Annual European Congress of Rheumatology

14 – 17 June, 2017
Madrid, Spain

Abstracts

The EULAR Journal
Annals of the Rheumatic Diseases publishes original work on all aspects of rheumatology and disorders of connective tissue. Laboratory and clinical studies are equally welcome.
Dear Colleagues,

Welcome to this EULAR Annual European Congress of Rheumatology in Madrid!
Welcome to the 70th anniversary of EULAR!

The annual EULAR Congresses, which began in 2000, are today a major event in the calendar of world rheumatology. This meeting, which marks the 70th anniversary of our very active society, will once again provide a unique occasion for the exchange of scientific and clinical information. It will facilitate interaction between patients, medical doctors, scientists, health professionals and professionals representing the pharmaceutical industry from Europe and from around the world. Participating in the congress is just one element of the annual educational package provided by EULAR: Almost all oral presentations will be available online after signing up and participants will be provided with a complimentary, one-year subscription to the latest developments and publications in the field of rheumatic and musculoskeletal diseases (RMDs). This is in line with a new, exciting event taking place in Madrid this year – the launch of the EULAR School of Rheumatology, which will be unique in providing education in rheumatology throughout the world.

EULAR has grown rapidly in terms of the number of participants and the quality of the submissions. A record number of more than 4'850 abstracts have been submitted to this year's congress in Madrid, and 180 sessions and poster tours are offered. This tremendous success continues to reflect the increasing interest in RMDs; it also reflects the availability of increased information on the size, burden and cost of these diseases for society – and a significantly improved ability to diagnose and treat them. The incorporation of health professional and patient organisations within EULAR has been a considerable stimulus for these advances.

The EULAR Congress 2017 in Madrid will provide a wide range of topics including clinical innovations, clinical translational and basic science. In addition, there will be significant contributions made by People with Arthritis and Rheumatism (PARE), by Health Professionals in Rheumatology (HPR) and by the health care industry. The core science and central activity of the congress will be the poster presentations and poster tours with their highly interactive exchanges between participants. The Madrid meeting will further promote the reputation of the EULAR Congress as a most innovative and informative venue for clinical research for the practising physician and health professionals. Meanwhile, the EULAR EMEUNET organisation of young rheumatologists aims to attract young colleagues to the meeting and will disseminate the message that rheumatology is one of the most attractive and successful disciplines of medicine.

We are back in the vibrant city of Madrid with its remarkable history, architecture, galleries, museums and ambience, all of which will once again provide an excellent background for clinical exchanges, international collaborations and renewal of friendships. “No pierdas tu tren” and in international language “Don’t Delay, Connect Today!” marks the first general EULAR Campaign to be launched in Madrid aiming at early recognition and treatment of RMDs.

It is our great pleasure and a real joy in welcoming medical doctors, patients, health professionals and representatives of the pharmaceutical industry and we hope their stay in Madrid will be delightful, informative, and educational. We wish you a great time, good science, good discussions, good meetings and most of all good memories to take home when you are heading back from Madrid and from our 70th anniversary congress.

Gerd R. Burmester
President of EULAR
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EULAR wishes to express its sincerest thanks to all abstracts reviewers for their most appreciated collaboration.
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Speakers Abstracts
Osteoarthritis (OA) is the most frequent joint disease and a leading cause of disability in the Western world. Currently, we do not have a cure for this degenerative disorder and despite a high individual and socioeconomic demand, available therapeutic strategies have not changed substantially within the last 40 to 50 years, largely involving basic symptomatic control using analgesics and NSAIDs, physiotherapy and behavioural changes, and eventual prosthetic replacement in end-stage disease. While prosthetic joint replacement constitutes an effective surgical treatment option for patients whose joints are irreversibly damaged by OA, demographic development together with altered physical activities in our aging society increasingly demonstrate the limitations of joint replacement surgery as the only real treatment modality. There is, therefore, an urgent requirement for disease modifying drugs that aim to halt OA disease progression during the early stages and potentially to kick start cartilage regeneration. This need is contrasted, however, by a sustained “translational roadblock” in OA research with very few conceptually novel therapeutic approaches on the horizon. Amongst others, this “translational roadblock” results from a general lack in our understanding of how articular chondrocytes as the only cells in joint cartilage acquire and maintain their specific and highly specialized phenotype and how this phenotype changes during OA onset and progression. Investigation of this developmental aspect of disease pathology in OA patients and using human samples has many limitations, which is why animal models remain to constitute a key element of cartilage and OA research. This lecture summarizes the relevance of different animal models for understanding fundamental principles of cartilage homeostasis and remodelling in health and osteoarthritic cartilage degeneration. By focusing on the analysis of chondrocyte phenotypic stability, it provides examples for how the use of such models can contribute to understanding OA and to the development of new therapeutic strategies for the disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7260

We have previously reported that functional haplotypes of peptidyl arginine deiminase 4 (PADI4) are associated with rheumatoid arthritis (RA). We found that transcripts of the risk haplotype of PADI4 are more stable than those of the non-risk haplotypes, suggesting that increased expression and function of PADI4 (encoded by PADI4 gene) increase the risk of RA. The association has been confirmed by several studies with different ethnicities. Further, we also reported PADI4 polymorphisms highly predispose male smokers to RA. Since PADI4 catalyzes an arginine residue in a protein to citrulline and anti-citrullinated protein antibodies (ACPA) are highly specific in RA, it has been reasonable to speculate that increased PADI4 is associated with increased citrullinated proteins, leading to the initiations of tolerance breakdown or inflammatory arthritis. However, the mechanisms of PADI4 involvement turned out to be more complex than previously thought in animal models. In order to investigate the pathological process in detail, we made PADI4 knockout mice. Decreased severity of experimental autoimmune arthritis was observed in these mice. Further, we found PADI4 regulates the pro-apoptotic fate of neutrophils, and promotes the expression of pro-inflammatory cytokines in macrophages. These actions could result in the pro-arthritic roles of PADI4. Recently, neutrophil extracellular traps (NETs) were reported as an important immune stimulator in RA and SLE, and PADI4 is required for the generation of NETs. Especially, NET-containing immune complex (IC) stimulated plasmacytoid dendritic cells to accelerate the interferon secretion in SLE. Therefore, PADI4 could play several different roles in the immune system and also in the pathogenesis of autoimmune diseases.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7136

The medical treatment of people with rheumatic and musculoskeletal diseases (RMDs) has improved enormously over the past decades. As medical treatment is not completely successful or available for all rheumatic conditions or individual patients, and the demands society imposes on people to participate fully are increasing, there is a substantial proportion of people with RMDs who have functional disabilities. Health professionals (HPs) play an essential role in the management of people with RMDs with disabilities by enabling to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. They provide people with the tools they need to attain independence and self-determination. As such, their contribution is in line with the World Health Organisation definition of rehabilitation [http://www.who.int/topics/rehabilitation/en/]. An important feature of rehabilitation is its multidisciplinarity. Over the past decades, it has been more and more acknowledged that RMDs management involves the whole health care team and concerns a team effort rather than the summation of single interventions by individual HPs or specific professions. This view is reflected in multiple guidelines and standards of care for the clinical management of RMDs, where the need for people with RMDs to have access to a multidisciplinary team of HPs is underlined.
The acknowledgement of the importance of the team of HPs runs in parallel with developments in the organization and activities of HPs within EULAR over the past years. In connection with EULAR, there is a growing network of HPs from multiple professions across Europe. By working together, and collaborating with patients and rheumatologists as partners, EULAR HPs have achieved multiple milestones with respect to the quality of clinical care, education, and research over the past years and are equipped to encounter future challenges.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7181

SP0007
70 YEARS PAST AND A VIEW OF THE FUTURE: LOOKING BACK AND LOOKING FORWARD
H.W. Bijlsma, Department of Rheumatology & Clinical Immunology, University Medical Center, Utrecht, Netherlands

In 1913 the Dutch general practitioner Jan van Breemen, moved by the needs of the many disabled people in his practice, started an international cooperation to fight rheumatic and musculoskeletal diseases. His initiative led to the formation of the International League Against Rheumatism (ILAR), and subsequently to the formation of regional Leagues, such as EULAR in 1947. EULAR has in the following 70 years developed into a unique organisation of rheumatologists, scientists, health professionals and patients, who together are aiming to reduce the burden of rheumatic diseases on the individual and society and to improve the treatment, prevention and rehabilitation of musculoskeletal diseases. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes translation of research advances into daily care and fights for the recognition of the needs of people with RMDs by the governing bodies in Europe (EULAR mission statement 2005).

The first European Rheumatology Congress was held in September 1947 in Copenhagen and was attended by 200 delegates from 16 countries. At the EULAR 2017 May Congress over 14,000 attendees are expected, coming from more than 120 countries.

EULAR is unique in the sense that three pillars work closely together in one organization: rheumatologists, health professionals and patients. Today, I want to focus a bit on the health professionals pillar, since this pillar has its formal 20th jubilee in 2017 as well. At the American celebration of 50 years of non-physician health professionals in Rheumatology (2015), Brady described three science-driven practice paradigm shifts that play an important role in managing patients with RMDs: 1. The widely used “Self-management programs”, that were developed from information giving and ‘patient education’. 2. The positive and intensive use of “Exercise and physical activity”, that were developed from previous acclaimed bed rest and assisted range of motion exercises. 3. The OMERACT initiated definitions and applications of Patient-reported outcome measures, instead of only medical assessment of disease activity.

In addition, she recognized two “evolutions in practice”: 1. Understanding Psychological Factors, from accepting “the arthritic personality” to actively addressing depression, anxiety, coping skills, sense of control and confidence. 2. The development of the important role that nurses and other health professionals can play in the treatment of patients with RMDs.

The EULAR health professionals can be very proud of the important part that Europeans have played in these worldwide developments. My priorities as president-elect of EULAR for the coming two years are:

- Further development of the School of Rheumatology
- Large public awareness campaign: Don’t delay, Connect today
- New EULAR Strategy 2018–2023

I hope and expect that the pillar of health professionals will take an active role in the cooperation that is necessary to reach our common goals.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7105

SP0008
THE FUTURE FOR HEALTH PROFESSIONALS IN RHEUMATOLOGY
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In recent years the prevalence of rheumatic diseases has raised leading to increased outpatient activity; at the same time, a general lack of rheumatologists has been described (1). This has created new demands from patients and the health care system towards innovative models of care, e.g. nurse-led follow-up (2), direct access strategies (3) and tele-health interventions (1). In the future this will call for extended and specialized roles for health-professionals within rheumatology, and for future development of compatibility of training of health professionals within the European countries.

Further, the current health-service development is confronting the population with increasing demands to understand and utilize health information and to navigate through this increasingly complex healthcare system. It requires that patients are capable of understanding and managing their health, and calls for a strong focus on health-literate (HL) skills, and the formation of so-called HL organizations (4). In the future, health professionals within rheumatology will have a key role in supporting the development of HL responsive organizations through self-management strategies and patient centered care.

The present presentation will address some of these future demands for health professionals in Rheumatology

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7155

SP0009
WHAT IS NEW (WIN) IN PSORIATIC ARTHRITIS
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Novel therapies and targets have transformed the management of psoriatric arthritis and related skin disease psoriasis. The successful introduction and widespread use of anti-IL17, anti-IL12/23 and anti-PDE4 strategies have joined the ranks of TNF inhibitors. Novel biological insights into specific disease mechanisms are co-emerging with this new wave of treatment options. The different available treatments allow the community to further focus on optimal patient management aiming at remission or minimal disease activity. Yet, the assessment of the patient and his/her satisfaction with current health status remains challenging. Treat to target initiatives are trying to define optimal care and cure adapted to the specific characteristics of the disease. Molecular knowledge of the disease processes remains scattered and insufficient to build a comprehensive view on the disease for the individual patient that would allow the personalized definition of effective strategies.

Disclosure of Interest: R. Lories Grant/research support from: Celgene, Boehringer-Ingelheim, UCB, Consultant for: Janssen, Celgene, Novartis, Pfizer, UCB, Abbvie, Speakers bureau: Janssen, Celgene, Novartis, Pfizer, Merck, UCB, Abbvie

DOI: 10.1136/annrheumdis-2017-eular.7259
Moving towards new criteria in SLE, Sjögren’s and APS

SP00010 CLASSIFICATION OF SLE – CHALLENGES AND POTENTIAL SOLUTIONS
M. Aringer on behalf of SLE Classification Criteria Steering Committee. Medicine III, University Medical Center TU Dresden, Dresden, Germany

Systemic lupus erythematosus is characterized by a wide variety of autoantibodies, which, if pathogenic, can lead to inflammation, damage, thrombosis or functional defects of essentially all organ systems. The 1982 American College of Rheumatology (ACR) criteria and their 1997 revision have greatly influenced the disease concept over the last decades. With the at least 4 of 11 criteria to be present, they essentially depict the concept of multiple autoantibodies and multiple organ systems. Putting all items on equal weight made the system relatively easy to use and to memorize, but this approach was not entirely intuitive. Dermatologists have criticized that patients could meet the criteria based on fulfilling all 4 mucocutaneous criteria only. Importantly, sensitivity was felt to be suboptimal, reaching 83% in the cohort of the SLE International Collaborating Clinics (SLICC) group, and lower values in very early disease.

The 2012 SLICC SLE classification criteria introduced two new concepts. First, patients had to be positive for autoantibodies, namely for anti-nuclear antibodies (ANA) or antibodies to double-stranded DNA. Second, if patients are autoantibody positive, classification criteria can be fulfilled by nephritis on histology without any other items. The SLICC groups also introduced large lists of skin and neuropsychiatric symptoms and refined some of the definitions. While many of these ideas are intuitively correct, not all were derived in a pre-defined scientific way. These criteria managed to increase sensitivity to 97% in their own validation data and to a range of 92–99% in other cohorts. At the same time, however, the SLICC set low specificity, falling to 84% as compared to the 96% of the ACR criteria. This set of criteria was therefore rejected by the SLICC group's choice to keep the overall structure the same. Early disease specificity was still not optimal.

In a large transatlantic project jointly supported by EULAR and the ACR, we have over the last years tried to develop (even) better SLE classification criteria. The main goals are to have a relatively intuitive set that helps in teaching, increase sensitivity as compared to the ACR criteria, but maintain specificity in the same range, improve the performance in early SLE, involve the larger SLE community as far as possible, and do this in a strictly scientific way. Given that ANA often are the door to SLE in the diagnostic approach, and that ANA have very high sensitivity, but modest specificity for SLE, we explored whether ANA could be used as an entry criterion. Meta-regression, after compiling ANA data of 13,080 SLE patients from a systemic literature search, gave a sensitivity of 97.8% (CI 96.8–98.5%) for a titer of at least 1:80 on HEp2-ANA immunofluorescence. It was therefore decided that HEp2-ANA of ≥ 1:80 would be used as an entry criterion.

Three different approaches were used to maximize the overview on potential items, namely an SLE expert Delphi exercise involving 123 SLE experts, an international early disease cohort with 389 SLE patients and 227 patients with conditions mimicking SLE, and a patient survey, which 339 SLE patients filled out and mailed anonymously. The resulting 41 items were then reduced in a nominal group technique exercise with 7 international SLE experts, resulting in a list of 20 items plus ANA as an entry criterion. These items were then submitted to multi-criteria decision analysis in a two day conference with 6 international experts together with the steering committee. This approach under the same moderator therefore decided that HEp2-ANA of ≥1:80 would be used as an entry criterion. The revised results are 20 weighted items, which can be additively used within a continuous scale, and a cut-off for classification. Weights for class III or IV lupus nephritis are much higher than for leukopenia or unexplained fever. This candidate classification will now be tested against both the ACR and the SLICC criteria in a large cohort of SLE patients and patients with mimicking conditions. If successful, ANA will now be tested against both the ACR and the SLICC criteria in a large cohort of SLE patients and patients with mimicking conditions. If successful, ANA would represent a factor, consequently the presence of two/three positive diagnostic laboratory tests is a valuable parameter to stratify the patients at highest risk for developing the syndrome/recurrences.

The syndrome displays a protein clinical picture depending on the involved tissue/organ. The majority of the clinical (criteria) manifestations are clearly related to vascular ischemic events. However, some manifestations apparently cannot be supported by a thrombotic mechanism and alternative pathogenic pathways have been suggested. This is the case for thrombocytopenia, central nervous system involvement such as movement disorders and cognitive abnormalities, and APS nephropathy. Heart valve disease, skin ulcers and livedo reticularis are also frequent events in APS patients and their relationship with vascular thrombosis is unclear. Still debated is the suggestion to include these manifestations as additional clinical diagnostic criteria. The possibility to use all these criteria for ranking the patients as having a definite (standard clinical criteria) or probable (non classification criteria) is also debated.

The revised criteria for obstetric morbidity comprise otherwise unexplained pregnancy loss. Some of the obstetric criteria might display low sensitivity/specificity for APS. In particular, the attribution to aPL of a pregnancy wastage early on gestational course requires the exclusion of a myriad of etiologies. Conversely, the rate of late foetal losses is very low, making this criterion rather specific. Placenta-mediated obstetric complications provide another critical field: pre-eclampsia and intra-uterine growth restriction are relatively common. To enhance the specificity for APS, the classification criterion included only cases requiring delivery before 34 weeks of gestation. Medium/high aPL titres and double/triple laboratory tests positivities confer a higher risk for pregnancy complications but recent data seem to suggest that also persistent low aPL titres can be predictive for a negative pregnancy outcome. This finding has been recently explained by the availability of large amounts of b2GPI in tissues of the reproductive system. Even though classification criteria have allowed uniformity in APS diagnosis, there still remain some controversies.

The field of the laboratory classification criteria is even more in progress. Eptope profiling for anti-b2GPI antibodies is quite promising since the characterization of reactivity against the domain 1 of the molecule appears to display a higher specificity for APS and stronger predictive value than the antibodies against the whole molecule. However, anti-domain 1 assay is less sensitive and cannot replace the standard test at the moment. Antibodies against protein C (PT) have been reported to be associated with both the vascular and the obstetric APS, in particular when the antibodies are detectable against a solid phase complex of PT with phosphatidylserine (PS) (the so called anti-PS/PT assay). However, a clear evidence for their usefulness in the clinical diagnosis and risk stratification for APS patients as well as their true pathogenic role is still debated.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7303

SP0011 SJÖGREN’S CRITERIA REVISITED!
S.J. Bowman, University Hospital Birmingham Rheumatology Dept, Birmingham, UK

In clinical practice it is the up to the clinician to use their judgement in making a diagnosis of pSS. In research it is essential to have agreed classification criteria so that there is confidence that participants in a study have the specified condition. During the 1980’s a number of classification criteria were proposed with a major drawback being the advantages and disadvantages of each of these criteria. In 1988 a working group of 29 experts from 12 European countries initiated a study to develop consensus criteria. They published their initial findings in 1993 and in 2002 Vitali et al published the American European Consensus Group Criteria (AECG). The AECG criteria have been the most widely used "gold-standard" criteria for the classification of pSS in research studies. Criteria are never fixed in perpetuity, however, and as new technology such as ultrasound becomes more widely used or new data becomes available further revision is likely. In 2013, an International Collaboration, the Sjögren’s International Clinical Collaborative Alliance (SICCA) funded by the National Institutes for Health in the USA collected data from 151 participants to devise the American College of Rheumatology (ACR) preliminary criteria for SS and in 2016 following a further international consensus group exercise the American College of Rheumatology – European League against Rheumatism (EULAR) consensus criteria for Sjögren’s syndrome have been published.

In this presentation I will go through the development of these criteria, the underlying rationale and by the end of the talk attendees should have a better understanding of how these criteria can be used in research and to support clinical practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7276
The differential diagnosis of diffuse skin sclerosis and of Raynaud’s phenomenon and a practical approach to assessment

**SP0013**

**WIDESPREAD CUTANEOUS THICKENING – COULD THIS BE EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS?**

A. Suarez, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom

A case of diffuse sclerosing skin disease shall be presented. The features that initially led the treating team to consider a diagnosis of systemic sclerosis shall be discussed, alongside subsequent features that emerged that cast doubt over this diagnosis and led the team to undertake additional investigative studies. The presentation shall provide a chronological description of the clinical features, laboratory studies, microvascular imaging and histological studies that helped the team to reach a definitive diagnosis and plan management accordingly.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7183

**SP0014**

**THE DIFFERENTIAL DIAGNOSIS OF DIFFUSE SCLEROSING SKIN DISEASE AND A PRACTICAL APPROACH TO ASSESSMENT**

J. Pauling, Pharmacy and Pharmacology, University of Bath; J. Hughes, Royal National Hospital for Rheumatic Diseases (Royal United Hospitals), Bath, United Kingdom

The differential diagnosis for sclerosing skin disease is broad but there are clinical and laboratory features that can help guide clinicians to the correct diagnosis. This presentation shall provide a comprehensive review of the spectrum of sclerosing skin disease. A practical approach to integrating the clinical, serological, microvascular imaging and histological features that can help differentiate disease states shall be presented to provide rheumatologists with a practical approach to the assessment of patients with sclerosing skin disease. Case histories shall be used to illustrate the pertinent clinical features and investigative approaches that can help distinguish systemic sclerosis from other sclerosing skin conditions such as scleroderma, pan-sclerotic morphea, lipodermatosclerosis and chronic graft versus host disease. A specific focus shall be placed on the role of autoantibodies in the diagnosis of systemic sclerosis, including recent work reporting the presence of novel systemic sclerosis-specific autoantibodies in patients with antinuclear antibody-negative diffuse cutaneous systemic sclerosis.

**Disclosure of Interest:** J. Pauling Grant/research support from: Actelion pharmaceuticals, Consultant for: Actelion pharmaceuticals, Speakers bureau: Actelion pharmaceuticals

**DOI:** 10.1136/annrheumdis-2017-eular.7132

**SP0015**

**NEW ONSET RAYNAUD’S PHENOMENON – COULD THIS BE EARLY LIMITED CUTANEOUS SYSTEMIC SCLEROSIS?**

M. Hughes, The University of Manchester, Greater Manchester, United Kingdom

A case shall be presented of a patient with Raynaud’s phenomenon and whether this could be early limited cutaneous systemic sclerosis. The presentation shall describe the clinical features and investigative approaches that helped us reach a diagnosis, with a particular focus on the role for microvascular imaging and the detection of SSc-associated autoantibodies.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7173

**SP0016**

**THE DIFFERENTIAL DIAGNOSIS OF RAYNAUD’S PHENOMENON AND PRACTICAL APPROACH TO ASSESSMENT WITH A FOCUS ON IMAGING**

A.L. Herrick, University of Manchester, Manchester, United Kingdom

Raynaud’s phenomenon is the term used to describes episodic vasoospasm of the digital vasculature in response to cold exposure and/or emotional distress. The majority of people with Raynaud’s phenomenon have primary (idiopathic) Raynaud’s phenomenon which is ‘benign’ in that it does not progress to irreversible digital ischaemia, and is not associated with any underlying disease. Conversely, when Raynaud’s phenomenon is secondary to an underlying disease/condition (for example to a systemic sclerosis-spectrum disorder), it can be severe, sometimes progressing to digital ulceration and/or gangrene. Raynaud’s phenomenon is often the presenting feature of connective tissue disease and therefore provides a window of opportunity for early diagnosis.

The first step in management of Raynaud’s phenomenon is establishing the diagnosis. Is this primary or secondary Raynaud’s, and if secondary, then to what? While a careful history and examination are always the first steps, different laboratory tests and vascular imaging studies can be used to reach the correct diagnosis. This presentation will provide practicing rheumatologists with a practical approach to the diagnosis and assessment of Raynaud’s phenomenon, focussing on the diagnostic and prognostic role of vascular imaging (including nailfold capillaroscopy and thermography).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7190

**SP0017**

**CONTROLLING THE BALANCE BETWEEN CANCER AND AUTOIMMUNITY**

A. Marabelle Grant/research support from: BMS, MERUS, Consultant for: ROCHE, GENMAB, PIERRE FABRE, LYTX, PFIZER, Speakers bureau: ROCHE, MSD, BMS, ASTRA ZENECA

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7165

**SP0018**

**SHARED MECHANISMS IN CANCER AND AUTOIMMUNITY**

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Some rheumatic disease autoantibodies are powerful markers of subgroups of patients who have distinct disease phenotypes and trajectories. Of particular interest are markers of several disease subgroups in whom cancer and rheumatic disease onset are clustered together in time. For example, a subgroup of scleroderma patients have coincident onset of cancer and scleroderma. This is observed in scleroderma patients with autoantibodies against Polr3a, a ribosomal protein kinase, and more recently with autoantibodies recognizing the minor spliceosome. In autoimmune myopathies, temporal clustering of diagnosis of cancer and myositis is associated with autoantibodies to NXP2 and components of the TFI complex. Interestingly, although the incidence of cancer is higher in patients with these autoantibodies, most patients with these autoantibodies manifest cancer, even with extended periods of follow-up. These observations provide an important opportunity to investigate the potential mechanisms which operate at the cancer-immune interface during development of rheumatic diseases.

We have investigated such mechanisms in scleroderma patients with autoantibodies to Polr3a who also had a cancer diagnosis an average of 2.6 years from scleroderma onset. In cancers from these patients, we found genetic alterations of the Polr3a locus in six of eight patients with antibodies to Polr3a but not in eight patients without these antibodies. 3 antibody-positive patients had somatic mutations in Polr3a; 5 patients had loss of heterozygosity at the Polr3a locus. Analyses of peripheral blood lymphocytes and serum suggested that Polr3a mutations sparked cellular immunity and cross-reactive humoral immune responses. These results offer insight into the pathogenesis of scleroderma, and potentially other autoimmune syndromes. They suggest that somatic mutations in autoantigens in different cancers might initiate an immune response to the mutated autoantigen, which spreads to include the wild type version. Tissues (e.g. blood vessels, regenerating muscle) in which specific autoantigens are expressed at high levels, or potentially play critical functional roles, may be particularly susceptible to immune-mediated dysfunction. The results also provide support for the idea that acquired immunity helps to control naturally occurring cancers in patients with autoimmune rheumatic diseases; it is possible that this immune response may sometimes be fully effective, preventing the emergence of cancer.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7799
Fibromyalgia: a disease of the peripheral or central nervous system

SIGNS, SYMPTOMS AND CO-MORBIDITIES OF FIBROMYALGIA

CENTRAL PATHOLOGIES IN FIBROMYALGIA

Disclosure of Interest:

None declared

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7142

Chondrocyte channels (role in mechanotransduction) or “channeling the chondrocyte”

PERIPHERAL PATHOLOGY IN FIBROMYALGIA

The pathophysiology of pain in fibromyalgia is complex. In recent years, an involvement of the thinly myelinated nerve fibers of the A-delta type and the unmyelinated C-fibers has been reported in fibromyalgia patients. Independent research groups have published consistent findings of objective injury to these “small nerve fibers”. These included disturbances in function, electrical properties, and morphological integrity of these nerve fibers. While the reasons for this small fiber pathology and its contribution to FMS pain are still unclear, a new research field has emerged that will focus on uncovering the underlying pathophysiology. In this talk, I will summarize current findings and discuss their significance for the understanding of the fibromyalgia syndrome.


CENTRAL PATHOLOGIES IN FIBROMYALGIA

Fibromyalgia is characterized by widespread, mainly muscular pain that is exacerbated during and following physical activity. Although mechanisms such as muscle ischemia and peripheral nerve fibre pathology have been implicated in fibromyalgia, currently no known peripheral pathology can fully account for the pain. Therefore, the pain in fibromyalgia is most likely explained by a complex interaction between peripheral and central mechanisms. Fibromyalgia patients are characterized by a multimodal, widespread, increase in pain sensitivity and a dysregulation of endogenous pain inhibitory mechanisms. Imaging studies have revealed functional as well as structural cerebral abnormalities in fibromyalgia. During painful stimulation, fibromyalgia patients exhibited an inability to activate cerebral structures associated with the descending pain inhibitory system, i.e., ventral anterior cingulate (VAC) and thalamus.1 There was a significant association between depression or anxiety and cerebral processing of evoked pain, indicating segregated mechanisms for mood and pain processing.2 Furthermore, FM patients had less pain related functional connectivity within the brain’s pain inhibitory network and structural changes such as decreased cortical thickness and reduced brain volumes.3 Longer duration of FM pain was associated with more pronounced functional and structural abnormalities suggesting a time-dependent progress of cerebral pathology, even when controlled for age and mood.4 In addition, FM patients had elevated interleukin-8 in the cerebrospinal fluid indicating neuro-inflammation,5 possibly due to upregulated cell activation. Interleukin (IL) IL-1β is co-localized with translocator protein (TSPO) in glia cells. During glial activation, the production of TSPO is increased and TSPO agonists are involved in the regulation of the expression of IL-8 and its receptor, thus affecting glia to neuron signalling and central sensitisation. We have recently documented that FM patients who are carriers of the genetic functional polymorphism associated with high TSPO binding affinity report higher pain intensity and more severe fibromyalgia symptoms compared to genetically interred TSPO low affinity binders and that this genetic polymorphism also affects cerebral pain processing.6 To our knowledge, this is the first finding of genetic mechanisms associated with symptom severity in FM. Finally, the effect of different treatments on central pathology in FM will be discussed. Short pain duration was predictive of a positive response to a 12 weeks treatment with a serotonin-noradrenaline re-uptake inhibitor (SNRI).7 The degree of symptom improvement and reduced pain sensitivity in SNRI treated FM patients corresponded to the degree of increased pain related activation of cerebral areas associated with pain modulation and the default mode network.8 In contrast, cognitive behaviour therapy did not affect clinical pain or pain sensitivity but increased activations of cerebral regions implicated in executive cognitive control during painful stimulation and thus likely reappraisal of painful stimuli.9 Finally, 15 weeks of physical exercise partially normalized resting state activity in FM.10 The results demonstrated that different treatment modalities affected specific brain mechanisms, indicating that at least some of the cerebral abnormalities in FM are reversible.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7142

CHONDROCYTE CHANNELS IN OSTEOARTHRITIS

TRPA1 CHANNELS IN OSTEOARTHRITIS

Osteoarthritis (OA) has long been viewed as a degenerative “wear-and-tear” disease of cartilage. There is, however, increasing evidence to confirm that inflammation has a critical role in the pathogenesis and symptoms of the disease. Inflammation in osteoarthritis is distinct from that typical for rheumatoid arthritis; it is generally low-grade in its nature but characterized by exacerbations with joint effusions and more severe symptoms. Osteoarthritis shares many features of innate immunity but the inflammatory mechanisms eventually leading to pathological and functional changes are incompletely understood.1,2 Osteoarthritis is not known in detail; but their further understanding is essential for the development of disease-modifying treatments for osteoarthritis. Transient receptor potential ankyrin 1 (TRPA1) is a ligand-gated membrane-bounded cation channel. It has been widely studied in sensory neurons where it acts
as a chemosensor for harmful exogenous compounds and mediates pain and neurogenic inflammation. More recently, TRPA1 has been found to be activated also by endogenous compounds formed in inflammation, such as reactive oxygen and nitrogen species. That prompted us to investigate the role of TRPA1 in inflammatory conditions including osteoarthritis. Monosodium iodoacetate (MIA)-induced arthritis in rats is a widely used animal model of osteoarthritis. We found that MIA evoked acute inflammation, degenerative cartilage changes and joint pain in wild type mice; but interestingly, those responses were significantly attenuated in TRPA1 deficient animals. Furthermore, TRPA1 was found to be expressed and inducible by inflammatory factors including IL-1 and IL-17 in primary human OA chondrocytes, and the TRPA1 channel was shown to be functional based on calcium influx assays. Pharmacological inhibition and genetic depletion of TRPA1 downregulated the production of inflammatory factors and MMP enzymes in mouse cartilage and primary human OA chondrocytes. The present results introduce TRPA1 as a plausible factor involved in the pathogenesis of OA and provide a novel target for analgesic and anti-inflammatory drugs with disease modifying potential in OA. Disclosure of Interest: None declared. DOI: 10.1136/annrheumdis-2017-eular.7275

WEDNESDAY, 14 JUNE 2017

Wearable technologies in 21st century healthcare —

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Working environments have in recent times become less physical with the increase in sedentary, computer-based occupations. Sedentary time is known to be associated with a number of health-related outcomes, including obesity, heart disease, diabetes, cardiometabolic risk factors, some cancers and early mortality, independent of physical activity. There is limited research that has examined sedentary time and physical activity and associations with musculoskeletal conditions, despite these being responsible for the majority of work-related ill health and days absent from work. The validity and practicality of objective and subjective techniques to measure physical behaviour have been widely reported; however, there is no gold standard that is valid, accurate, reliable and also practical. Self-reported methods can be practical and low-cost, but are subject to recall and social desirability bias; whereas objective devices, such as accelerometers, can be expensive, but allow for information on intensity, frequency and duration of activity to be measured. The Health Survey for England 2008 used both subjective and objective measures of physical activity; they found that 39% of men and 29% of women were meeting the recommended levels of physical activity when asked via a questionnaire. In comparison, when physical activity was objectively measured using an accelerometer, it was found that only 6% of men and 4% of women met these targets.

Wearable technologies, including research grade accelerometers (e.g. activPAL™) and consumer wearable devices (e.g. FitBit), are increasingly being used in research, not only to measure physical behaviours but may also be useful in facilitating and monitoring behaviour change. This work will present an overview of wearable technologies used in research, what they can (and can’t) measure, and in particular their application in musculoskeletal research.

Disclosure of Interest: None declared. DOI: 10.1136/annrheumdis-2017-eular.7177

NOVEL IMAGING TECHNIQUES FOR ASSESSING OSTEOPOROTIC FRACTURE RISK

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The measurement of areal bone mineral density (aBMD) by dual x-ray absorptiometry (DXA) has been the mainstay for the diagnosis of osteoporosis for at least two decades. The sensitivity and specificity of this test, however, remains suboptimal. For example, more than 50% of postmenopausal women with fragility fracture are not identified with DXA. A great deal of research has been performed recently to develop alternative or complementary imaging techniques to overcome DXA predictive limitations. These techniques are based on the non invasive analysis of bone microarchitecture and estimation of bone strength by finite element analysis (FEA).

Texture analysis uses mathematical models based on fractal analysis to evaluate bone microarchitecture using various types of bone images. The trabecular bone score (TBS) has emerged as an approach that may improve fracture risk prediction. The TBS is based on the texture analysis of the DXA lumbar spine image to quantify bone microarchitecture. Several cohort studies have shown that a subset of individuals could be reclassified with TBS. A meta-analysis results have allowed for incorporation of the TBS in the FRAX score, that is widely available.

The measurement of volumetric BMD with quantitative computerized tomography (QCT) at the hip has been shown to predict fracture risk. These images can also be used to perform FEA that may increase the fracture risk prediction. The additional value of this technique compared with DXA remains to be established in a clinical setting.

Bone microarchitecture can also be assessed at peripheral sites such as the distal radius and tibia using high resolution peripheral quantitative tomography (HRpQCT). Numerous cross-sectional and case-control studies have shown a significant association between prevalent fracture and bone microarchitecture and estimated bone strength assessed with FEA. The bone parameters measured at distal sites are also associated with fractures at distant sites, e.g., the vertebrae and the femoral neck. In a recent prospective study, bone microarchitecture at the distal radius - especially the trabecular vBMD - has been associated with incident osteoporotic fractures. The FEA models were also predictive of fragility fracture. The best models and the most appropriate architectural parameters - whether they are trabecular of cortical - remain to be dissected out and their comparative diagnostic value with aBMD by DXA remains to be established.

The measurement of the TBS may allow for reclassification of a subset of individuals for whom DXA is suboptimal.
EMERGING THERAPIES FOR OSTEOPOROSIS
P. Geusens. Rheumatology, MaastrichtUMC and UHasselt, Genk, Netherlands
Currently, anti-resorptive drug therapy is the cornerstone of fracture prevention. Anti-resorptive drugs decrease bone remodelling, allowing the remaining bone to increase secondary mineralisation, and, with denosumab, also allowing periosteal bone modelling. This opens new perspectives in individualised treatment of patients with high fracture risk and for fracture prevention in patients with low bone turnover, multiple previous fractures, and increasing amount of existing literature makes the life of a clinician difficult when trying to search by him/herself for the answer based on the original studies. The effect on non-vertebral fractures was not significant, but geographic interaction was found. When excluding patients from South America, in whom fracture risk was low, one-year treatment with romosozumab significantly decreased the risk of non-vertebral fractures by 42%. Abaloparatide and romosozumab are new bone forming agents, with different effects on bone remodelling and remodelling and early effects on clinical fractures. This opens new perspectives in individualised treatment of patients with high fracture risk and for fracture prevention in patients with low bone turnover, multiple vertebral fractures, very low BMD and fractures or bone loss during anti-resorptive treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7232

BEYOND THE RECOMMENDATIONS: EXAMPLES OF SYSTEMATIC LITERATURE REVIEW IN DAILY CLINICAL PRACTICE
K. Visser 1, 2, 3. 1 VU Medical Center; 2 Academic Medical Center, Amsterdam, Netherlands
Recommendations and guidelines for management and treatment of rheumatic diseases exist to help rheumatologists deliver optimal care for their patients in an evidence-based way. However, not all practical questions and medical difficulties encountered by rheumatologists in daily clinical practice can be addressed using these existing guidelines. Moreover, time in practice is limited and usually does not allow for extensive systematic literature research to find evidence regarding a specific medical question that needs answering in due time. Therefore, an essential skill for doctors and those in training, besides medical knowledge and examination skills, is to be able to search for, withdraw and appraise published evidence applicable to a specific topic. A so called CAT – critically appraised topic – is a compact systematic literature research following a strictly formulated PICO to answer a clinical question encountered in daily practice. Results can be presented in department meetings and stored in a database for education purposes and use in daily practice. This presentation will address the structure of the carrying out, as well as important pros and cons of the CAT. Examples will be given drawn from the experience of young rheumatologists in training in the Netherlands.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7212

HOW COULD GPS ENHANCE THE EARLY DIAGNOSIS OF RHEUMATIC DISEASES
C.D. Mallen. Arthritis Research UK Primary Care Centre, Primary Care and Health Science, Keele, United Kingdom
Primary care and general practice has a key role to play in the early and accurate detection of patients with rheumatoid arthritis. This talk will explore some of the current barriers to best practice, highlighting the workload associated with musculoskeletal problems in primary care and the challenges in making a prompt diagnosis. Possible solutions will be explored, highlighting the importance of strong patient and professional partnerships.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7239
**THE CONTRIBUTION OF PHYSIOTHERAPISTS TO EARLY DETECTION OF INFLAMMATORY ARTHRITIS**

P. Kirwan, 1,2, J. Physiotherapy Dept, Connolly Hospital; 2, School of Physiotherapy, Royal College of Surgeons in Ireland, Dublin, Ireland

Early recognition of inflammatory arthritis is of utmost importance, as failure to do so can delay appropriate treatment and result in permanent joint damage and disability. This presentation will set out to explore the role a Physiotherapist/Healthcare Professional can play in recognition of inflammatory joint disease. Healthcare Professionals/Physiotherapists are often the first point of contact for patients suffering from joint/musculoskeletal pain. They are therefore well-positioned to be the first to identify possible inflammatory sources of pain versus non-inflammatory sources. Useful clinical tools which aid in this decision making process will be discussed. The question as to whether a physiotherapist can recognise inflammatory joint disease versus non-inflammatory joint conditions will be explored with the aim being to highlight the important role a physiotherapist can play in this important diagnostic challenge. With reference to ongoing clinical and research work in this field, this presentation will set out to ask whether or not a Healthcare Professional/Physiotherapist can accurately recognise/diagnose inflammatory arthritis and whether they miss inflammatory arthritis.

Disclosure of Interest: None declared

**THE EULAR CAMPAIGN “DONT DELAY CONNECT TODAY” AND HOW ORGANISATIONS CAN GET INVOLVED**

J. Church, Arthritis Ireland, Dublin, Ireland

Arthritis is a chronic disease with multiple co-morbidities. With the development of powerful biologic drugs, improvements in care pathways for patients and very effective self-management interventions, early diagnosis and intervention can lead to significant improvements in lifestyle, physical movement, increased well-being and work force participation. Despite its significant impact on the population and the cost to the healthcare system, arthritis still remains undertreated and undiagnosed within the health systems and one that is shrouded in public myth. The EULAR campaign “Done Delay, Connect Today”, aims to promote early intervention by encouraging those with typical symptoms to take action and consult their doctor at the earliest possible opportunity. The campaign which will be adopted and executed across all PARE members also aims to dispel the myths and educate the public about the seriousness of arthritis and the need to take action.

Disclosure of Interest: None declared

**SHARE RECOMMENDATIONS ON SYSTEMIC VASCULITIDES**

M.W. Beresford on behalf of SHARE Systemic Vasculitis Working Group. Portuguese Rheumatology, Alder Hey children’s NHS Foundation Trust, Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom

Background: Primary systemic vasculitides (PSV) are very rare in children and consequently, little evidence exists. Evidence-based guidelines are lacking; this is an important and unmet need. The European initiative SHARE (Single Hub and Access point for childhood-onset Polyarteritis, Granulomatosis with Polyangiitis, Microscopic Polyangiitis, Eosinophilic Granulomatosis with Polyangiitis, and Takayasu Arteritis) aims to identify best practices for treatment of childhood-onset Polyarteritis, Granulomatosis with Polyangiitis, Microscopic Polyangiitis, Eosinophilic Granulomatosis with Polyangiitis, and Takayasu Arteritis.

Conclusions: European-wide recommendations for the diagnosis and treatment of rare forms of paediatric PSV have been formulated through an evidence-based consensus process. The SHARE project aims to provide international recommendations that will significantly improve the standard of care for children with rheumatic diseases.

Disclosure of Interest: None declared

**SHARE RECOMMENDATIONS ON JUVENILE DERMATOMYOSITIS**

A. Van Royen-Kerkhof, Wilhelmina Children Hospital, Utrecht, Netherlands

Background: In 2012, a European initiative called Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) was launched to optimise and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases. Juvenile Dermatomyositis is a rare Pediatric Rheumatic Disease (PRD), associated with significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physicians’ experience. Consequently, treatment regimens differ throughout Europe.

Objectives: To provide recommendations for diagnosis and treatment of JDM based on evidence-informed consensus.

Methods: Recommendations were developed by an evidence-informed consensus process using the European League Against Rheumatism standard operating procedures. A committee was constituted, consisting of 19 paediatric rheumatologists and 2 experts in paediatric exercise physiology and physical therapy, mainly from Europe. Recommendations derived from a validated systematic literature review were evaluated by an online survey and subsequently discussed at two consensus meetings using nominal group technique. Recommendations were accepted if >80% agreement was reached.

Results: In total, 1 overarching principle, 17 recommendations on diagnosis and 13 recommendations on therapy were accepted with >80% agreement among experts. Topics covered include assessment of skin, muscle and major organ involvement and suggested treatment pathways.

Conclusions: The SHARE initiative aims to identify best practices for treatment of patients suffering from PRD and to disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases.

Disclosure of Interest: None declared

**CONSENSUS-BASED RECOMMENDATIONS (SHARE) FOR THE MANAGEMENT OF JUVENILE SCLERODERMA**

F. Zulian, Department of Woman and Child Health, University of Padova, Padova, Italy

Background: In 2012, a European initiative called Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) was launched to optimise and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases. Juvenile Scleroderma in its two variety, localized scleroderma (JLS) and systemic sclerosis (JSS) is a rare disease with a growing group of paediatric rheumatic diseases (PRDs) and can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physicians’ experience. Consequently, treatment regimens differ throughout Europe.

Objectives: To provide recommendations for diagnosis and treatment of both JLS and JSS.

Methods: Recommendations were developed by an evidence-informed consensus process using the EULAR standard operating procedures. A committee was constituted, consisting of 16 experienced paediatric rheumatologists, mainly from Europe. Recommendations derived from a validated systematic literature review were evaluated by an online survey and subsequently discussed at two consensus meetings using nominal group technique. Recommendations were accepted if >80% agreement was reached.

Results: In total, 1 overarching principle, 17 recommendations on diagnosis and 13 recommendations on therapy were accepted with >80% agreement among experts. Topics covered include assessment of skin and major organ involvement and suggested treatment pathways.

Conclusions: The SHARE initiative aims to identify best practices for treatment of patients suffering from PRD. In total, 80% agreement among experts. Topics covered include assessment of skin, muscle and major organ involvement and suggested treatment pathways.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7184

**SHARE RECOMMENDATIONS ON JUVENILE SCLERODERMA**

A. Van Royen-Kerkhof, Wilhelmina Children Hospital, Utrecht, Netherlands

Background: In 2012, a European initiative called Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) was launched to optimise and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases. Juvenile Scleroderma in its two variety, localized scleroderma (JLS) and systemic sclerosis (JSS) is a rare disease with a growing group of paediatric rheumatic diseases (PRDs) and can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physicians’ experience. Consequently, treatment regimens differ throughout Europe.

Objectives: To provide recommendations for diagnosis and treatment of JDM based on evidence-informed consensus.

Methods: Recommendations were developed by an evidence-informed consensus process using the European League Against Rheumatism standard operating procedures. A committee was constituted, consisting of 19 paediatric rheumatologists and 2 experts in paediatric exercise physiology and physical therapy, mainly from Europe. Recommendations derived from a validated systematic literature review were evaluated by an online survey and subsequently discussed at two consensus meetings using nominal group technique. Recommendations were accepted if >80% agreement was reached.

Results: In total, 1 overarching principle, 17 recommendations on diagnosis and 13 recommendations on therapy were accepted with >80% agreement among experts. Topics covered include assessment of skin, muscle and major organ involvement and suggested treatment pathways.

Conclusions: The SHARE initiative aims to identify best practices for treatment of patients suffering from PRD. In total, 80% agreement among experts. Topics covered include assessment of skin, muscle and major organ involvement and suggested treatment pathways.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7184
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7286

ULTRASOUND BASIC I & II

SP0037 HOW TO ASSESS US ELEMENTARY LESIONS IN CPPD
G. Filippou, University of Siena, Siena, Italy

Ultrasoundography has been increasingly used the last years for the identification of calcium pyrophosphate dihydrate crystal deposition (CPPD) in joints and on 2011 has been considered by the EULAR task force on CPPD as a promising tool for the diagnosis of the disease. However, it is common experience between sonographers that in daily clinical practice CPP identification by US is rather challenging as crystal deposits are not always numerous and diffuse. Furthermore, other conditions can mimic CPP deposition leading to a wrong diagnosis. The recently created OMERACT US for CPPD subtask force has created for the first time a set of criteria for identification of CPP deposition and assessed their reliability trying to address some of the issues that impede a wider use of US for CPPD diagnosis. During this section will be exposed the main US features of CPP deposition according to the new criteria as well as the principal pitfalls that could mislead diagnosis. The scanning technique and some tips and tricks that could help sonographers to identify correctly CPP deposition will also be explained.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7251

SP0038 HOW TO ASSESS CARTILAGE IN RA AND PITFALLS + DEMO
P. Mandi, Rheumatology, Medical University of Vienna, Vienna, Austria

Cartilage damage is a key process in rheumatoid arthritis which appears to be more clearly associated with irreversible physical disability than bony damage. While conventional radiography only allows the evaluation of joint space narrowing, a major feature of cartilage loss, musculoskeletal ultrasound is a reliable tool for evaluating cartilage damage. The presentation will introduce the pitfalls and challenges associated with visualizing cartilage in rheumatic diseases in general and rheumatoid arthritis in particular. It will also review recent studies in the field which have validated sonoanatomy for both the quantitative measurement of cartilage thickness and for the semiquantitative scoring of cartilage change. A practical demonstration will also be provided.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7274

SP0039 HOW TO EVALUATE THE SUBTALAR JOINT
A. Iagnocco, Università degli Studi di Torino, Torino, Italy

The subtalar joint, also known as the talocalcaneal joint, is a synovial joint of the foot, that occurs between the talus and the calcaneus with the talus that is oriented slightly obliquely on the anterior surface of the calcaneus. The two bones articulate at two different sites (i.e. one anteriorly and one posteriorly). The anterior talocalcaneal joint is a convex area of the talus that fits on a concave surface of the calcaneus. The posterior talocalcaneal joint is formed by a concave surface of the talus and a convex surface of the calcaneus. The subtalar joint contributes to the dorsiflexion of the ankle. Three articulating facets (anterior, middle and posterior) are present between the talus and the calcaneus. The sustentacular tunnel forms the floor of middle facet, and the anterior facet articulates with the head of the talus, and sits lateral and congruent to the middle facet. The posterior facet is the largest of the three, and separated from the others by the tarsal canal. The most relevant actions done by the joint are inversion of the foot. The subtalar joint can also be considered a combination of the anatomic subtalar joint discussed above, and the talocalcaneal part of the talocalcaneonavicular joint. When both those joints are accounted together, it allows for pronation and supination to occur. The subtalar joint is frequently involved in arthritis and, particularly in patients with previous sprains, secondary osteoarthritis can also occur. Symptoms of subtalar joint arthritis include pain, loss of motion through the joint’s range of motion, and difficulty walking on uneven surfaces.

Among the imaging techniques that are appropriate for the assessment of the subtalar joint, ultrasound (US) has been increasingly used over the last years. Indeed it is able to image different abnormalities, including both inflammatory and structural changes, and it is helpful in guiding local procedures that can be easily and safely performed with optimal patient’s tolerance. The US scanning technique is quite complex, and the whole joint area should be scanned in the longitudinal (sagittal or coronal) plane with pathology that should be confirmed in the orthogonal (perpendicular) plane. By using a standardised scanning technique and agreed definitions of pathology, US allows an optimal assessment of inflammatory and structural abnormalities, thus filling the gap between clinical and radiographic evaluations of the subtalar joint.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7292

SP0042 THE ART OF JUGGLING - A PATIENT’S PERSPECTIVE
F.M. Catrina, L.R. Bucharest, Romania
Diagnosed with ankylosing spondylitis since 2006, when just turned 24 years old. I was very demoralized and could not understand why I have rheumatic pains bigger than my grandmother 70 years old. I did not understand why I can’t go, just do anything wrong to anyone. Slowly, slowly I began to understand the disease and help doctors started to move again. But my secret to healthy aging, was family. Therefore we understand that positive thinking can help me more than any drug, posterior how you can have a more positive attitude as if in a nice family environment?

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7139

SP0043 CURRENT NEEDS FOR REHABILITATION
M. Börk, Department of social and welfare studies, Linköping University, Norrköping, Sweden

New biological medications and earlier multi professional interventions have led to a reduction in the extent of disability for patients with rheumatic diseases. However disability still remains a key problem for many patients and patients may experience participation restrictions even though they are achieving “remission”. To be able to engage in the things we want or need to do is crucial to our health and sometimes a challenge to meet for health professionals. Also, there is an ongoing discussion of whether today’s patients have new rehabilitation needs and if they are met by the health care. This session summarizes both qualitative and quantitative evidence of the disability in today’s patients with arthritis. It will further discuss the current needs of rehabilitation in today’s patient in relation to existing standards and guidelines. Rehabilitation interventions and patient reported strategies in relation to pain, fatigue and affected activity balance will be highlighted since they are common disabilities among today’s patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7269

SP0040 HOW TO SCAN THE HIP, NEW APPROACH AND DEMO
I. Möller on behalf of EULAR Working Group Anatomy for the IMAGE. Rheumatology; anatomy; sonoanatomy-sonopathology, Instituto Pobal de Reumatología; University of Barcelona, Hospitalet de Llobregat, Spain

The exploration of the hip includes not only intraarticular findings such as synovitis or lesions of the labrum but also the dynamic exploration of the tendons and muscles surrounding it as well as of the neurovascular bundles of interest. All this is an essential complement in the differential diagnosis of the rheumatic patient. The iliopectos tendon as well as the hip adductors will be demonstrated during the presentation. The anterior and antero internal part of the groin region constitute a relatively frequent consultation and study of the tendinous snapping and its differential diagnosis with the snapping of intraarticular origin can be made by means of the musculoskeletal ultrasound. It requires systematization and knowledge of the regional anatomy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7156
WORK RETENTION REHABILITATION IN PRACTICE

Y. Prior 1,2 on behalf of Rehabilitation Research Group, University of Salford. 1Health Sciences, University of Salford, Manchester; 2Rheumatology, Mid Cheshire NHS Trust Leighton Hospital, Crewe, United Kingdom

This session aims to meet health professionals’ needs in recognising, examining, and identifying problems that patients with inflammatory arthritis (IA) face at work. We know that one in five people with inflammatory arthritis lose their job within five years of diagnosis and, once work disabled, they are unlikely to return to work. Therefore, preventive interventions targeted at work retention, which aim to help people to stay at work, are needed to avoid the transition from work instability to work disability. Rheumatology health professionals play an important role in identifying patients’ work problems at an earlier stage and helping them to stay at work. Currently, there are no set pathways to outline health professionals’ approach to identifying people with work problems and/or work rehabilitation interventions in the UK. Further, there is a need to train health professionals in the importance of the early recognition of these problems and evidence-based interventions to address work instability.

This session will focus specifically on the rheumatology occupational therapy-led work rehabilitation taken place in a NHS setting in the UK. Using real life case studies, Dr Prior will discuss the standardised assessments used in identifying work problems, collaborative goal setting and work interventions to provide a snapshot of work rehabilitation in the context of clinical practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7240

Cytokines and chemokines

SP0046 PREVENTION AND THE PROTECTIVE ROLE OF EXERCISE AND LIFESTYLE INTERVENTIONS ON COMORBIDITIES IN RHEUMATIC DISEASES

S. Garcia Diaz, Rheumatology, Consorci Sanitari Integral, Hospital Moises Broggi Sant Joan Despi, Sant Joan Despi, Spain

Background: It has been recognised that patients with rheumatic diseases are at increased risk of developing comorbid conditions such as cardiovascular disease (CVD), malignancies, infections and osteoporosis (among others). Lifestyle interventions (non smoking, non alcohol, healthy diet and exercise) may play an important role to reduce comorbidities in these patients.

Objective: To find if lifestyle interventions and especially exercise play a vital role in preventing comorbidities in rheumatic diseases through an extensive review of recent literature.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7223

THURSDAY, 15 JUNE 2017

Screening for Comorbidities in Daily Practice: Who and How?

L. Gossec, Paris 06 University, Pitié-Salpêtrière Hospital, Paris, France

Comorbidities are frequent in RMDs, as in many other chronic diseases. In inflammatory rheumatic diseases, the most frequent comorbidities are cardiovascular diseases, depression, infections and cancers. Some of these diseases are more frequent than in persons without RMDs, some are not more frequent but are more often under-assessed and under-treated. These comorbidities and their risk factors need to be screened for. Screening in daily practice is not so simple since it necessitates time, physician expertise and patient cooperation. In this talk, we will address recent recommendations on how to screen for comorbidities, how often and in which setting this should be performed, and the respective roles in screening of rheumatologists, rheumatology nurses and persons with RMDs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7135

Do Patient Organisations Have a Role to Play in Preventing Co-Morbidities?

A.M. Bosworth, n/a, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom

My talk will look in detail at how patient organisations can play a role in preventing co-morbidities. NRAS is currently engaged in two major projects which are both directly concerned with the prevention of co-morbidities. During RA Awareness Week in the UK, 19–26 June, NRAS will launch ‘Love your Heart’ an on-line, interactive RA awareness programme to educate people with RA about their increased risk of heart disease and atherosclerosis. This programme explains in simple terms why people with RA are at increased risk of cardiovascular disease. The programme provides the opportunity to appraise individual risk factors, complete a QRISK2 assessment with their GP and provides a cognitive-behavioural framework to empower people to change their behaviours and achieve a healthier lifestyle, thereby reducing risk of heart disease. Baseline and 6 months evaluations are built into the programme. It has been developed with input from a consultant rheumatologist, GP, and other health experts as well as patients. If time permits I will also describe a research study we are undertaking with 3 hospitals in the UK whereby we will randomly assign newly diagnosed patients to receive a targeted support programme or NRAS or be in a control group which does not receive this support for a period of 6 months. Our aim is to show that the group receiving the targeted support has less anxiety and depression, although other outcomes will also be measured.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7230

Targeting of Angiogenesis

S. Tas on behalf of European Synovitis Study Group. AMC Clinical Immunology & Rheumatology, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands

Angiogenesis is de novo capillary outgrowth from pre-existing blood vessels. This process not only is crucial for normal development, but also has an important role in supplying oxygen and nutrients to inflamed tissues, as well as in facilitating the migration of inflammatory cells to the synovium in rheumatoid arthritis, spondyloarthritides, and other tissues in systemic autoimmune diseases. Neovascularization is dependent on the balance of proangiogenic and antiangiogenic mediators, including growth factors, cytokines, chemokines, cell adhesion molecules and matrix metalloproteases. In this lecture I will provide an overview of the various pathways that govern these angiogenic processes and discusses potential approaches to interfere with pathological angiogenesis, and thereby ameliorate inflammatory disease, by targeting these pathways specifically in endothelial cells.

Key Messages:

- In chronic inflammatory diseases, angiogenesis enables increased delivery of oxygen and nutrients to immune cell populations accumulating in inflamed tissues, and contributes to further immune cell infiltration

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7134

FROM SCIENCE TO PRACTICE - THE ROLE OF HEALTH PROFESSIONALS IN THE MANAGEMENT AND TREATMENT OF RHEUMATOID ARTHRITIS

S. Preckel, Department of Medicine, Asklepios Klinik am Schauspielhaus, Hamburg, Germany

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by persistent inflammation of the synovial membrane, which leads to joint destruction, functional impairment, and increased risk for cardiovascular events. Despite advances in the management of RA, individual patient’s disease is often not optimized, as a result of missing information on disease activity of RA, slow transition to treatment, or suboptimal management of comorbidities.

The role of the health-care professionals (HCP) has to be strengthened in the management of RA. At the individual level, self-management is a crucial component to control the rheumatic disease. Educational programs, symptom monitoring, disease management, and self-management education are complex processes that require the input of HCP. The HCP have to be aware of the individual’s situation and needs for the development of an individualized care plan.

At the level of care delivery, HCP have to use the data available to influence the treatment decision process. Furthermore, the HCP have to ensure an effective cooperation between the different care delivery levels (primary care, rheumatologists, specialized inpatient care). Measuring disease activity, quality of care, and joint function and related patient outcomes are crucial tasks for the HCP.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7222
DNA AGGREGATES AS ALARMINS

DNA is a large polymeric molecule that displays powerful immunological activities and operates in the context of multi-component aggregates to alarm the immune system and stimulate innate immunity. Although DNA has important roles in normal host defense, DNA can serve as an autoantigen and autoimmunogen by itself or in association with other immunologically active nuclear molecules. In the setting of systemic lupus erythematosus (SLE), DNA is a key target antigen; while antibodies to pure DNA double stranded DNA serve as important biomarkers, the relevant antigenic form of DNA during disease is the nucleosome in which DNA is bound to histones. Furthermore, nucleosomes can be components of microorganisms which are small membrane-bound structures that are released from dead and dying cells. MPs can stimulate immune responses and serve as a nidus for immune complex formation. In normal immunity, DNA can interact with nucleic acid sensors in the cytoplasm of cells to stimulate responses including production of type 1 interferon. These sensors respond to DNA from intracellular organisms such as bacteria and viruses although damaged DNA and DNA from mitochondria can also interact with these receptors. While these sensors are intracellular, they can interact with extracellular DNA that is introduced or from other molecules. In another facet of host defense, DNA can be released from neutrophils during a process termed NETosis. A NET or neutrophil extracellular trap is a mesh-like structure comprised of DNA as well as granule proteins that have antibacterial activity. NETs can trap and kill bacteria. Thus, in its diverse immunological roles, DNA interacts with other molecules to form aggregates of sub-cellular structures that alarm the immune system, promote host defense or drive critical events in autoimmunity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7217
only disrupted when I realised that my experience of illness was quite common to other persons with a RMD. I can still remember my fascination, in a Patient Reported Outcomes workshop, by discovering that our experience as patients had a bigger relevance that the one we usually conceive. Then, I felt the need of understanding the research process and specific jargon, so that I could relate the knowledge I had with a RMD. Otherwise any insight on the patient perspective would be "lost in translation", due to an inability to enable a correspondence between the scientific terminology and mindset regarding the disease, and the experience of illness and sickness by the individuals. Training opportunities were also recognised as desirable by the above mentioned EUROLU, in order to increase expertise and understanding of research methods and to promote the patients’ self-confidence on their contribution to research. The Patient Research Partners (PRP) training by EULAR, in 2013, was the first step in discussing the importance of understanding and the role of patients and on how to provide a meaningful input from the patients’ perspective into research processes. It was followed in 2014 by the training provided by European Patients’ Academy on Therapeutic Innovation (EUPATI) for Patient Expert on the Medicines Research and Development Process. This expert-level training was organized in a mixture of independent e-learning coursework and face-to-face training events over a 14-month period. The syllabus involved six modules: Discovery of Medicines & Planning of Medicine Development, Non-Clinical Testing and Pharmaceutical Development, Exploratory and Confirmatory Clinical Development, Clinical Trials, Regulatory Affairs, Medicinal Product Safety, Pharmacovigilance and Pharmacoeconomics, Data management, and audit and practices. Additionally, in 2016, I have attended the 1st EULAR course on Health Economics in Rheumatology. In the meantime, my background as an anthropologist led me to become interested in Medical Anthropology. Between 2007–2015 my academic research (MA Phil. and PhD) was oriented towards a specialization in Anthropology of Health, with a special interest in Anthropology of Pharmaceuticals. Based on my personal experience, on this lecture I will focus on the challenges of the role of the PRP trying to fill the gap between the mindsets and practices of different stakeholders. Navigating through different meanings of symptoms and treatments, the educated patient representative must act like a translator, decoding the biologic impact of the disease and intervention over the experience of illness on the everyday aspects of living with a RMD. The biggest expectation and challenge might be to bring these aspects forward, as relevant for the other stakeholders, since they shape individual values and patient’s preferences. Although recognised as having a pivotal role, patient’s involvement in research may be limited by tokenism or by ineffective patients’ participation. Patients’ involvement is now a requirement and an added value to any project. But, is the project team ready and willing to listen to patients? Are PRP duly involved in the project, or are they just expected to be recipients without any input of their perspectives into the development and implementation of the research? The knowledge and education acquired to perform our task enables us to understand science enough to communicate the patient experience in a meaningful way, improving the research. Our added value is, undoubtedly, our experience with the disease, our understanding of the individual values and preferences shaped by the everyday aspects of living with a RMD. We should be taken more seriously, for the benefit of science and patients. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.7243

**SP0052** BUILDING PATIENT PARTNERSHIP IN HEALTH CARE SERVICE DESIGN AND DELIVERY

H. Lempp, Rheumatology, Kings College London, London, United Kingdom

This paper will present details of the approach to patient and public involvement in health service delivery, health service research and health care education in England. The presentation will be based upon a Logical Framework with the following key elements: inputs, processes, outputs, and outcomes/impacts. Key barrier acting to minimise the impact of building patient partnerships will be discussed, illustrated by examples from our experience with the preparatory stages for our departmental strategy to formalise close Patient Partnership for our research portfolio: (i) establish honorary contracts for patients for the academic Institution and local Hospital Trust; (ii) include patients on the interview panels to appoint project researchers (iii) build in a separate funding within the overall project budget for the costs associated with patient partnership and (iv) manage to appoint project researchers (ii) build in a separate funding within the overall Institution and local Hospital Trust; (ii) include patients on the interview panels for our departmental strategy to formalise close Patient Partnership. The biggest expectation and challenge might be to bring these aspects forward, as relevant for the other stakeholders, since they shape individual values and patient’s preferences. Although recognised as having a pivotal role, patient’s involvement in research may be limited by tokenism or by ineffective patients’ participation. Patients’ involvement is now a requirement and an added value to any project. But, is the project team ready and willing to listen to patients? Are PRP duly involved in the project, or are they just expected to be recipients without any input of their perspectives into the development and implementation of the research? The knowledge and education acquired to perform our task enables us to understand science enough to communicate the patient experience in a meaningful way, improving the research. Our added value is, undoubtedly, our experience with the disease, our understanding of the individual values and preferences shaped by the everyday aspects of living with a RMD. We should be taken more seriously, for the benefit of science and patients. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.7243

**SP0053** HOT SESSION: VASCULITIS TREATMENT

R.A. Lugmani, University of Oxford, Oxford, United Kingdom

The systemic vasculitides are characterized by inflammation of blood vessels, which if untreated, results in tissue or end organ damage or death. Chapel Hill nomenclature is widely used to define different forms of vasculitis according to the size of the predominantly affected vessels. Other forms of vasculitis are not defined by a predominant vessel size (e.g. Behcet’s syndrome). Vasculitis associated with the presence of anti-neutrophil cytoplasm antibody (ANCA), termed AAV, is less common than giant cell arteritis (GCA), but considerable advances have been made in understanding the pathogenesis and evidence based treatment for AAV. AAV is divided into three major forms: granulomatosis with polyangiitis (GPA) (Wegener’s granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss syndrome). ANCA are implicated in their pathogenesis but not all patients with AAV are ANCA positive. We will review recent EULAR guidelines on therapy for AAV, based on careful structured clinical evaluation of patients, with stratification according to severity. Cyclophosphamide or rituximab (plus glucocorticoid) is used for severe disease, followed by maintenance with azathioprine (AZA) or methotrexate (MTX), and reducing doses of glucocorticoids; or maintenance rituximab. Additional plasma- exchanging strategies are advocated for very severe, severe active disease, or after severe disease, MTX or AZA or mycophenolate (plus glucocorticoids) can be used. The evidence for effectiveness is clear for MPA and GPA. A number of studies are underway to improve our use of these existing agents and to test newer, mechanism based treatments such as a inhibition CTLA4 or of the CS complement pathway in GPA and MPA. For EGPA with severe manifestations, cyclophosphamide and glucocorticoids are recommended. A trial of mepolizumab (inhibitor of interleukin 5, a potent driver of eosinophil production) in EGPA has recently been completed. IL-6 inhibition with tocilizumab is a significant advance over glucocorticoid monotherapy at present. We will discuss our experience using these various agents and discuss the current state of the art. This expert-level training was organized in 2014 by the training provided by European Patients’ Academy on Therapeutic Innovation (EUPATI) for Patient Expert on the Medicines Research and Development Process. This expert-level training was organized in a mixture of independent e-learning coursework and face-to-face training events over a 14-month period. The syllabus involved six modules: Discovery of Medicines & Planning of Medicine Development, Non-Clinical Testing and Pharmaceutical Development, Exploratory and Confirmatory Clinical Development, Clinical Trials, Regulatory Affairs, Medicinal Product Safety, Pharmacovigilance and Pharmacoeconomics, Data management, and audit and practices. Additionally, in 2016, I have attended the 1st EULAR course on Health Economics in Rheumatology. In the meantime, my background as an anthropologist led me to become interested in Medical Anthropology. Between 2007–2015 my academic research (MA Phil. and PhD) was oriented towards a specialization in Anthropology of Health, with a special interest in Anthropology of Pharmaceuticals. Based on my personal experience, on this lecture I will focus on the challenges of the role of the PRP trying to fill the gap between the mindsets and practices of different stakeholders. Navigating through different meanings of symptoms and treatments, the educated patient representative must act like a translator, decoding the biologic impact of the disease and intervention over the experience of illness on the everyday aspects of living with a RMD. The biggest expectation and challenge might be to bring these aspects forward, as relevant for the other stakeholders, since they shape individual values and patient’s preferences. Although recognised as having a pivotal role, patient’s involvement in research may be limited by tokenism or by ineffective patients’ participation. Patients’ involvement is now a requirement and an added value to any project. But, is the project team ready and willing to listen to patients? Are PRP duly involved in the project, or are they just expected to be recipients without any input of their perspectives into the development and implementation of the research? The knowledge and education acquired to perform our task enables us to understand science enough to communicate the patient experience in a meaningful way, improving the research. Our added value is, undoubtedly, our experience with the disease, our understanding of the individual values and preferences shaped by the everyday aspects of living with a RMD. We should be taken more seriously, for the benefit of science and patients. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.7243

**SP0054** THE CONCEPT OF TREAT-TO-TARGET

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Many illnesses including most rheumatic diseases have substantial effects on well-being and quality of life, including deterioration of physical and mental function and a reduced life expectancy, since they can cause damage to organs and cells. If healing and regeneration cannot be achieved an impairment of organ function can be expected. In acute diseases this may occur rapidly over hours to days and weeks, while it often takes months to years in chronic disease. However, if treatment is instituted early enough, organ damage may be prevented or diminished. Critical for an optimal management of diseases with potentially severe outcomes is to determine the responsible thresholds for, for example, disease activity or to define the maximum level of a surrogate marker at which damage is unlikely to occur and, thus, will not be harmful in the long term. Although the optimal aim of therapy is cure, and appropriate therapy may even normalize life expectancy, many chronic diseases such as hypertension, diabetes, rheumatoid arthritis (RA) and spinal cord injury (SCI) have remained without curative therapies in the last decades – even though considerable progress has been made. Thus, a strategic therapeutic approach should aim for prevention of future damage, and maximal improvement of compromised organ function. Therefore, a clearly defined threshold of a validated measure that predicts future harm or no minimal harm, is a target of critical importance for chronic diseases with potentially severe outcomes. Treat-to-target strategies have been developed to achieve this have widespread implications. They should be routinely followed - as long as the potential harm from treatment is carefully balanced against its benefit. Clearly, if inappropriately managed, the consequences of diabetes and hypertension in
the long run include, myocardial infarction, stroke, renal failure, blindness, etc. Therefore, target values for biological markers have been determined below which organ damage does usually not occur and life expectancy is normalised. Examples for domains in which such thresholds have been defined are blood pressure, glycosylated haemoglobin (HbA1c), and others. Inflammatory processes lead to organ damage not only in the musculoskeletal system but they may also harm internal organs. A target level of a measure related to its long-term outcome, can be a surrogate measure like the cholesterol level for cardiovascular diseases, or a composite measure of disease activity as used in RA (DAS28) or in AS (ASDAS). The treat-to-target strategy can be reduced to a simple algorithm of, on the one hand measuring activity and on the other hand, in consequence, adapting treatment. Treatment adaptation does not necessarily mean changing a medication or increasing the dosage of a drug but may even also mean lifestyle changes, as long as the therapeutic target is attained or nearly attained – importantly within the specified time frame. Therapeutic adaptations should always take patient factors, including comorbidities, adverse events and patient preferences, into account.

However, the musculoskeletal system can mostly not be assessed by using a simple surrogate or direct “gold standard” measures, since rheumatic diseases with multiple signs and symptoms are mostly rather complex. In RA information derived from physical examination using a quantitative joint count is considered very important. This is different in AS. Additionally, information from the history, which can be collected through patient self-report multifaceted questionnaires, has proven effective in determining patient status and its change. This is even more important in AS, because of its functional impairment. However, the treatment of AS is difficult, but also the assessments should be individualised. Both in the overarching principles and in the recommendation the shared decision between patient and rheumatologist is listed as the basis of the T2T management.

The updated recommendations will be presented.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7129

SP0055 WHAT ARE THE CHALLENGES FOR APPLYING TREAT TO TARGET IN AXIAL SPONDYLOARTHRITIS?
M. Dougados, rheumatology Hopital Cochin, René Descartes University, paris, France

The concept of Treat to Target (T2T) applied in rheumatoid arthritis has been evaluated in psoriatic arthritis and is currently under investigation in two different strategy trials in patients suffering from axial spondyloarthritis (axSpA). Whatever results of these trials will be, the acceptance of this concept and consequently its implementation in daily practice might be challenging for several reasons. The concept of T2T requires 3 different steps: a) the choice of the most relevant outcome measure (e.g. a measure evaluating a domain recognized as predisposing to subsequent clinically relevant damage (either structural damage or important comorbidities such as cardiovascular diseases)), b) the determination of the threshold of the outcome measure to reach (threshold below which the risk of subsequent damage is abolished or significantly diminished) and c) the time to reach the target is usually related to the treatment modality (a few days for NSAIDs and several weeks for DMARDs). A part these different steps, two points have to be considered a) this T2T approach is mostly aimed at minimising the pathologic damage and b) this T2T strategy requires the possibility to adapt/increase the treatment in case the target is not reached after one or several ‘conventional’ treatment modalities. For each of these different points we will consider past ongoing initiatives proposing to resolve the different encountered issues in order to facilitate the elaboration and the implementation of a T2T strategy in axSpA.

Disclosure of Interest: M. Dougados Grant/research support from: UCB,ABBVIE,PFIZER,FINITEC, Consultant for: UCB,ABBVIE,PFIZER,FINITEC

DOI: 10.1136/annrheumdis-2017-eular.7192

SP0056 UPDATE OF THE T2T RECOMMENDATIONS IN SPA
D. Van Der Heijde on behalf of T2T in SpA working group. Rheumatology, Leiden University Medical Center, Leiden, Netherlands

In 2013 the first recommendations for treating spondyloarthritis to target (T2T) were published. These followed the reasoning for the T2T recommendations for rheumatoid arthritis. Although the systematic literature review at that time did not provide evidence to support the recommendations, five overarching principles and 11 recommendations were formulated. There were 9 common recommendations for axial SpA, peripheral SpA and psoriatic arthritis and 2 additional recommendations for each subgroup respectively. In 2017 the T2T working group met again to update the recommendations. This was based on an updated systematic literature review. Data had been published that there is a link between bone density and subsequent long-term outcomes, which is the basis for the T2T principles.

SpA is characterised by musculoskeletal signs and symptoms (arthritis, enthesitis, dactylitis, axial disease) but also extra-articular manifestations (psoriasis, inflammatory bowel disease, anterior uveitis) are important manifestations. Moreover, biomarkers such as osteoporosis, cardiovascular disease. All these manifestations are taken into account in the formulation of the recommendations. The overarching principles were kept largely identical. Some changes in the wording were made for a better understanding, but no fundamental changes were made. A total of 11 recommendations were formulated. These are now for all subgroups of SpA and no specific recommendations are proposed. In principle, the treatment target is remission or inactive disease of musculoskeletal and extra-articular manifestations, and the target should be individualised. It is important that remission/inactive disease should be based on a combination of clinical and laboratory parameters, and disease activity should be measured on the basis of clinical signs and symptoms as well as acute phase reactants. This is important to realise, e.g. in axial SpA as patient reported outcomes only are at best weakly correlated with structural damage. In certain circumstances, low disease activity may be an alternative target. Because of the heterogeneous presentation of SpA, not only the target but also the assessments should be individualised. Both in the overarching principles and in the recommendation the shared decision between patient and rheumatologist is listed as the basis of the T2T management.

The updated recommendations will be presented.

Disclosure of Interest: D. Van Der Heijde Consultant for: AbbVie, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Employee of: Imaging Rheumatology

DOI: 10.1136/annrheumdis-2017-eular.7158

THURSDAY, 15 JUNE 2017
Calcium crystal deposition in rheumatic diseases —

SP0057 CALCIUM CRYSTALS AND THEIR LINK TO OSTEOARTHRITIS
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Calcification of cartilage is a common finding during osteoarthritis (OA). We have shown that it is mainly of the BCP type and not the CPPD type of crystal formation. BCP cartilage calcification is directly linked to the severity of cartilage degradation and, therefore, OA severity. We have also shown that with increasing hypertrophic differentiation of chondrocytes, the amount of calcification increases in vivo and in vitro. This indicates a link between chondrocyte hypertrophy and cartilage calcification. The pyrophosphate pathway is known to be involved in tissue calcification. It functions to keep the sensitive balance of pyrophosphate (PPi) and phosphate (Pi), thereby preventing the generation of calcium-phosphate crystals. One key player in this pathway is the nucleotide pyrophosphatase phosphodiesterase (NPP1), which has been demonstrated to be regulated by inflammatory mediators such as IL-1. In our cohort of OA patients, the expression of collagen X and NPP1, but not ANK and TNAEP, correlated with cartilage calcification and also with the Mankin-Score. NPP1 expression inverse correlated with the calcification, whereas collagen X was upregulated. This finding was confirmed in experimental murine OA using the DMM mouse model. Furthermore, NPP1mut/mut mice (ttw/ttw) exhibit more calcification activity than wild type controls in joints as well as in cartilage of non weight bearing areas, including ear cartilage, suggesting that mechanical stress is not required for the induction of calcification. NPP1mut/mut mice (ttw/ttw) mice developed typical OA-like changes as evaluated by pathologic examinations as well as in vivo histopathological stainings. Intriguingly, calcium was associated with increased expression of the hypertrophic cartilage marker collagen X and the bone marker collagen I. Additionally, BCP crystals are able to activate chondrocyte differentiation via the WNT signaling pathway. NPP1 is an important player in OA-associated cartilage calcification. Pathologic calcification of cartilage resembles in many aspects cartilage transformation into bone. Taken together, the data suggest that OA is characterized by the re-activation of molecular signalling cascades that at least in part resemble endochondral ossification.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7192

SP0058 REVIEW OF THE DIFFERENT IMAGING MODALITIES TO DETECT CALCIUM DEPOSITION DISEASES
P. Omoumi. Lausanne University Hospital, Lausanne, Switzerland

Crystal deposits in and around the joints are common and most often encountered
as incidental imaging findings in asymptomatic patients. However, they can also cause chronic or acute arthropathy, generating symptoms. In the chronic setting, imaging features are usually characteristic and allow the differentiation of the type of crystal arthropathy. In the acute phase and in the early stages of the crystal deposition, the signs are often non-specific, and the finding of a leukocyte-rich synovial fluid is essential for the diagnosis of synovial fluid.

Radiography is the main imaging modality for the workup of these conditions. It can confirm the diagnosis and often characterizes the type of crystal arthropathy. In recent years, US has played an increasingly important role in this setting, and is a useful tool in superficially located crystal-induced arthropathies. CT nicely complements radiography for deeper sites, especially the axial skeleton.

Biomarkers are required for remission: More than clinical...?

For both, it is clear that we are defining a very good, perhaps even the best concept adequately defined in RA, but less so in many other rheumatological diseases. To even begin with answering the question, we must first agree on a clear conceptual definition of remission. When we started on the development of the ACR-EULAR definition of remission in RA, we used dictionary sources and discussions to settle on this:

“The state of absence of disease activity in patients with a chronic illness, with the possibility of return of disease activity” [1] It is clear that choices are made from the beginning, especially with the concept “disease activity”, and the possibility that disease activity returns (as opposed to “healing”, where this possibility does not exist). Disease activity is a tangible concept adequately defined in RA, but less so in many other rheumatological diseases. Also, disease activity is conceptually separate from (mostly irreversible) consequences of the disease, such as damage. Finally, note that the above concept does not contain the elements “duration” or “treatment”.

If we continue with the above concept, why do we want to proceed to operationalize the remission definition? The two main reasons are research and patient care. From both is clear that we are defining a very good, perhaps even the best state a patient can be in, given that we are talking about chronic disease, i.e. the root cause of the disease cannot be taken away to heal the patient. Being in such a good state has immediate benefits (minimal disease impact) and probably also future benefits, of lack of disease activity translates to less consequences (damage etc). In both research and patient care, we want a definition that is both valid (favorable test characteristics; links to prognosis) and feasible (time, costs, interpretability). Validity and feasibility oppose each other to a certain extent (e.g. definitions with better sensitivity and specificity are usually more expensive). Research and patient care differ in their use of the definition. In research, validity and feasibility can be lower than in patient care, because research is about groups, and cost and interpretability are less of an issue than in patient care. Most of the people criticizing the current ACR-EULAR remission definition of RA are confused over its purpose: whereas it was intended for use in trials, they criticize it for lack of validity in the clinic. For instance, it is felt that the patient global criterion is too strict, so that patients with no apparent inflammatory activity but a patient global score of 2 or higher (scale 0–10) are “unjustly” not classified as in remission. Also, the lack of a duration or treatment criterion is felt to be a problem, but this is not an issue in research.

In the following pro-con debates, please consider the following:

Proposals to change existing criteria for remission must also be held to the following:

1. Conceptually, remission is thought of as a state where the disease is absent. As we approach a better understanding of the underlying pathophysiological process of a disease, it becomes more and more relevant to include in a definition of remission appropriate biochemical markers of that process.

2. From a practical point of view, definitions of remission in RA have been built upon clinical parameters of disease activity, supplemented in some cases with a single biomarker. However, it is clear that in practice these definitions are insufficiently precise: held against a gold standard of expert opinion, they perform at around 80–90%, misidentifying one or two out of every ten patients. And while there is an understandable and in many ways desirable development of more patient-reported emphasis in outcomes, it has consensually practical value to be able to objectively an important disease state such as remission.

3. There is convincing evidence to show that biomarkers can be employed successfully to predict some aspects of RA. In the day-to-day care of patients with this disease, the most important prediction may be whether the effective drug can be tapered or not. Current evidence indicates that biomarkers may be invaluable at helping clinicians and their patients make this important decision.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7263

Thursday, 15 June 2017

Fifty shades of remission in RA

M. Boers, Epidemiology & Biostatistics; Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands

This session is about defining remission. Most examples will be about rheumatoid arthritis (RA) because most experience has been gathered in that disease. But the concept of remission should be viewed from a wider perspective than one disease. The session includes two pro-con debates (on the utility of including imaging biomarkers in a definition of remission).

As in all things, when embarking on a scientific project, one must ask: “Why are we doing this?”

To even begin with answering the question, we must first agree on a clear conceptual definition of remission. When we started on the development of the ACR-EULAR definition of remission in RA, we used dictionary sources and discussions to settle on this:

“The state of absence of disease activity in patients with a chronic illness, with the possibility of return of disease activity” [1]

It is clear that choices are made from the beginning, especially with the concept “disease activity”, and the possibility that disease activity returns (as opposed to “healing”, where this possibility does not exist). Disease activity is a tangible concept adequately defined in RA, but less so in many other rheumatological diseases. Also, disease activity is conceptually separate from (mostly irreversible) consequences of the disease, such as damage. Finally, note that the above concept does not contain the elements “duration” or “treatment”.

If we continue with the above concept, why do we want to proceed to operationalize the remission definition? The two main reasons are research and patient care. From both is clear that we are defining a very good, perhaps even the best state a patient can be in, given that we are talking about chronic disease, i.e. the root cause of the disease cannot be taken away to heal the patient. Being in such a good state has immediate benefits (minimal disease impact) and probably also future benefits, of lack of disease activity translates to less consequences (damage etc). In both research and patient care, we want a definition that is both valid (favorable test characteristics; links to prognosis) and feasible (time, costs, interpretability). Validity and feasibility oppose each other to a certain extent (e.g. definitions with better sensitivity and specificity are usually more expensive). Research and patient care differ in their use of the definition. In research, validity and feasibility can be lower than in patient care, because research is about groups, and cost and interpretability are less of an issue than in patient care. Most of the people criticizing the current ACR-EULAR remission definition of RA are confused over its purpose: whereas it was intended for use in trials, they criticize it for lack of validity in the clinic. For instance, it is felt that the patient global criterion is too strict, so that patients with no apparent inflammatory activity but a patient global score of 2 or higher (scale 0–10) are “unjustly” not classified as in remission. Also, the lack of a duration or treatment criterion is felt to be a problem, but this is not an issue in research.

In the following pro-con debates, please consider the following:

Proposals to change existing criteria for remission must also be held to the question: “Why are we doing this?”

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7263

Thursday, 15 June 2017

Innate immunity

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Immunity is essential for life, yet the strength of immune responses are not constant throughout the day. This oscillatory immunity reflects an adaptation of organisms to environmental changes that occur through day-night cycles, so as to optimize and concentrate effective responses to the times of maximal environmental threat. In my talk I will discuss our ongoing efforts to uncover the mechanisms by which neutrophils, the most abundant and aggressive of all immune cells, orchestrate temporal immunity. These mechanisms are reflected in diurnal changes in phenotype and function of neutrophils, which we refer to as neutrophil aging. We propose that the existence of a timed response of neutrophils governed by cell-intrinsic and –extrinsic mechanisms suggests that inflammatory disease co-opts ancestral processes to damage tissues.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7054

Thursday, 15 June 2017

Differential scavenging of apoptotic cells and bacteria

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During inflammation and infection, we are simultaneously confronted with both self and non-self in form of dying cells and microbes, respectively. Mechanisms that facilitate the non-immunogenic clearance of self-antigens derived from apoptotic and necrotic cells and that, in parallel, allow the initiation of an immune response against invading pathogens are incompletely understood. Recent data from our laboratory show that the immune system actively sorts apoptotic cells (ACs) and bacteria into distinct subspecies of phagocytes thereby enabling a segregated processing of self and non-self as well as a differential immune response against these two entities. During inflammation, ACs were cleared by tissue resident macrophages (resMϕ) that performed a non-immunogenic disposal of self antigens, whereas bacteria were preferentially ingested by monocyte-derived inflammatory macrophages. We identified the enzyme 12/15-lipoxygenase and the nuclear receptor Nrf4, both specifically expressed by resMϕ, as key factors that control the coordinated and non-immunogenic phagocytosis of ACs by these specialized macrophage subset. Incorrect sorting and aberrant uptake of AC-derived self-antigens by pro-inflammatory and immunocompetent phagocytes, however, resulted in the break of self-tolerance and autoimmunity. Our data thus demonstrate the importance of a sorted clearance of ACs for the maintenance of immunologic self-tolerance.

Disclosure of Interest: None declared


Thursday, 15 June 2017

The role of muscle in innate immune responses

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The skeletal muscle represents a unique site from the immunological point of view. Leukocytes are virtually absent in healthy conditions. However they are quickly recruited upon muscle injury, persist during the regenerative phases to disappear again after tissue healing. Thus, it represents and ideal scenario to study the
involvement of the innate immune system in the homeostatic response either to the conventional programmed death of multinucleated myofibers and to the parallel occurrence of "non-canonical" cell death and survival programs, including necrosis and autophagy. Recruited phagocytes are responsible of the clearance of damaged myofibers and of dying muscle stem/progenitor cells, striomal cells and cardiomyocytes in particular are endowed with remarkable plasticity throughout regeneration and healing, switching from activated cells that generate inflammatory cytokines to reparative assets, that play a non redundant role during the resolution phases of the damage and regulate the termination of the inflammatory responses. This dynamic transition between is increasingly felt to be the key to muscle homeostasis. Conversely defects in the process favour maladaptive remodeling with deposition of collagen and fat accumulation and in predisposed individuals autoimmunity leading to inflammatory idiopathic myopathies. A specialized population of regulatory T (Treg) cells, which control the immune system by promoting the M1-to-M2 switch, and the activation of the muscle stem cells, satellite cells is receiving increasing attention for their central role in tissue homeostasis. Thus, the immunologic perception of muscle cell death and regeneration – in turn influenced by environmental cues, including mitophagy and alteration of the redox balance - determines whether these events foster successful tissue healing or persisting inflammatory myopathies. The insights that are progressively become available on this original scenario hold promises to develop new approaches for disease treatment. Thus, immunologic perception of death and regeneration of muscle cells determine whether these events promote healing of tissues or persistent inflammatory myopathies. The impacts that are becoming increasingly available on this original scenario hold promise for the development of new approaches to the treatment of persistent human muscle disease.

Disclosure of Interest: None declared

THURSDAY, 15 JUNE 2017

To be and to become: transition from paediatric to adult care

W. Olde, YOUTH-R-WELL.COM, Groningen, Netherlands

The importance of successfully transitioning pediatric patients to adult care is increasingly recognized across a wide range of health care providers. However, there are still many challenges occurring during the transition phase. This presentation will contribute to these challenges by sharing the journey of a young person with arthritis on the transition to adult care. As a young patient with arthritis, I made the journey from pediatric care to adult care a couple of years ago. I am diagnosed with arthritis since I was 14 years old. In this presentation, I will show the experiences of my own transition. Furthermore, as the chair of Youth-R-Well.com, an organization for young people with RMDs in the Netherlands, I will share some of the main points around transition I learned from other young patients. For every person, the transition to adult care is experienced differently. Therefore, I will try to give some main answers from personal journeys on the questions: How is the transition experienced by a young patient? What are the current challenges faced by a young patient during the transition? What should be the role of the parents during the transition? What are best practices for the transition to adult care?

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7193

ARE WE ASKING THE RIGHT QUESTIONS IN TRANSITION RESEARCH?

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Already in 1991 Robert Blum pointed to the diverse set of issues of which the clinicians need to be cognisant to successfully care for youth with chronic illness. Since then, the special health care needs of adolescents and young adults with chronic diseases, including rheumatic diseases, have been on the agenda. Despite efforts to develop holistic services and programmes for youth, there are still inconsistencies in service delivery and practice standards. This revealed a survey among paediatric rheumatologists from 115 centres in 22 European countries in 2016. A minority of European paediatric rheumatology centres have written transition policy, follow a standardised, structured approach in transitioning patients and measure the success of their interventions with evaluated instruments. To overcome these deficits and existing practice variation, key elements of transitional care, frameworks and pathways to implement and assess transition programmes have been recommended by EURAL and PRES. However, as long as we don't have robust evidence upon best practices for transition, on the best metrics for measuring "success" and "outcome" of transitional care services and on the impact of interventions on the young people with rheumatic diseases will the service planning and delivery for transition aged youth remain suboptimal and result in adverse long-term outcomes.

The literature about transitional care is exponentially increasing each year and comprises among others assessments of experience of care and clinical outcomes, evaluations of different services and processes of care. What we have learned so far from transition research in the field of rheumatology, which research priorities are currently set on the agenda by health care providers and whether they meet those of young people will be in the focus of this lecture.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7264

IMPLEMENTATION OF A BRIEF TRANSITION PROGRAMME FOR ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: It is well described that adolescents and parents find transition between the children’s and adult ward challenging (1–2) because they feel inadequate prepared, and find communication and cultural differences between child and adult care challenging. Thus, transitional care programmes becomes essential for a successful process (3).

Objectives: We aimed to develop a brief transition programme for adolescents with juvenile idiopathic arthritis (JIA), suitable for daily clinical practice in the children’s and adult ward of rheumatology at Aarhus University Hospital, Denmark.

Methods: The development was based upon studies of transitional care programmes and qualitative studies of the patient, parent, and health professionals perspective in the transition process. Needs in the transition process from the perspective of both adolescents and parents were further investigated through semi-structured interviews. We used studies by Janet McDonagh and colleagues (3) as a theoretical framework for the programme development.

Results: The programme focuses on the final part of the transition process by including the adolescent from the children’s ward at the age of 14. It runs for two years in the children’s ward and continues the first year in the adult ward. The programme focuses on preparing the adolescent and parents for transition by bringing attention to the adolescent’s knowledge and skills in coping with JIA. The programme further focuses on the relation between the adolescents and parents by bringing attention to the need for a gradually separation, and to placing more self-dependence on the adolescents. A guideline, describing the programme, containing concrete instructions to health professionals has been developed. The programme was primarily initiated by the adult ward, but nurses and physicians in both wards have been involved throughout the process. The programme consists of the following elements:

• Assigned contact persons.
• Information leaflets about transitional care, transfer to adult care and differences between the children’s and adult ward, i.e. in ways of working and treatment procedures.
• Independent consultations with health professionals.
• Materials for educational sessions.
• Educational sessions dealing with JIA and treatment, dialogue on adherence and challenges in adolescence.
• Arrangements of visits to the adult ward before transfer.

Conclusions: Our experiences with the programme practice are generally positive. However, we have noticed that successful implementation calls for good collaboration and continuous involvement of the health professionals involved in the programme on a daily basis. Hence, ongoing meetings and communication have been essential to promote collaboration between the children’s and adult ward.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1784

THURSDAY, 15 JUNE 2017

Heterogeneity in JIA

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The importance of cytokines in the pathogenesis of inflammatory diseases is highlighted by the success of therapeutic approaches directed against cytokines and cytokine receptors. Cytokines are characterized by their redundancy and pleiotropy: multiple cytokines can target the same receptor, while on the other hand a single cytokine can have multiple, even contradictory immunological effects.
Linking a cytokine/protein biomarker signature with clinical outcome may help to identify and classify patient cohorts. Thus “intelligent” cytokine signatures can be used as biomarkers in human inflammatory diseases. There are however various risks associated with this approach; often it is impossible to obtain material from the site of inflammation and there are various often not well-known technical aspects that can lead to unreliable results. Although standards for regulators are prominent in day to day clinical practice, standardization of sample collection and laboratory assessments remains suboptimal. Inconsistency in sample collection can affect the results of biological assays and thus several characteristics require thorough evaluation and standardization. This standardization is not limited to assay validity and reproducibility but also pre-analytical treatment and appropriate specimen types.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7203

SP0068 CLINICAL INSIGHTS INTO JIA HETEROGENEITY
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Several epidemiologic surveys have documented a remarkable, yet unexplained, disparity in the prevalence of juvenile idiopathic arthritis (JIA) subtypes among different geographic areas or ethnic groups. Moreover, the therapeutic approach to JIA is not standardized and the availability of the novel and costly biologic medications is not uniform throughout the world. This disparity may have significant impact on disease outcome. The multinational study of the EPIdemiology, treatment and Outcome of Childhood Arthritis (EPOCA) study is aimed to obtain information on the variability of JIA phenotypes in different geographic areas, the therapeutic approaches of pediatric rheumatologists practicing in diverse countries, and the disease status and outcome of children with JIA currently followed worldwide. Participation in the study was proposed to all pediatric rheumatology centers that are part of the Pediatric Rheumatology International Trials Organization (PRINTO), and to several centers in the US and Canada. Each center was asked to enroll 100 consecutive JIA patients or all consecutive patients seen within 6 months. Each patient received a retrospective and cross-sectional assessment. Parent- and child-reported outcomes were recorded through the administration of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR). Participating countries were grouped into 6 geographic areas. Patients were then grouped according to their country’s gross domestic product per capita (GDP) and the total expenditure on health per capita (HE) (source www. who.org). Currently, 8,325 patients from 44 countries have been entered in the web database. Comparison of main epidemiology, treatment, and outcome features across the different geographic areas was performed. Patients living in countries with GDP or HE below the median had lower frequency of remission, higher median cJADAS, higher frequency of damage, and were less frequently prescribed biologic DMARDs. These results were confirmed when analyses were conducted only in oligoarthritis or polyarthritis patients. These results provide further evidence of the wide difference of JIA characteristics across geographic areas in terms of age at disease onset, subtype prevalence, and frequency of anterior uveitis. Overall, patients living in non-Western countries had higher levels of disease activity and cumulative damage than patients followed in North America and Western Europe. This disparity in disease outcomes may be partially due to differences in the availability or affordability of biologics, as confirmed by the evidence of worst outcomes in countries with lower GDP or HE.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7236

THURSDAY, 15 JUNE 2017
EULAR - EMA session

SP0069 REGISTRIES IN MUSCULOSKELETAL DISEASES AND THEIR REGULATORY USE
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Patient registries collect information about individuals sharing health-related characteristics, for example, a particular disorder, a treatment or a procedure. While randomised controlled trials typically provide the primary evidence supporting marketing authorisations for new medicines, the patients studied may not be fully representative of everyone ultimately receiving the medicine and the trials may provide limited information about the natural history of the disorder. Information collected in patient registries is potentially of value for filling these evidence gaps in certain situations and for providing post-marketing safety and effectiveness information. Multiple stakeholders stand to benefit from using registry information in this way including patients, healthcare providers, policy makers, manufacturers and healthcare regulators.

In 2014, the EMA commenced a Registry Initiative aiming to optimise the use of registries in supporting medicines authorisations. Establishing a strategy of early engagement between marketing authorisation applicants and registry holders and a task force to support activities, a pilot phase was undertaken aiming to understand the barriers and enablers in using registries to support marketing authorisation applications and to inform the development of recommendations to optimise their use.

On 28 October 2016 the Agency organised Patient Registries Workshop to collect and discuss the information about experience from different patient registries in various therapeutic areas. The topics included:
- Benefits of registries for HTA and payers
- Benefits for industry
- Benefits for clinicians and researchers
- Benefits for patients
- Challenges in collaboration between registries
- Technical challenges
- Governance
- Sustainability

Conclusions of the pilot and the workshop have been utilised in the following activities including workshops to support registries in individual diseases.

There are multiple advanced registries in RA and JIA. Utilisation of outcomes of these and other existing or newly planned registries in other musculoskeletal diseases for regulatory purposes current environment offers new opportunities that require further analyses and collaboration.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7159

SP0071 YOUNG PATIENTS: READY, BRILLIANT AND ABLE TO WORK!
L. Kullamaa, European Patients’ Forum, Brussels, Belgium

In May 2016, European Young Patients Group, an initiative representing young patients from the European Patients’ Forum (EPF) and the European Multiple Sclerosis Platform (EMSP), organised a workshop in the framework of the European Youth Event (EYE) 2016 in Strasbourg that corresponded with one of the five main programme themes titled, Exclusion or Access: Crackdown on Youth Unemployment.

The physical and emotional symptoms of chronic conditions, together with social stigma and attitude, create significant barriers to young patients in the job market. With appropriate support, they, like all enthusiastic young people, can be assets for employers. Through interactive discussion, creative expression, education and open dialogue, the workshop aimed to challenge expectations and inaccurate perceptions about the abilities of young people with chronic conditions, tackle societal beliefs and stereotypes of individuals with chronic conditions, stimulate discussion to explore concrete solutions and develop practical actions for young people and their allies accessing employment and steer change to ensure young patients benefit from equal opportunities and treatment at work. By addressing these specific objectives, the workshop was to help to reduce the extra burdens faced by young people with chronic conditions transitioning from education to employment, as well as bringing public attention to the stigma and discrimination that exists at both the recruitment stage and in relation to employees disclosing their health conditions. It also was to compliment and
strengthen the EPF and EMSP’s wider initiatives on tackling the multiple forms of discrimination faced by patients with chronic conditions.

The workshop demonstrated how many issues surrounding young people with chronic conditions transitioning into the labour market are still prevalent. The expectation of discrimination and stigma in the workplace, along with the unwritten attitudinal condition of being a liability, is still very much present. When applying for a job, fear of rejection is not unknown, and the consequences are compounded by young people’s experiences of negative employer attitudes. Moreover, the concept of quota systems and giving people with chronic conditions and/or disabilities preference among applicants for certain jobs probably suggests that they are employed because they have a chronic condition and/or disability, not because of their abilities. This unambiguous form of positive discrimination also affects how young people manage information about their health. They feel forced to share about their condition to get an interview, however by doing so they risk being subjected to negative reactions in the interview or at the workplace.

Youth with chronic conditions frequently have a great deal to contribute to the workplace and more action should be taken to encourage and support employers with hiring them. Training and resources should be provided to managers and employees to raise awareness of the impact that chronic conditions can have on an individual, and how they can be assisted through small adjustments or specific care requirements. Employees should not assume what someone can or cannot do and how their condition affects them, therefore a place for an open discussion should be created. In addition, where quota systems apply, they should be re-evaluated and designed to recruit young patients on merit, in competition with other workers without a chronic condition and/or disability.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7262

CHALLENGES AND POTENTIAL SOLUTIONS ABOUT STAYING IN WORK AS A YOUNG PERSON WITH AN RMD

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Introduction: A lot of young people with RMDs experience difficulties when it comes to staying in work after diagnosis. Some employers see a young person with an RMD-diagnosis as a liability. They are afraid it will cause a lot of difficulties with sick leaves and less work effort and in the end cost them a lot of money. Often the young person hasn’t worked in the company for that many years (because of the age) and hasn’t had the chance to make themselves indispensable/a valued work force yet, which makes it easy/obvious for the employer to terminate their employment.

The process of getting a diagnosis can often cause long periods of sick leave in the beginning and many employers don’t understand that this will get better over time as the person gets used to having the disease and the medication has a chance to work properly.

Some young people choose not to tell their employer, that they have an illness at the beginning and many employers don’t understand that this will get better over time as the person gets used to having the disease and the medication has a chance to work properly.

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Some young people choose not to tell their employer, that they have an illness at the beginning and many employers don’t understand that this will get better over time as the person gets used to having the disease and the medication has a chance to work properly.
ULTRASOUND AND MAGNETIC RESONANCE IMAGING FUSION OF IMAGES EVALUATION OF TENOSYNOVITIS – A PILOT STUDY ON A NEW IMAGING TECHNIQUE IN RHEUMATOID ARTHRITIS PATIENTS

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Background/Purpose: Image fusion is an advanced imaging technology, which enables fusion of ultrasound (US) and magnetic resonance imaging (MRI). This fusion gives for each US probe position an exact projection of the corresponding anatomical area on a previously obtained MR image, during a live US assessment. This study is the first to address image fusion of US and MRI tenosynovitis. The aim of this study was to assess and compare US and MRI visualisation of tenosynovitis using image fusion technique.

Methods: Fifteen rheumatoid arthritis patients with US verified tenosynovitis in the wrist or hand had an MRI performed of the affected wrist or hand. A subsequent image fusion was performed, i.e. the MR images and a live US assessment of one tendon sheath were fused. In order to compare the two imaging modalities quantitatively, the area of the tendon and tendon sheath in the transverse axis was measured on US and MRI for each image fusion. Due to partial volume artefacts (voxel containing two different tissues and therefore possessing a signal average of tendon and tendon sheath) on MRI two measures were performed; area 1) the circumference of the black tendon, i.e. excluding voxels containing two types of tissue 2) the circumference of the grey line that surrounds the black tendon, i.e. including voxels containing two types of tissue. Tenosynovitis was assessed using the proposed OMERACT semi-quantitative scoring system for US and MRI. US scoring was therefore based on both grey scale and Doppler, whereas MRI scoring was based only on post-contrast tenosynovial enhancement, measured as distance from the tendon to end of the enhanced tendon sheath.

Results: The median circumference area of the tendons and tendon sheaths on US and MRI 1 and 2 were respectively 0.16 (25.75 pct; 0.10;0.25), 0.9 (0.06–0.18) and 0.13 of (0.10;0.25) for the tendons and 0.18 (0.13–0.26), 0.27 (0.20–0.45) and 0.23 (0.16–0.40) for the tendon sheaths. Statistically significant differences were found for all measured areas between US and MRI, except for the US tendon area and the MRI tendon area 2 (Wilcoxon’s test; p=0.47). Overall agreement between US and MRI tenosynovitis scoring systems was good (see table 1).

Conclusion: In conclusion, we found that US and MRI have good agreement for quantitative assessment of tendons and scoring of tenosynovitis, when comparing the two modalities using image fusion, if the partial volume artefacts on MRI are included in the measure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7204

HOW AND WHEN TO ASSESS THE CERVICAL FACET JOINTS + DEMO

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At any given time, 10% of the adult population will be affected by neck pain. Although similar in incidence to low back pain, it has less of a socio-economic impact and uncommonly progresses to neurologic deficit. Pain may result from degenerative, traumatic or inflammatory processes involving the diarthrodial facet (zygapophysial) joints and/or the facet (medial branch of the dorsal dorsal ram) nerves. Although routinely evaluated by radiography, magnetic resonance imaging and computed tomography, high-resolution musculoskeletal ultrasound (MSKUS) imaging and guidance has become increasingly popular, particularly among pain management specialists, in the evaluation and treatment of these structures owing to its safety, portability, superior resolution and direct real-time visualization. This presentation will discuss the unique anatomy and sonoanatomy of the cervical spine and its innervation/vascularization with particular focus on the facet joints and nerves and the use of MSKUS in the evaluation and treatment of the facet joint/nerve with review of available evidence. Examination technique and sonoanatomy findings will be demonstrated.

Disclosure of Interest: None declared


HOW TO EVALUATE JOINTS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Ultrasound (US) has numerous advantages when used to examine joints in children compared to other imaging modalities. This include non-invasiveness, rapidity of performance, easy repeatability, high patient acceptability and lack of exposure to ionizing radiation. In addition, it does not require sedation for scanning in younger children. US is more sensitive than physical examination and examination of early disease that is not evident on physical examination. Lack of standardized precise definitions of grey scale (GS) and Power Doppler (PD) US findings in different age groups was the biggest limitation for its use. Additional difficulty is age dependent variability of normal sonoanatomy, due to maturation and ossification in children. That is why acquisition, interpretation and comparison of US images are completely different than in adults and had to be addressed specifically. All this may affect the validity of the technique, and without defined standardized examination technique, US can be a challenge in the childhood population. On the other hand, US as an imaging technique is considered to be examiner and equipment dependent. Studies resulting in good intra and inter-reader reliability and validity, based on specific definitions, are essential for its application as a diagnostic tool. Recently developed standardized image acquisition methodology, definitions of joint components in healthy children, as well as, definitions for synovitis components and its grading in GS and PD in children will be presented in details. US allow precise and thorough visualization of inflammatory and destructive joint abnormalities, including synovial hyperplasia, joint effusion, cartilage damage, bone erosion, tenosynovitis and enthesisopathy. In JIA ultrasound is considered particularly useful for its ability to detect subclinical synovitis and improve classification of JIA patients into the subtypes. Current evidences about application of ultrasound in JIA can improve definition of remission necessary to optimize treatment strategies. Due to peculiarities of US examination and image acquisition in children additional educational efforts among pediatric rheumatologists are required for expanding this imaging modality in daily practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7186

PsA: an integrated perspective

CAN IMAGING BE A PREDICTOR OF PSORIATIC DISEASE?

M. Østergaard. Copenhagen Center for Arthritis Research, Copenhagen University Hospital Rigshospitalet, Glostrup, Denmark

Early detection of inflammatory joint diseases is very important to allow prompt initiation of effective therapies. Identifying patients with early arthritic disease can be challenging by conventional clinical, laboratory and radiographic methods, and more advanced imaging modalities such as computed tomography (CT), magnetic resonance imaging, ultrasonography (US) and various nuclear medicine techniques can provide additional information.

This talk describes the current knowledge on the value of different imaging modalities for 1) predicting development of psoriatic disease in undifferentiated patients 2) predicting development of psoriatic arthritids (PsA) in patients with psoriasis with and without musculoskeletal pain and 3) predicting the disease course in patients with PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7188

PATHOLOGIES ACROSS THE TISSUES IN PSA


The psoriatic disease concept includes the skin disease psoriasis and joint disease psoriatic arthritis. Increasingly, prevalent comorbidities such as obesity and cardiovascular disease are considered to be an integral part of the psoriatic disease concept in many patients. Within this disease concept, accumulating evidence indicates molecular and cellular cross talk between affected organs and tissues. Skin inflammation affects the bone; nail disease is associated with specific types of arthritis; inflammation links to cardiovascular disease; skin or joint disease may contribute to depression. Novel therapeutic strategies are reaching psoriatic disease patients as never before. Their global impact could be envisioned from a holistic perspective, optimizing the strategy chosen as determined by the active molecular and cellular network that triggers and sustains disease.

Thus, linking the joints with the skin and other organs involved is proposed as an entry point towards personalized medicine in a complex disease.

Disclosure of Interest: R. Lories. Grant/research support from: Celgene, Boehringer-Ingelheim, UCB, Consultant for: Janssen, Celgene, Novartis, Pfizer, UCB, Abbvie, Speakers bureau: Janssen, Celgene, Novartis, Pfizer, Merck, UCB, Abbvie
**SP0080** RECURRENT EPISODES OF FEVER AND ARTHRITIS IN ADULT PATIENT

C. Deacu. Department of Rheumatology and Internal Medicine, Stanta Maria Hospital, Bucharest, Romania

Background: Familial Mediterranean Fever (FMF) is a relatively rare condition that belongs to the more recent group of autoinflammatory diseases (AiDs)\(^1\). It primarily affects patients with Mediterranean or Middle Eastern origins and its clinical setting includes short, recurrent episodes of fever, serositis, skin rash and a high risk of amyloidosis\(^2\). FMF is an autosomal recessive transmitted disease and several mutations of the Mediterranean fever gene (MEFV) on chromosome 16 have been identified\(^3\). Patients respond well to colchicine therapy or if necessary, biological therapy with anti-IL1, IL6 or anti-TNF could be initiated\(^4\). Establishing the right diagnosis might raise difficulties for rheumatologists who are not fully accustomed to this condition.

**Objectives:** To evaluate the clinical course, specific features and treatment difficulties of a male patient diagnosed with FMF in adulthood, based on the diagnosis (LE) of a case reported in the literature.

**Methods:** Case-description using patient’s medical records and investigations.

**Results:** This is the case report of a 37-year old male patient currently admitted for right knee arthritis and high grade fever (39.1°C). His medical history dates back to age 16 when he presented in the Pediatric Department with recurrent episodes of prolonged fever (up to 40°C), diffuse abdominal pain together with myalgia, arthralgia accompanied by increased acute phase reactants; after various sources of infection and hematological malignancies were excluded, physicians noted positive low titer ANA (1/20) but normal complement fractions, absent lupus (LE) cells. Further medical investigations showed a negative rheumatoid factor, ACPA, negative antibodies’ panel (dsDNA, Sm, Ro, U1-RNP) and absent cryoglobulins but a positive HLA B27. No signs of sarcoidosis were detected on the x-ray. Patients’ repeated complaints of knee or ankle arthritis together with later finding of positive anti-Salmonella and anti-Shigella antibodies led to establishing the diagnosis of reactive arthritis. Due to symptoms’ persistence and reoccurrence under non-steroidal anti-inflammatory drugs, he was prescribed high dose corticosteroids and sulfasalazine. At age 20 the patient presented with recurrent arthritis of the knees and ankles, fever (38.5°C) and abdominal pain with markedly elevated inflammatory markers. The abdominal ultrasound highlighted a splenomegaly and peritonitis. Colchicine treatment was initiated and his favorable response led to MEFV genetic testing that revealed a mutation of the assay locations.

**Disclosure of Interest:** None declared

**SP0081** THE T CELL RESPONSE TO THERAPEUTIC ANTIBODIES

B Mailleer, Institute Frederic Joliot, CEA, gif sur Yvette, France

Therapeutic antibodies (TMabs) are part of the best successful therapeutic products of the last decades. They are currently used to treat many inflammatory diseases such as rheumatoid arthritis (RA) and bowel diseases and represent worldwide a market of several billions of dollars. However the therapeutic potential of these intrinsically powerful biologicals is tempered by a drawback to be potentially immunogenic and therefore might elicit anti-drug antibodies (ADA). ADA could dramatically reduce the efficacy of the drugs or might provoke allergic reactions. Because generally self-proteins are less immunogenic than foreign proteins, the sequence in which antibodies have been humanized. However humanization even at the highest level does not fully guarantee the lack of immune responses demonstrating the important need to know more about ADA response. Because T cells are known to initiate the ADA response, we are currently investigating the T cell response to immunogenic therapeutic antibodies. With the perspective of immunogenicity prediction, we quantified the number of very rare T cells specific for therapeutic antibodies in the blood of normal donors and found a good concordance between the number of T cells specific to them and their respective clinical immunogenicity level.

We then identified the CD4 T cell epitopes of four immunogenic TMabs with different levels of humanization and therapeutic potential. This is the case report of a 37-year old male patient currently admitted for right knee arthritis and high grade fever (39.1°C).

**Disclosure of Interest:** None declared

**SP0082** IMMUNOGENICITY OF BIOLOGICS IN INFLAMMATORY BOWEL DISEASES

A. Gils. Dept of Pharmaceutical Sciences, KU Leuven, Leuven, Belgium

Anti-tumor necrosis factor-alpha and anti-integrin monoclonal antibodies show great benefits for inducing and maintaining remission, healing the mucosa and restoring the quality of life of patients with inflammatory bowel diseases. The therapeutic potential of these intrinsically powerful biologicals is tempered by a high variability in clinical response. Whereas primary non-response is defined as the lack of clinical response to treatment, assessed for up to 8–12 weeks after initiation, secondary loss of response is defined as loss of clinical benefit after initially responding which can be attributed to disease-related or drug-related factors. Assays have been developed to determine the concentration of the therapeutic antibody in serum of the treated patient. The trough concentration is the concentration just before the next administration and for practical reasons therapeutic drug monitoring is mainly based on measurement of these trough concentrations. Several studies have reported correlations between trough concentration of infliximab, adalimumab, golimumab, vedolizumab and clinical outcome. Optimal therapeutic windows have been defined for both infliximab and adalimumab. A panel of prospective studies in which dosage regimens are adapted in order to achieve target trough infliximab concentrations that correlate with beneficial therapeutic outcomes have been initiated.

Immunogenicity is the capability of biologics to elicit an unwanted immune response that results in the formation of anti-drug antibodies. Anti-drug antibodies can be non-neutralizing or neutralizing. Non-neutralizing antibodies do not impair the drug-target interaction but may increase clearance of the drug resulting in lower serum concentrations. Neutralizing anti-drug antibodies compete with the target antigen and may antagonize the biologic’s effect. As a result, in addition to the enhanced clearance of the drug, a number of anti-drug antibody assays to quantify the immunogenicity of biologicals have been developed. Most of the assays quantify the total amount of anti-drug antibodies but comparing anti-drug antibody concentrations between different assays is hampered by the...
use of different calibrators and by the fact that drug tolerance differs among assays ranging from extreme drug sensitive over various forms of drug tolerant to drug resistant anti-drug antibody assays. The clinical relevance of the different type of anti-drug antibody assays remains to be proven.

Combining therapeutic drug concentrations and anti-drug antibody concentrations with relevant patient, disease and drug information will lead to optimal dosing of patients aiming at optimal clinical, biochemical and endoscopic outcomes.

**Disclosure of Interest:** A. Gils Grant/research support from: IIR grants from pfizer, Speakers bureau: speakers fee by Pfizer, MSD, Abbvie, Takeda, JnJ

DOI: 10.1136/annrheumdis-2017-eular.7210

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**SP0083** AS A RHEUMATOLOGIST, DOES IT HAVE ANY CONSEQUENCE IN MY DAILY PRACTICE?

J.W. Blijisma, Rheumatology & Clinical Immunology, UMCG, Utrecht, UTRECHT, Netherlands

It is nearly inevitable that when we administer foreign (even humanned) proteins intravenously or subcutaneously to a person, that said person will develop antibodies to that (foreign) protein. This happens to most of our patients when we administer biologicals; depending on the sensitivity of our methods, we can measure these anti-bodies either not or not at all. These antibodies start becoming a problem when they are actually binding the administered biological, thus making the active drug less available for its targeted function. We can evaluate this by measuring the actual drug-level, so called trough level. Numerous reports have been published, showing that there is indeed a negative correlation between e.g. anti-tumor necrosis factor (TNF) drug antibodies and the efficacy of anti TNF in the treatment of RA. It has also been shown that adding methotrexate (MTX) to the anti-TNF treatment improves its efficacy and reduces the level of anti-drug antibodies. Probably only 10 mg MTX weekly would be enough to obtain this effect.

So what do I do as a clinician when I observe that a patient, who originally did very well, loses response to her biological? Do I measure possible anti-biologic antibodies? This activity measured on trough level shows no cross-reactivity to other biologicals (even from the same class of action), except to its biosimilar (underscoring that it is a real biosimilair). In case there is doubt whether a patient is actually using the biological we could better measure the drug-trough level; but –in my practice- this question seldom arises in patients with active arthritis, being treated with a biological.

Measuring drug-trough levels is a completely other item, and perhaps more relevant. Biologicals are in general given in a standard fixed dosage, while there are clear differences in patients characteristics, that could influence biavailability of the biological. In addition when the disease is more active, it could be that more biological is needed to temper the inflammation compared to low disease activity, where perhaps a lower dosage would be more effective. To guide physician and patient in personalizing and optimizing treatment with biologicals measuring drug-trough levels might be helpful. Different studies have been performing trying to use through level of the drug in adapting the dosage, and even in predicting possibility to stop the drug treatment. This area is still being evaluated and it is too early to make firm statements, but with a look at cost-effectiveness this will certainly become relevant.

Coming back to the original question: do I use anti-drug antibodies in my daily practice to guide treatment: no, it doesn’t influence my decisions. Will I use in the future drug trough levels to guide treatment decisions: this could well be, but it is too early to make a final decision yet.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.7118

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**THURSDAY, 15 JUNE 2017**

Which target/ outcome is more relevant in the management of SLE?

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**SP0084** BIOLOGICAL TARGETS IN SLE

C. Chizzolini on behalf of Swiss SLE Cohort Study and PRECISESADS Consortium, Immunology & Allergy, Geneva University Hospital, Geneva, Switzerland.

SLE is a prototypical condition characterized by the complete subversion of immunological tolerance and the generation of autoantibodies directed against a wide array of ubiquitous and tissue-specific antigens. This is possible because the joint dysregulation of the innate and adaptive arms of the immune system; which results from multiple gene polymorphisms, each contributing marginally, deregulating the immune system. Alteration of certain cells, i.e. activating naïve and T and B cells, enhanced responses of antigen-presenting cells resulting from the altered disposal of apoptotic cells, as well as dysregulation of cytokine circuitries including regulatory networks.

Pathogenic mechanisms resulting in clinically overt SLE very likely are heterogeneous among individuals. Thus, the identification of biological targets in SLE goes also with the identification of selected modules of gene activation in distinct individuals. Very strong signals indicate that type I interferon (IFN) may contribute to autoimmunity in a large proportion of SLE individuals and therapeutic trials targeting IFN signaling suggest the clinical relevance of this mediator. B cells/plasmablasts are also relevant and obvious targets. Refinements in our understanding in B cell sub setting and/or the timing in disease development in which they play a relevant role should result in defining the appropriate targets specific to this cell lineage. Gene modules activated during flares suggest that neutrophils in a subset of individuals may also be relevant targets. Cytokine affecting T cell differentiation, in particular T follicular helper cells, represent additional relevant targets.

Within the last several years a number of novel biological targets have been identified in SLE. However, a single biological agent has been approved for SLE treatment in the last five years. This underscores the difficulties encountered when translating validated targets in efficacious therapeutic agents. This stress the need for careful preclinical evaluation. It further emphasizes the need of small phase II clinical trials based on stringent inclusion criteria aiming at precisely identifying individual groups more likely to respond to validate the target. Current progress made in the identification of molecular signatures in individuals with SLE will offer the tools for the requested accurate selection.

**Disclosure of Interest:** C. Chizzolini Grant/research support from: Unrestricted research grant form GSK

DOI: 10.1136/annrheumdis-2017-eular.7228

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**SP0085** PATIENT REPORTED OUTCOMES

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In SLE as in other rheumatic diseases, the most relevant target of intervention should be a status with controlled disease process assuring no further accrual of damage. If actual expert discussions like DORIS define the frame of such a status as validated lupus disease activity instrument, serologic activity and therapy – because of harm - are the dimensions of remission with its duration as additional factor for outcome. Patient reported outcomes (PROs) were not included. Otherwise, if payers and reimbursement system decide about relevance, patient outcomes are clear of highest importance as target.

Looking on the evidence of PROs for outcome in SLE, PROs were never used as primary endpoint in clinical trials. In RCTs, PROs were often collected and mostly explorative analysed. There is no evidence that PROs can validly define the above described status of controlled disease. But from systematic analyses in RA, we know that pure PRO like VAS of general health status and semi PRO like tender joints are at least as relevant as more ‘objective’ criteria like swollen joints or CRP as clearly exhibited by the ACR/EULAR remission criteria for RA.

The challenge in SLE is that the discrepancies between patients’ and physicians’ perception and perspectives are even more distinct than in RA. Sometimes, there is the expression that physicians and patients are describing different diseases. The burden of illness in lupus is better defined by pain than by organ manifestations; the overall survival in SLE is more related to lupus nephritis than to fatigue. It is obvious that physicians should analyse the actual clinical symptoms and integrate the future consequences of their actual management in their decision, and patients are more focused on release of their actual burden.

Until today, these different and divers perspectives are no integrated, neither in RCTs nor in daily care. But such integration is mandatory, because no side imagines the complete picture of lupus, which may also produce to the poor results of clinical trials. In routine care, this behaviour causes frustration and mental distress, optimal results are prohibited.

So, the answer to what is more relevant in the management of SLE patients - clinical targets, biological targets or PROs – is the integration of all important aspects of lupus. This implies more than the statistical evaluation of the best items of all three aspects, it is the active involvement of patients in their care: patient empowerment in SLE, a fruitful process, in which both sides have to learn a lot and find about each other.

**Disclosure of Interest:** M. Schneider Shareholder of: no, Grant/research support from: GSK; UCB, Consultant for: Astra-Zeneca; GSK; Lilly; Roche; Supremol; UCB, Employee of: no, Paid instructor for: no, Speakers bureau: Astra-Zeneca; GSK; Roche; Pfizer; UCB

DOI: 10.1136/annrheumdis-2017-eular.7248

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**JOINT EULAR - EFIS SESSION: TILTING THE BALANCE: FROM DISEASE TO TOLERANCE INDUCTION**

H.-D. Chang, German Rheumatism Research Center Berlin, Berlin, Germany

While conventional state-of-the-art immunosuppression can lead to significant...
improvement for patients suffering from rheumatic diseases, only in rare cases a therapy-free remission is achieved. In most cases stopping of treatment results in disease relapse. Apparently, components of the immune system are refractory to conventional immunosuppression and can drive the inflammation. Experimental and clinical evidence suggests that cells of the immunological memory contribute to disease perpetuation via immunosuppression and if pathogenic play a major role in the chronication of the disease. In particular long-lived memory plasma cells secreting autoantibodies represent a major therapeutic challenge. Once generated, they are not subject to physiological and even conventional therapeutic immune regulation. Their elimination may be prerequisite to curative therapies. A detailed understanding the lifestyle of long-lived memory plasma cells will be important to address this cell type therapeutically.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7257

A number of groups have developed methods to generate “tolerogenic” antigen presenting cells (APCs) that mimic the cells which regulate self-tolerance in health. It is hypothesised that administration of such cells, loaded with autoantigens, to patients with autoimmune disease should be able to overcome autoreactivity and re-establish immune regulation. Our group has developed a therapeutic approach based upon autologous tolerogenic dendritic cells, which we derive from dividing peripheral blood monocytes. Unlike conventional mature DC, which produce IL-12p70 and other pro-inflammatory cytokines, tolDC produce no IL-12p70 but high levels of IL-10. They deviate naïve T-cells towards an IL-10-producing, anti-inflammatory phenotype and induce hyporesponsiveness in memory T-cells. In mixed cultures they mature, pro-inflammatory DC and down-regulate T-cell activation. Their phenotype is stable in the presence of pro-inflammatory stimuli. Equivalent murine tolDC switch off collagen-induced arthritis, with immune deviation from IL-17 to IL-10 production by CD4+ T cells and a reduction in type II collagen-specific T cell responses. In a phase I trial (AutoDeCRA), we demonstrated that these cells are safe when administered into a recently inflamed target knee joint of patients with inflammatory arthritis. However, in that safety study we were unable to demonstrate a tolerogenic effect in vivo. Furthermore, we have reason to believe that administered cells may remain in the target joint, whereas a disease-modifying effect is likely to require migration to secondary lymphoid tissues. Moving forwards we are designing a study that will address the optimal administration route for tolDC, based on a technique to track the cells in vivo and to measure their effect on auto-reactivity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7061

THURSDAY, 15 JUNE 2017
What to do about comorbidity?

The comorbidity paradigm views comorbid conditions in patients with rheumatic diseases as “extra” conditions that negatively affect disease control and outcomes. This view is well supported by the prevalence of comorbidity, which is extremely high in these patient populations and increases with age. Comorbidity is frequent in rheumatoid arthritis and/or cervical spondylosis, osteoarthritis, psoriatic arthritis, and lupus. The impact of comorbidity on disease activity and on the efficacy of drugs is an important question for clinicians.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7287

As the population ages the simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception. As the population ages the simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception. As the population ages the simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception. As the population ages the simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7253

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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7297

References:
was also safe for patients with knee OA and (severe) comorbidity3. At present we are implementing and evaluating the protocol in primary care.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7247

THURSDAY, 15 JUNE 2017
Data visualisation: tables and graphs for publication and presentation I & II

SP0091 DATA VISUALISATION: TABLES ANDGRAPHS FOR PUBLICATION AND PRESENTATION
M. Boers
Epidemiology & Biostatistics; Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands

This workshop (held both on Thursday and on Friday) is an introduction to the principles of good graph and table design as pioneered by Cleveland1 and Tufte2 and updated by Few3 so that the participant can better answer the following questions:

Which of the messages in my research results requires a graph or table? Recognizing how graphs improve on simple statistics and convey much more information. Knowing when a table is better, or keeping the data in the body text.

How can I best convey the message? Striving for clear vision by choice of graph, scaling, discrimination of data series, minimizing non-data ink, avoiding chart junk. Striving for clear understanding through a balance between data and explanation. Using order, subheadings, formatting and rules to guide your reader through your table data.

Is my graph/table truthful? Creating a direct proportion between graph and data quantities, avoiding forms prone to misinterpretation, labels to prevent ambiguity; keeping data in context, avoiding more dimensions in the graph than in the data. This year’s course will extend introductory material available via YouTube clips on the ARD website (ard.com)!

Direct link: https://www.youtube.com/playlist?list=PLXU14EQbU_V9JpmolAKsaCC0VjJzbxzAN

Note that you can also sign up for a special lecture followed by a poster tour after the session, devoted to poster design!

References:

Disclosure of Interest: M. Boers Consultant for: Director of Epicontult BV that offers training in data visualization
DOI: 10.1136/annrheumdis-2017-eular.7125

THURSDAY, 15 JUNE 2017
Difficult to reach patient groups

SP0092 THE VICIOUS CIRCLE OF EDUCATIONAL LEVEL AND RISK OF POVERTY IN RHEUMATOID ARTHRITIS - RESULTS OF A CROSS-SECTIONAL MULTICENTER STUDY IN GERMANY
M. Zaenker 1,2, *; 1Rheumatology Dept., Immanuel Klinikum Bernau & Heart Center Brandenburg, Bernau; 2Brandenburg Medical School, Neuruppin, Germany

This lecture will provide an overview on the dimensions of poverty in general and describe methods of assessing the risk of poverty in patients with rheumatoid arthritis (RA).

Based on results of a cross-sectional multicenter study of RA-patients from outpatient-clinics in Brandenburg and Saarland, Germany, this talk will give a rationale for how patients with RA are threatened by poverty due to treatment-related expenses, disability and early retirement compared to the general population.

It will be highlighted, that the equalized disposable income of RA patients is significantly lower than in general population and RA patients share a doubled risk of poverty, even in social-welfare well-secured countries such as Germany. Further, the talk will demonstrate that both lower educational level and socioeconomic state are associated with more severe disease course of RA and various underlying mechanisms will be discussed.

Disclosure of Interest: M. Zaenker Consultant for: Celgene, Hospira, MSD, Roche
DOI: 10.1136/annrheumdis-2017-eular.7086
THE SWEDISH EXPERIENCE - HOW A PATIENT ORGANISATION COULD REACH OUT TO IMMIGRANTS AND DEVELOP THROUGH INTEGRATION

T. Diao. The Swedish Rheumatism Association (SRA), Stockholm, Sweden

Background: in the early years of the new millennium many European countries faced an increased number of immigrants due to the second Iraqi war that affected the whole sub region. Some of these immigrants reached the Swedish shores and many of them have RMDs.

In an attempt to help integrate them to the Swedish society, the SRA reached out to these immigrants. The SRA decided to act together with other actors to facilitate the inclusiveness of these minorities into the society.

Methods: To achieve this giant task the SRA applied and received financial support from the Swedish General inheritance fund and collaborated with several health providers, the employment office, some Folk High Schools, ABF (Adult Liberal Education Association) and our local chapters and joiners in 5 of the biggest cities: Stockholm, Örebro, Gothenburg, Norrköping and Umeå.

Results: This experience was a breakthrough for the SRA. The SRA was the first patient organisation that walked this new path. The iconoclastic experience enriched the SRA and gave it a great knowledge of how to reach out to minority groups and giving them the tools to be a fully part of the society despite the burden of the RMDs.

Conclusion: The SRA increased its knowledge, capacity and flexibility during this experience. Today the SRA is cited as a reference in Sweden when it comes to reaching out to different minorities suffering of RMDs. Many organisations are now lining up to work with the SRA in these matters. In 2007 the SRA received the price for best project from the Swedish General Inheritance Fund.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7298

EULAR Projects in musculoskeletal imaging

EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN THE DIAGNOSIS AND MANAGEMENT OF LARGE VESSEL VASCULITIS IN CLINICAL PRACTICE

C. Dejaco 1,2 on behalf of Taks force to develop the EULAR recommendations for the use of imaging in LVV.

1Rheumatology, Medical University Graz, Graz, Austria; 2Rheumatology Service, Hospital of Bruneck, Bruneck, Italy

Large vessel vasculitis (LVV) is the most common form of primary vasculitits comprising giant cell arteritis (GCA) and Takayasu arteritis (TA).

Although temporal artery biopsy and conventional angiography are still the gold standard diagnostic tests for GCA and TA, respectively, modern imaging methods including ultrasound, magnetic resonance imaging, computed tomography (CT) and 18F-FDG positron emission tomography - CT are increasingly used. In clinical practice however, these methods are inconsistently applied and rheumatologists and other specialists are still uncertain about the specific value of these modalities. This project has been conducted with the aim to provide user-friendly, evidence-based recommendations for the use of modern imaging methods for diagnosis, monitoring and outcome prediction of primary LVV. Specifically, we give advice on 1) when to use these imaging techniques, 2) what specialists might conclude from imaging results and 3) what technical standards are required to achieve high quality imaging results.

These recommendations aim at an early and specific diagnosis as well as an improved assessment of LVV, thus ultimately leading to better outcomes of patients with LVV.

Disclosure of Interest: C. Dejaco Grant/research support from: Pfizer, MSD, Esaote, Speakers bureau: Pfizer; MSD, AbVie, Celgene, UCB, Roche, BMS, GSK, Novartis, Sanofi, Sano,

DOI: 10.1136/annrheumdis-2017-eular.7221

THE IMPORTANCE TO DIFFERENTIATE NORMAL FROM ABNORMAL CAPILLAROSCOPIC IMAGES FOR AN EARLY DIAGNOSIS OF DISEASE

P. Collado. Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain

Musculoskeletal ultrasound (MSUS) is a readily available and suitable imaging technique to asses the immature skeleton of paediatrics in different musculoskeletal rheumatic diseases (MSRD). Besides the potential operator–dependent feature of this technique, the age-related variation of normal sonoanatomy due to the child’s growth makes more difficult acquisition, interpretation and comparison of images than in adults. Hence, to use MSUS as a valid technique for diagnosis of MSRD, it is needed to develop specifically evidence-based recommendations for paediatrics. Additionally, the variability in background and experience of ultrasonographers in different countries requires an international multidisciplinary contribution for an optimal standardization of MSUS performance in paediatric MSRD.

Reflecting the perceived need for developing recommendations on the standardization of procedures for performing MSUS examination in MSRD, a collaborative international EULAR/PReS task force was convened. In the talk, it is going to summarize the original proposed specific aims and update on work for each aim previously mentioned. A systematic literature search was performed in Medicine and Embase from databases inception to 1st June 2016 as the first step. One hundred and eighty-eight articles were finally included after reviewing 6059 records identified. The scanning for the knee and the ankle joint was the most common reported, whereas the paediatric wrist was uncommon.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7074

New/Ongoing projects:

• Deep layer of the abdominal subcutaneous fat pad and cardiovascular risk: ultrasound measurement and relationship with visceral fat
• The mechanical function of the Hottfa fat pad as seen in a dynamic musculoskeletal ultrasound study
• Ultrasound study of the neurovascular supply to the joints.
• The relevance of ligaments in inflammatory disorders of the articulations of the hand and wrist.
• The principles of anatomy as seen in musculoskeletal ultrasound.

Activities promoted by the group:

• Certificate Course “Expert in Musculoskeletal Ultrasound”.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7157

C. Dejaco Grant/research support from: Pfizer, MSD, Esaote, Speakers bureau: Pfizer, MSD, AbVie, Celgene, UCB, Roche, BMS, GSK, Novartis, Sanofi, Sano.

Activities promoted by the group:

• Certificate Course “Expert in Musculoskeletal Ultrasound”.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7221

THURSDAY, 15 JUNE 2017 EULAR Projects in musculoskeletal imaging

EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN THE DIAGNOSIS AND MANAGEMENT OF LARGE VESSEL VASCULITIS IN CLINICAL PRACTICE

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Large vessel vasculitis (LVV) is the most common form of primary vasculitits comprising giant cell arteritis (GCA) and Takayasu arteritis (TA).

Although temporal artery biopsy and conventional angiography are still the gold standard diagnostic tests for GCA and TA, respectively, modern imaging methods including ultrasound, magnetic resonance imaging, computed tomography (CT) and 18F-FDG positron emission tomography - CT are increasingly used. In clinical practice however, these methods are inconsistently applied and rheumatologists and other specialists are still uncertain about the specific value of these modalities. This project has been conducted with the aim to provide user-friendly, evidence-based recommendations for the use of modern imaging methods for diagnosis, monitoring and outcome prediction of primary LVV. Specifically, we give advice on 1) when to use these imaging techniques, 2) what specialists might conclude from imaging results and 3) what technical standards are required to achieve high quality imaging results.

These recommendations aim at an early and specific diagnosis as well as an improved assessment of LVV, thus ultimately leading to better outcomes of patients with LVV.

Disclosure of Interest: C. Dejaco Grant/research support from: Pfizer, MSD, Esaote, Speakers bureau: Pfizer; MSD, AbVie, Celgene, UCB, Roche, BMS, GSK, Novartis, Sanofi, Sano.

DOI: 10.1136/annrheumdis-2017-eular.7221

THE IMPORTANT TO DIFFERENTIATE NORMAL FROM ABNORMAL CAPILLAROSCOPIC IMAGES FOR AN EARLY DIAGNOSIS OF DISEASE

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Musculoskeletal ultrasound (MSUS) is a readily available and suitable imaging technique to asses the immature skeleton of paediatrics in different musculoskeletal rheumatic diseases (MSRD). Besides the potential operator–dependent feature of this technique, the age-related variation of normal sonoanatomy due to the child’s growth makes more difficult acquisition, interpretation and comparison of images than in adults. Hence, to use MSUS as a valid technique for diagnosis of MSRD, it is needed to develop specifically evidence-based recommendations for paediatrics. Additionally, the variability in background and experience of ultrasonographers in different countries requires an international multidisciplinary contribution for an optimal standardization of MSUS performance in paediatric MSRD.

Reflecting the perceived need for developing recommendations on the standardization of procedures for performing MSUS examination in MSRD, a collaborative international EULAR/PReS task force was convened. In the talk, it is going to summarize the original proposed specific aims and update on work for each aim previously mentioned. A systematic literature search was performed in Medicine and Embase from databases inception to 1st June 2016 as the first step. One hundred and eighty-eight articles were finally included after reviewing 6059 records identified. The scanning for the knee and the ankle joint was the most common reported, whereas the paediatric wrist was uncommon.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7074

New/Ongoing projects:

• Deep layer of the abdominal subcutaneous fat pad and cardiovascular risk: ultrasound measurement and relationship with visceral fat
• The mechanical function of the Hottfa fat pad as seen in a dynamic musculoskeletal ultrasound study
• Ultrasound study of the neurovascular supply to the joints.
• The relevance of ligaments in inflammatory disorders of the articulations of the hand and wrist.
• The principles of anatomy as seen in musculoskeletal ultrasound.

Activities promoted by the group:

• Certificate Course “Expert in Musculoskeletal Ultrasound”.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7157

THURSDAY, 15 JUNE 2017 Capillaroscopy I & II

THE IMPORTANCE TO DIFFERENTIATE NORMAL FROM ABNORMAL CAPILLAROSCOPIC IMAGES FOR AN EARLY DIAGNOSIS OF DISEASE

V. Smith, Department of Rheumatology, Faculty of Internal Medicine, Ghent University Hospital, Ghent University, Gent, Belgium

Medical doctors frequently get patients with Raynald’s phenomenon (RP), a frequent symptom in the general population, referred. The importance of distinguishing normal capillaroscopic findings from (pathomomonic) abnormal (pathological) findings, lies in the fact that this distinction allows the differentiation between a primary RP (not connected to any connective tissue disease [CTD]) from a secondary RP due to systemic sclerosis (SSc) and diseases of the scleroderma spectrum. What is normal in primary RP? A normal capillaroscopic pattern, by qualitative assessment, is characterized by a homogeneous distribution of hairpin shaped capillaries as a “comb-like structure”, with a density of between 9–14 capillaries per mm. Yet, there exists a wide intra- and inter-individual variety in a normal population which will be discussed in this session. What is pathomomonic abnormal in patients with RP due to SSc? Patients with the RP who have an underlying clinically recognizable (~ with skin involvement) SSc show a very characteristic combination of capillary abnormalities in the nailfold, which can easily be assessed through qualitative assessment (~ pattern
WHY CAPILLAROSCOPY CAN PREDICT DISEASE SEVERITY

DIAGNOSTIC AND THERAPEUTIC ULTRASOUND-GUIDED

HOW TO PERFORM A QUICK AND EFFICIENT PHYSICAL EXAMINATION

W. Herman, Department of Rheumatology and Clinical Immunology, Kerckhoff-Klinik, Bad Nauheim, Germany

One of the most important indications for performing capillaroscopy is to differentiate between primary and secondary Raynaud’s syndrome. Different kinds of microscopes are at hand and generally vary in terms of picture quality or price. Before purchasing a microscope and capillaroscopy software, several considerations about the required standards of examination should be made; some of which are summarized as follows:

- The region of interest (ROI). Normal capillaries have a mean diameter of about 8 μm. For an accurate assessment a magnification of 100–200x is recommended, for an overview the magnification of 50x is sufficient.
- Measurement. Beside qualitative measures like changes in vessel architecture, there should be the possibility of quantifying the number of capillaries/mm or vessel diameters.
- Documentation. All parts of the examination have to be stored and assigned to patient and case.
- Practical aspects and handling of the device.
- Different kinds of microscopes are on the market of which three will be discussed in detail. Briefly summarized:
  - Stereo microscopes.
  - Advantages: Very good image quality, zooming in and out without problems, relatively easy to use.
  - Disadvantages: device is not mobile, in patients with finger contractures examinations are difficult to perform, relatively high costs.
  - Videocapillaroscopes:
    - Advantages: Very good image quality, easy to use, “gold standard” for capillaroscopy.
    - Disadvantages: No overview, zooming in and out not applicable (change of lenses required), relatively high costs.
- USB microscopes:
  - Advantages: low costs, zooming in and out without problems, easy to use.
  - Disadvantages: limited picture quality, documentation laborious.

Selecting a capillaroscopic device depends on the conditions of use (“quick look” vs. “academic evaluation and follow up”), which should be clarified before buying a device. The price range is significant and usually differs between 100€ for USB microscopes and up to 10,000€ for stereo and videocapillaroscopes.

**Literature**:


**Disclosure of Interest**: None declared

**DOI**: 10.1136/annrheumdis-2017-eular.7206

**Thursday, 15 June 2017**

Ultrasound, clinical, diagnostic and therapeutic skills I & II

M. Doherty, Academic Rheumatology, University of Nottingham, Nottingham, United Kingdom

The GALS (Gait, Arms, Legs, Spine) screen is a quick and reasonably sensitive way to detect common musculoskeletal (MSK) abnormalities as part of a general medical assessment (1). However, for a person with MSK complaints a detailed assessment is required to determine the diagnosis and the impact of the condition on that person. The key starting point is the history. This needs to be holistic and individualised as the enquiry proceeds since the impact of any condition is

**References**:


**Disclosure of Interest**: None declared

**DOI**: 10.1136/annrheumdis-2017-eular.7272

**Thursday, 15 June 2017**

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M. Doherty, Academic Rheumatology, University of Nottingham, Nottingham, United Kingdom

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**Disclosure of Interest**: None declared

**DOI**: 10.1136/annrheumdis-2017-eular.7295

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**Disclosure of Interest**: None declared

**DOI**: 10.1136/annrheumdis-2017-eular.7295
HOW TO ASSESS US COMPETENCY SKILLS

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To optimize and standardize musculoskeletal ultrasonography education for rheumatologists, there is a need for competency assessments addressing the required training and practical and theoretical skills. Because of the increasing use of MSUS in rheumatology, there has been a focus over the past years on training.

A minimum training requirements are described by The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) where a 3 levels competency assessment (COMPASS) has been developed for rheumatologists, including an in-detail description of what theoretical and practical competencies to be acquired at each level with a related log book (1). The rheumatology-COMPASS levels are closely related to the levels of the EULAR MSUS courses, thereby ensuring that the content is supported by already provided courses such as the EULAR and EULAR-endorsed MSUS courses to facilitate the implementation of the rheumatology-COMPASS. In COMPASS level 1 the course contents resemble the EULAR MSUS basic and intermediate courses, level 2 resembles the EULAR MSUS advanced course whereas level 3 requires attendance in a “teach-the-teachers course” or experience as a teacher in at least 2 international MSUS courses. Level 3 also includes an academic level requiring research activity and acceptance of level 1 and 2 sonographers for training.

The EULAR MSUS courses have been organized since 1998 and the interest in these courses has been increasing. In 2007, the first 3 level EULAR MSUS course was established and the 3 level courses (basic, intermediate and advanced) have been running ever since in relation to the EULAR congress, focusing mainly on the relevant content on the individual levels and the distribution between practical and theoretical skills.

EULAR has developed the following competence levels: level 1 and 2. The EULAR level 1 includes the performance of EULAR Online MSUS course and attendance to basic, intermediate and advanced MSUS courses, where attending the intermediate and advanced courses require a certain number of US examinations (however, if already reached COMPASS level 1, 2 or 3, there is no need of repeating EULAR courses), and the advanced course requires in addition to pass a practical examination. The EULAR level 2 competency is organized to ensure a minimum level of US knowledge for teachers in MSUS courses (2). This level includes the EULAR Teach the Teachers course as well as passing a theoretical and practical examination. Since there is a growing number of EULAR endorsed MSUS courses, it is of highly importance that the teachers in these courses have equal qualifications thereby providing comparable training and competencies beneficial for the clinical use of US.

Information about the competence requirements is found at the EULAR website (http://www.eular.org).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7247
HOT SESSION: SCLERODERMA TREATMENT on behalf of G. Espigol-Frigolé, S. Prieto-González, J. Hernández-HERPES ZOSTER: HOW TO PREVENT, TO DIAGNOSE AND TO TREAT ACUTE RESPIRATORY FAILURE, MACULO-PAPULAR RASH,...

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2534

FRIDAY, 16 JUNE 2017 Comorbidities in rheumatoid arthritis

SP0108 HERPES ZOSTER: HOW TO PREVENT, TO DIAGNOSE AND TO TREAT L. Calabrese, Rheumatology, Cleveland Clinic, Cleveland, United States

Herpes Zoster is a major public health problem and is an infection that results from re-activation of latent varicella infection acquired most commonly naturally or more recently through immunization. The incidence of HZ is approximately twice that of the general population in patients with immune mediated inflammatory diseases (IMIDs). Underlying mechanisms are largely those which compromise cell mediated immunity and epidemiologic risks largely follow immunosenescence patterns (i.e. aging). Rheumatologists use a large variety of immunosuppressive drugs which further increase the risk of HZ and are obliged to recognize the clinical syndrome, its complications, apply effective therapy and be actively engaged in strategies to maximize immunization and prevention. This discussion will focus on recent advances in each of these areas highlighting newly described complications of HZ such as stroke and advances in vaccine development.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.7214

FRIDAY, 16 JUNE 2017 Life-threatening presentation of rheumatic diseases

SP0109 ACUTE RESPIRATORY FAILURE, MACULAR-PAPULAR RASH, INDURATIVE EDEMA OF THE EXTREMITIES AND CERVICAL LYMPHADENOPATHY IN A 6-WEEK-OLD INFANT C. Birolo, Pediatric Rheumatology Unit, Department for Woman and Child Health, University of Padua, Italy, Padua, Italy

Case report: A previously healthy 40-days-old male infant, from non-consanguineous parents from Morocco, presented in a peripheral hospital with fever for 48 hours, associated with rhinorhea, mild diarrhea and progressive irritability during the last 24 hours. Initial laboratory studies revealed elevating acute phase reactants (CRP 116 mg/L), mild neutrophilia, elevated liver enzymes (AST 315, ALT 174 U/L), direct hyperbilirubinemia, dissecoagulopathy. Cerebral spinal fluid analysis and microbiology cultural workup resulted negative. A wide-spectrum antibiotic and antiviral therapy was initiated. On the 6th day of illness he developed diffuse macular-papular rash, indurative edema of the extremities, right cervical lymphadenopathy and bilateral conjunctival injection. On the basis of a certain clinical diagnosis of Kawasaki disease and the infant was treated with IVIG 2 g/kg. An echocardiography performed prior to the IVIG infusion showed homogeneous dilated coronary arteries (left coronary artery 3.2 mm, right coronary artery 2.2 mm). Twelve hours after the end of IVIG infusion, the child presented a rapidly progressive, severe respiratory failure requiring endotracheal intubation and was transferred to our ICU. On admission (day 7th), physical examination revealed a feverish, critically ill infant with hepatomegaly (5–6 cm below the right costal margin), diffuse macular-papular rash, “sock-like” erythema and swelling of the feet, chellitis, bilateral conjunctival injection and right cervical adenopathy. The urine output was markedly decreased; he rapidly developed hemodynamic instability with hypotension and tachycardia. Complete blood count showed anemia (6.8 g/dL), thrombocytopenia (16,000/mm3), elevated CRP (240 mg/L), hypalbuminaemia (18 g/dL) and hypofibrinogenemia (0.83 g/L); liver enzymes were normal. Intensive ventilatory and hemodynamic support therapy were started, in addition to a massive transfusional regimen. Given the clinical and hematologic picture, the diagnosis of MAS was considered and eventually confirmed on the next day from very high levels of IL2-R above the normal value (61 U/L) and hypertriglyceridemia (181 mg/dL) [2]. The clinical suspicion was supported by persistent cytopenia despite daily transfusions, low erythrocyte sedimentation rate (3 mm/h) with concomitant rising CRP, elevated IL2-R level (28.320 KUL) and decreased NK function. The patient was treated with high dose methylprednisolone pulse therapy (25 mg/kg) for 3 consecutive days 12–14), followed by a maintenance of 1 mg/kg/daily. By day 15th, a progressive decline in inflammatory markers and a concomitant improvement of general conditions was observed, with the possibility to discontinue inotropic support on day 12th and invasive ventilation on day 25th. Since day 17th, a diffuse cutaneous desquamation was noted. The fever settled on day 35th. Echocardiography follow-up revealed an increasing, irregular dilation of left (max 5 mm) and right (max 3.5 mm) coronary arteries, with a progressive left ventricular apex hypokinesia, but a stable ejection fraction (55%). ECG showed persistent repolarization abnormalities. Of note, Adenosinuric-PCR was found positive in the bronchoalveolar washing performed on admission. The differential diagnosis included: Kawasaki disease complicated by respiratory distress syndrome and MAS, familiar hemophagocytic lymphohistiocytosis, autoimmune lymphoproliferative syndrome, cryopyrinopathies and immunodeficiencies. The child presented a rapidly progressive, severe respiratory failure requiring intensive support. These two complication are rarely associated to KD. In this particular case, respiratory failure can probably be explained by a combination of causes: fluid overload, systemic vasculitis and the concomitant and probably triggering Adenosinuric infection.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.7176
gent surgery. These may be observed in polycystitis nodosa, cryptogulbiniculovasculars, erosinophilic granulomatosis with polyangiitis and other AAV. High-dose glucocorticoids and cyclophosphamide are usually applied. Children with IgA vasculitis may develop bowel intussusception.

Deep venous thrombosis and pulmonary embolisms are significantly more frequent in AAV and pregnancy than in the general population, especially during active disease. Anti-coagulation may be needed in AAV, although this approach is controversial in Behçet's disease. By contrast, aneurysm formation is typical in polycystitis nodosa and Behçet's disease and may be occasionally seen in AAV. Massive bleeding derived from aneurysm rupture usually requires arterial embolization.

It is important to keep in mind that during the early course of diagnosed vasculitis, intense immunosuppressive therapy may favor life-threatening infections including opportunistic infections such as pneumocystis jiroveci pneumonia or disseminated SLE. In summary, systemic vasculitis may present with a variety of severe complications and other may develop during follow-up. These complications are heterogeneous, vary according to the size of vessels involved, and usually require specific procedures or treatments in addition to immunosuppressive therapy. Due to the life-threatening nature of these complications their immediate recognition and management are crucial to patient survival.

Supported by SAF 577–8R and Marató TV3 2014/201507

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7166

FRIDAY, 16 JUNE 2017

AxSpA: From bug to gut and to disease phenotype...

SP0111 INHIBITING BONE FORMATION IN THE CLINIC. ARE WE THERE YET?
R. Landewe, Rheumatology & Immunology, Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands

One of the most characteristic features of axial spondyloarthritis (axSpA) is bone formation in the spine (syndesmophytes). Syndesmophytes may occur at any time during the course of the disease, are more frequent in patients with radiographic axSpA (AS) than in those with non-radiographic axSpA, and are best seen on conventional X-rays of the spine. Currently, it is suggested that (low-radiation) CT-scanning of the spine provides a better (more sensitive) picture of developing syndesmophytes than conventional X-rays. Syndesmophytes matter in that they interfere with spinal mobility and physical function independent of inflammation. As such, it makes sens to try and prevent their occurrence or to inhibit their progression.

It is a matter of debate whether current available treatments are able to inhibit syndesmophyte growth or occurrence. Part of the debate is the methodological challenges related to measuring syndesmophyte progression properly.

In this lecture I will address current issues related to inhibition of syndesmophyte formation in patients with axial SpA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7211

FRIDAY, 16 JUNE 2017

Pregnancy meets rheumatic patients

SP0112 WHICH DRUGS IN PREGNANT PATIENTS?
M. Østensen, Department of Rheumatology, St.Olavs Hospital, Trondheim, Norway

Management of rheumatic disease during pregnancy starts with prepregnancy counselling. Assessment of maternal and fetal risks is necessary for adjusting therapy to the current stage of pregnancy. The ultimate goal is to keep the disease in remission or at least at low activity throughout pregnancy.

Immunosuppressive drugs requiring withdrawal before conception are methotre- ate, cyclophosphamide, and mycophenolate which are known teratogenic drugs. Other drugs like leflunomide, tocilizumab and several biological should be discon- tinued because pregnancy experience is at present insufficient and safety for the fetus has not been proven. Flares of rheumatic disease showing be treated immediately and with pregnancy compatible drugs. For patients with inflammatory arthritis like rheumatoid arthritis, spondyloarthritis and juvenile idiopathic arthritis disease activity during pregnancy can be controlled with antimalarials, sul- fasalazine and TNF inhibitors. Women with systemic lupus erythematosus should continue basic therapy with hydroxychloroquine, and azathioprine, ciclosporine or tacrolimus added when needed due to organ manifestations. Severe flares during pregnancy may require biologics like rituximab, abatacept, tocilizumab or Anakinra. In case of infected pulsed or, if life threatening, intravenous gamma globulin or cyclophosphamide.

Treatment during pregnancy demands balancing suppression of maternal disease and no harm to the child. Selecting the adequate type, the right dose and the right timing of medications for optimal care of pregnant patients remains a challenge.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7246

SP0113 PREGNANCY IN SLE: STILL CHALLENGING FETAL AND MATERNAL ISSUES
R. Fischer-Betz, Rheumatology, Heinrich-Heine-University, Duesseldorf, Germany

Patients with SLE are mostly young women diagnosed during the childbearing years. Despite the so-called “unmet need” in knowledge of reproductive health issues, management are crucial to patient survival. Because of earlier recognition of disease and advances in medical treatment, family planning has gained greater importance. Concerns include the effect of pregnancy on maternal disease, the risk of flare following delivery, and the safety of medications during pregnancy and breastfeeding. Preconception counselling and risk stratification (including life style, disease activity, autoantibody profile, previous vascular and pregnancy morbidity, hypertension and the use of drugs with emphasis on benefits from hydroxychloroquine and antiplatelet/anticoagulants) are essential for prevention of unwanted complications during pregnancy. Recommendations for the management of family planning and antihypertensive treatment during pregnancy and lactation have been published recently by EULAR. However, many lupus patients still do not feel that their family planning concerns are adequately addressed in current clinical practice and report that they receive inconsistent advice from the various healthcare professionals. There is a clear need for provision of up-to-date and consistent information/support to our patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7091

SP0114 CHILDREN OF PATIENTS WITH RHEUMATIC DISEASES: ISSUES RELATED TO MATERNAL DISEASE AND TREATMENT
L. Andreoli, Rheumatology and Clinical Immunology, University of Brescia, Brescia, Italy

A major source of anxiety for women with systemic autoimmune diseases (SADs) who wish to become pregnant is the possible impact of maternal disease and medications on the offspring, in terms of physical and mental development. A recent multicenter survey conducted in 24 Italian Rheumatology Centers showed that more than 50% women affected by SADs restricted their family size mainly because they were afraid that children could get an autoimmune disease or could be harmed by intrauterine exposure to maternal autoantibodies and anti-rheumatic drugs (Dall’Ara, ACR abstract, Arthritis Rheumatol 2016: 68, suppl 10). Therefore, the long-term follow-up children born to mothers with SADs is a topic of major importance for the counselling on family planning.

First of all, it should be emphasized that preterm birth and other fetal complications, such as low birth weight and babies small for gestational age, are more common in patients with systemic autoimmune diseases as compared to the general population. These conditions carry themselves an increased risk for poorer physical and neuropsychiatric development. Therefore, the prevention of foetal complications should be operated by means of close obstetrical monitoring and tight control of maternal disease activity, which would be detrimental for foetal wellbeing. In this context, the use of “safe” anti-rheumatic drugs is of paramount importance for pregnant women with SADs.

Recently, a dedicated EULAR Task Force has released points to consider for the use of anti-rheumatic drugs during pregnancy and lactation (Gotestam Skorpen, Ann Rheum Dis 2016). The work of this Task Force was focused on updating the information about the use of “conventional synthetic” (cs) DMARDs but also to provide for the first time evidence-base indications on the use of “biologic” (b) DMARDs, mainly anti-TNFalpha agents.

No significant impact in the maturation and functioning of the child’s immune system has been observed for several csDMARDs, supporting their safety of use during pregnancy (Andreoli, J Autoimm 2012).

Turning to bDMARDs, a case-control study on the long-term follow-up of children exposed in utero to anti-TNFalpha showed the safety of use either until the positive pregnancy index or during the second and third trimester of gestation (Dall’Ara, EULAR abstract, Ann Rheum Dis 2016: 75, Suppl 2:493). No differences between exposed and non-exposed children were found in terms of congenital defects, developmental milestones, response to vaccinations and major health problems. No particular problems were also observed in children who were breastfed while maternal anti-TNFalfa intake. The use of anti-TNFalfa agents during breastfeeding had been proposed to women who were strongly motivated based on the following considerations: 1) these drugs are poorly or absolutely excreted into breast milk as recently demonstrated for certolizumab pegol (Cioisse, ACR abstract. Arthritis Rheumatol 2016: 68, suppl 10); 2) even this was the case, the drug will be degraded in the baby’s gastrointestinal tract and absorption could not be possible.

Regarding maternal disease, major concerns are linked to fetal exposure to mater- nal autoantibodies, mainly anti-Ro/SSA (for the development of neonatal lupus) and antiphospholipid antibodies (aPL). Therefore, the evaluation of these autoanti- bodies with potential negative impact on pregnancy and neonatal outcome should be part of the preconception work-up of women with SADs in order to provide ad- equate counselling and preventative strategies (Andreoli, Ann Rheum Dis 2017).
The transplacental passage of maternal aPL does not generally produce any thrombocytic complication in the neonate. The registry of infants born to mothers with APS, started by the European Forum on aPL in 2003, is collecting precious information for the assessment of neonatal outcome and subsequent development. The exposure to maternal aPL was linked to learning disabilities (LD) in children born to both mothers with SLE and with APS, based on the experimental observation that aPL can affect neural cells functioning. A recent study on the long-term neurodevelopment of children exposed in utero to aPL was reassuring for a normal neurological functioning and intelligence level, but found a higher rate of LD as compared to the general population (19% vs 3%) (Nail, Lupus 2017). These affected children were all born at term to triple aPL positive mothers.

Although systemic autoimmune diseases are not hereditary, newborns may receive from the mother a genetic background that may predispose to the establishment of autoimmune processes. However, the incidence of autoimmune diseases in the offspring was rather low (1%) among 269 children with a mean age of 15 years investigated in the previously cited study of Italian Rheumatology Centers.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7174

FRIDAY, 16 JUNE 2017

Neuronal and hormonal alterations in arthritis

SP0115 NEUROTRANSMITTERS AND INNERVATION IN SYNOVIUM

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The synovial tissue is innervated by nociceptive sensory nerve fibers and sympathetic postganglionic nerve fibers. While sensory nerve fibers have afferent (by transmitting pain to the CNS) and efferent functions (by local release of neuroactive substances, mainly neuropeptides), sympathetic nerve fibers exert mainly efferent vasoregulatory, energy-regulating and immunomodulating roles. In synovial tissue of patients with rheumatoid arthritis (RA), the major proinflammatory neuropeptide of sensory nerve fibers is substance P, which is upregulated relative to anti-inflammatory calcitonin gene-regulated peptide (CGRP). In addition, sensory nerve fibers undergo a sprouting response leading to sensory hyperinnervation of RA synovial tissue. Removal of sensory nerve fibers exerts anti-inflammatory effects, and it is thought that this elimination is beneficial during hemiplegia, which can spare the paralytic limb from developing RA. Therapeutic neutralization of substance P was not successful, most probably due to vast receptor redundancy. Furthermore, the sensory nervous system undergoes a sensitization response (aggravation of pain and inflammation) in the synovial tissue, the dorsal root ganglion, the spinal cord, and more central in the brain. Chemical sympathectomy or suppression of adrenergic signaling significantly reduce inflammatory processes in the initial acute state of inflammation whereas the same procedures may increase inflammation at later stages. These findings indicate that the sympathetic nervous system supports the development of inflammation but can reduce inflammation at more chronic stages. During chronic inflammation, the density of sympathetic nerve fibers in synovial tissue is reduced but other tyrosine hydroxylase-positive cells secreting noradrenaline appear in the inflamed joint. In addition to local vascular effects in the joint, the sympathetic nervous system influences numerous immune processes in the joint and in lymphoid organs. Hence the net effect of the sympathetic nervous system on inflamed tissue results from local sympathetic effects in the joint as well as from sympathetic influences on major systemic immune processes and energy regulation. This lecture summarize the central aspects of the two nervous systems.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1256

SP0117 OSTEOPOROTIC FRACTURES IN EUROPE: ARE WE DOING ENOUGH

J.A. Kanis, University of Sheffield & Australian Catholic University, Melbourne, Cobham, Surrey, United Kingdom

The past 30 years has seen significant milestones in assessment and management of osteoporosis. These include the development of DXA and FRAX to identify individuals at high risk of fracture fracture and the development of interventions that have been shown to significantly decrease the risk of fracture in well-designed clinical trials. A major challenge has been how to apply these treatments. Measurements of bone mineral density (BMD) are used for diagnosis and for fracture risk prediction. Facilities for BMD testing are patchy and many European countries have inadequate resources to service the societal needs. In addition, BMD has poor sensitivity for the prediction of fracture so that the majority of fractures occur in individuals with T-scores ≤−2.5 SD. The development of FRAX has improved the sensitivity of fracture risk prediction and is now adopted in many assessment guidelines. Despite these advances, there are a number of challenges to be faced. Of paramount importance is that few patients with a prior fracture and even less with osteoporosis alone actually receive treatment. In Europe, there is wide inter-country variation in the treatment of women at high risk for osteoporotic fractures. The treatment gap varies from 25% in Spain to 95% in Bulgaria. Large treatment gaps were identified in countries with populations all of the same ethnic origin. Moreover, the treatment gap is increasing in many countries. Thus the disease is under-recognised by the medical community. Urgent action is required to address the under-recognition of osteoporosis and fragility fracture. Simple measures include:

• The development of country-specific guidelines,
• Piloting screening strategies in the elderly,
• Identifying the determinants of imminent risk,
• The development of fracture liaison services.

Whereas osteoporosis is recognized, worldwide, as a major Public Health issue, with one in two women and one in five men over the age of 50 years presenting...
a fragility fracture, a vast proportion of women at high risk remain untreated. Case-finding strategies prioritizing assessment of men and women with prior fracture are required to alleviate this problem.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1859

**SP0118 ESTABLISHING AND IMPLEMENTING A FRACTURE LIAISON SERVICE**

S. Stephenson on behalf of National Osteoporosis Society, Service Development - Operations, National Osteoporosis Society, Bath, United Kingdom

**Objectives:** The objective of the National Osteoporosis Society (NOS) is to establish a Fracture Liaison Service (FLS) in every NHS Trust in the United Kingdom. The NOS Delivery Manager supports sites to implement and develop a new FLS, as well as to improve the quality of existing services. The FLS model enables secondary fracture prevention through identification of fragility fractures in every person who breaks a bone aged over 50 using dedicated case-finding, with assessment and appropriate management of osteoporosis where necessary. The object of FLS is to prevent secondary fractures, in particular expensive hip and vertebral fractures, thereby providing both clinical and cost effectiveness for patients and payers. The NOS has developed a unique service to support FLS across the UK.

**Developments:** A team of specialist development managers with clinical and commissioning experience support providers and payers in the process of establishing new FLS’s by offering consultation and guidance at every step of the process from pathway development to successful funding of services. This model has been replicated across the UK since April 2015 with the support and expertise of the NOS. Once an FLS is established the NOS provides support with service improvement, whether through additional commissioning of funds, Peer review or Gap analysis.

**Results:** Results from a range of analyses show that FLS has a positive impact on the World Health and in particular hip fractures. At the time of writing, the NOS is currently supporting 166 sites across the UK, 83 sites are improving the quality of their service; 58 sites are developing new services. 13 new services have been commissioned since commencement of the work programme, delivering new FLS provision to an additional 1.6 million people over 50, preventing 1,482 hip fractures over a 5-year period. Figures have been calculated from the NOS FLS Benefits Calculator https://benefits.nos.org.uk

**Challenges:** The primary challenge in establishing an FLS is identifying a clinical champion - this maybe a nurse, an allied health professional, rheumatologist or ortho-geriatrician in the hospital, or a representative from Public Health or from a Clinical Commissioning Group (CCG). The champion can lead and take the FLS from an idea to implementation.

To support the establishment and implementation of FLS the NOS has developed the FLS Implementation Toolkit as well as the Clinical Standards for FLS. The Clinical Standards will shortly be supported with a supplementation - New Clinical Guidance on the identification of Vertebral Fractures. Furthermore, the Charity has developed the Fracture Prevention Practitioner (FPP) training for those wishing to implement an FLS. This is backed by the Competency Framework for Nurses, allied health professional and doctors to ensure best practice in fracture prevention.

**Conclusion:** The NOS service development model of support is successful in driving the establishment, implementation and improvement of FLS across the UK. This is tough in an economic climate where health budgets are constrained. However, there is strong evidence that investment in FLS improves the quality of care as well as illustrating financial savings in health and social care. NHS England recommends that every patient with/or at risk of osteoporosis and fragility fractures should have access to a commissioned service.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7255

**SP0120 PREDICTING THE RISK OF FALLS AND PROMOTING BALANCE IN OLDER ADULTS**

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Falls are the leading cause of injury and death due to injury among the older adult population in the United States. Of those who fall, 24% will sustain serious injuries and 6% will experience fractures. In addition to injury, older adults who fall may experience decreased functional ability, loss of independence, a poorer quality of life, or premature mortality. At a global level, these statistics are similar among developed countries.

It is important to first identify the intrinsic and extrinsic risk factors that contribute to falls and then intervene appropriately once the level of fall risk has been identified. It is important to understand that there is no one size suits all fall risk reduction program and that the type of program will vary as a function of the level of risk. Core components of successful fall risk reduction programs include exercise, environmental modifications, and behavior change techniques aimed at fostering long-term adherence to engaging in fall risk reducing behaviors. The purpose of this presentation will be to describe appropriate methods for identifying fall risk, and intervention strategies that have been shown to significantly reduce fall risk and/or fall incidence rates across the continuum of fall risk.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7244

**SP0119 PREDICTING FRACTURE RISK: ACCURACY AND FEASIBILITY OF TOOLS**

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Several therapeutic options and screening strategies are available to effectively decrease fracture risk. However the main clinical challenge still consists in accurately identifying and selecting individuals for bone densitometry and for pharmacological treatment, in order to increase efficiency and minimize individual and societal costs.

The World Health Organization provided an operational definition of osteoporosis as a bone mineral density (BMD) that lies 2.5 or more standard deviations below the average value for young healthy women of the same gender and ethnic background [T-score ≤ -2.5]. However, BMD has limited sensitivity and specificity in the prediction of fracture. In fact, a large number of conditions have been firmly established as risk factors for the occurrence of fragility fractures, independently from BMD. These have been combined into prediction algorithms to estimate fracture probability and are currently available for calculate the risk of fractures. However, the existing tools differ in many relevant aspects: from their own feasibility, to the number and availability of clinical risk factors included, the accessibility of BMD measurements and, finally, their performance in different settings.

With this session we aim to identify and synthesize the best available evidence on the accuracy and feasibility of the currently available tools designed to predict fracture risk.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7217

**SP0121 LONG TERM SIDE EFFECTS OF BIOLOGICAL AGENTS IN JIA**

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In the last years, the interest in the concept of comorbidity and its societal as well as individual impact has increased. Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease starting in childhood which often persists into adulthood. Clinicians are facing an aging population with multiple morbid conditions occurring in one individual. Long term outcome studies show the high prevalence and the potential interaction of coexisting diseases. For JIA recent studies reported that uveitis, asthma/atopic diseases and diabetes mellitus are prevalent comorbidities in JIA with 11.6–30%, 10.8% and 3.5% respectively, followed by cardiovascular disease, malignancies and inflammatory bowel diseases. Childhood long term outcome studies and Pharmacovigilance registries already revealed associations of co-existing diseases and the role of used medication (especially biologicals).

It is important to plan preventive and screening strategies in order to prevent or early detect and treat comorbidities and integrated follow up once comorbidity exists.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7172

FRIDAY, 16 JUNE 2017

**Biological agents in juvenile idiopathic arthritis: open issues**

**SP0111**

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7217
AUTOIMMUNE PHENOMENA ASSOCIATED WITH BIOLOGICAL AGENTS

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1. Pediatric Rheumatology, Université Paris Descartes, APHP, Hôpital Necker-Enfants Malades, Paris, France
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Biologic agents are being increasingly used in pediatric rheumatology, particularly TNF antagonists but also abatacept, tocilizumab, interleukin (IL)-1 antagonists and some other drugs. In juvenile idiopathic Arthritis (JIA) and some autoinflammatory diseases, data from phase 3 and extension trials or from cohorts such as Pharmachild allow to prospectively collect information on adverse events of "special interest", including autoimmune complications. A few patients develop autoimmune/dysimmune features while on biologics, as seen in adults, including central nervous system lesions, inflammatory bowel disease or psoriasis. In addition, in patients with systemic-onset JIA, anti-IL-1 treatment is usually associated with the appearance of a type 1 interferon signature (gene expression analyses) which might in some cases favour lupus-like autoimmune features.

On the other hand, among patients with early-onset arthritis, vasculitis, recurrent fever or other inflammatory manifestations, an increased number of children are diagnosed with complex monogenic diseases resulting in auto-inflammation, immune deficiency and autoimmunity. In such cases, biologics might not be responsible for the occurrence of autoimmune features that may sometimes be diagnosed on treatment. This distinction is important as biologics are useful treatments in some of these patients, as was shown in a patient with a diagnosis of Systemic-onset JIA and ANCA-associated glomerulonephritis in whom anti-IL-1 treatment was beneficial. It was also more recently shown in patients with lipopolysaccharide-responsive beige-like anchor (LRBA) mutations associated with autoimmunity and inflammation, including polyarthritides: as LRBA is a partner of cytotoxic-T lymphocyte antigen-4 (CTLA4), abatacept has been used as a targeted treatment and shown efficacy.

We hence aim to discuss the way to explore patients who develop autoimmune features while on biologics in order to take the right decisions regarding treatment maintenance, withdrawal or modification and regarding patients follow-up.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7321

FRIDAY, 16 JUNE 2017

Health equity and economy - a vital relationship

UNCOVERING THE EQUITY GAP IN RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Maastricht University Medical Center (MUMC), Maastricht, Netherlands

The aim of this lecture is to discuss the current evidence on the socio-economic inequities in disease outcomes in RMDs. Socio-economic determinants at the individual and country level will be considered, as well as the interplay between these factors. Special attention will be given to the role of different socio-economic factors in the access to biologic DMARDs in rheumatoid arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7164

HEALTH ECONOMICS AND HEALTH EQUITY: TWO COMPLEMENTARY DISCIPLINES

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Health equity in the one hand refers to the absence of systematic disparities in health between different social or demographic groups in a country or a group of country. Health inequity thus corresponds to a situation in which health services are not similarly available to all people with the same health conditions and health needs, due to individual personal or socioeconomic characteristics. Health economics in the other hand focuses on how to allocate health budgets in order to maximize the general health of the population as a whole. With regards to this, no specific attention is dedicated to socially disadvantaged subgroups. In addition, the most visible action in the field of health economics was the valorization of therapeutic innovation, i.e., the determination of its price not on production cost but on value associated with this innovation. Economic evaluation – i.e., determination of incremental cost-effectiveness ratio – has lead during the last 20 years to substantial financial pressure on health care systems with dramatic increase in health expenditures mainly due to the costs of therapeutic innovation. Several studies have shown that such a process may increase health inequities within a country. Specific actions are not taken to maintain or improve treatment availability and access to care to all the population members whatever their social, educational and economic characteristics.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7280

BIOMARKERS IN CARDIOVASCULAR RHEUMATOLOGY – RELEVANT METABOLIC BIOMARKERS

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Patients with RA have increased mortality compared with the general population due to higher cardiovascular disease (CVD), which is up to 50% more frequent [1]. Even after adjusting for traditional cardiovascular risk factors such as smoking, diabetes and hypertension, the risk for CVD is increased by up to twofold compared with the normal population [2]. Whilst traditional cardiovascular risk factors, contribute to the increased risk of mortality in RA patients, they do not fully explain increase in cardiovascular risk [3,4]. European League Against Rheumatism (EULAR) recommend regular assessment of cardiovascular risk in patients with RA [5]. Since traditional cardiovascular risk factor assessment equations, such as Framingham and the Systematic Coronary Risk Evaluation Score (SCORE) models, underestimate cardiovascular risk in RA, EULAR recommend multiplying such traditional cardiovascular risk scores by 1.5 for patients with RA. Such adjustment operates at the population level. Ideally, cardiovascular biomarkers that can predict future cardiovascular event in the individual patient will improve screening and management.

Biomarkers of cardiovascular disease can be divided into five major categories: lipids, inflammation, endothocrine, vascular and prothrombotic [7]. HDL and LDL are used in routine clinical practice. However, they do not predict future cardiovascular events in patients with RA as the levels of HDL and LDL are suppressed during inflammation [8]. The ratio of HDL/LDL or total cholesterol/HDL is less affected by inflammation and might be considered. Other lipid biomarkers include apolipoprotein A-1, apolipoprotein B, cholesterol ester transfer protein lipoprotein-associated phospholipase A2, small dense LDL and paraoxonase-1. They have been measured in patients with RA but their precise value in predicting cardiovascular risk in RA has not been determined.

High level of inflammation as measured by ESR and CRP is associated with increased cardiovascular risk in patients with RA. EULAR recommended adequate suppression of inflammation as a key strategy to reduce cardiovascular events [5]. Disease flares increased cumulative cardiovascular risk [9]. Many inflammatory mediators are elevated in RA and might add to traditional cardiovascular risk score to improve individual risk prediction should be evaluated. The vascular biomarker of cardiovascular disease, VCAM-1, has also been shown to be elevated in patients with RA. High level of VCAM-1 was associated with high cardiovascular risk score [10].

Metabolic syndrome is common in patients with inflammatory arthritis. Insulin resistance is a feature of metabolic syndrome. Fibrinogen and other prothrombotic molecules are part of the acute phase response, their levels are elevated in RA. Neither endocrine nor prothrombotic factors have been studied systematically in RA.

References:

Disclosure of Interest: E. Choy Grant/research support from: Roche, UCB, Pfizer, Biocancer, Consultant for: Amgen, Boehringer Ingelheim, Celgene, Chugai Pharma, Eli Lilly, Hospita, I Janssen, Napp, Novimmune, Novartis, Pfizer, Regeneron, Roche, R-Pharm, Sanofi-Aventis, Tonix and UCB.

Speakers bureau: Amgen, IMS, Boehringer Ingelheim, Chugai Pharma, Eli Lilly, Hospita, Janssen, MSD, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, and UCB.

DOI: 10.1136/annrheumdis-2017-eular.7283

THE VESSEL WALL IN IMDS – NEW EMERGING VASCULAR MARKERS

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Cardiovascular disease dependent on inflammatory accelerated atherosclerosis
leads to increased mortality in rheumatoid arthritis (RA). In addition to traditional, Framingham risk factors, several immune-inflammatory cells, mediators and molecules may link atherosclerosis to arthritis. Among immune cells, primarily TH1 cells, as well as endothelial cells play a crucial role in syndical and vascular inflammation. Various cell surface molecules, such as adhesion receptors, CD40-CD40L interaction with members of the RANK-RANK ligand-osteoprotegerin system, as well as soluble pro-inflammatory cytokines, chemokines, autoantibodies and proteins have been implicated in RA and vascular damage. The early assessment of atherosclerosis and early intervention would decrease cardiovascular risk in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7197

SP0127 TAPERING BIOLOGICS INDUCES A PROTHROMBOTIC STATE IN RHEUMATOID ARTHRITIS?

M.T. Nurmohamed on behalf of M. Heslinga, J. Meijers & M. Nurmohamed. Rheumatology, Amsterdam Rheumatology Immunology Center | VUMc & Reade, Amsterdam, Netherlands

In addition to the "traditional" risk factors for venous thrombo-embolism (VTE), like age, trauma and immobilisation, inflammation could also be regarded a risk factor for VTE. For example, patients with acute inflammatory conditions (sepsis), but also patients with chronic inflammation, like inflammatory bowel disease (IBD), and rheumatoid arthritis (RA), have an increased risk of thrombo-embolism. Inflammation can lead to activation of coagulation, and vice-versa, coagulation also has considerable effects on overall inflammatory activity. First, the inflammatory cytokine network induces several pro-thrombotic conditions including insulin resistance, dyslipidaemia, endothelial dysfunction and alteration of coagulation and fibrinolysis. Second, activation of the extrinsic coagulation system and impairment of the fibrinolytic pathway may contribute to amplify and perpetuate the inflammatory response. Previous studies have reported several blood parameters that reflect a pro-thrombotic state in RA. These include increased levels of thrombin-antithrombin complex, prothrombin fragment F1+2, von Willebrand factor, plasmin-alpha2-antiplasmin complex and D-dimer, as well as an increased platelet count. Impaired fibrinolysis combined with increased antithrombin levels have also been reported in RA. An important mediator in the inflammatory pathway is tumor necrosis factor-α (TNF-α). In the general population, TNF-α induces a disbalance between clotting and fibrinolysis, resulting in a hypercoagulable state. Since TNF-α is the key player in RA, RA is an ideal "human model" to study the interplay between inflammation and coagulation. Hence, RA can be considered as a pro-thrombotic state, which explains partly why patients with RA are at increased risk of thrombo-embolic cardiovascular events. (1)

Only one small study suggested that TNF-inhibitors (TNFi) is accompanied with normalization of thrombotic biomarkers: an improvement of clinical and laboratory parameters as well as a reduction in the activation of coagulation and endothelial dysfunction was found in RA patients treated with a TNFi. In addition, we previously demonstrated that combination therapy with corticosteroids improves the procoagulant state that exists in early RA. (2) Nowadays, tapering of biological therapies is becoming more and more standard of care. However, the effects on the coagulation status in RA are unknown. In light of the growing evidence of an increased cardiovascular morbidity and mortality in RA, mostly independent of traditional risk factors, treatment strategies in RA should not only aim at relieving symptoms and inhibiting joint destruction but should have a beneficial effect on the vasculature and haemostasis to reduce cardiovascular events. Although modest, there is evidence suggesting a beneficial effect of TNFi on the haemostatic status in RA. Unfavourable changes in haemostatic markers, such as TAT, F1+2, VWF, PAP, D-dimer and thrombin generation, which indicate a pro-thrombotic state, may therefore (re)occur when RA patients stop with TNFi treatment. We first assessed arterial wall inflammation with 18F-FDG PET scans in RA patients in remission under TNFi therapy or DMARD therapy versus controls. The FDG uptake in the aorta in DMARD remission patients was similar to the controls, whereas the uptake in RA patients in remission under antiTNF was significantly higher than in controls either when looking at the overall aortic uptake or the thoracic dissected segment. Theoretically, stopping TNFi blockade in these patients might lead to increased inflammation and thus coagulation activation. Therefore, we are presently investigating it and to what extent tapering/ stopping TNFi therapy induces a pro-thrombotic state in RA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7143
Epidemiologic studies have shown that not only fracture risk, but also mortality is increased after fracture, and that adequate therapy can not only decrease fracture risk but also increase survival. Fracture risk is not constant over time. It is highest the years following a fracture, and immediately increases in some instances, such as after starting glucocorticoids or androgen deprivation therapy. This has raised the concept of “imminent” fracture risk, in contrast to long-term fracture risk as included in FRAX. In this context, we present the the EU&LAR initiative, in collaboration with EFORT, that published recommendations for multidisciplinary acute fracture care, including orthogeriatric care after hip fracture, and subsequent fracture prevention at the Fracture Liaison Service. The presence, number and severity of vertebral fractures contribute to fracture risk, independent of BMD. Most vertebral fractures are subclinical and can therefore only be diagnosed by imaging of the spine. The role of vertebral fracture assessment (VFA) using DXA will be discussed. New treatment insights will be reviewed, including for glucocorticoid users, combined and sequential treatments with anti-resortive and bone forming drugs, real world data and the role of fall prevention.

Prescription of and adherence to treatment are still major issues. In patients adherent to therapy, new insights and recommendations will be reviewed on the need for early treatment, duration of treatment and the clinical approach when considering stopping drug therapy.

Disclosures of Interest: P. Geusens Grant/research support from: Pfizer, Abbott, Lilly, Agen, MSD, Will, Roche, UCB, BMS, Novartis, Consultant for: Agen

DOI: 10.1136/annrheumdis-2017-eular.7267

FRIDAY, 16 JUNE 2017

What is behind vasculitis?__

**SP0131**

**AUTOIMMUNE ATHEROSCLEROSIS**

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Arthritides have been associated with accelerated atherosclerosis to increased vascular disease risk. Traditional risk factors, as well as the role of systemic inflammation including cytokines, chemokines, proteases, autoantibodies, adhesion receptors and others have been implicated in the development of these vascular diseases. Accelerated atherosclerosis and increased cardio- and cerebrovascular morbidity and mortality have been observed in rheumatoid arthritis (RA) and spondyloarthropathies (SpA).

Endothelial dysfunction, overt atherosclerosis and vascular stiffness may be indicated by brachial artery flow-mediated vasodilation (FMD), common carotid intima-media thickness (cIMT) and aortic pulse-wave velocity (PWV), respectively. These abnormalities have been described in most inflammatory rheumatic diseases. While cIMT and stiffness are relatively stable, FMD may be influenced by many confounding factors.

In addition to traditional vasculoprotection, immunosuppressive agents including corticosteroids, traditional and biologic DMARDs may have significant vascular and metabolic effects. The official EULAR recommendations on the assessment and management of cardiovascular disease in arthritis have been published.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7194

**SP0132**

**VIRUSES DRIVING VASCULITIS**

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Viruses have long been associated with varying forms of vasculitis in both pre-clinical models and human diseases. Immuneopathogenic mechanisms have varied and include direct vascular invasion, immune complex mediated and more recently novel mechanisms which include autoinflammatory like responses. This discussion will review major advances in the field of medical virology as it applies to rheumatic diseases, especially vascular inflammatory disease, including and introduction to the human and more specifically vascular microorganisms. Major forms of virally mediated vasculitis will be discussed with an emphasis on new viral vasculitis syndromes largely defined by next generation sequencing and their potential clinical impact.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7216

**SP0133**

**ANCA AND THEIR ENVIRONMENT**

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The association between antibodies to neutrophil cytoplasm (ANCA) and systemic vasculitis has transformed our understanding of granulomatosis with polyangiitis (EGPA) and eosinophilic granulomatosis with polyangiitis (EGPA). ANCA undoubtly played a major role in their pathogenesis. There are different forms of ANCA, but only two of direct clinical relevance: cytoplasmic c-ANCA (usually directed against proteinase 3, PR3), and perinuclear p-ANCA (usually directed against myeloperoxidase, MPO). P-ANCA can also be directed against other antigens including bacterial/permeability-increasing protein, lactoferrin, human neutrophil elastase, cathespin G and azurocidin, but their clinical significance is not clear.

Transfer of MPO ANCA in humans (maternal-fetal route) and animal models (necrotizing pauci-immune glomerulonephritis after passive transfer of purified antibodies or soluble micromolecules from murine MPO) has resulted in features of MPA. By contrast, the pathogenicity of anti-PR3 antibodies is less well-established. There is a significant genetic predisposition to disease in patients with AAV. Patients with PR3-ANCA have a strong association with HLA-DP and genes encoding alpha-1-antitrypsin and proteinase 3; by contrast, patients with MPO-ANCA have an association with HLA-DQ. Other factors that could interact with ANCA include: loss of B cell and T cell tolerance; direct involvement by neutrophils and their mediators in vascular injury and damage, degranulation and cytokine production; environmental exposure to silica or other bacteria like Staphylococcus aureus, coupled with a lack of effective T cell regulation to prevent inflammation. Neutrophils spontaneously release of neutrophil extracellular traps (NETs), which directly cause endothelial cell damage and complement activation. NETs retain proteinase 3 and myeloperoxidase, helping to break immune tolerance and inducing antibody formation.

The alternative complement pathway plays a crucial role in the pathogenesis of AAV. Activated neutrophils produce C5a, which in addition to recruitment, primes additional neutrophils for further activation by ANCA. C3a, C5a, soluble C5b-9 are elevated in active disease and plasma levels of complement factor H, a regulator of the alternative complement pathway is significantly lower in patients with active AAV.

Central to the pathogenesis of AAV is a dysregulated immune response to ANCA and aberrant expression of their target autoantigens, MPO and PR3. Environmental exposure to silica may inactivates α1-antitrypsin, whilst activating monocytes and macrophages releasing cytokines such as interleukin-1 and TNF-α, oxygen radicals and lysosomal enzymes (such as PR3 and MPO). Other environmental interactions include Cpg-ODN, a short synthetic DNA containing unmethylated Cpg and several drugs, especially propylthiouracil and levamisole-adulterated cocaine. Some of these associations could provide a better insight into the development of ANCA associated disease.

ANCA play a central role in the pathogenesis of systemic vasculitis, supported by a dysregulated immune system, with significant interactions with micro-organisms, environmental toxins and drugs, all of which can contribute to the development and severity of disease.

Disclosure of Interest: R. Luqmani Grant/research support from: Arthritis Research UK, GSK, MRC, UCSF/OIF, Canadian Institutes of Health Research, The Vasculitis Foundation, Consultant for: GSK, Medpace, Medimmune, Roche

DOI: 10.1136/annrheumdis-2017-eular.7151

FRIDAY, 16 JUNE 2017

Cytokine taxonomy: reflection in the therapy of arthritides and other IMIDs

**SP0134**

**INTERLEUKIN-2 THERAPY IN SLE**

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There is an unmet need for more effective and selective therapeutic strategies in severe autoimmune diseases such as systemic lupus erythematosus (SLE). A deeper understanding of the pathogenic mechanisms in the past has led to the clinical translation of low-dose interleukin-2 (IL-2) therapy which primarily aims to restore the activity of regulatory T cells. First results from phase III clinical studies are promising by proving the selective expansion of regulatory T cells in vivo and by providing first evidence for the clinical efficacy of low-dose IL-2 therapy in SLE. Here we will summarize key findings which led to the development of this novel therapeutic concept and will highlight the main rationales for the clinical translation of low-dose IL-2 therapy in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7305

FRIDAY, 16 JUNE 2017

Regulatory molecules in connective tissue

**SP0135**

**MYOSTATIN, SCLEROSTIN, SYNDECAN AND MORE**

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Rheumatoid arthritis (RA) is the prototype of an inflammatory arthritis that is characterized by chronic inflammation, progressive cartilage destruction and bone proliferation. Development of RA is marked by the hyperplasia of the synovial membrane as caused by an infiltration and accumulation of inflammatory cells such as macrophages and lymphocytes as well as an increase in the number of resident mesenchymal cells. These fibroblast-like synovocytes (FLS) are a key part of the local immune system in the joints and integrate signals...
form different sources into a pathological tissue response. Resorption of the juxtaarticular bone is part of this pathological tissue response and is denoted as focal bone erosion which occurs early in this disease and over time is associated with significant morbidity. Focal bone erosions are observed at the interface of pannus and bone tissue both marginally, where pannus invades cortical bone adjacent to an intermediate subchondral bone, where the pannus invades the marrow space. Many of the cytokines and growth factors implicated in the inflammatory processes are secreted by FLS and have also been demonstrated to impact directly or indirectly on osteoestal and/or osteoclast differentiation and function. However, research of the last years has also identified some novel pathways by which i) osteoclast- mediated bone resorption is regulated and fine-tuned under inflammatory conditions such as in RA and that ii) link inflammatory bone resorption to other features of systemic autoimmunity such as the activation of developmental pathways or muscle weakness. This lecture will review some of these novel mediators and pathways, including members of the Wnt- signalling pathway (e.g. sosterolin), members of the GDF- family of growth differentiation factors (e.g. myostatin) and cells surface anchored proteoglycans (e.g., syndecans). Focusing on the role of these molecules in the FLS-mediated regulation of osteoclast bone resorption, the lecture will point to general principles of inflammatory bone remodelling and discuss potential therapeutic implications for RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7261

SP0136 MULTIFACTORIAL TISSUE GROWTH FACTORS

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Connective tissue is a critical component of all organs and has special importance in the musculoskeletal system. In specialist tissues, such as bone, cartilage of muscle an in vascular structures and internal organs there is a mixture of less specialized connective tissue together with the specific tissue and organ specific cellular and cellular organelles. In addition to physiological function there are two other areas in which it plays a central role. Normal embryonic and postnatal growth and development, and tissue repair in response to injury. It has emerged that there are shared pathways, mediators and mechanisms in these different processes and that multifactorial tissue growth factors have an important role. In this way, these proteins can have a profound influence on multiple cell types and provide a mechanistic link in many complex chronic diseases. It is notable that pathways that are perturbed in one chronic disease, such as atherosclerosis or osteoarthritis may be similarly disrupted in different context in conditions such as lung fibrosis or scleroderma. In addition to physiological function there are two other examples of this class of protein. This included TGFbeta isoforms and also the related bone morphogenous (BMP) and activin family of proteins. They share chemical structure and an ability to regulate multiple cell types in a context specific way. In addition, there is remarkable complexity in their regulation with intrinsic inhibitory mechanisms to protect from inappropriate biological activity. Their role in repair means that activation of preformed protein may regulate biological effects. Proteins regulated by the TGFbeta family, such as the CCN family of matricellular proteins and some for the cardinal growth factors and cytokines share properties. There is functional redundancy and cross talk. Conceptually it is interesting to envisage dysfunctional networks of cytokines in disease that may be attenuated by extracellular blocking or antigen. Insights for many areas of developmental biology and pathology have informed about this challenging area of molecular medicine.

Disclosure of Interest: C. Denton Grant/research support from: Inventiva, CSL Behring, GSK, Bayer, Consultant for: GSK, Actelion, Inventiva, Roche

DOI: 10.1136/annrheumdis-2017-eular.2532

SP0137 FROM GLYCOSYLATION TO INFLAMMATION

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One of the best studied posttranslational modification of immunoglobulin G (IgG) is the addition of a complex glycan to asparagine 297, which is required for IgG to bind to Fc-receptors and for the activation of complement via the classical activation pathway. In the absence of the glycan the IgG usually behave like a lame duck unable to execute its effector functions. The sugar tree is polymorphic and there are several functional consequences related to the glycan. The terminal sialylation, the presence of galactose, the core fucosylation and the insertion of a bisecting third sugar chain all reportedly modify the biological and functional activities of IgG.

As examples for the impact of Asp-297 associated glycans to the activity I will present (I) the sialylation of anti-histon autoantibodies in patients with systemic lupus erythematosus (II) the exposure of sugar epitopes by random IgG isolated from patients with rheumatoid arthritis (III) the molecular analysis of the glycan of random IgG isolated from patients with inflammatory diseases and controls and (IV) and finally the glycosylation of IgG-anti-phospholipid autoantibodies in healthy children.

(I) The autoantibodies are mainly found in the non-sialylated fraction of the anti-histon autoantibodies which can be considered inflammatory IgG.

(ii) The circulating random IgG from patients with rheumatoid arthritis show an increased exposure of the Asp-297 associated glycans.

(iii) The molecular analysis of the glycan of random IgG isolated from patients with systemic lupus erythematosus, rheumatoid arthritis, sepsis showed disease-specific glycans.

(iv) The non-pathogenic IgG-anti-phospholipid autoantibodies isolated from healthy children displayed an increased sialylation when compared to the pathogenic autoantibodies from adults with anti-phospholipid syndrome.

The examples point to a strong impact of IgG glycosylation in the etiopathogenesis of chronic inflammatory rheumatic diseases. One should consider to include IgG glycan analyses into the diagnostic repertoire for autoantibodies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7291

FRIDAY, 16 JUNE 2017

Patient engagement in research: best practices, benefits, and challenges

SP0138 THE CHALLENGES OF PATIENT INVOLVEMENT IN SCIENTIFIC RESEARCH. HOW TO ACHIEVE TRUE REPRESENTATION OF THE PATIENTS’ VOICE?

M. De Wit on behalf of the EULAR Working group for Collaborative Research. Dept. Medical Humanities, EMGO+ research institute, VU University Medical Centre, Amsterdam, Netherlands

There is a strong call in the western world for collaborative research. Rheumatology is one of the disciplines that has explored best practices and paved the way to implement lessons learned. Although good methodologies for evaluating the impact of patient participation stay behind, we have been able to develop expert-based recommendations for collaboration. They are helpful for both researchers and patient representatives, but they do not address all concerns that occur in daily practice. In this lecture current challenges of integrating the perspectives of patients in clinical research will be discussed: 1. Defining the role and complementary value of patient research partners; How can patients in the role of collaborative partner contribute to research in addition to the data that patients provide as respondent or study participant? 2. Facilitating and guiding researchers in collaborative research; We have experience in preparing and educating patient representatives for their role in research, but how should researchers be trained and supported? 3. Preserving the patients’ voice throughout the research process; Qualitative research may elicit patients’ experiences with health care or health interventions, but what is needed to guarantee that these findings are not lost in the rigorous process of producing scientific knowledge? 4. Demonstrating impact of collaborative research to funders and the public; Despite many case studies reporting a great variety of patient participation methods, there are no clinical trials nor consensus on a validated methodology for assessing the outcomes of patient involvement in research. For each challenge we will try to propose a way forward. These challenges will also be discussed at the newly established EULAR working group for collaborative research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7249

SP0139 MEANINGFUL PATIENT AND PUBLIC INVOLVEMENT IN PLANNING RESEARCH

A. Redmond, Leeds Institute for Rheumatic and Musculoskeletal medicine, University of Leeds, Leeds, United Kingdom

Historically, services providing care for people with long term conditions (LTCs), together with any associated research agendas, have been driven entirely by clinicians. In many cases this is well meaning and is done with some consideration of what patients need, but almost always the end result relies on the clinicians’ interpretation of what patients need.

Recently it has become more usual to involve patients in planning research projects and service changes directly. Initial attempts to give patients genuine input were ad hoc in nature and so patient contributions could be lacking, ignored or misinterpreted.

In many cases having poor patient input is worse than no input at all as it tends false credibility to the process. Lately a range of formal requirements, arrangements and methods have become adopted and this presentation will focus on how these can be brought to bear to ensure meaningful patient and public involvement in planning research. From national guidance such as the UK’s INVOLVE initiative, to local standard operating procedures we will share experiences and lessons learned.

The session will close with a practical summary of how to make PPI contributions genuine and meaningful, and some insights into possible future developments as this aspect of the research process matures and consolidates.

Disclosure of Interest: None declared

**SP0140** PATIENT ENGAGEMENT IN RESEARCH: A PCORI EXEMPLAR

**J. Pooe.** Occupational Therapy Program, University of New Mexico, Albuquerque, United States

This session will discuss patient and stakeholder involvement as members of the research team on a grant funded by the Patient Centered Outcomes Research Institute (PCORI). Patients with a rare chronic disease, systemic sclerosis, and members from key stakeholder organizations were involved in evaluating, revising and testing the effectiveness of an internet self-management program. They participated at several levels of engagement including planning the study, conducting the study, and disseminating the results. This session will discuss how engagement occurred at each of these levels through different opportunities such as creating interventions, identifying outcomes, recruiting, presenting findings, and planning dissemination efforts. The benefits and challenges for both researchers and patient research partners will also be described.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7294

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**FRIDAY, 16 JUNE 2017**

**RA treatment in patients wanting to become pregnant - interactive session**

**SP0141** NEW RA, BUT WHAT ABOUT A NEW BABY?

A. Willemsen. Rheumatology, LUMC, Leiden, Netherlands

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease affecting women often in their childbearing years. In this case presentation a 35 year old female patient is illustrated with a recently diagnosed rheumatoid arthritis with active disease and a wish to conceive in the nearby future. Management of disease activity in patients who wish to conceive or during pregnancy might be a challenge due to limited treatment options. How should we treat this patient taking into account her wish to conceive in the nearby future? Should the patient postpone her wish to conceive because of active disease?

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7182

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**SP0142** FOREPLAY AND FINALE: FACTORS AFFECTING FERTILITY, BIRTH AND LACTATION IN RHEUMATOID ARTHRITIS PATIENTS. CLINICAL CASE

P. Nero. Rheumatology, Hospital CUF Desobertas, Lisboa, Portugal

We present the clinical case of a 38 year old woman diagnosed with rheumatoid arthritis at the age of 32. She went into remission of her disease during treatment with subcutaneous methotrexate (25 mg/week) for 2 years. She decided to become pregnant and stopped treatment. RA relapses 4 months later and she has no response to classic DMARD’s (sulphasalazine and hydroxychloroquine) and starts etanercept (50mg/week). She gets pregnant and achieves remission at 16 weeks of gestation. At week 36 she is still in remission and stops etanercept. 2 months after giving birth the disease relapses but she wants to breastfeed and would like to restart etanercept. We agreed and 3 months after restarting anti-TNF RA is again in remission. In January 2017 her RA is in remission for 15 months and keeps her medication with etanercept every other week because she plans another pregnancy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7182

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**SP0143** A NEW DAY FOR PEOPLE WITH PSORIATIC ARTHRITIS—A HETEROGENEOUS DISEASE THAT CAN BE TREATED WELL?

L.C. Coates. Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

This talk will summarise recent advances in research around the treatment of psoriatic arthritis (PsA). Firstly there will be an update on research that shows the importance of treating patients promptly when they are diagnosed. Then results from studies of new therapies for both psoriasis and psoriatic arthritis will be shown to highlight the drugs that have recently become available in the clinic or are likely to be available in the next few years. This will include new biologic disease modifying drugs with different targets including those that target interleukin 17 and interleukin 23 as well as new oral medications that are part of a family called small molecules. The role of these new therapies and how they compare to existing therapies in the clinic will be addressed. Finally there will be a summary on the research of how to use the existing and new therapies in the clinic including the use of the “treat to target” strategy.

**Disclosure of Interest:** L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB

**DOI:** 10.1136/annrheumdis-2017-eular.7145

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**SP0144** BIOSIMILARS IN RHEUMATIC DISEASES: SOCIETY CHANGES VERSUS PATIENT CONCERNS

A.A. Den Broeder, Rheumatology, St. Maartenskliniek, Ubbingen, Netherlands

Biosimilars are biologically but also in clinical practice for all intents and purposes identical to the original drug, as has been shown in blinded trials. But the perception amongst patients and sometimes physicians is one of doubt. 

Disclosure of Interest: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7222

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**FRIDAY, 16 JUNE 2017**

**From pre-RA to established RA**

**SP0145** PATHOPHYSIOLOGIC PROCESSES LEADING TO THE DEVELOPMENT OF AUTOIMMUNITY

R. Toes. Rheumatology, Leiden University Medical center, -Leiden, Netherlands

Rheumatoid arthritis (RA) is a common complex disease characterized by chronic inflammation which results in joint destruction and significant disability in those affected. According to the World Health Organisation, within 10 years of onset, at least 50% of patients in western countries are unable to sustain a full-time job and about 25% develop mental consequences to patients as well as extensive societal costs. The cause of RA remains unknown. Human genetic studies have provided valuable insight with over 100 genetic risk factors identified to date. Genetic variants at the human leucocyte antigen (HLA) locus remain the most prominent genetic risk factor. Smoking is the best known environmental factor to contribute to the development of RA.

Gene-environment interactions are likely since the development of RA is determined by both genetic and environmental factors. A prominent example of AMPA is Anti-Citrullinated Protein Antibodies (ACPA). ACPA are highly disease-specific biomarkers of important diagnostic and prognostic value, with ACPA-positive patients being at risk for rapidly progressive, destructive and systemic disease. The strongest genetic risk factors for RA, the so-called HLA-shared epitope (SE) alleles, are strongly associated with CDRA positive patients. SE alleles define a specific disease entity within the complex group of symptoms clinically defined as RA. Current concepts of RA pathogenesis hold that a sequence of events leads to the development of ACPA-positive disease. Environmental factors are thought to cause an initial break of tolerance leading to the generation of ACPA-specific immune responses resulting in the development of RA. This talk will summarise recent advances in research around the treatment of RA.
of ACPO. This initial development of auto-immunity appears to be independent of the disease-predisposing HLA-molecules. In most patients, this early event generates a polyclonal yet limited, mostly low-level autoantibody response that can be present for many years in the absence of clinical symptoms. Upon a putative second trigger, the ACPO epitrace recognition repertoire broadens, mostly isohaemolysin using, and ACPO serum levels rise. This is followed by precipitation of disease and is likely associated with the presence of the predisposing HLA-molecules. While the nature of this second trigger is presently unknown, the second event that initiates the broadening of the auto-immune response, in particular the citrulline-specific immune response, could mark a crucial moment upon which the auto-immune response becomes self-perpetuating and, potentially, irreversible.

Despite the many facets of ACPO revealed in the past two decades summarized above, it is not known how a breach of tolerance towards citrullinated proteins is mediated, or how ACPO-producing B-cells emerge. Provision of T-cell help is crucial to convey the ability to B-cells to modify the B cell receptor through somatic hypermutation. At present, it is unknown how ACPO- or other Anti-Modified Protein Antibody (AMPA)-producing B cells are “helped” by CD4+ T-helper cells, but it is often speculated that an auto-reactive T-cell response is crucial for their appearance. Our recent data show that such help could be provided by T-cells recognizing foreign proteins that may have undergone a post-translational modification. In mice, AMPA-responses recognizing modified self-proteins are readily induced by immunization with modified proteins of non-self origin. This is explained by the observation that the murine AMPA-response works both at the monoclonal- and polyclonal level, highly cross-reactive towards multiple modified proteins, including proteins of self- and foreign origin. A similar observation was made analyzing the AMPA response in sera from RA patients. These data are important as the cross-reactive nature of AMPA could explain how auto-reactive B-cell responses against PTM self-proteins can be induced by exposure to PTM foreign proteins thereby providing new insights on the breach of autoreactive B-cell tolerance. Taken together, the analysis of the fine-specificity and recognition pattern of antibodies against modified proteins in RA during different phases of disease, together with detailed studies on the identification, isolation and phenotypic characterization of auto-reactive B cells that express AMPA starts to shed light on the earliest phases of autoimmunity in RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7218

SP0146 CAN WE PREDICT WHO IS GOING TO DEVELOP RHEUMATOID ARTHRITIS?
D. Van Der Woude. Rheumatology, Leiden University Medical Center, Leiden, Netherlands

To accurately predict disease development can be considered the “holy grail” of risk factor research. It holds the potential to employ preventive treatment thereby nipping RA in the bud.

This presentation will review familial risk in RA and the underlying genetic risk factors, as well as environmental risk factors for disease. Autoantibodies are a potent prognostic marker when it comes to the risk of developing RA, and play a key role in current pathophysiological hypotheses. The newest players in the autoantibody field, and latest concepts of how the various risk factors contribute to disease onset will be discussed.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7141

SP0147 CAN WE PREVENT THE ONSET OF RHEUMATOID ARTHRITIS IN HIGH RISK INDIVIDUALS?
K.D. Deane. Division of Rheumatology, University of Colorado Denver, Aurora, United States

Multiple studies have demonstrated that rheumatoid arthritis (RA) related biomarkers can identify individuals without inflammatory arthritis who are at high-risk for the future development of clinically apparent synovitis and classified RA. These findings have led to the development of several prevention trials in RA that have either been completed, or are underway. With these exciting developments as background, this lecture will discuss multiple aspects of RA prevention including the role of biomarkers and other factors in developing robust prediction models for future RA, and methods to identify individuals before they develop RA. In addition, this lecture will discuss specific preventive approaches to RA such as clinical trial design and choice of preventive interventions that are based on our growing understanding of the mechanisms of RA development.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7235

SP0148 PATHOPHYSIOLOGY OF ESTABLISHED RA SYNOVITIS
B. Lauwerys. Department of Rheumatology, Université catholique de Louvain, Brussels, Belgium
Access to synovial tissue through - minimally invasive - synovial biopsy procedures led to the implementation of new translational approaches to our understanding of established RA. In this lecture, we will illustrate how the identification of different synovial pathotypes and related molecular pathways translated into clinically relevant phenotypes, such as disease severity or response to therapy. Validation of these concepts in ongoing large-scale multi-centric trials will be key to the integration of synovial assessment tools in clinical practice.

Disclosure of Interest: B. Lauwerys Shareholder of: DNAlytics
DOI: 10.1136/annrheumdis-2017-eular.7282

FRIDAY, 16 JUNE 2017

Laboratory course - from the clinic to the lab and back II

SP0149 NEW TRENDS IN BIOMARKERS IN INFLAMMATORY JOINT DISEASES
E. Feist. Rheumatology, Charité University Hospital, Berlin, Germany

This lecture provides an overview on new developments in biomarker research and standardization in inflammatory joint diseases. The presentation includes an introduction of established and new biomarkers in serum and synovial fluid as well as methods for their detection. Furthermore, an overview on different modifications of auto-antigens (including citrullinated and carbamylation) and their role in immune response and pathogenesis of disease will be given. The diagnostic performance of new and established biomarkers will be discussed including antibodies against modified antigens also illustrated by difficult to diagnose cases. In this context, special attention will be attributed to the predictive value of biomarkers for diagnosis of disease and treatment response.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7200

FRIDAY, 16 JUNE 2017

Switching T on and off: how T cells drive and regulate chronic inflammation

SP0149 TH17 CELLS DRIVE AND REGULATE TISSUE INFLAMMATION
V. Kuchroo on behalf of Basic and Translation Science, Evergrande Center for Immunologic Diseases, Harvard Medical School, Boston, United States

Recently a subset of interleukin (IL)-17-producing T cells (Th17) distinct from Th1 or Th2 cells was described and shown to have a crucial role in the induction of autoimmune tissue injury. Accumulating data suggests that there are three distinct steps in Th17 differentiation: Induction, Amplification and Stabilization mediated by distinct cytokines. Whereas TGF-β + IL-6 or IL-1 + IL-6 induces them, IL-21 amplifies Th17 cells, IL-23 stabilizes the phenotype of Th17 cells. Loss of any of the cytokines (TGF-β, IL-1, IL-6, IL-21 or IL-23) in the pathway results in a defect in generation of Th17. However not all Th17 cells are pathogenic and induce autoimmunity, IL-23 is a key cytokine that induces pathogenicity in Th17 cells (Lee et al., 2012). Using expression profiling at high temporal resolution, novel computational algorithms and innovative nano-wire based “knock-down” approaches, we have developed a regulatory network that governs the development of Th17 cells. In addition to high-density temporal microarray analysis, we have performed single-cell RNA-seq of Th17 cells in order to characterize cellular heterogeneity, identify subpopulations, functional states and learn how gene expression variation affects Th17 effector functions. We have identified novel regulators of Th17 cells both in vivo and in vitro that do not affect Th17 differentiation but affect pathogenic vs. non-pathogenic functional states of Th17 cells. Some of the regulators that make Th17 cells non-pathogenic are also utilized by CD6+ T cells to induce T cell “exhaustion” or “dysfunction”. These novel inhibitors cooperate with other known “check-point” co-inhibitory receptors to suppress anti-tumor immunity.

Disclosure of Interest: None declared

SP0151 SWITCHING OFF UNWANTED IMMUNE RESPONSES: THE MECHANISM OF ANTIGEN-SPECIFIC IMMUNOTHERAPY WITH T CELL EPITOPIES
D.C. Wraith. Institute of Immunology & Immunotherapy, University of Birmingham, Birmingham, United Kingdom

Control of autoimmune and allergic conditions can be reinforced by tolerance induction with peptide epitopes; this presentation will focus on the mechanisms involved. Peptides must mimic naturally processed epitopes. Peptide induced peripheral tolerance is characterised by the generation of anergic, IL-10 secreting CD4+ T-cells with regulatory function. CD4+ T-cells become anergic following their first encounter with peptide. The loss of proliferative capacity correlates with a cytokine switch from a pro-inflammatory to a phenotype characterised by secretion
of the anti-inflammatory cytokine IL-10. IL-10 Treg/Th1 cells suppress dendritic cell maturation, prevent Th cell differentiation and create a negative feedback loop for Th driven immune pathology. Tolerance induction involves upregulation of transcription factors controlling IL-10 and inhibitory receptors limiting T cell signalling. Results from clinical trials of peptide immunotherapy will be discussed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7209

SATURDAY, 17 JUNE 2017

Reverse translation - learning from clinical trials in SLE, Sjögren’s and APS

LEARNING FROM CLINICAL TRIALS IN SYSTEMIC LUPUS ERYTHEMATOSUS

D.A. Isenberg, University College London/University College Hospital London, London, United Kingdom

An enormous sense of frustration has surrounded the results of clinical trials in patients with systemic lupus erythematosus (SLE). A steady stream of trials involving those studying the effects of Epratuzumab, Abatacept, Rituximab, Tabalumab and Silfalimumab have failed to meet their endpoints. Even though Benlysta (which blocks the B-cell activating factor BAFF) did meet its endpoints, it only demonstrated a difference of around 10% between the Benlysta-treated and placebo-treated arms in trials involving over 800 patients.

However, there are some bright spots on the horizon. Trials comparing the use of interferon-alpha with other classic immunosuppressive drugs clearly showed it to be as good as Cyclophosphamide in getting patients into renal remission and demonstrated its superiority in maintaining that remission compared to Azathioprine(1). The use of Atacicept which blocks two B-cell activating factors has shown some extremely promising results(2) as have trials of both Rontalizumab and Anifrolumab(3) (which block interleukin-alpha).

Some key messages learnt from the running of the lupus trials include the importance of minimising the concomitant steroids and immunosuppression; ensuring the quality of those assessors participating in the clinical trials and the utility of employing an independent peer-review panel to monitor data as it is collected from the participating centres during the course of the trial. It is also evident that selecting patients who are more serologically active is likely to be of benefit both in clinical trials and in the clinic. However, we still need better biomarkers to help guide us; the identification of individuals expressing a high interferon alpha signature (and who thus might better benefit from an interferon alpha blocker) is one such example.

It remains ironic that Rituximab, the most widely used monoclonal antibody in SLE, failed its endpoint in two clinical trials. However, detailed analyses of data from those trials have shown some encouraging trends including falls in DNA abnormalities and improvement in some clinical parameters.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7196

LESSONS FROM APS TRIALS

M. Khamashta, 1, 2, 3 Rheumatology Dept, Dubai Hospital, Dubai, United Arab Emirates; 4 Lupus Research Unit, St Thomas Hospital, London, United Kingdom

Prevention of thrombosis in patients with APS remains a vexing clinical problem. In patients with a history of thrombosis, there is considerable risk of recurrence, and long-term anticoagulation treatment with warfarin is effective in most cases. Existing evidence suggest that the use of DOACs for secondary thromboprophylaxis for APS patients with previous VTE is promising. Until new data from ongoing clinical trials are available, there is not enough evidence to consider using DOACs in patients with APS and previous arterial events. The efficacy of heparin and low-dose aspirin in APS patients with previous pregnancy losses is supported by 3 meta-analysis available on the topic. In patients with antiphospho-lipid antibodies but without a previous thrombotic event, most physicians in the field recommend thromboprophylaxis with low-dose aspirin. Given the diversity of clinical presentations and medical specialties involved, it is not surprising that treatment of APS has been subject of intense debate. Due to the difficulty in conducting trials in the setting of a relatively rare condition, well designed multicenter studies (such as registries) using actual classification criteria and standardized tests should be performed in the future to answer all the opened questions regarding management of APS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7248

SATURDAY, 17 JUNE 2017

Genomic imprinting and post-translational modifications

RATIONALIZE TO TARGET IMMUNE MEMORY RESIDING IN INFILLED TISSUES

H.-D. Chang, German Rheumatism Research Center Berlin, Berlin, Germany

T helper (Th) lymphocytes play a major role in the regulation of immune responses and are thought to initiate and drive chronic rheumatoid inflammation. Memory Th lymphocytes persist in the inflamed tissue and are refractory to therapy. Inflammation in Th lymphocytes have undergone molecular adaptations, such as the upregulation of Twist1 and the microRNA miR-148a, which are not found in circulating Th lymphocytes, and support the survival of the Th cells within the inflamed tissue. Within the inflamed tissue, the Th lymphocytes constantly recruit and activate inflammatory cells, such as monocytes/macrophages and granulocytes through the secretion of particular chemokines and interleukins. The monocytes/macrophages in turn can recruit more Th cells into the inflamed tissue. Disrupting this vicious circle by specifically targeting the memory Th cells resident in the inflamed tissue by interfering with their molecular adaptations could be an interesting therapeutic option.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7219

THE ROLE OF POST-TRANSLATIONAL MODIFICATION AND AUTOREACTIVITY

R. Toes, Rheumatology, Leiden University Medical Center, -Leiden, Netherlands

Rheumatoid arthritis (RA) is a prototype autoimmune disease, with the hallmark signs of synovial inflammation and the presence of autoantibodies. Of the different autoantibody systems present in RA, rheumatoid factors (RF) are probably the best studied. Their presence was first detected > 70 years and it was in the late 1950s when it was realized that RF reacted to gamma globulins. Since the discovery of RF several other autoantibody systems have been discovered in RA, many of them directed against post-translationally modified protein antigens. The most prominent example of such autoantibodies are anti-citrullinated protein antibodies (ACPAs), which are directed against a wide array of citrullinated proteins. Now RF and ACPA determination are the two major diagnostic laboratory tests for RA and part of the EULAR and ACR criteria for RA.

In the past few years, it has become clear that the autoantibody response present in RA extends towards several other modified proteins, such as proteins modified by acetylation or carboxylation. As all these auto-antibodies recognize Post-Translationally Modified (PTM) proteins, these antibodies are collectively called Anti-Modified Protein Antibodies (AMPA). In the context of this presentation, I will focus on the auto-antibody response against citrullinated, carbamylated and acetylated proteins.

Carbamylations lead to the formation of homocitrulline. Structurally, homocitrulline greatly resembles citrulline but is one methylene group longer. Citrulline is generated when PAD enzymes modify the amino acid arginine. In contrast, the amino acid homocitrulline is generated by a chemical reaction in which cyanate reacts with the amino acid lysine. Arginine and lysine are located at different positions in the amino acid sequence of proteins, and therefore these modifications occur at different positions in proteins with different flanking amino acids. Intriguingly, although homocitrulline residues can also be recognised by auto-antibodies, these auto-antibodies often do not crossreact with citrulline.

Acetylation is a process where acetyl groups are added to free amines of lysine residues by acetyl transferases. Acetylated lysine does not resemble citrulline but bears similarity to homocitrulline except at the side chain terminal amine, which is replaced by a methyl moiety.

By now it is clear that AMPA consist of different auto-antibody families that are largely distinct, but that they also display a certain degree of cross-reactivity. Therefore, the notion is emerging that, although cross-reactivity exist, different classes of AMPAs are generally seen as distinct auto-antibody families that target different antigens, but intriguingly often co-occur. As the AMPA-responses in RA are often found together, it indicates that –somehow- AMPA-reactivity has a commonality that is currently not understood.

Although, the reason why an immune response starts against PTM proteins is not known, it appears crucial to obtain understanding on the break of tolerance towards PTM proteins as the immune response against these proteins has been intimately implicated in disease-pathogenesis. Understanding the full AMPA response, the triggers that drive AMPA production, their mutual crosstalk and the pathways by which AMPA and/or AMPA-expressing B cells possibly contribute to RA will be important for the development of curative interventions in RA. In the context of this presentation, some of these aspects will be discussed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7219
SP0156 HOW BIG DATA HELP US UNDERSTAND NEW AND OLD THERAPY TARGETS

P.E. Lipsky, Ampel Biosolutions, Charlottesville, United States

Gene expression profiling is a valuable tool to identify the altered cellular state and to meta-analyze expression profiles from multiple gene expression microarrays. In this study, we performed metaexpression analysis of 556 independently conducted microarray expression profiling studies (comprising 1,152 samples), which were deposited in the GEO database (GSE accession number GSE109791). The studies covered a wide range of human tissues and diseases, including cancer, inflammation, and metabolic diseases. We used a custom algorithm to identify differentially expressed genes and to meta-analyze these genes across studies. The algorithm takes into account the statistical significance of the expression changes and the biological relevance of the genes. We identified a set of genes that were consistently upregulated across multiple studies and that were enriched in biological pathways related to inflammation and cancer. These genes include regulators of the immune response, such as interferon genes, and genes involved in metabolic processes, such as adipokine expression. The results of this study suggest that metaexpression analysis can be a powerful tool for identifying new drug targets and for understanding the molecular mechanisms of disease.
**IS DIABETES AN INFLAMMATORY DISEASE AND SHOULD BE TREATED LIKE THAT?**

A. Schaeffer, Department of Internal Medicine-III, Endocrinology and Diabetes, University of Giessen, Germany, Giessen, Germany

It is a well-known clinical observation that inflammatory diseases are accompanied by metabolic implications such as hyperglycemia, insulin resistance and increased fatty acids. On the other hand, metabolic diseases have inflammatory implications. There is a chronic and low-grade state of inflammation in obesity and type 2 diabetes. Physiological insulin resistance during infection or inflammation redistribute glucose and fatty acids to immune cells. On the basis of systemic and adipose tissue inflammation such as MCP-1/LTR-4-driven macrophage infiltration and pro-inflammatory polarization of these cells, this lecture will give a summary of anti-diabetic effects of anti-inflammatory drugs used in rheumatology. What is the evidence from clinical studies using anti-inflammatory approaches to treat patients with type 2 diabetes mellitus? Basically, TNF plays an important role in insulin resistance in rodents. Blocking TNF in rodents reverses obesity-related diabetes. There are no state of the art clinical studies showing convincing evidence of an anti-diabetic potential due to underpowered cohorts and short duration of the studies. Only one single study over 6 months showed a 10% improvement of fasting glucose levels in 40 prediabetic obese patients. Diacerein belongs to the chemical group of anthranoids. Although the mechanism of action is unknown, diacerein decreases the levels of TNF and of IL-1b and has therefore been used in rheumatic diseases. Diacerein has potent effects on insulin secretion and glycemic control with a reduction of HbA1c level by 1.6%. IL-1 receptor antagonists such as anakinra (a recombinant human IL-1 receptor antagonist) have also been studied in diabetes. Anakinra was able to improve glycemia, inflammation and insulin secretion. Two additional studies in patients with impaired glucose tolerance or prediabetes demonstrated positive effects of anakinra on beta cell secretory capacity. Since anakinra requires daily injections and often causes adverse effects at the injection site, humanized antibodies against IL-1b have been developed. Each of these antibodies had beneficial effects in patients with type 2 diabetes. However, studies were either underpowered or showed only little improvements of glycosylated HbA1c levels, probably due to low pre-study levels. Inhibition of the IKK/NFkB pathway might also be of benefit in insulin resistance. Salsalate improves insulin sensitivity, insulin secretion and glycemic control to a moderate extent of 0.4–0.5%. Salsalate also has effects in prediabetic patients and in drug-naive type 2 diabetic patients. There is upcoming evidence of potential beneficial effects of CCR2 antagonism in diabetes.

Obesity causes an increased flux of fatty acids into muscle and liver with an accumulation of DAG in these organs. DAG activates specific isoforms of protein kinases, that is PKC T in muscle and PKC E in the liver. These isoforms cause an inhibitory phosphorylation of IRS-1 and the insulin receptor itself leading to insulin resistance. Weight reduction by diet, physical activity and bariatric surgery remove ectopic fat and are able reverse diabetes. Most interestingly, PKC-isoform specific inhibitors such as FGF-21 might represent new drug targets.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7055

**THE ROLE OF ADIPOSE TISSUE IN OSTEOARTHRITIS**

A. Ioan-Facsinay, Leiden University Medical Center, Leiden, Netherlands

The association between obesity and osteoarthritis (OA) is nowadays well-accepted. This association is present both in weight-bearing and non-weight-bearing joints, indicating that next to local effects, systemic effects associated with obesity could play a role in disease. The relative contribution of local and systemic effects could be different in each joint. In this presentation, I will summarize the current knowledge about the contribution of local and systemic adipose tissues to osteoarthritis in different joints, with emphasis on knee OA. Moreover, obesity-associated changes and their role in OA will be highlighted.

The key messages I would like to convey are:

- Mechanical stress is a major contributor to knee OA
- The infrapatellar fat pad (IFP), an intra-articular adipose tissue in the knee, is distinctly different from other adipose tissues and could play a role in knee OA
- Only few obesity-related features have been described in IFP in OA

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7207

**ADIPOKINES IN THE PATHOPHYSIOLOGY OF CARTILAGE**

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Fat mass dysregulation is a marked characteristic of overweight and obesity. Obesity is, historically, a classic risk factor for osteoarthritis development and progression and shares with osteoarthritis a huge societal impact but also several common biochemical features that are strongly related to the low-grade inflammatory status. Even though OA has been considered during decades a disabling degenerative disease related to mechanical, age and genetic factors with poor inflammatory component, the current consensus is that OA, in particular OA associated with metabolic alterations, is a global muscle-skeletal diseases in which pro-inflammatory and catabolic mediators, most of them produced by a dysregulated visceral or periarticular white adipose tissue (WAT), are at play. The coexistence of obesity and OA is a clinical reality and is changing the traditional view of this degenerative disorder. Thus, chronic low-grade inflammation is a common characteristic shared by both obesity and OA. It has been demonstrated that obesity increases the incidence of OA, particularly in weight-bearing joints such as knees. However, the fact that obese individuals have an increased risk of developing OA in non-weight bearing joints such as hands and wrists suggests that factors produced by WAT play a role in the onset and/or progression of OA. In addition to a growing body of evidence demonstrating that obesity has a direct mechanical effect joint cartilage, recent research shows that pro-inflammatory factors produced by WAT (collectively known as adipokines) promote further inflammation and degradation of cartilage, also influencing the whole joint environment (i.e. synovium, muscle, bone and immune cells). Accumulating evidence shows another potential source of inflammatory adipokines in the joint is the Hoffa infrapatellar fat pad. Adipokines including leptin adiponectin, visfatin and lipocalin 2 have been demonstrated to exhibit a wide spectrum of biological activity including the activation of pro-inflammatory and catabolic pathways mediated by elevated levels of NO, ROS, MMPs and PGE2. The discovery of adipokines has made a major contribution to our understanding of the complex relationship between diabesity and OA, encompassing a variety of factors that include the immune system, metabolism and biomechanics. A critical aspect that must constantly be borne in mind is that diabesity and OA share a low-grade inflammatory state that heavily influences the course of OA progression. Therefore, the prevention and correction of diabesity should be the first line approach for tackling the detrimental effects of weight gain, adiposity and altered metabolic WAT function in OA. The aim of this lecture is to summarize the role of adipokines in bone and cartilage function, as well as in inflammatory and degenerative joint disease. We discuss clinical implications and then survey attempts to exploit this role for therapeutic gain, which holds potential as a novel approach for drug development in bone and joint disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7081

**INTERVENTIONS TO IMPROVE MEDICATION ADHERENCE IN PATIENTS WITH INFLAMMATORY ARTHRITIS**

J.E. Vriezelaar, Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands

Non-adherence to medication in rheumatic diseases is a major concern for patient’s health, because incorrect use can result in less therapeutic benefits of treatment, including more disease activity and increased radiological damage. As a consequence, non-adherence may lead to more disability and lower health-related quality of life. Using Lowe’s taxonomy, the current state of evidence around medication adherence interventions will be presented. Examples of promising intervention strategies will be highlighted.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7199

**T r i a l s and tribulations of medication adherence **

Saturday, 17 June 2017
**BARRIERS AND FACILITATORS TO ADHERENCE TO MEDICATION IN PATIENTS WITH INFAMMATORY ARTHRITIS**

K. Koutsogianni, The Arthritis Foundation of Crete, Heraklion, Crete, Greece

**Background:** Inflammatory arthritis can cause pain, stiffness, joint damage and even disability. From diagnosis and early treatment. The full benefit of several treatments recommended, can be achieved if patients strictly follow drug regimens. However, rates of adherence to prescribed medications in patients with inflammatory arthritis seem to be suboptimal.

**Objectives:** To identify the barriers and facilitators for adherence to medication in patients with inflammatory arthritis seem to be suboptimal. However, rates of adherence to prescribed medications in patients with inflammatory arthritis tend to be quite low and range from 30–80%.

**Methods:** A survey conducted among patients of the Arthritis Foundation of Crete aiming to assess the degree of their adherence to MTX therapy. A survey conducted among patients with inflammatory arthritis. Experiencing beneficial effects of the medications and being able to maintain autonomy and social participation, receiving clear and understandable information about the treatment options, having support from family and friends, having a good relationship with the treating physician and being involved in shared decision-making process are the keys for leading the patients to better adherence.

**Conclusion:** A good patient-health professional relationship, knowledge about the treatment options, having support from family and friends, having a good relationship with the treating physician and being involved in shared decision-making process are the keys for leading the patients to better adherence.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7133

**CAN MUSCULOSKELETAL ULTRASOUND INFORM HEALTH BELIEFS AND PLAY A ROLE FOR MEDICATION ADHERENCE?**

K. Kumar, University of Manchester, Manchester, United Kingdom

Rheumatoid Arthritis (RA) is a condition with no cure and can cause disability. RA affects nearly 1 in 100 adults. Early disease is characterised by pain and other features of inflammation, such as heat, swelling of joints, and loss of function. RA is associated with increased costs of co-morbid conditions (such as cardiovascular (CVD)) associated with RA.

Medication can ease symptoms and limit disease progression in RA. Despite this, non-adherence to medication is common in RA. In the UK, we found that patients’ joint swelling via musculoskeletal ultrasound scan as an educational tool helped to increase beliefs about the necessity of treatment.

Our study provided a deeper understanding of adherence to disease modifying anti-rheumatic drugs (DMARDs) in patients with RA. Improving adherence is likely to be facilitated by incorporating visual representations of the disease process and better explanations from the consequences of poorly controlled RA into the consultation. This session will uncover some suggestions around the use of musculoskeletal ultrasound in improving adherence to DMARDs.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7085
HORIZON 2020: OPPORTUNITIES FOR MEDICAL RESEARCH AND INNOVATION

S. Hogan, DG Research, Directorate Health, European Commission, Brussels, Belgium

Horizon 2020 is the largest EU Research and Innovation programme ever with nearly €80 billion of funding available over 7 years (2014 to 2020). It is an opportunity for supporting excellence and collaboration in research, and on a scale and scope that is seldom feasible at global level. Horizon 2020 contributes to the Innovation Union, a Europe 2020 flagship initiative aimed at securing Europe’s global competitiveness. By coupling research and innovation, Horizon 2020 is helping to achieve this with its emphasis on excellent science, industrial leadership and tackling societal challenges. The goal is to ensure Europe produces world-class science, removes barriers to innovation and makes it easier for the public and private sectors to work together in delivering innovation. This is seen as a means to drive economic growth and create jobs.

SATURDAY, 17 JUNE 2017
EULAR Projects - challenging projects in education and training

SP0168 THEORY OF POSTER DESIGN AND PRESENTATION

M. Boers, Epidemiology & Biostatistics; Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands

This lecture introduces basic elements of poster design, and is followed after the session by a special poster tour devoted to design. It strongly links to the concepts discussed in my workshop on data visualization. To design an effective poster, its message and the intended audience must be clear. Effective posters stand out because they convey their main message almost instantly, and then seduce participants to stay longer and learn more. Much more than oral presentations, posters are about selling your work in competition with all those other people presenting in your session. In a good poster, all elements work together like a symphony orchestra: Title, headings, text, tables, graphs, format, colors, layout, handouts, gimmicks, and... you! For the design process, you need a good plan (including timelines!), good tools (templates, software!) and a ruthless editor. Editing is about throwing out more and more stuff, until finally you reach the point where throwing out more destroys understanding. So the “orchestra” has single instrumentation, and is wonderfully transparent.

Posters are not "comprehensive"! All the details you love can go into a specially designed handout (NOT an exact replica of your poster). Your role as presenter is special: you must be visible but unobtrusive, and flexible to accommodate different viewer styles, and have different modes of presentation (eg, walkthrough, answer questions, respond to critique). Also make sure your contact details are visible and correct (if no handout, be sure to have business cards). If you are playful you can use gimmicks to increase your visibility: match your clothes to your color scheme, make something in real 3D on your poster, use sound, etc. But don’t overdo it: this is just the icing on the cake: this is a science, not a commercial exhibit.

When we go to assess posters in the upcoming poster tour, we will be looking for the following elements:
1. Overall message clear?
2. Text quality: brevity, clarity
3. Table quality: clear vision, clear understanding
4. Graph quality: clear vision, clear understanding
5. Design elements: layout, choice of font, color
6. Handout: not a replica, elements 1–5 repeated
7. Presenter: style, contact details

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7225

SATURDAY, 17 JUNE 2017
EULAR SCHOOL OF RHEUMATOLOGY, A CHALLENGING EDUCATIONAL EULAR PROJECT. WHERE ARE WE NOW?

J.W. Bijlsma, Rheumatology & Clinical Immunology, UMCU, Utrecht, UTRECHT, Netherlands

In the last decade EULAR has further developed its educational portfolio. Apart from very educational tracks in the EULAR Congress, EULAR offers:
• on-line courses (Rheumatology, Connective Tissue Diseases, Scleroderma, Paediatrics, Ultrasound, Health Professionals), that are being followed by thousands of students all over the world
• text-books, based on the on-line courses
• live courses, such as the Postgraduate Course, Ultrasound courses, capillaroscopy, epidemiology, immunology, teach the teachers
• exchange programs, for trainees, scientists, health professionals and patients
• on-line image library, on-line outcome registry
• learning DVDs for medical students
• scientific endorsement of other courses

To bring all these offerings under one umbrella, EULAR decided to found the School of Rheumatology. But the School is doing substantially more: we identified 7 areas (classrooms) where we bring enthusiastic and involved people together to evaluate the present needs in those areas and to prioritize new educational activities for those unmet needs. The following classrooms are actively developing new products:
Classroom medical students: formulating standard curriculum for musculoskeletal diseases arbs and providing video-matials to support teachers and students.
Classroom trainees in rheumatology: start of a journal club, evaluating possibilities to install a European (EULAR) examination to become a rheumatologist, imaging on-line course.
Classroom teachers: course on assessment questions was already held, a teach the teachers event is planned.
Classroom rheumatologists: development of a pocket primer on rheumatic diseases, to be used as an app.
Classroom scientist: preparing a possible on-line course on epidemiology and clinical (trial) research, evaluating possible webinars for basic science methodology.
Classroom health professionals: preparing an accreditation system for health professionals; expanding on-line courses.
Classroom patients: implementing and distributing lays versions of recommenda-
tion; development of a patient partner program in research; webinars on actual items in the form of questions and answers (eg biosimilars).

Some of the items on this agenda can be organised within one year, for some others many years are foreseen; it will be a dynamic process. Ideas and support are very welcome via the EULAR Standing Committee on Education, or directly to the EULAR office, attention of the education program manager.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7108

SP0170 ASSESSING RHEUMATOLOGY SKILLS

C. Haines, The Medical School, The University of Nottingham, Nottingham, United Kingdom

Medical Education is making great advances in understanding the power of assessment. Modern learners seek frequent, faster feedback on their learning to study more effectively. It is now common for examinations to be statistically monitored in order to show that acceptable levels of reliability have been reached. But, a test is only as good as its questions. Clinicians are not often trained in how to create valid and reliable test questions. This session will describe some basic principles for creating valid and reliable tests for the knowledge, skills and attitudes which are required by practising rheumatologists. The speaker is currently the Eular Educationalist, who advises Eular on how to continually enhance assessment processes for the online courses and the new trainee examination.

As a result of the session participants will be better able to:
• Describe reliability fairly validly and apply Eular assessments
• Describe the differences between formative assessment for learning and summative assessment for grading
• Identify improvements which they could make to test questions
• Identify improvements which they could make to tests

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7202

SP0171 HOW TO SELECT THE MOST APPROPRIATE CAPILLAROSCOPIC DEVICE: PROS AND CONS

F. Iaconelli, Dept. of Clinical Sciences and Community Health, Università degli Studi di Milano, ASST Gaetano Pini, MILANO, Italy

Nailfold capillaroscopy is a simple noninvasive imaging technique mainly used to observe capillaries within the first few micrometers from the skin surface. After application of a drop of immersion oil, capillaries can be observed with a magnification lens because they run parallel to the epidermis at the nail bed area. The study of the morphology of superficial nailfold capillaries provides clinically
relevant information in the management of patients with scleroderma-spectrum diseases. Recently, an international survey on non-invasive techniques to assess the microcirculation performed under the aegis of members of the European League Against Rheumatism (EULAR) Study Group on Microcirculation in Rheumatic diseases (SG_MC/RD) showed that nailfold videocapillaroscopy was the one most used technique in both clinical and research settings by adult physicians and paediatric rheumatologists to assess patients with Raynaud’s phenomenon. A number of different instruments are available to perform the exam. They have different characteristics in terms of their cost, quality of images, magnifications, training period, portability, software for image analysis and storage. Some of these instruments can be used both in clinical and research settings such as the stereomicroscope and the videocapillaroscope. The stereomicroscope allows the widefield visualization of the nailfold with low magnifications, the training is relatively short, but the examination is difficult to perform in patients with digital flexion contractures. There appears to be consensus regarding the use of videocapillaroscopy that allows a detailed visualisation of capillary morphology using higher magnifications (100–300x). Contact probe with polarized light microscopy permits easier observation of the skin surface, and the training period is briefer. Specific softwares are available for images analysis, storage, and complete medical reports (text + images) can be produced. By contrast, in a clinical setting, nailfold capillaries can generally be visualised using more simple but also efficient tools such as a dermatoscope, USB microscope, ophtamloscope or smartphone device. The quality of images can be quite good, although the lower magnification means that some details are unlikely to be seen, and they often lack the possibility of image storage and measurement. In particular, the dermatoscope with magnification of the order of x10 is a small, inexpensive and easily portable piece of equipment that has been suggested to be comparable to videocapillaroscopy in routine clinical practice.

Disclosure of Interest: None declared


SP0172 MANAGING VOLUNTEERS- A UK PERSPECTIVE

C.B. Jacklin. External Affairs, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom

Volunteers are an integral part of any charity and it would be impossible to run a charitable organisation without the support of volunteers. Like paid staff they need to be trained, nurtured and rewarded but as volunteers they need to be handled in a very different way to employees. People who volunteer do so for many different reasons and not always perhaps for the right reasons so managing volunteers takes great skill and diplomacy. My talk will cover how to value volunteers, lessons we have learned from observation of the skin surface, and the training period is briefer. Specific softwares are available for images analysis, storage, and complete medical reports (text + images) can be produced. By contrast, in a clinical setting, nailfold capillaries can generally be visualised using more simple but also efficient tools such as a dermatoscope, USB microscope, ophtamloscope or smartphone device. The quality of images can be quite good, although the lower magnification means that some details are unlikely to be seen, and they often lack the possibility of image storage and measurement. In particular, the dermatoscope with magnification of the order of x10 is a small, inexpensive and easily portable piece of equipment that has been suggested to be comparable to videocapillaroscopy in routine clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7227

SP0173 THE CHALLENGES OF A SMALL ORGANIZATION

M. Kosanovic, Association of Rheumatic Diseases Patients of the Republic of Serbia (ORS), Belgrade, Serbia

When a group of citizens establishes a non-profit and a non-government organisation in our country, those volunteers are carried by great enthusiasm. At the beginning when founding an NGO the main problems are lack of experience and financial resources. Those deficiencies can be overcome by some other qualities such as the personal competencies of volunteers. As NGOs are seen by the public rather critically in our country, our organization had to face several additional challenges. In my presentation I will illustrate the following aspects: the non-attractiveness of NGOs for volunteers, the lack of awareness how volunteering is important for a society, the lack of knowledge how to attract volunteers and how to manage them, the lack of knowledge how to define the volunteers’ positions and how to monitor their work, the lack of their systemic, continuing education and the lack of rewards, recognition and appreciation to acknowledge the most dedicated volunteers.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7187

SP0174 WAYS OF SUPPORTING VOLUNTEERS

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The promotion of volunteer workers is an indispensable part of the human resources policy of self-help organizations and requires specific concepts. Using the example of the rheumatism league Baden-Württemberg -an organization with 65,000 members, 3,000 volunteers and 10 fulltime employees- there will be shown best-practice examples. A successful concept covers the areas of recruitment, training, support and integration.

1. The support of volunteers should include four key areas:
   1. Transfer of knowledge and professional competences
   2. Individual support for personal development
   3. Promotion of teamwork and social skills
   4. Framework conditions (insurance cover, reimbursement of expenses)

The implementation of these requirements should be carried out by specifically trained volunteer managers on the basis of a strong and motivating personal relationship.

This strategy can be seen as a precondition for establishing a long-term relationship of the volunteer with the association, a successful local work, satisfied members and volunteers who perceive their work as satisfying and fulfilling.

Slik Szymank
Deputy managing director
Rheumatism League Baden-Württemberg e.V., Germany

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7084

SATURDAY, 17 JUNE 2017

WIN & HOT session...

SP0175 WHAT IS NEW IN JUVENILE IDIOPATHIC ARTHRITIS

N.M. Wulffraat. Dept. of Paediatrics, University Medical Center Utrecht, Dept. Pediatric Rheumatology, Utrecht, Netherlands

Juvenile Idiopathic Arthritis comprises 7 subcategories. As the insights in pathogenesis progress so does the need for reclassification that is based more on biology than on clinical phenotypes. After a series of clinical trials for new biologicals, now trials are started that test specific treatment strategies such as treat to target an d step down studies. Especially rapid induction of remission is currently a major aim, followed by biomarked guided tapering of medication.

The expanding number of potential biomarkers forms the basis for the creation of personalized medicine, a strategy aimed at providing individualized medication choices. Since most pediatric rheumatic conditions are rare, international collaboration is vital. The recently created European Reference Networks (ERN) will prove instrumental here.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7281

SATURDAY, 17 JUNE 2017

Systemic sclerosis

SP0176 TARGETING VASCULOPATHY FROM THE BEGINNING

M. Cutolo on behalf of EULAR Study Group on Microcirculation in Rheumatic Diseases, Internal Medicine, Research Lab Division Rheumatology University of Genova, genova, Italy

In systemic sclerosis (SSc), the natural history of microvascular damage progresses from capillary dilation to capillary loss and reactive angiogenesis, as detectable by nailfold videocapillaroscopy (NVC) [1]. The process is systemic and determines multiple clinical manifestations, from the early appearance of Raynaud’s phenomenon, trough formation of digital ulcers (DUs), until severe organ involvement, impairing patient’s quality of life or leading to main death causes, including interstitial lung disease and pulmonary arterial hypertension (PAH), hearth involvement, sclerodema renal crisis [2,3]. Although microvascular and macrovascular abnormalities frequently coexist in disease such as diabetes mellitus and other vascular diseases, the possible association between microvascular failure and macrovasculopathy in SSc patients has not been deeply investigated. However, significant correlations seem to exist between increased Inntima-Media Thickness (IMT) of periferic small-caliber arteries (microcirculation) and altered peripheral BF (LASCA) at the level of hand microvessels (microcirculation) in SSc patients.

Silin addition, significant capillary loss, observed at NVC, is peculiar of the “Late” scleroderma pattern of microangiopathy and is mainly preceded by progressive capillary enlargement, microhemorrhages and their collapse, leading to presence of large avascular areas [4]. The importance of capillary loss was already demonstrated by a simple and reliable prognostic index, capable to predict digital trophic lesion development in SSc-related microvascular disease, when evaluated as part of the semi-quantitative NVC scoring [5]. Moreover, microvascular function and its alterations in SSc, can be reliably assessed by laser-doppler flowmetry (LDF) and laser speckled contrast analysis (LASCA), evaluating blood perfusion at fingertips or at larger body areas [6–9]. The most frequently used drugs for treatment of complications in SSc patients, approved with evidence grade la, are vasoactive drugs. In particular, for severe...
NEW APPROACHES BY TARGETING SOLUBLE MEDIATORS

GUT DYSBIOSIS AND OTHER CHALLENGES PRECIPITATE success and interpretation of studies targeting soluble mediators to define target

References:

Disclosure of Interest: M. Cutolo Grant/research support from: actelion, italfarma,

SP0181  FAILURE OF NATURAL REGULATORY AUTOANTIBODY NETWORK AS CAUSE OF AUTOIMMUNE
O.C. Marques on behalf of Lubeck University. Prof. Riemekasten. Reumathology, University of Lubeck, 23562 Lubeck, Germany

The role of autoantibodies in normal physiology is under debate. In investigating autoantibody (aab) concentrations against G protein-coupled receptors (GPCR) in different autoimmune diseases, we found both increased and decreased aab concentrations, which suggests physiological anti-GPCR aab levels may be dysregulated in autoimmune diseases. During our analysis of healthy donor antibodies to 16 GPCR and 15 growth factors and related signaling molecules, we discovered several clusters of correlations in these antibody concentrations. Possible functional interactions of these 31 autoantibody target molecules were studied by STRING, DAVID, and enriched Gene Ontology analyses. Through these analyses, a network of GPCR, growth factors, and signaling molecules with endothelin receptor type A (ETAR) in the center was revealed. Migration and adhesion assays were suggested to be the most significant functions regulated by the antibody network. Accordingly, IgG from healthy donors induced both IL-8 expression by peripheral blood mononuclear cells (PBMCs) as well as migration of neutrophils and tumor cells, which was specifically diminished by the ETAR antibody. It thus seems that a set of factors can influence the development of the antibody network. Accordingly, IgG from healthy donors induced both IL-8 expression by peripheral blood mononuclear cells (PBMCs) as well as migration of neutrophils and tumor cells, which was specifically diminished by the ETAR antibody. It thus seems that a set of factors can influence the development of the antibody network. This notion is supported by the observation that additional F(ab)-glosses are not found on ACAP-igG. How F(ab)-glosses facilitate the emergence and/or expansion of autoimmune B cells in this context, however, remains unclear. Using recently developed technology to identify and isolate citrullinated antigen-specific B cells from patients, we can now address this question by studying the frequency and localization of F(ab)-glosses in the antibody repertoire and by studying the phenotype and functional characteristics of ACAP-expressing B cells. Together with our investigations on the modulation of ACAP F(ab)-glosses, these studies provide a deeper understanding of mechanisms that allow the development of autoimmunity as such, and of the mechanisms that underlie the progression from systemic autoimmunity towards overt autoimmune disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2218

SP0182  ALTERATIONS IN THE ANTIBODY REPERTOIRE AND SUGAR MODULATION AS CAUSE FOR AUTOIMMUNITY
H.U. Scherer, Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

Many autoimmune diseases are hallmarked by the presence of auto-reactive B cells that can develop into antibody-secreting plasma cells. In most cases, the secreted autoantibodies have extensively been studied in their role as disease-associated biomarkers, and for some, specific pathogenic effector functions have been demonstrated supporting the use of interventions that target the plasma cell compartment. In other cases such as rheumatoid arthritis (RA), however, the pathogenicity of specific autoantibodies is less clear, and the therapeutic efficacy of B cell depleting therapy that spares the plasma cell compartment indicates that auto-reactive B cells themselves can have pathogenic effector functions that contribute to disease. In this context, it is of great interest to understand the mechanisms that allow auto-reactive B cells to emerge from the naive repertoire, a process that marks the onset of systemic autoimmunity and frequently precedes the clinical onset of disease. RA is characterized by a remarkable appearance of autoantibodies that target post-translational modifications of proteins, of which anti-citrullinated protein antibodies (ACPA) display the highest specificity for disease. In addition, ACPA are expressed by both plasma cells and plasma cell-like dendritic cells, which can evolve and contribute to the development of such diseases. Furthermore, therapeutic approaches aiming to overcome these Treg cell defects and to restore Treg cell activity in the patients will be discussed.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2218

SP0183  FAILURE OF TREG CONTROL TO UNDERSTAND AUTOIMMUNITY
J.Y. Humrich, Department of Rheumatology and Clinical Immunology, University Hospital Schleswig-Holstein, Campus Luebeck, Luebeck, Germany

Regulatory T cells (Treg) expressing the transcription factor FoxP3 are crucial for the maintenance of immunological tolerance to self and thus for the control of autoimmunity. There is strong evidence that numeric or functional defects in Treg cell biology are involved in the pathogenesis of particular autoimmune diseases. Here we will focus on the fundamental role of Treg cells in diverse autoimmune and rheumatic diseases and will explain how a failure of the Treg cell system can evolve and contribute to the development of such diseases. Furthermore, therapeutic approaches aiming to overcome these Treg cell defects and to restore Treg cell activity in the patients will be discussed.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7179

SP0184  ROLE OF MICROENVIRONMENT AND ENDOGENOUS PATHWAYS TO BREAK TOLERANCE
P. Lampecht, Universität Zu Lübeck, Lübeck, Germany

Break of tolerance driving autoimmune disease is initiated by a combination of predisposing genetic and environmental factors resulting in self-perpetuating chronic inflammation and tissue damage. Effector molecules and cells targeting tissues housing the inciting autoantigen(s) maintain tissue damage and the autoimmune response. Granulomatosis with polyangiitis (GPA, formerly Wegener’s granulomatosis) is a prototypic autoimmune disease characterized by extravascularizing granulomatous inflammation and specific autoantibodies to 16 GPCR and 15 growth factors and related signaling molecules, which is mainly induced by T cells that provide help to B cells. As ~90% of all ACPA-IgG molecules carry such F(ab)-linked N-glycans, and as protective antibodies in the same individuals and many autoantibodies in other diseases do not show this feature, it is conceivable that the contribution of F(ab)-glosses by ACAP-IgG is a T cell –mediated process that provides a selective advantage to ACAP-expressing B cells. This notion is supported by the observation that additional F(ab)-glosses are not found on ACAP-IgG. How F(ab)-glosses facilitate the emergence and/or expansion of auto-reactive B cells in this context, however, remains unclear. Using recently developed technology to identify and isolate citrullinated antigen-specific B cells from patients, we can now address this question by studying the frequency and localization of N-glycosylation sites in the antibody repertoire and by studying the phenotype and functional characteristics of ACAP-expressing B cells. Together with our investigations on the modulation of ACAP F(ab)-glosses, these studies provide a deeper understanding of mechanisms that allow the development of autoimmunity as such, and of the mechanisms that underlie the progression from systemic autoimmunity towards overt autoimmune disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7306

This clinical form of OA may be associated with a so called “erosive” radiographic aspect marked by subchondral erosions of the finger joints and ankylosis. Many mediators of inflammation have been involved in the pathogenesis of osteoarthritis such as prostaglandin E2, free radicals and main cytokines (IL1B, IL6, and TNFa). Using Doppler power ultrasonography and magnetic resonance imaging, it has been shown that synovial fluid is frequently associated with HOA and correlates with pain and with disease progression. Taking all these considerations together, it appears logical to target synovitis in HOA, especially with an erosive form. Because erosive hand OA is a polyarticular disease, the treatment is more systemic than local.

Local or oral NSAIDS are out of scope because this presentation focuses on systemic than local.

HOA, especially with an erosive form.

Using anti-IL1B strategy, a decrease in pain has been observed in 3 patients subgroup of patient with clinically inflamed IP joints.

In the long term trial published by Verbruggen G, the incidence of new erosive lesions was decreased in Adalimumab group compared to placebo, only in a subgroup of patient with clinically inflamed IP joints.

Using anti-IL1B, there is still a decrease in pain has been observed in 3 patients subgroup of patient with clinically inflamed IP joints.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7304
DIVERGENCES BETWEEN OBJECTIVE AND SELF-REPORTED PHYSICAL FUNCTION IN FIBROMYALGIA

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In fibromyalgia (FM), intolerance to physical activity, with increased pain and experience of early muscle fatigue, is a predominant feature. Furthermore, shorter endurance times and higher perceived effort during physical activity compared with healthy controls are characteristic. However, there are discrepancies between physical functioning as perceived by the patients and as measured objectively or during performance tests. For example, in 840 FM patients and 122 healthy controls, we found reduced muscle strength in approximately 50% of the FM patients. However, the patients with subnormal muscle strength did not self-report worse symptoms or more physical disability than those with normal muscle strength. Much like central sensitization of pain, it has been suggested that impaired sensory-motor interaction is present in FM, which may be a cause for observed discrepancies between perceived and objective signs of muscle fatigue. That is, the sensory inputs to the central nervous system during a physical activity are over-interpreted, leading to amplified sensations of fatigue and discomfort normally associated with the confounding muscle work. To illuminate this we conducted a controlled experiment, in which FM patients and health controls completed a muscle exhaustion test, while objective measures of muscle fatigue were collected by electromyography in parallel with reporting of perceived muscle fatigue. The results suggest that among FM patients, central nervous system processes normally associated with muscular fatigue were present, yet without any evidence of peripheral muscle fatigue. The study supports a hypothesis about abnormal sensory-motor interaction among FM patients that can explain the discrepancies between perceived and observed physical disability in FM.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7186

COGNITIVE FOG: SUBJECTIVE AND OBJECTIVE UNDERSTANDINGS OF THE SYMPTOM OF DYSCOGNITION

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Dyscognition refers to the complaint that a person's ability to perform thinking tasks is impaired. This complaint is colloquially known as "brain fog". It is a major symptom of a variety of disorders and associated with considerable work and social disability for those experiencing it. However, attempts to demonstrate objective cognitive impairment in persons reporting "brain fog" have not been straightforward. In this lecture, the symptom of cognitive dysfunction will be described from the patient's point of view, using fibromyalgia as a disease model. The cognitive tests used to determine objective alterations in cognitive ability will be reviewed, the amount of objective impairment demonstrated in fibromyalgia will be placed into clinical context, and the "disconnect" between what the experience of dyscognition is and the cognitive content measured by modern testing will be discussed. The poor relationship between the magnitude of subjective dyscognition and objective cognitive performance will be examined, and evidence gleaned from neurological imaging studies. In conclusion, the experience of cognitive fog is not well captured by current testing paradigms. Subjective complaint is a poor predictor of objective cognitive performance. The neuronal mechanisms responsible for the experience of cognitive fog may be separate from those required to perform cognitive tasks.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7148

ASSOCIATIONS OF PAIN-RELATED COGNITIONS WITH THE DISCORDANCE BETWEEN SUBJECTIVE AND OBJECTIVE PHYSICAL FUNCTION IN FIBROMYALGIA: THE AL-ÁNDALUS PROJECT

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Background: In fibromyalgia, there is a disagreement between patients' self-reports and performances; i.e., subjective and objective status, respectively.

Objectives: First, to test the discordance between subjective and objective measures of physical function. Second, to determine whether catastrophizing and self-efficacy are independently associated with this discordance.

Methods: Four hundred and five fibromyalgia females and 193 age-matched female controls. Participants filled out the Pain Catastrophizing Scale, Chronic Pain Self-efficacy Scale, and physical functioning subscales of the Revised Fibromyalgia Impact Questionnaire (FIQ-R) and Short Form-36 (SF-36) health survey. Objective physical function was measured with a battery of performance-based tasks (e.g., 6-min walk-test). Subjective and objective physical function were expressed as deviation from the general population in standard deviation (SD) units using means and SD of the control group.

Results: Fibromyalgia patients reported a worse physical function than performed (p<.001). We found a consistent association of higher catastrophizing with higher discordance between subjective and objective physical function. A significant association of higher self-efficacy with lower discordance was only found when subjective physical function was reported on the SF-36 but not on the FIQR.

Conclusion: Although both are markedly impaired, subjective physical function is more impaired than objective physical function in fibromyalgia. Catastrophizing is associated with this discordance. In rehabilitation settings, physical function of fibromyalgia females should be evaluated by both subjective and objective assessments to fully understand their physical function.

Disclosure of Interest: This work was supported by the Spanish Ministry of Economy and Competitiveness [I+D+i DEP2010–15639, I+D+i DEP2013–40908-R, and BES-2014–067612].

DOI: 10.1136/annrheumdis-2017-eular.7185

THE DRUGS DON'T WORK

L. Piggott, Fibromyalgia, Nantwich, United Kingdom

This presentation will depict the journey of Louise, a previous school teacher and a single mother of two, living with Fibromyalgia as well as multiple other diagnoses. Louise will discuss her feelings around being diagnosed with Fibromyalgia, how this was communicated to her and what this meant for her career and family life. Following this, Louise will share her journey through the secondary care as a Fibromyalgia patient, and her own search for answers and cure to Fibromyalgia in an attempt to salvage her life and independence, prior to accepting that this is a long-term condition which will require self-management and perseverance. In addition, Louise will share her thoughts on pain and fatigue in Fibromyalgia, and how the “drugs don’t work”.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7191

SATURDAY, 17 JUNE 2017

Interactive cases from the HOT and WIN sessions —

HOT SESSION: INTERACTIVE CLINICAL ASPECTS AND CASES ON VASCULITIS TREATMENT

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The systemic vasculitides are characterized by inflammation of blood vessels resulting in end organ, or tissue damage or necrosis. They are defined by the Chapel Hill nomenclature according to the calibre of the predominantly affected vessels. Other forms of vasculitis not defined by a predominant vessel size are also recognized (e.g., Behcet's syndrome). Large vessel vasculitides include giant cell arteritis and Takayasu arteritis; medium vessel vasculitides includes Kawasaki disease and PAN; small vessel vasculitides are divided into: immune complex small vessel vasculitis and anti-neutrophil cytoplasm antibody (ANCA) - associated vasculitis (AAV). The immune complex group, with moderate to marked vessel wall deposits of immunoglobulin and/or complement, is represented by anti-glomerular basement membrane disease, cryoglobulinaemic vasculitis, hypocomplementaemic urticarial vasculitis (anti-C1q vasculitis) and IgA vasculitis (Henoch–Schönlein). By contrast, AAV has few or no immune deposits associated with (in most cases) the presence of ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA). Depending on their clinical presentation and ANCA specificity, AAV is divided into three major variants: granulomatosis with polyangiitis (GPA) (Wegener’s granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss syndrome). In some cases, vasculitis is relatively trivial and may lead to minor, often asymptomatic clinical features such as splinter haemorrhages. However, in severe forms of ANCA associated vasculitis, the consequences of rapid onset of ischaemia and occlusion of blood vessels can lead to organ failure and death. The multisystem involvement in most forms of vasculitis can be a real challenge. Patients may present to different specialists resulting in diagnostic delay. The investigation of patients with suspected vasculitis should follow on from a careful history and examination to determine the likely diagnosis. The differential diagnosis is very wide. It is important to correctly identify patients with vasculitis as early as possible, but it is also important to rule out more common causes. In acutely unwell patients, the differential diagnosis depends on the combination of clinical features. Vasculitides tend to involve multiple organ systems. In fact, the more organ systems affected, the more likely it is that the patient has vasculitis.
We will review some examples of cases with what might appear to be unusual clinical features which form a more consistent pattern. Initial treatment is generally straightforward, but the evaluation of patients during the course of their illness is often difficult due to variation in disease, as well as drug toxicity, damage and co-morbidity. We will discuss examples of patients where relapse is suspected but not always confirmed.

In this overview we will summarise current practice in vasculitis, illustrated by cases to provide a clinical context in which to interpret and implement evidence based management of vasculitis.

Disclosure of Interest: R. Luqmani Grant/research support from: Arthritis Research UK, GSK, MRC, UCSF-CF, Canadian Institutes of Health Research.
The Vasculitis Foundation., Consultant for: GSK, Medpace, MedImmune, Roche

DOI: 10.1136/annrheumdis-2017-eular.7152

SATURDAY, 17 JUNE 2017
Suffering in silence. Optimizing the management of psychological well-being for people with RMDs

SP0190
FACTS AND FIGURES: HOW MENTAL HEALTH CARE ADDRESSES THE PSYCHOLOGICAL BURDEN OF RMD’S IN EUROPE
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University of the West of England, BRISTOL, Bristol, United Kingdom

It is recognised that patients have to make behaviour changes and psychological adjustments to address the impact of inflammatory arthritis on their lives. Challenges include fluctuating pain, fatigue and flares of disease activity, and emotional consequences. Meeting these challenges effectively requires patients to engage in medical management, role management, and emotional management.

For some patients this can be a struggle, and the rheumatology team can be a valuable source of support.

This session will examine patient perspectives on the psychological impact of inflammatory arthritis and the role of the rheumatology team in meeting the associated support needs. It will look at the relationship between psychological distress, well-being and self-management, and will highlight patients’ views on the characteristics of patient-centred, collaborative care. It will look at factors that influence psychological impact, adaptation and self-management; present data from patients on ways in which well-being and self-management can be enhanced or diminished through clinical interactions with the rheumatology team; and will consider the implications for clinical practice, including the training needs of the rheumatology team.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7121

SATURDAY, 17 JUNE 2017
Showcasing the EULAR Online Course for Health Professionals

SP0191
PRINCIPLES OF NON-PHARMACOLOGICAL MANAGEMENT OF REGIONAL MUSCULOSKELETAL DISORDERS
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The two main components of non-pharmacological management of regional musculoskeletal disorders are a thorough assessment followed by rehabilitative care.

Assessment includes a careful history, level of daily activities and participation, including occupation, rehabilitative care to date, possible presence of psychosocial problems, sports and hobbies. Special attention must be given to patient’s expectations and personal objectives. A systemic enquiry is also important, as regional pain may be due to an underlying medical condition. Clinical examination consists of observation of posture, mobility, and whether there is evidence of wasting, asymmetry, deformity, or muscle imbalances. Palpation of soft tissue and bony structures follows to identify areas of tenderness, lumps, myofascial trigger points, tendon crepitus. Assessment of active and passive movements in all planes follows looking for specific restrictions. Examination is not restricted to the site of pain; as for example upper limb pain syndromes may be referred from the neck. In some patients further medical investigation is necessary when a thorough history, examination, and ultrasonography do not provide sufficient diagnostic information. This may involve blood tests, plain radiography, CT or MRI.

Rehabilitative care is a customized process, which aims to achieve an optimal functional outcome and participation in all aspects of life. Active rehabilitation and a gradual return to normal activities are key points in successful treatment of regional pain syndromes. Progressive exercise is a fundamental part of the treatment of most regional musculoskeletal complaints. The goal is to work towards full, specific, pain free functional activity. In myofascial pain syndromes and non specific arm pain in particular, there is a need for review of postural issues and ergonomics and building aerobic fitness. In addition, providing information to the patient about the nature of the condition, beneficial and negative habits and activities, self help exercises, expected response to treatment and outcome should all be part of the approach to these patients. Psychological interventions may complement rehabilitative care. Cognitive and behavioral methods focus on changing the patient’s interpretation and reaction to pain. The main assumption of a behavioral approach is that pain and pain disability are influenced by somatic pathology and also by psychosocial factors (e.g. patient’s attitudes and beliefs, psychological distress and illness behavior). Consequently, the behavioral treatment of regional musculoskeletal disorders does not primarily focus on removing an underlying organic pathology, but on the reduction of disability through modification of environmental contingencies and cognitive processes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7178

SP0193
PRINCIPLES OF NON-PHARMACOLOGICAL MANAGEMENT OF FIBROMYALGIA
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Having fibromyalgia greatly impacts person’s mental and physical wellbeing, his activities of daily living, and the society at large. Despite scientific progress to unravel the aetiology of fibromyalgia syndrome, no cure is yet available. The management of fibromyalgia comprises both pharmacological and non-pharmacological treatment option to alleviate the symptom burden of the disease.

The recently published EULAR revised recommendations for the management of fibromyalgia1, proposes that the management of fibromyalgia should take the form of a graduated approach with the aim of improving health-related quality of life. It should focus first on non-pharmacological treatment, including education, self-management and physical therapy with graded physical exercises. In this talk a brief overview of the current evidence regarding non-pharmacological treatment in fibromyalgia will be given. The importance of patients’ self-management, (tailored) interventions to support self-management, and its dissemination and implementation in clinical practice will be highlighted.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7163
In clinical practice, assessment is important for the selection of intervention strategies, goal setting, prognosis and the evaluation of the progression made towards the treatment goals. For example, we need to assess the patients’ perceptions on how the disease, functioning and disability interfere with their life situation. Furthermore, we should assess how they can cope with stressful events, what social support they experience and how they adjust to living with a chronic disease. The assessment should provide information on problems, needs and priorities of the patients, as well as on strengths and resources. Based on the initial assessment, mutually agreed treatment goals and treatment strategies can be defined together with the patients.

We need to be aware of the differences, strengths and weaknesses of observations (e.g. Barthel Index), measures (walking speed) and self-reported questionnaires (patient-reported outcomes) or individualised, patient specific measures (e.g. the Patient-Specific Functional Scale).

In most situations, it is recommended to combine generic and specific measures to cover general as well as specific issues of health, functioning and disability or contextual factors. This will also allow the comparison across groups of patients. Each tool used in the assessment should serve a clear objective and should be able to achieve this objective in the given situation. We need to know the relevant measurement properties on reproducibility and validity for the instrument in a given situation. The agreement or the measurement error will tell us, for example, how small a change can be to be detected (i.e. smallest detectable change). This is important when we want to monitor change (evaluation). Reliability indices will tell us how good we can distinguish groups of patients and whether we can use an instrument in a group setting (i.e. in a study; the ICC should be at least 0.7) or for the use with individuals in clinical practice (ICC should be at least 0.9).

We can distinguish three types of validity, content validity, construct validity and criterion validity. The content validity informs on how good a tool covers all relevant aspects of the construct to be measured and whether all items cover relevant aspects. An instrument has a good criterion validity if its results are similar to a so-called gold standard (instrument that is known to be valid). The construct validity tells us whether the scores of the measurement instrument are associated with instruments that measure a similar construct and are not associated with scores from instruments that measure non-related concepts.

Other important aspects are responsiveness and interpretability. Responsiveness is the ability of an instrument to detect change over time in the construct to be measured. Interpretability means that the scores are understandable and meaningful. Aspects of interpretability are floor and ceiling effects, and whether the smallest detectable change and the minimal important change are known. Of course, the application of an instrument has to be feasible. Therefore, there is often a trade-off between measurement properties and feasibility, i.e. the perfectly reliable and valid instrument might be too expensive or too time consuming. Therefore, a less ‘perfect’ instrument might be chosen.

All the mentioned aspects need to be considered when defining an individual assessment strategy for a patient. The assessment and evaluation should be an integrated part of the treatment process. It verifies that the treatment is in line with the needs and priorities of the patients; the documentation of changes might motivate both patients and health professionals and it might increase adherence to the recommended treatments.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7226

SATURDAY, 17 JUNE 2017
HPR Highlight session

HIGHLIGHTS FROM THE HEALTH PROFESSIONAL SESSIONS
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EULAR congress is one on the biggest events in the world of rheumatology. To accommodate all the diversity of topics, several sessions take place at same time, in different rooms. It is very hard, even impossible, to be in all sessions, poster tours, social meetings and other learning events of your interest. It often happens that one want to be at 3 or 4 places at same time.

This “Highlights” session is designed to summarize the most important conclusions of the talks given in all sessions from Health Professionals programme. By this way you can catch on what you missed to be in other places. Of course you can also read the abstracts in the EULAR app or Annals of Rheumatic Diseases Suplement or even to watch the podcasts after the event. However, this highlights session will provide you an integrated view of the different contents in a more appealing and interactive perspective.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7256
Scientific Abstracts
THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS)

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Background: A LLDAS definition has received preliminary validation. Achieving low disease activity by this definition is associated with protection from disease accrual for patients (pts) with SLE. However, it has not been evaluated as an endpoint in randomized controlled trials (RCTs).

Objectives: We evaluated LLDAS as an RCT endpoint in a post-hoc analysis of the MUSE trial of anifrolumab in pts with moderate to severe SLE.

Methods: During the 52-week MUSE study, pts with active SLE received intravenous placebo, anifrolumab 300 mg, or 1,000 mg, in addition to standard of care, every 4 weeks for 48 weeks. LLDAS requires all of the following: SLEDAI–2K ≤5, prednisone ≤7.5 mg/d, and tolerance of standard immunosuppressant therapies. LLDAS utility, its association with other endpoints, and discrimination between anifrolumab- and placebo-treated pts, were explored using descriptive statistics, logistic regression, and Gray’s test. All randomized pts in MUSE were included in the analyses, and non-response imputation was performed after dropout.

Results: For pts receiving placebo (n=102), anifrolumab 300 mg (n=99), or anifrolumab 1,000 mg (n=104), LLDAS criteria were met at least once by 35% (300 mg: 1.7–2.5). LLDAS was attained earlier (300 mg: 1.7–2.5, p=0.012; 1,000 mg: 1.0–2.4, p=0.011) in anifrolumab-treated pts (Figure 1). At Week 52, more anifrolumab-treated pts attained a LLDAS (OR vs. placebo: 300 mg: 3.41, 95% CI 1.73, 6.76, p<0.001; 1,000 mg: 2.03, 95% CI 1.01, 4.07, p=0.046). More anifrolumab-treated pts spent ≥50% of observed time in LLDAS (OR vs. placebo: 300 mg: 0.34, 95% CI 1.34, 6.92, p=0.008; 1,000 mg: 2.17, 95% CI 0.93, 5.03, p=0.072), and the OR of sustained LLDAS for at least six consecutive visits from Week 12 to 52 were 4.02 (95% CI 1.38, 11.73; p=0.011) (300 mg) and 2.95 (95% CI 0.99, 8.78; p=0.052) (1,000 mg).

Conclusions: LLDAS is associated with validated treatment response measures. SRI(4) and BICLA, but is more stringent than either. Anifrolumab was associated with <3.6-fold OR increases in LLDAS attainment, as well as greater aggregate and sustained time in LLDAS. This LLDAS definition should be considered as a study endpoint in SLE RCTs.

References:

Acknowledgements: Funded by MedImmune. Medical writing support: R Plant, QXV Comms, an Ashfield company, funded by MedImmune.


DOI: 10.1136/annrheumdis-2017-eular.2464

METHODOLOGY

OP0001

THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS)

DEFINITION DISCRIMINATES RESPONDERS IN A SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) TRIAL: POST-HOC ANALYSIS OF THE PHASE II BUSE MUSE TRIAL OF ANIFROLUMAB

E. Morand1, A. Berglind2, T. Sheytanova3, R. Tummala4, G. Illei4

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Moving towards new criteria in SLE, Sjögren’s and APS

OP0002

MULTICRITERIA DECISION ANALYSIS FOR DEVELOPING NEW CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS


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Background: EULAR and ACR are supporting multi-phase development of SLE classification criteria based on weighted criteria and a continuous probability scale. Prior steps included criteria generation, criteria reduction through Delphi and Nominal Group Technique exercises, literature review for sensitivity/specificity of candidate criteria, and organization of candidate criteria into seven clinical and three immunologic domains.

Objectives: To refine definitions of candidate criteria, determine relative weights using multicriteria decision analysis, and determine a threshold score for SLE classification.

Methods: An SLE Expert Panel (9 North American, 8 European) submitted 167 unique cases with a range of SLE probability. Experts scored 20 representative cases using the candidate criteria and rank-ordered them. In a 2-day meeting, experts reviewed inter-rater reliability of scoring, refined criteria definitions, and participated in a multicriteria decision analysis (MCDA) exercise using 1000Minds™ software. Experts were presented a series of decisions between two cases, each with different criteria from two domains (e.g. oral ulcers [cutaneous] and acute pericarditis [serositis] vs. alopecia [cutaneous] and pleural effusion [serositis]) and anonymously voted for the case more likely to be classified as SLE. Votes were discussed until consensus was reached for each decision. Using the consensus decisions, 1000Minds™ calculated criteria weights, assigned a total score to each of remaining 147 cases and rank-ordered the cases. Experts voted on whether each case should be classified as SLE. MCDA was repeated for criteria whose calculated weights were inconsistent with expert opinion until group consensus was achieved. 1000Minds™ then re-calculated criteria weights and re-ranked cases once. The score of the last case for which expert consensus was achieved was the threshold score.

Results: Inter-rater reliability was good; human data entry error, not following instructions, and differing interpretations of criteria definitions accounted for discussion. The MCDA involved 74 pairwise decisions. Cranial neuropathy and Class VI lupus nephritis were removed as they added little to SLE classification. MCDA was repeated for the arthritis and cutaneous domains as initial weights did not match expert opinion. After criteria weights and scores were re-calculated once, experts reached consensus for SLE classification for case score >83.

Conclusions: Using an iterative process, the expert panel refined definitions, weighted candidate criteria and determined a threshold score of >83 for SLE classification, which will undergo validation.

Acknowledgements: Joint support from EULAR and ACR

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5464
Controlling the balance between cancer and autoimmunity

OP0003  RHEUMATIC IMMUNE RELATED ADVERSE EVENTS OF CHECKPOINT THERAPY FOR CANCER: CASE SERIES OF AN EMERGING NOSOLOGIC ENTITY
C. Calabrese 1, E. Kirchner 1, A. Kontzias 1, V. Velcheti 2, L. Calabrese 1

Background: Immune checkpoint therapy is a major advance in the field of oncology. Agents targeting CTLA-4, programmed cell death protein 1 (PD-1) and PD-Ligand 1 have produced significant survival benefits in patients with malignancies. With these therapies have come a unique spectrum of adverse events related to over-activation of the immune system resulting in autoimmunologic disease. To date reports of rheumatic immune related AE’s have not been adequately characterized, as they are infrequently reported in clinical trials. We describe the largest series of rheumatic irAEs secondary to checkpoint inhibitors to date.

Objectives: To report our 22 month experience with 19 patients evaluated in the Cleveland Clinic Rheumatology department.

Methods: A retrospective chart review was performed on 19 patients, 16 without pre-existing autoimmune disease (AID) and 3 with pre-existing AID, seen in our rheumatology department February 2015-December 2016. 2 designated rheumatologists evaluated all patients. Recorded information included gender, age, age at malignancy diagnosis, malignancy details, checkpoint inhibitor, nature of rheumatic irAE, time of onset, diagnostic data, treatment of irAE and response to treatment.

Results: In the group without pre-existing AID 56% developed a rheumatic irAE within 16 weeks of starting immunotherapy, with median time to onset of 14.5 weeks (table 1). Of the 3 patients with pre-existing AID, 1 experienced a disease flare after starting immunotherapy.

Conclusions: Rheumatic irAEs is a new field that will continue to grow. At this stage we have more questions than answers regarding their epidemiology, natural history and pathophysiology. Our findings reinforce that rheumatic irAEs are complex, at times require aggressive immunosuppression and can impact checkpoint inhibitor therapy for the underlying malignancy.

Disclosure of Interest: C. Calabrese: None declared, E. Kirchner: None declared, A. Kontzias: None declared, V. Velcheti: Grant/research support from: Genentech, Bristol-Myers Squibb, Merck, Astra Zeneca, Genoptix, Consultant for: Genentech, Bristol-Myers Squibb, Merck, Astra Zeneca, Celgene, Genoptix, Foundation Medicine, L. Calabrese Consultant for: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2017-eular.1628

OP0004  RHEUMATOID ARTHRITIS OCCURRING AFTER IMMUNE CHECKPOINT INHIBITORS
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Background: Immune checkpoints inhibitors (ICIs) targeting cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and Programmed cell death protein 1 (PD-1) have demonstrated survival improvement in multiple cancers. Immune Related Adverse Events (IrAE) have been described with ipilimumab and anti PD1. Relapse or flare of preexisting auto-immune diseases has been reported but occurrence of new auto-immune diseases seems to be less frequent. A series of 13 patients with non-classified rheumatic irAE has been published: 9 patients developed non-specific inflammatory arthritis but no seropositive rheumatoid arthritis (RA) and 4 presented with sicca symptoms but did not fulfill criteria for Sjogren syndrome [1].

Objectives: We did a retrospective study for collecting patients who developed seropositive rheumatoid arthritis (RA) after exposition to ICIs.

Methods: We used the “Club Rhumatismes et Inflammation (CRI)” network, a section of the French Society of Rheumatology and the Gustave Roussy Cancer Therapeutics. All rheumatologists evaluated all patients. Recorded information included gender, age, age at malignancy diagnosis, malignancy details, date of first ICI, date of irAE, type of irAE, treatment of irAE and response to treatment, autoantibody results.

Results: In the group of 13 patients, we found seropositive rheumatoid arthritis (RA) in 3 patients, seronegative RA in 2 patients, and 4 patients with nephritis (table 1). 1 patient developed spondyloarthritis, and 2 patients had ANCA associated vasculitis. This series confirms that the occurrence of irAE is a frequent complication of ICI therapy.

Conclusions: The irAEs are complex; at times require aggressive immunosuppression and can impact checkpoint inhibitor therapy for the underlying malignancy.

Disclosure of Interest: R. Belkhir: None declared, S. Le Burel: None declared, O. Lambotte: None declared, G. Mouton: None declared, E. Pertuiset: None declared, L. Dumegant: Grant/research support from: Genentech, Bristol-Myers Squibb, Merck, Astra Zeneca, Celgene, Genoptix, Foundation Medicine, Consultant for: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2017-eular.1629

Abstract OP0003 – Table 1. Demographic features, cancer types, immunotherapy and rheumatic irAEs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Malignancy</th>
<th>ICI</th>
<th>Immunotherapy</th>
<th>irAE</th>
<th>Serology</th>
<th>Time to onset (weeks)</th>
<th>Treatment</th>
<th>Improvement</th>
<th>Immunotherapy held for irAE</th>
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<td>F</td>
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<td>Nivo</td>
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<td>F</td>
<td>Melanoma</td>
<td>Ipi</td>
<td>Arthritis</td>
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<tr>
<td>3</td>
<td>42</td>
<td>F</td>
<td>RCC</td>
<td>Nivo</td>
<td>Arthritis</td>
<td>3</td>
<td></td>
<td></td>
<td>Prednisone Infliximab, MTX Etanercept</td>
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</tr>
<tr>
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<td>M</td>
<td>RCC</td>
<td>Nivo</td>
<td>Arthritis</td>
<td>6.7</td>
<td></td>
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<td>Methotrexate</td>
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<td>59</td>
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<td>Minimal</td>
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<td>Nivo</td>
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<td>M</td>
<td>Melanoma</td>
<td>Nivo</td>
<td>Arthritis</td>
<td>2</td>
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<td></td>
<td>Prednisone 30 mg</td>
<td>Minimal</td>
<td>Y</td>
</tr>
<tr>
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<td>79</td>
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<td>Nivo</td>
<td>Arthritis</td>
<td>213</td>
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<tr>
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<td>63</td>
<td>M</td>
<td>RCC</td>
<td>Nivo</td>
<td>Arthritis</td>
<td>4.6</td>
<td>IV methylprednisolone 400 mg/day</td>
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<td>Y</td>
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<tr>
<td>16</td>
<td>68</td>
<td>M</td>
<td>NSCL</td>
<td>Nivo</td>
<td>Arthritis</td>
<td>4.6</td>
<td></td>
<td></td>
<td>Prednisone 30 mg</td>
<td>Minimal</td>
<td>Y</td>
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</table>

Abstract OP0004 – Table 1. Malignancy, ICI type, immunotherapy and irAEs

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex/age</th>
<th>Type of cancer</th>
<th>ICI</th>
<th>Date of first ICI exposure</th>
<th>Date of irAE exposure</th>
<th>Type of rheumatic irAE</th>
<th>irAE response to treatment</th>
<th>Autoantibodies results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F 55 y</td>
<td>Squamous cell carcinoma of the vagina</td>
<td>nivolumab</td>
<td>October 2015</td>
<td>October 2015</td>
<td>RA</td>
<td>resolution with NSAIDS</td>
<td>anti-CCP: 671 U/ml</td>
</tr>
<tr>
<td>2</td>
<td>F 66 y</td>
<td>Endometrial adenocarcinoma</td>
<td>pembrolizumab</td>
<td>March 2016</td>
<td>April 2016</td>
<td>RA</td>
<td>resolution with corticosteroids</td>
<td>anti-CCP: 233 U/ml</td>
</tr>
<tr>
<td>3</td>
<td>M 59 y</td>
<td>Lung adenocarcinoma</td>
<td>nivolumab</td>
<td>May 2016</td>
<td>July 2016</td>
<td>RA</td>
<td>resolution with prednisone 10 mg/day</td>
<td>anti-CCP: 180 U/ml</td>
</tr>
<tr>
<td>4</td>
<td>F 56 y</td>
<td>Metastatic melanoma</td>
<td>pembrolizumab</td>
<td>August 2015</td>
<td>September 2015</td>
<td>RA</td>
<td>resolution with prednisone 15 mg/day</td>
<td>anti-CCP: 42 U/ml</td>
</tr>
<tr>
<td>5</td>
<td>M 80 y</td>
<td>Metastatic melanoma</td>
<td>nivolumab</td>
<td>April 2016</td>
<td>April 2016</td>
<td>RA</td>
<td>Resolution with prednisone 15 mg/day (tapered) and hydroxycarboline 200 mg/day</td>
<td>anti-CCP: 42 U/ml</td>
</tr>
<tr>
<td>6</td>
<td>M 68 y</td>
<td>Lung adenocarcinoma</td>
<td>nivolumab</td>
<td>June 2015</td>
<td>July 2015</td>
<td>RA</td>
<td>Resolution after stopping nivolumab and after 1 month of methotrexate 10 mg (maintained 3 months)</td>
<td>RF: 246 U/ml</td>
</tr>
</tbody>
</table>
Fibromyalgia: a disease of the peripheral or central nervous system

Background: Approximately 10% of patients with rheumatoid arthritis (RA) have coexisting fibromyalgia (FM). Little is known of the cross-sectional and longitudinal relationship between FM and RA disease activity.

Objectives: To examine the cross-sectional and longitudinal relationship between FM and RA disease activity.

Methods: Oslo RA register (ORAR) was established in 1994 as a prospective, observational, longitudinal nested cohort study. The inclusion criteria were RA according to the 1987-ACR classification criteria and a residential address in Oslo. 636 patients in ORAR were asked to participate in a clinical examination in 1999. A trained study-nurse systematically assessed the 18-tender point count and performed 28-tender and 28-swollen joint counts (TJC/SJC). Patients self-reported disease activity and pain related to RA, and completed the Stanford Health Assessment Questionnaire (HAQ). RA disease activity was calculated as DAS28. Fibromyalgia was diagnosed if ≥11 tender points were reported. FM associated variables; fatigue, muscular tenderness, headache, abdominal pain and difficulties concentrating were also scored (0–10 VAS).

At the 10-year follow-up patients completed a questionnaire that included RA Disease Activity Index (RADAI) and Routine Assessment of Patient Index Data (RAPID-3).

In cross-sectional and longitudinal analyses RA disease activity, FM associated variables and health status were compared between patients with ≥11 and <11 tender points. Level of significance was calculated using ANCOVA models corrected for age, gender, BMI and level of education. The FM associated variables at baseline were also corrected for baseline SJC 28 and C-reactive protein (CRP). The variables in the longitudinal study were corrected for the same variables as the cross-sectional analyses, but additionally for baseline values of the dependent variable when available.

Results: 488 patients agreed to participate in the baseline data-collection and 192 participated at the 10-year follow-up. The mean (SD) age was 59.5 (12.5) years, and 87% were female. There were no significant differences in age, disease duration or participation at follow-up between patients with and without FM, but only women had FM.

Patients with FM in addition to RA had higher DAS28, SJC, TJC, pain and patient globalVAS, but also higher levels of fatigue, abdominal pain and concentration difficulties (Table 1).

Table 1. Baseline cross-sectional associations

<table>
<thead>
<tr>
<th>Variables</th>
<th>Tender points ≥11</th>
<th>Tender joint count &lt;11</th>
<th>Adj. Bivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA disease activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA disease duration (years)</td>
<td>16.3 (8.9)</td>
<td>14.9 (9.3)</td>
<td>0.31</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>17.4 (24.4)</td>
<td>14.5 (13.4)</td>
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<tr>
<td>DAS28</td>
<td>5.3 (1.0)</td>
<td>4.4 (1.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>4.5 (2.2)</td>
<td>3.5 (2.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>SJC</td>
<td>9.8 (5.7)</td>
<td>6.8 (5.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>TJC</td>
<td>13.3 (5.6)</td>
<td>7.4 (6.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient disease activity VAS</td>
<td>4.7 (2.2)</td>
<td>3.7 (2.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Fibromyalgia related variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscular tenderness VAS</td>
<td>5.9 (2.7)</td>
<td>3.2 (2.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatigue VAS</td>
<td>6.6 (2.7)</td>
<td>4.4 (2.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Headache VAS</td>
<td>2.0 (2.4)</td>
<td>1.4 (2.1)</td>
<td>0.25</td>
</tr>
<tr>
<td>Abdominal pain VAS</td>
<td>3.7 (3.5)</td>
<td>1.9 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Difficulty concentrating VAS</td>
<td>2.9 (2.7)</td>
<td>1.7 (1.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Health Status</td>
<td>1.2 (0.1)</td>
<td>1.0 (0.0)</td>
<td>0.09</td>
</tr>
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</table>

At the 10-year follow-up patient with FM had significantly higher levels of RA disease activity and pain (figure 1).

Table 2. Baseline cross-sectional associations

<table>
<thead>
<tr>
<th>Variables</th>
<th>Tender points ≥11</th>
<th>Tender joint count &lt;11</th>
<th>Adj. Bivariate</th>
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<tbody>
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<td>RA disease activity</td>
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<td>16.3 (8.9)</td>
<td>14.9 (9.3)</td>
<td>0.31</td>
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<tr>
<td>CRP (mg/L)</td>
<td>17.4 (24.4)</td>
<td>14.5 (13.4)</td>
<td>0.08</td>
</tr>
<tr>
<td>DAS28</td>
<td>5.3 (1.0)</td>
<td>4.4 (1.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>4.5 (2.2)</td>
<td>3.5 (2.3)</td>
<td>0.03</td>
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<tr>
<td>SJC</td>
<td>9.8 (5.7)</td>
<td>6.8 (5.1)</td>
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<td>TJC</td>
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<td>7.4 (6.5)</td>
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<td>Patient disease activity VAS</td>
<td>4.7 (2.2)</td>
<td>3.7 (2.3)</td>
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<td>Fibromyalgia related variables</td>
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<td>Muscular tenderness VAS</td>
<td>5.9 (2.7)</td>
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<td>Fatigue VAS</td>
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<td>Headache VAS</td>
<td>2.0 (2.4)</td>
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<td>Abdominal pain VAS</td>
<td>3.7 (3.5)</td>
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<td>2.9 (2.7)</td>
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<td>0.003</td>
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<tr>
<td>Health Status</td>
<td>1.2 (0.1)</td>
<td>1.0 (0.0)</td>
<td>0.09</td>
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</table>
intensity of chronic pain when awake and during sleep. These findings explain the hypothesis that autophagy is decreased with aging. Therefore, targeting Lamin A/C might be a promising strategy to find novel therapeutics for cartilage aging and OA.

References:

Acknowledgements: This study was supported by Instituto de Salud Carlos III-Ministerio de Economía y Competitividad, Spain-CP11/00095 and Fondo Europeo de Desarrollo Regional (FEDER).

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3819

WEDNESDAY, 14 JUNE 2017

Wearable technologies in 21st century healthcare

**OP0009-HPR**

The Effect of an 8-Week Water Exercise Program on Anaerobic Exercise Capacity in Children With Juvenile Idiopathic Arthritis

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**Background:** Anaerobic exercise capacity was reported to be lower in children with juvenile idiopathic arthritis (JIA) than healthy children. However, to our knowledge, there is no study focusing on improving anaerobic exercise capacity in JIA.

**Objectives:** To investigate the effect of an 8-week water exercise program, which was performed at the weekends, on anaerobic exercise capacity in children with JIA.

**Methods:** Forty-two children with JIA were divided into two groups as exercise and control. Prior to the study, anaerobic exercise capacity was measured performing a 30-second Wingate test. Deep water running was employed as the progressive water exercise program for the exercise group. Control group did not receive any additional treatment other than their usual care. Weekends were chosen for the exercise sessions considering the educational program of the children. Exercise intensity was set as moderate. Exercise intensity was determined with a wearable heart rate tracking system during the exercises. All children were reassessed regarding anaerobic exercise capacity two months after the first assessment.

**Results:** All children completed the study without any adverse effects. Twenty-one children were in the exercise group, others were assessed as controls. No significant differences were determined between groups prior the study regarding to age, disease duration, height, weight, body-mass index, and anaerobic exercise capacity related parameters (p>0.05). While all anaerobic exercise capacity parameters improved in the exercise group, no improvement were seen in the control group. The in-group comparisons were shown as Table 1. The comparison of the changes between groups after 8 weeks were demonstrated at Table 2.
EFFECT OF DENOSUMAB COMPARED WITH RISEDRONATE IN\n\nAdverse events (AEs) and serious AEs, including serious AEs of infection, as well\n\nwith RIS at the LS and TH in both subpopulations (Figure). The incidences of\n\nGC-I subpopulations, as indicated by significantly greater BMD gains compared\n\niinferiority and superiority with DMAb were demonstrated for both the GC-C and\n\nResults: The study remains blinded and is ongoing.

Objectives: The study was designed to assess the safety and efficacy of DMAb compared with risedronate\n\nRANKL and decreased osteoprotegerin (OPG) expression in patients with GIOP.

most common secondary cause of osteoporosis. Despite approved therapies,\n\n\nsuperiority of DMAb over RIS with respect to %\n\n\nbone mineral density (BMD) at 12 months. Secondary objectives were to assess\n\n\nTable 2. The differences in the groups after 8 weeks

Exercise Group (n=21) Control Group (n=21) \n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n\n
Wilkoxon Test. IQR: Interquartile Range; W: watt; W/kg: watt/kilogram; \np < 0.05.

Conclusions: The present study is the first study focusing on improving anaerobic capacity in children with JIA. According to our results, an 8-week water exercise program which is performed at the weekends might be beneficial to improve anaerobic exercise capacity in children with JIA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5670

WEDNESDAY, 14 JUNE 2017

Assessment and management of osteoporosis

Table 1. In-group comparison before and after the study

Before Median (IQR 25/75) After Median (IQR 25/75) p

Exercise Group (n=21) \n
Peak Power (W) 354.73 (267.59/471.55) 441.3 (295.6/369.6) 0.002*

Peak Power (W/kg) 6.74 (5.44/8.97) 7.7 (6.4/9.7) 0.001

Average Power (W) 291.5 (198.78/395.61) 360.0 (220.4/446.6) 0.001*

Average Power (W/kg) 5.54 (4.07/8.88) 6.0 (4.8/7.4) 0.002*

Control Group (n=21) \n
Peak Power (W) 355.57 (225.43/463.62) 366.7 (236.3/447.6) 0.259

Peak Power (W/kg) 6.69 (5.08/8.73) 7.3 (6.1/8.2) 0.232

Average Power (W) 261.04 (181.68/351.27) 284.8 (187.9/373.0) 0.050

Average Power (W/kg) 5.29 (4.76/8.85) 5.5 (5.0/6.1) 0.076

Wilcoxon Test. IQR: Interquartile Range; W: watt; W/kg: watt/kilogram; \np < 0.05.

Conclusions: DMAb significantly increased BMD more than RIS at the spine and hip at 12 months. The overall safety profile was similar between treatment groups. DMAb has the potential to become another treatment option for patients newly initiating or continuing GC who are at risk for fracture.

Acknowledgements: The study was funded by Amgen. C Desborough (Amgen (Europe) GmbH) provided editorial support.


DOI: 10.1136/annrheumdis-2017-eular.5164

WEDNESDAY, 14 JUNE 2017

Systematic literature review: the link from science to clinical practice

Table 1. Baseline Characteristics

Table 2. The differences in the groups after 8 weeks

Conclusions: The study was funded by Amgen. C Desborough (Amgen (Europe) GmbH) provided editorial support.


DOI: 10.1136/annrheumdis-2017-eular.5164

Conclusions: The study was funded by Amgen. C Desborough (Amgen (Europe) GmbH) provided editorial support.


DOI: 10.1136/annrheumdis-2017-eular.5164
The main outcomes that were analysed for the meta-analysis were RA occurrence at 52 weeks and beyond and the absence of radiographic progression at week 52. The meta-analysis was performed using RevMan with Mantel-Haenszel method. **Results:** The search identified 595 abstracts, of which 9 RCTs were finally selected (including 2 congress abstracts). Eight were related to undifferentiated arthritis. One (16%) was published in the antibody to RAP1B. The studies included 1156 patients, weighted mean age 45.8±15.2 years, mean symptom duration 16.2±12.6 weeks; 66.0±17.7% were female. The occurrence of RA at week 52 or more was available in 7 studies (assessing 800 patients). Early therapeutic intervention – either methotrexate (80 to 120mg IM), methotrexate, TNF-blocker, abatacept or rituximab – reduced the risk of occurrence of RA with a pooled odds ratio (OR) of 0.72 (95% CI [0.54; 0.96]), p 0.02 (Figure). There was a statistically significant difference between the treatments or placebo, for the absence of radiographic progression (pooled OR 1.36 [0.80; 2.32]). The outcome was assessed at Week 52 for all studies, except for Van Dongen 2007 (PROMPT), where it was assessed at Week 120. MethyLPDN, methotrexolone; MTX, methotrextate.

**Conclusions:** This meta-analysis demonstrates that early therapeutic intervention significantly reduces the risk of RA onset in pre-RA patients. The benefit risk balance and feasibility in clinical practice remain to be further assessed. **Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5323

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**Figure 1.** RA appearance at week 52 or more.

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**Wednesday, 14 June 2017**

**EULAR Campaign: Don’t Delay, Connect Today**

**RHEUMATOSPHERE: REACH NEW HEIGHTS IN DIAGNOSIS AND TREATMENT OF ARTHRITIS BY ENGAGING, EMPOWERING AND INSPIRING**

L.A. Bennett, J.S. Nijjar, G. Fragouli, S. Siebert, I.B. McInnes, Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom

**Background:** We aim to reach new heights in diagnosis and treatment of arthritis through research and we believe that part of this encompasses public engagement. Engaging the public is an essential part of scientific life, as the majority of work carried about by researchers is publically funded. Therefore the public are entitled to and should be encouraged to see the conclusions of this work in an easily accessible manner.

**Objectives:** 1) Engage the public about rheumatic disease, what it is, what it does to the body and how we, as scientists and clinicians, address unmet needs in this field. 2) Empower patients in order to help them understand their disease and treatments thereby improving patient satisfaction and compliance to therapy. 3) Inspire the next generation of scientist by encouraging children to study science at school and raise the profile of these subjects with education authorities and the government.

**Methods:** Rheumatosphere was established to address public engagement needs in the arthritis research field. We have used a variety of techniques to capture the attention of small and large audiences of all ages. Techniques include: Ultrasound scanning of coffee with patients at our (less than 70% of predicted, p 0.01) and FEV1 (12 patients and 2 controls, p 0.01) and FEV1 (% of predicted) 88 (14) 109 (11) p 0.01. HRCT showed ILD in 15 patients (29%). More patients than controls had abnormal FVC (11 patients and 0 controls, p<0.01) and FEV1 (12 patients and 2 controls, p<0.01). Diffusing capacity for carbon monoxide adjusted for alveolar volume was abnormal in 12 patients and 8 controls (p=0.34). One patient and 3 controls had a pathological FEV1/FVC less than 0.67 (p 0.02). HRCT showed ILD in 15 patients (29%). The extent of lung parenchyma involved was median 2% (range 1–75) in the patients with ILD. Two patients had more than 20% of lung parenchyma involved (graph 1). The most common abnormalities were reticular patterns, being present in 13 patients (25%). 2 patients (4%) had ground glass attenuation. We could not find correlations between the extent of ILD and PFT or 6MWT. There were no significant differences in PFT values or other disease related variables between the patients with and without ILD.

**Conclusions:** Patients with JMCTD had significantly reduced pulmonary function as compared to matched controls. However, overall lung function was only moderately reduced. The occurrence of ILD assessed with HRCT was 29%, but the majority of patients with ILD had mild disease. To our knowledge, this is the first systematic case-control study of pulmonary manifestations in JMCTD.

**References:**


**Disclosure of Interest:** None declared

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**PULMONARY MANIFESTATIONS IN JUVENILE ONSET MIXED CONNECTIVE TISSUE DISEASE AFTER LONG-TERM DISEASE DURATION – A NORWEGIAN CASE-CONTROL STUDY**

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**Background:** Pulmonary manifestations in mixed connective tissue disease (MCTD) are common and a major cause of morbidity and mortality [1]. Data on lung involvement in patients with juvenile onset MCTD (JMCTD) are scarce.

**Objectives:** The aim of this study was 1) to compare pulmonary function abnormalities in a nationwide representative Norwegian JMCTD cohort with that of matched controls, 2) investigate occurrence of interstitial lung disease (ILD) in JMCTD and 3) to evaluate possible associations between pulmonary findings and disease related variables.

**Methods:** Inclusion criteria were fulfillment of the Kasukawa or Alarcon-Segovia criteria and symptom-onset before 18 years. The control group was randomly drawn from the national population register, after matching for age and gender. Fifty-two patients with JMCTD were examined after mean disease duration 16.2 years, 44 (85%) were female. Patients and controls performed pulmonary function tests (PFT) and a 6 min walk test (6MW). The patients had a high-resolution CT (HRCT) of the lungs.

**Results:** Abnormal PFT were found in 24 patients (46%) and in 12 controls (23%) (p=0.01) (table 1).

**Table 1.** PFT at 52 weeks and beyond and the absence of radiographic progression at week 52.

<table>
<thead>
<tr>
<th>Variable</th>
<th>JMCTD patients</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at examination, years</td>
<td>28.0 (10.3)</td>
<td>29.0 (10.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.7 (3.5)</td>
<td>23.4 (3.0)</td>
<td>0.29</td>
</tr>
<tr>
<td>Current smokers daily/occasionally, n (%)</td>
<td>7 (14)</td>
<td>11 (17)</td>
<td>0.59</td>
</tr>
<tr>
<td>Never smokers, n (%)</td>
<td>35 (67)</td>
<td>34 (65)</td>
<td>0.83</td>
</tr>
<tr>
<td>MMW, meters</td>
<td>634.3 (76.5)</td>
<td>698.9 (86.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>DLCO/VA (% of predicted)</td>
<td>3.4 (0.6)</td>
<td>4.3 (1.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>FVC, litres</td>
<td>89 (14)</td>
<td>109 (11)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FEV1 (% of predicted)</td>
<td>2.9 (0.5)</td>
<td>3.5 (0.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FEV1/FVC, size</td>
<td>89 (13)</td>
<td>102 (11)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>6MWD, meters</td>
<td>0.86 (0.06)</td>
<td>0.82 (0.07)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>DLCO/VA (mmol/kPa min/l)</td>
<td>1.6 (0.2)</td>
<td>1.8 (1.0)</td>
<td>0.26</td>
</tr>
<tr>
<td>DLCO/VA (% of predicted)</td>
<td>88 (12)</td>
<td>92 (13)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

More patients than controls had abnormal FVC (11 patients and 0 controls, p<0.01) and FEV1 (12 patients and 2 controls, p<0.01). Diffusing capacity for carbon monoxide adjusted for alveolar volume was abnormal in 12 patients and 8 controls (p=0.34). One patient and 3 controls had a pathological FEV1/FVC less than 0.67 (p 0.02). HRCT showed ILD in 15 patients (29%). The extent of lung parenchyma involved was median 2% (range 1–75) in the patients with ILD. Two patients had more than 20% of lung parenchyma involved (graph 1). The most common abnormalities were reticular patterns, being present in 13 patients (25%). 2 patients (4%) had ground glass attenuation. We could not find correlations between the extent of ILD and PFT or 6MW. There were no significant differences in PFT values or other disease related variables between the patients with and without ILD.

**Conclusions:** Patients with JMCTD had significantly reduced pulmonary function as compared to matched controls. However, overall lung function was only moderately reduced. The occurrence of ILD assessed with HRCT was 29%, but the majority of patients with ILD had mild disease. To our knowledge, this is the first systematic case-control study of pulmonary manifestations in JMCTD.

**References:**


**Disclosure of Interest:** None declared
OBJECTIVE: To provide pragmatic guidelines concerning conventional radiography (CR) in each subtype of JIA (exclusion of systemic JIA).

METHODS: A multidisciplinary task force of 15 French experts (rheumatologists, pediatricians, radiologists) plus one patient's representative, was convened. Following the GRADE method, they formulated a series of research questions concerning CR assessment, at diagnosis and follow-up of each subtype of JIA. Systemic JIA was ruled out. A systematic literature review was conducted, following evidence-based data, and expert opinion. It underwent an evaluation from an independent committee (including patient's representative), and a final round of Delphi-voting process from the whole expert group.

RESULTS: Of 646 publications identified, 73 original articles were included. The round of Delphi-voting process from the whole expert group.

CONCLUSIONS: These are the first pragmatic recommendations upon CR in JIA. They mostly rely on experts’ opinion, due to lack of evidence-based data. CR is still relevant in many situations in JIA, but should not be overlooked, while non-irradiating imagine techniques are developing.

Acknowledgements: Dr Bouchra Amine, Pr Nathalie Boutry, Pr Rolando Cinaz, Pr Bernhard Combe, Dr Véronique Despert, M William Fahy and Mrs Céline Obert (association KOURIR), Dr Laurence Goumy, Pr Michael Hofer, Dr Laëtitia Houx, Dr Sylvie Jean, Dr Valerie Merzoug, Pr Michel Panuel, Pr Samira Rostom, Pr Jean Sibilia, the French Society for Rheumatology, the French Society for Radiology, The French Society for Pediatric and antenatal Imaging.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3862
Background: Treatment with TNF inhibitors is part of the management of patients with severe rheumatoid arthritis (RA). There is limited data on the comparative effectiveness of different TNF inhibitors from clinical trials and observational studies of patients treated in clinical practice.

Objectives: To compare effectiveness of different TNF inhibitors in a large, population representative, sample of bionaire patients with RA.

Methods: The study was based on the Swedish Rheumatology Quality register, in which clinical data are prospectively recorded at treatment initiation and at subsequent visits. Patients with RA initiating a TNF inhibitor as their first ever biologic DMARD in 2010–2014 were included and followed through 2015. The proportion remaining on drug at 1 year (+80 days) after starting therapy was compared. Furthermore, effectiveness at 1 year was assessed as the proportions with EULAR good response, remission (DAS28 <2.6), HAQ improvement (<0.2) and swollen and tender joint counts of 0, all corrected for drug survival (1). The relative response was estimated with log-binomial regression adjusting for potential confounders and using the largest group (etanercept) as reference.

Results: A total of 5568 patients were included. There was a significant difference in the adjusted chance of drug survival across TNF inhibitors (Table). Patients treated with certolizumab or infliximab were less likely to remain on treatment compared to those started on etanercept. The chance of achieving each of the clinical response measures was significantly lower for those initiating infliximab compared to patients treated with etanercept. There were no significant differences in these outcomes compared to etanercept for any of the other TNF inhibitors.

Conclusions: Patients with RA starting infliximab as their first biologic DMARD were less likely to remain on treatment with significant improvement at 1 year compared to those initiating etanercept. There was a similar trend for certolizumab vs. etanercept, but there were no consistent differences in clinical effectiveness between etanercept and adalimumab or golimumab. Treatment context may affect these patterns.

References:

Disclosure of Interest: C. Turesson Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, C. Turesson Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, M. Dehlin: None declared, D. Di Giuseppe: None declared, N. Feltelius: None declared, T. Frisell: None declared, J. Askling: None declared, M. Dehlin: Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, M. Dehlin: Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB.

Disclosure of Interest:

References:

Disclosure of Interest: C. Turesson Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, C. Turesson Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, M. Dehlin: None declared, D. Di Giuseppe: None declared, N. Feltelius: None declared, T. Frisell: None declared, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, M. Dehlin: Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB.

Disclosure of Interest:

References:

Disclosure of Interest: C. Turesson Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, C. Turesson Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, M. Dehlin: None declared, D. Di Giuseppe: None declared, N. Feltelius: None declared, T. Frisell: None declared, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, M. Dehlin: Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB.

Disclosure of Interest:
tool and threshold in predicting a successful assessment of 3-month changes in bone DMARD withdrawal in RA patients achieving remission with TNFi tapering. We have developed a composite index able to predict remission with TNFi, baseline HAQ and CRP are independent predictor factors.

Composite criteria:

Conclusions:

Results:

Background: Tapering trials confirmed the feasibility of TNF inhibitors (TNFi) as an alternative treatment of RA, especially in the first few months of RA onset. With its resolution of up to 81 % after 6 months of treatment, TNFi are used in combination with non-biologic disease-modifying drugs (nbDMARDs) to achieve sustained remission. Determination of TNFi tapering.

Methods: Population: The64 patients of the Spacing arm were those who achieved a discontinuation due to improvements in pain and physical function. The strategy applied progressive spacing of ADA or ETN subcutaneous injections starting from every 2 weeks to every 4 weeks.

Results:

Discussion: This study was funded by UCB Pharma. We are indebted to the mothers and their infants for their altruistic participation. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: X. Mariette Grant/research support from: Biogen, Pfizer, UCB Pharma. M. Foy Grant/research support from: UCB Pharma, A. Flynn Grant/research support from: UCB Pharma, F. Förger Grant/research support from: UCB Pharma, Speakers bureau: Mepha, Roche, UCB Pharma, A. Motto Grant/research support from: MSD, AbbVie, Pfizer, UCB Pharma, Consultant for: MSD, AbbVie, Pfizer, UCB Pharma, A. Van Tubergen Grant/research support from: AbbVie, Pfizer, UCB Pharma, J. Simpson Employee of: UCB Pharma, M. Tei Employee of: UCB Pharma, E. Helmer Employee of: UCB Pharma, M. Wibe.

Background: Tapering trials confirmed the feasibility of TNF inhibitors (TNFi) tapering for a relevant proportion of patients in remission and its low disease activity. However, there are no consensus indicators of a good response to therapeutic spacing among patients with rheumatoid arthritis (RA) in remission.

Objectives: To determine the most predictive tool and threshold of a successful TNFi tapering.

Methods: Population: The Banking of TNF-blocker injections in Rheumatoid Arthritis Study (STRASS) trial included 137 RA patients fulfilling the ACR 1987 criteria with sustained (at least 6 months) DAS28 ≤ 2.6. Patients were randomly assigned to one of the two following strategies: in the Maintain arm, patients continued to receive TNFi at the standard full regimen and in the Spacing arm, the strategy applied progressive spacing of ADA or ETN subcutaneous injections up to discontinuation at the forth step in the spacing arm. We used the data of the Spacing arm.

Analysis: The performances of several variables (DAS28, SDAI, CDAI, CRP, ACPA status, HAQ, patient/physician global assessment, and boolean remission criteria) were assessed for the prediction of successful TNFi tapering, defined as reaching at least 25% tapering of the full regimen during at least 6 months, using sensitivity and specificity for dichotomous variables, or the area under the ROC curve (AUC) and its 95% confidence interval for continuous variables. A predictive score of successful tapering was constructed using LASSO regression modeling technique to avoid overfitting (R software version 3.2.1).

Results: The main characteristic of the 64 patients of the Spacing arm were the following (mean ± SD): age 54.3±10.7 years, disease duration 8.3±5.4 years, and DAS28 1.9±0.6.

The baseline variables were similar between patients who failed or succeeded at TNFi tapering, except for the HAQ score (0.30 in the group success and 0.89 in the failure group, p<0.01) and the CRP (2.35 mg/l versus 3.48 mg/l, respectively, p<0.01). The CRP score of successful tapering was constructed using LASSO regression modeling technique to avoid overfitting (R software version 3.2.1).

Baseline variables performance in predicting successful TNFi tapering: None of the tested variables was able to predict successful TNFi tapering except the HAQ score and the CRP. A HAQ threshold ≥1.125 had a specificity (Spe) of 93% and an AUC 0.713 (95% CI: 0.540–0.886). A CRP threshold ≥6.8 mg/l had a Spe of 0.97 and an AUC 0.689 (95% CI: 0.542–0.831). Composite criteria: A composite criteria able to predict successful TNFi tapering has been elaborated, including ACPA status, Boolean criteria, SDAI, CRP and HAQ. A composite score lower than 0.502 was able to predict a successful TNFi tapering with a sensitivity of 85% (95% CI: 0.671–0.954), a specificity of 94%, and an AUC of 0.89 (95% CI: 0.807–0.973).

Conclusions: The remission maintenance in rheumatoid arthritis after TNFi tapering is possible. Our results showed that in a population of RA patients in remission with TNFi, baseline HAQ and CRP are independent predictor factors of successful tapering. We have developed a composite index able to predict successful TNFi tapering with an AUC of 0.89 (95% CI: 0.671–0.954), a sensitivity and specificity of 94%, and an AUC of 0.89 (95% CI: 0.807–0.973). A validation study will be needed to confirm its ability to select patients for treatment decrease.

Disclosure of Interest: None declared

DOI: 10.1136/AnnRheumDis-2017-eular.1640
increases in erosion volume at MCH2 and wrist despite low disease activity (Fig. B). In the anti-TNFα group, joint space width and volume of the MCP joints decreased significantly from BL to 3M and were positively correlated with erosion volume changes. Although microstructural parameters at the wrist and MCP remained largely unchanged, erosion volume changes were significantly negatively correlated with changes of trabecular BMD in the anti-TNFα group (Fig. C). No significant correlations were observed between HR-pQCT parameters and RAMRIS and DAS scores.

Table 1. Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=26)</th>
<th>MTX only (n=9)</th>
<th>Anti-TNFα (n=17)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.9±15.4</td>
<td>60.2±15.1</td>
<td>47.7±13.9</td>
<td>0.056</td>
</tr>
<tr>
<td>Sex (Female:Male)</td>
<td>21:5</td>
<td>6:3</td>
<td>15:2</td>
<td>0.331</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>6.5±5.4</td>
<td>7.5±5.0</td>
<td>5.7±5.6</td>
<td>0.518</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.3±7.1</td>
<td>25.2±5.1</td>
<td>30.1±7.6</td>
<td>0.109</td>
</tr>
<tr>
<td>DAS28-ESR</td>
<td>4.27±2.03</td>
<td>2.17±0.53</td>
<td>5.78±1.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>3.82±1.88</td>
<td>1.93±0.61</td>
<td>5.19±1.09</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure. (A) Comparisons of changes of DAS 28 ESR and CRP from baseline (BL) to 3-months (3M). (B) Comparisons of changes of bone microarchitecture parameters from BL to 3M. *p<0.05; paired T test. (C) Spearman correlations between changes of erosion volume and each bone parameter in MCP in the anti-TNFα group.

Conclusions: We found that anti-TNFα treatment can prevent erosion progression and deterioration of bone microarchitecture within the first 3 months of treatment. HR-pQCT can serve as a sensitive and powerful tool to quantify bone changes and monitor RA treatment even over short time periods.

References:

Acknowledgements: The study was supported by UCB Pharma Inc.

Disclosure of Interest: None declared

Background: TNF inhibitors (TNFi) can be used as monotherapy (mono) or in combination (combo) with conventional DMARDs (cDMARDs). Data from randomized clinical trials and European registries suggest there is evidence of better effectiveness of TNFi combo therapy than mono. Effectiveness of TNFi mono vs combo in US clinical practice, in particular among biologic naïve and experienced patients, has not been assessed. There have also been no assessments of tofacitinib (tola) mono vs tola combo nor tola mono vs TNFi combo in US clinical practice. Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA.

Objectives: This study quantifies the prevalence and effectiveness of TNFi monotherapy use compared to TNFi combination therapy by line of therapy in US clinical practice. Secondary objectives were to compare tola monotherapy use and effectiveness separately to tola combo and to TNFi combo therapies.

Methods: RA patients initiating a TNFi (adalimumab, etanercept, infliximab, golimumab, certolizumab pegol) or tola with a six month follow-up in Corrona were identified. A subcohort of TNFi initiators after 11/6/2012 (market approval of tola) were used for comparisons with tola initiators. We defined combo therapy as TNFi or tola used with MTX only and mono as no use of any cDMARD. The primary outcome was achieving LDA (low disease activity) or remission at 6 months. Patients switching to another biologic prior to 6 months were defined as non-responders. Secondary outcomes included modified ACR20/50/70 and mean change in CDAI. Combo and mono initiators were matched within line of therapy using a propensity score. Covariates for the model were selected if the standardized mean difference between the groups > 0.1.

Results: From 10/2001 to 8/2016 there were 7976 eligible TNFi initiations in Corrona, with 2511 (31%) mono initiations. Mono by line of therapy was 21%, 36% and 42% for 2nd, 3rd and 4th line therapy, respectively. There were 555 tola initiations with 338 (61%) mono and mono rates of 47%, 58% and 63% for 2nd, 3rd and 4th line therapy, respectively. In the matched populations, across outcome measures (Table 1), TNFi combo was more effective than TNFi mono in 2nd line therapy (55.6% LDA vs 47.1% LDA) and differences diminished with 3rd line (43.2% vs 36.6%) and 4th line (32.0% vs 34.0%). Tofa combo therapy was similar to mono in the matched 3rd and 4th line populations (35.1% LDA vs 31.1% LDA). Tola mono was similar to TNFi combo therapy in the matched 3rd and 4th line populations combined (33.6% LDA vs 37.5% LDA).

Conclusions: TNFi monotherapy is common in U.S. clinical practice. TNFi monotherapy is less effective than combination therapy especially in biologic naïve patients or with one prior biologic. There is no evidence that tofacitinib monotherapy is less effective than combination therapy or TNFi combination therapy in the outcome measures reported.

Acknowledgements: This study is sponsored by Corrona, LLC. The Corrona RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, AstraZeneca, BMS, Crescendo, Eli Lilly and Company, Gilead, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Disclosure of Interest: G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, R. Gerber Shareholder of: Pfizer, Employee of: Pfizer, Y. Shan Employee of: Pfizer, D. Gruben Employee of: Pfizer, G. Wallenstein Shareholder of: Pfizer, Employee of: Pfizer, J. Kremer Shareholder of: Corrona, LLC, Employee of: Pfizer, D. van der Heijde 1, X. Baraliakos 2, K.G. Hermann 3, R. Landewé 4, P.M. Machado 5, W. Maksymyych 6, O. Davies 7, N. de Peyrecave 8, B. Hoeppken 9, L. Bauer 10, T. Nürménien 11, J. Braun 12, Leiden University Medical Center, Leiden, Netherlands; 13 Ruhr-University Bochum, Herne; 14 Charité Medical Center, Berlin, Germany; 15 Academic Medical Center, Amsterdam & Atman Medical Center Heerlen, Amsterdam, Netherlands; 16 University College London, London, United Kingdom; 1 University of Alberta, Edmonton, Canada; 17 UCB Pharma, Slough, United Kingdom; 18 UCB Pharma, Monheim; 19 Rheumazentrum Ruhrgoebiet, Herne, Germany.

Background: RAPID-axSpA (NCT01087782) was a long-term study in patients (pts) with axial spondyloarthritis (axSpA) treated with certolizumab pegol (CZP). This is the first report of 4-year imaging results in CZP-treated axSpA pts, including ankylosing spondylitis (AS) and non-radiographic (nr)-axSpA.

Objectives: To report 4-year X-ray and MRI data in CZP-treated axSpA pts.

Methods: RAPID-axSpA was double-blind and placebo (PBO)-controlled to Week 24, dose-blind to Week 48, and open-label to Week 204. Pts fulfilling ASAS axSpA criteria were stratified using a local read according to presence/absence of radiographic sacroiliitis (AS/nr-axSpA) at randomization and had active disease. Week 204 CZP-randomized pts (200mg CZP/400mg C4W) continued assigned dose; PBO pts received CZP after Week 16/24. Centrally-read lateral X-rays of cervical/lumbar spine at baseline (BL), Week 96, and Week 204 were assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS); Sacroiliac (SI) joint X-rays were scored for sacroiliitis at BL and Week 204. MRI scans performed at Week 12, 48, 96, and 204 were assessed using Spondyloarthritis Research Consortium of Canada (SPARCC) score for SI joints and Berlin score for spine.

Results: Of 315 CZP-treated pts, 196 had available spinal X-rays and were included in MMRM analyses (BL mean mSASSS: 9.47). 158 pts had MRI assessments (BL mean SPARCC: 8.17 [n=151]; Berlin score: 6.10 [n=153]; 137 pts had SI joint X-rays at BL and Week 204 (67.9% radiographic sacroiliitis). In AS pts, mean mSASSS change between BL and Week 204 was 0.98; 0.67 from BL to Week 96, and 0.31 from Week 96 to Week 204 (0.06, -0.01, and 0.07 respectively for nr-axSpA) (Table A). MMRM estimates were similar to observed values (0.62 and 0.70, respectively [axSpA Week 204 mean change]). Limited changes in SI joint X-ray grading were observed to Week 204: only 4.5% of pts progressed to AS, whilst 4.3% moved from an AS classification to nr-axSpA. MRI assessments showed sustained improvement (Table B).

Table A: Mixed model for repeated measures (MMRM) estimates of mSASSS to Week 204 of the RAPID-axSpA study for all patients treated with CZP

Table B: MRI outcomes to Week 204 of the RAPID-axSpA study for all patients treated with CZP (observed values)

Conclusions: This is the first trial to report imaging data in both AS and nr-axSpA pts over 4 years. Limited spinal radiographic progression was observed in CZP-treated pts with lower progression between Wks96 and 204 compared with the first 96 wks. Limited change in radiographic sacroiliitis was observed. Early reductions in MRI inflammation were maintained to Wk204.

References:

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Schering-Plough, UCB Pharma; Employee: A. Stassen is the guarantor of this study. J. Luwisch Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Daiichi, Eli-Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Speakers bureau: Abbbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, UCB Pharma, K. G. Hermann Speakers bureau: AbbVie, MSD, Pfizer, UCB Pharma, R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Consultant for: Abbott, Abyln, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Chugai, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Merck, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, P. Machado Consultant for: AbbVie, Centocor, Janssen, MSD, Novartis, Pfizer, Speakers bureau: AbbVie, Centocor, Janssen, MSD, Novartis, Pfizer, W. Maksymowych Grant/research support from: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, Consultant for: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, K. G.Hermann Speaker: UCB Pharma. O. Davies Shareholder of: UCB Pharma, Employee of: UCB Pharma. L. Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, N. de Peyrecave Employee of: UCB Pharma, B. Hoepken Employee of: UCB Pharma, L. Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, T. Nurmienen Employee of: UCB Pharma, J. Braun Grant/research support from: Abbott, Bristol-Myers Squibb, Celgene, Chugai, Roche, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Consultant for: Abbott, Bristol-Myers Squibb, Celgene, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma.

Background: Immuno sorbent assay for anti-drug antibodies is a reliable and sensitive test to detect anti-drug antibodies. However, it is not widely available and the test needs to be performed in a research laboratory. Moreover, anti-drug antibodies can be detected in samples without the corresponding clinical picture of adverse events. Therefore, we aimed to evaluate the association between anti-drug antibodies and adverse events.

Objectives: The objective of this study was to evaluate the association between anti-drug antibodies and adverse events in patients treated with adalimumab.

Methods: Adalimumab was administered in patients with moderate to severe rheumatoid arthritis and an inadequate response to nonsteroidal anti-inflammatory drugs. Anti-drug antibodies were determined by a commercial ELISA (Meso Scale Discovery, Gaithersburg, MD). The presence of antibodies was confirmed by using a second ELISA and retesting was performed in case of positive results. Adverse events were collected on a standardized form. The results were analyzed by comparing the group of patients with anti-drug antibodies with the group of patients without anti-drug antibodies.

Results: 313 patients with anti-drug antibodies were included in the study and 339 patients were included in the control group. The prevalence of anti-drug antibodies was 50.1% in the group of patients with adverse events and 41.8% in the group of patients without adverse events. The prevalence of adverse events was 60.1% in the group of patients with anti-drug antibodies and 44.7% in the group of patients without anti-drug antibodies. The difference in prevalence of adverse events between the two groups was statistically significant (p = 0.025) using the chi-square test.

Conclusion: Anti-drug antibodies are associated with an increased risk of adverse events in patients treated with adalimumab.

Disclosure of Interest: The authors declare that they have no conflict of interest.


Acknowledgements: The study was supported by the University of Athens, Greece.
(0.9–4.3) and 9.5 (5.3–13.3), p=0.000. When patients tested positive in the ARIA, ABT and the 2-sided ELISA almost all patients had undetectable drug levels.

Conclusions: The fast majority of the AS patients develop ADA. The ARIA detects more ADA compared to the assays susceptible for drug interference, the ABT and the more frequently used 2-sided ELISA. Immunogenicity data should be interpreted with the knowledge of the assay and in context of drug levels.

Disclosure of Interest: J. Ruwaard: None declared, A. Marsman: None declared, M. Nurmohamed: None declared, H. te Velthuis: None declared, K. Bloem: None declared, T. Rispens Speakers bureau: Pfizer, AbbVie, G. J. Wolbink Grant/research support from: Pfizer, Speakers bureau: Pfizer, AbbVie, UCB

DOI: 10.1136/annrheumdis-2017-eular.6149

OP0026 HIGH DRUG-FREE REMISSION IN EARLY PERIPHERAL SPONDYLOARTHRITIS AFTER INDUCTION THERAPY WITH GOLIMUMAB

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Background: In rheumatoid arthritis there is accumulating evidence for a so-called “window of opportunity” remission induction treatment at an early stage of the disease. Whether a similar concept also applies to Spondyloarthritis is currently unknown. Given the higher chance of obtaining remission or low disease activity with early aggressive (biologic) treatment in early axial SpA, one could speculate that there is at least also a possibility of a “window of opportunity” for drug-free remission in peripheral SpA (pSpA).

Objectives: To evaluate sustained drug-free clinical remission after induction therapy with golimumab in patients with active peripheral Spondyloarthritis in a very early stage of the disease.

Methods: CRESPA (Clinical REmission in peripheral SPondyloArthritis) is an ongoing monocentric study of golimumab treatment in pSpA patients. Eligible patients were ≥18 years and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for pSpA. All patients had a symptom duration <12 weeks. Patients were randomized 2:1 to receive golimumab 50 mg every 4 weeks or matching placebo for 24 weeks. The primary endpoint was the percentage of patients achieving clinical remission at week 24, defined as the absence of arthritis, enthesitis and dactylitis on clinical examination. If patients were in clinical remission at two consecutive visits (major evaluations at week 12, 24, 36 and 48) treatment was stopped. These patients were prospectively followed to assess the percentage of patients in sustained drug-free clinical remission, compared to those experiencing a clinical relapse of arthritis, dactylitis or enthesitis. In case of clinical relapse patients were retreated with open-label golimumab in the extension part of this trial.

Results: In total 60 patients were randomized of whom 20 received placebo and 40 golimumab. Baseline demographics and disease characteristics were generally similar between the 2 groups. At week 24 a significantly higher percentage of patients receiving golimumab achieved clinical remission compared to patients receiving placebo (75% (30/40) versus 20% (4/20); P<0.001). At week 12 similar results were observed (70% (28/40) versus 15% (3/20); P<0.001). In 49 out of the 60 patients treatment could be stopped because they fulfilled sustained clinical remission at 2 major consecutive visits. All patients had at least a follow up of 12 months after discontinuation of treatment with a maximum of follow-up of 58 months. 53% (26/49) of these patients are still in drug-free sustained clinical remission and 47% (23/49) had a clinical relapse after withdrawal. The majority of relapsed patients experienced their flare within 6 months after discontinuation.

Conclusions: In patients with active, very early peripheral spondyloarthritis, treatment with golimumab led to high percentages of clinical remission at week 12 and 24. A remarkably high percentage of patients are still in sustained drug-free clinical remission after induction therapy with golimumab which indicates a window of opportunity for drug-free remission in this disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1656

OP0027 WITHDRAWN

WITHDRAWN
LOW DOSE IL-2 THERAPY CAN RECOVERY TH17/TREG CELL BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Recent studies have shown that increased number of Th17 cells and decreased number of Treg cells in the peripheral blood contribute to ankylosing spondylitis (AS). However, current therapy for AS, including biological agents, immunosuppressant and glucocorticoid, can not correct the imbalance of Th17 and Regulatory T (Treg) cells in AS patients effectively. It has been reported that low dose IL-2 can selectively expand Treg cells and had a critical effect on homoeostatic balance between the Th17 and Treg cells.

Objectives: The study is to explore the effect of low dose IL-2 therapy on the balance of Treg and Th17 cells in patients with AS and observe the efficiency and side effects of the therapy.

Methods: Seventeen patients, who met the 1984 modified New York criteria and had evidence of active inflammatory spondylitis (defined as Bath AS Disease Activity Index (BASDAI) score >4) despite of receiving standard therapy including glucocorticoid, immune-suppressants, biological agents or combination of them, were enrolled. These patients were not only given traditional treatment, but also injected subcutaneously low-dose IL-2 (50 IU/day for 5 days). Clinical and laboratory indicators were compared before and after IL-2 treatment. The side effects were observed in the course of therapy.

Results: The number of Treg cells significantly increased after the treatment by 44.1% of patients had a global benefit of at least 50% at D15, 63.6% at M1, 25.6% at M3 and 33.3% at M6. There was no decrease of the BASDAI, BASFI, ESR, CRP, ASDAS ESR and ASDAS CRP. Moreover, no relationship was found between the efficiency of sacroiliac infiltrations in terms of global benefit as well as of decrease of the VAS at least of 50% and the presence of sacroiliac images on the MRI. Neither when looking at the different subtypes of sacroiliitis lesions (bone marrow oedema, synovitis, osteitis). Among the non active sacroiliac structural lesions (erosions, subchondral sclerosis, bone bridges…), only fatty involution was statistically more present in the group with a global improvement or a VAS of less than 50%.

Conclusions: Long acting corticosteroid infiltrations of the sacroiliac joints are useful in patients suffering from inflammatory sacroiliitis pain. However, the majority of sacroiliac joints images found on a concomitant MRI does not predict the treatment response except fatty involution that seems to be associated with a lower response. Likewise, composite indexes/scores as well as parameters of systemic inflammation are not relevant for the patients follow up in that indication.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2303

INEQUITY IN BIOLOGIC DMARD PRESCRIPTION FOR SPA ACROSS THE GLOBE. RESULTS FROM THE ASAS COMOSPA STUDY

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Background: The value of biologic DMARDs (bDMARDs) in SpA is well recognized but global access to these treatments can be limited due to high cost and other factors.

Objectives: This study explores variation in the use of bDMARDs in SpA across countries and to what extent socio-economic (SE) factors may explain variation.

Methods: Patients fulfilling the ASAS SpA criteria in the multi-national, cross-sectional ASAS COMOSPA study were studied. Multi-level logistic regression models with random intercept for country were constructed with current use of bDMARDs as the dependent variable. Contribution of socio-economic factors using country health expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) as independent country-level factors, was explored in models adjusted for socio-demographic as well as clinical variables known to determine bDMARD-use in SpA.

Results: In total, 3370 patients from 22 countries were included (mean [SD] age 43 [14] years; 66% male; 88% axial disease). Across countries, 1275 (38%) were bDMARD users. Crude mean bDMARD-use varied between 5% (China) to 74% (Belgium). After adjustment for relevant socio-demographic and clinical variables, important variation in bDMARD-use across countries remained (Figure, p<0.001). Country-level socio-economic factors, specifically higher health...
expenditures were related to higher bDMARD uptake (Table), though not meeting statistical significance (OR 1.91; 95% CI 0.93,3.92). Similar findings were found with country GDP (OR 1.72;95% CI 0.83,3.57).

Conclusions: There remains important residual variation across countries in bDMARD uptake of patients with SpA followed in specialized SpA centers. This is in line with other similar studies report on variability in the use of other therapies for SpA, which may be related to different reimbursement strategies and differences in the disease burden in the countries.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4480

WEDNESDAY, 14 JUNE 2017

Early diagnosis of systemic sclerosis and myositis: biomarkers and diagnostic tool

OP0031 DEVELOPMENT OF A NOVEL EPITOPE-BASED DIAGNOSTIC ASSAY FOR SYSTEMIC SCLEROSIS

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Background: We described the conformational PDGFRα biomarkers and diagnostic tool

Methods: i. The large PDGFRα peptide library used for epitope mapping of monoclonal anti-PDGFRα antibodies was screened with 25 SSC (12 limited, 13 diffuse) and 25 healthy control (HC) serum samples. ii. A smaller PDGFRα peptide library containing only the top 20 conformational binders plus 20 linear and 20 conformational controls was synthesized. 60 conformational and linear peptides of a cognate protein forming a molecular complex with PDGFRα were included in the array. 20 scrambled peptides were added as negative controls. This library was synthesized by Pepscan Presto, Netherlands. Statistical analysis was performed by Wilcoxon-Mann-Whitney test. Correlations between serological results and clinical status were made.

Results: i. An immunodominant peptide discriminating SSC from HC serum samples was identified in the first library. This was confirmed by the second library, which highlighted also one immunodominant epitope from the cognate protein. Statistical analysis identified two cohorts of SSC samples (reactive vs. nonreactive, the latter undistinguishable from HC) each composed by limited and diffuse SSC subtypes.iii. The third peptide library identified the chimeric peptide recognized exclusively by the reactive SSC serum samples, which were taken from patients with active, progressive disease regardless of limited vs diffuse classification, whereas the nonreactive SSC samples were taken from subjects with less active, non progressive disease.

Conclusions: We developed a conformational epitope-based assay detecting SSC-specific, agonistic, serum autoantibodies. The preliminary results suggest that this novel assay may identify SSC patients with active disease, regardless of the canonical classification criteria. We propose this assay for prospective screening of large cohorts of patients affected by, or suspected for, SSCs, to validate it as a tool for disease activity assessment and/or early diagnosis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6814

OP0032 IS IMMUNOHISTOCHEMISTRY USEFUL TO PREDICT RESPONSE TO TREATMENT IN NECROTIZING MYOPATHIES?

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Background: Muscle biopsy is the gold standard for the diagnosis of inflammatory myopathies, but the role of immunohistochemistry in Necrotizing Myopathies (NM) has not been fully characterized yet.

Objectives: To determine if MHC-I expression and pattern of Csβ-9 deposition in biopsies correlate with clinical phenotype and response to treatment in NM.

Methods: The Neuropathology Departmental database was searched to identify patients with a histological diagnosis of NM and follow up data for at least 6 months (30 patients). Electronic patient records were reviewed retrospectively to record demographics, autoimmune diseases, treatments, treatment, proximal muscle power at 3, 6 and 12 months by Manual Muscle Testing (MMT) (2), levels of CK and flares. Patients were classified as responders when there was improvement of MMT >20% and non-responders when MMT improvement was <20% (3). All biopsies were reviewed blindly by an experienced neuropathologist. MHC-I expression was classified as positive only if over expressed in all fibers. The patterns of Csβ-9 deposition in endomysial capillaries were classified as specific (solid), non-specific (granular) or negative.

Results: MHC-I positive group (n=16/30) had a higher proportion of responders (62.5% vs 7.7%, p<0.002), higher number of patients with total recovery of muscle power (n=4, 15.4%) when compared to the MHC-I negative group (n=4-14). 17 patients were positive for auto-antibodies of which 9 were myositis specific antibodies (SRP [n=6], HMGCaCoA reductase [n=1], Jo-1 [n=1], P15S140 [n=1]) and 4 were myositis associated antibodies [Ro-52 [n=2], KU [n=1], PrmScl [n=1]]. 13/30 patients had Csβ-9 deposition, with a specific pattern in 5 and non-specific in 8. The specific pattern group had a greater reduction of CK after 6 months compared to non-specific and negative respectively (98% vs. 77% vs. 56.8%, p=0.006), greater reduction in CK after 12 months (98.6% vs. 68.9% vs. 59.6%, p=0.015), and higher rate of responders (91.6% vs. 56% vs. 18.8%, p=0.001). Six patients were on immunosuppressants (azathioprine/hydroxychloroquine, n=2), steroids (n=3) or both (n=1) for a minimum of 4 weeks when the biopsy was performed. Differences in age, gender, clinical features or treatment were not found to be statistically significant.

Conclusions: Upregulation of MHC I and solid staining pattern of Csβ-9 in the capillaries of NM patients appears to be associated with a better outcome.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6814

OP0033 SPECT- AND PET/CT IMAGING IN NEWLY ONSET IDIOPATHIC INFLAMMATORY MYOPATHY

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Background: Diagnosis of idiopathic inflammatory myopathies (IIMs) is challenging. Most patients harbor no pathognomonic features on imaging by imaging. Few radiologic imaging techniques have been tested for this purpose, mainly 99mTc-pyrophosphate planar imaging and 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT). However, 99mTc-PYP uptake has been assessed visually and at best graded semi-quantitatively.

Objectives: We aimed for quantitative 99mTc-PYP and 18F-FDG-PET/CT imaging in a group of newly onset IIM patients.

Methods: Thirty patients (mean age 62 years) with newly diagnosed, untreated IIM were included. 99mTc-PYP SPECT/CT and 18F-FDG-PET/CT imaging of the thorax, pelvis, and thighs. Seven of the patients also had a whole-body 99mTc-PYP PET scan. Forty-nine healthy controls (mean age 59 years) underwent 99mTc-PYP SPECT/CT and 26 healthy controls (mean age 57 years) had a 18F-FDG PET/CT scan done. Voltages of interest (VOIs) covering the right biceps, triceps, and quadriceps muscles were drawn manually on each series. Registered 99mTc-PYP and 18F-FDG uptake values (SU/mL) were analyzed.

Results: In the IIM group there was a greater uptake of 99mTc-PYP and 18F-FDG (75% vs. 35.7%, p=0.030) when compared to the IIM-group negative (n=14). The uptake was significantly higher (99mTc-PYP SUV [g/mL] 1.95 (0.25-4.26) vs. 0.42 (0.19-1.41), 18F-FDG SUV [g/mL] 2.93 (0.19-5.1) vs. 0.76 (0.09-2.08), p=0.001) in IIM patients compared to controls.

Conclusions: 99mTc-PYP and 18F-FDG-PET/CT imaging is useful for the diagnosis and assessment of the activity of inflammatory myopathies in newly onset IIM patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6009
Results: IIM patients had visible tracer uptake in the skeletal muscles of the extremities. The muscular 99mTc-PYP uptake was significantly higher in upper limbs of patients than the uptake in the same muscle groups in healthy controls (uptake[biceps] 0.46 vs. 0.31 g mL\(^{-1}\), p=0.01; uptake[triceps] 0.40 vs. 0.27 g mL\(^{-1}\), p<0.003). The 99mTc-PYP uptake tended to be higher in the lower limbs of patients than controls (in the lower limb 99mTc-PYP uptake of 0.74 ± 0.53 g mL\(^{-1}\)), (p=0.006; SUV\(_{max}\)[biceps] 0.91 vs. 0.44 g mL\(^{-1}\), p=0.008) and lower limbs (SUV\(_{max}\)[quadriceps] 0.84 vs. 0.62 g mL\(^{-1}\), p<0.0001). The muscular FDG uptake values were consequently higher than the 99mTc-PYP uptake values, although not by a constant factor.

Conclusions: Quantitative 99mTc-PYP SPECT/CT as well as 18F-FDG PET/CT imaging revealed muscular inflammation in patients with newly onset, untreated IIM. Patients had a tracer uptake in skeletal muscles groups than healthy controls. Quantification of muscular tracer uptake with the potential to objectively distinguish physiology from pathology could be a valuable tool in the challenging diagnosis of IIMs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6000

**OP0035 PRELIMINARY ANALYSIS OF NAILFOLD CAPILLAROSCOPY IN THE VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS (VEDOSS): THE CAP-DI -VEDOSS EXPERIENCE**

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Background: In Systemic Sclerosis (SSc), before the onset of clinical signs of fibrosis, puffy fingers, specific autoantibodies and microcirculatory modifications are present and are identified in the VEDOSS criteria for ‘very early’ disease. No previous studies are available indicating the prevalence of nailfold capillaroscopic (NVC) SSc patterns or quantitated capillaroscopic characteristics in a ‘very early’ cohort.

Objectives: Evaluation of the prevalence of SSc patterns and quantitated capillaroscopic characteristics in a ‘very early’ cross sectional SSc cohort.

Methods: Multicentre observational cohort study of patients with two strata (Figure): 1RAYNAUD’s phenomenon (RP), Anti Nuclear Antibody (ANA) positive (+), 2. RP, ANA negative (-). ‘Target’ (RP+, ANA, puffy finger [PF] +/-, SSc-antibody (SSc-Ab), NVC+) and ‘control’ (RP-, ANA, SSc-Ab, NVC-) subsets were described. NVC patterns (non-specific abnormalities, SSc-patterns) were entered into database. Generalized Estimating Equations (GEE) were used to assess differences in prevalence of NVC patterns between strata, taking clusters of patients within centers into account.

Results: 1085 RP patients from 40 centres (median number [n] of pt 12 (minimum [min] 1-maximum [max] 393) per centre were enrolled in the VEDOSS online database. Due to erroneous included/missing data (e.g. erroneously absence/missing information on RP, presence of former ACR criteria for SSc, skin involvement at baseline; missing info on: ANA positivity, PF, Cap, SSc-Ab) 750 patients (median n= 7 min=1-max=271) were retained for the analysis. Scoring of capillaroscopy (NVC-patterns) with “Active”, “Late”; “Sclerodermlike” and quantitative (“absent”=“none” or “rare”) and “present” (≈“moderate” or “extensive”) capillaroscopic alterations for giants, haemorrhages, capillary loss and abnormal capillaroscopic characteristics were evaluated. Generalized Estimating Equations (GEE) were used to assess differences in prevalence of NVC patterns between strata, taking clusters of patients within centers into account.

Conclusions: More than 40% of early-diagnosed SSc-PAH patients in the DETECT cohort who were followed over time had disease progression during a rather short follow-up time, with male gender, functional capacity, and pulmonary function (low FVC) also significantly associated with progression. This suggests that even mild and early detected PAH should be regarded as a high-risk complication of SSC, and every effort to make an early diagnosis is valuable.

Acknowledgements: The authors thank all investigators and patients involved in
Conclusions: The VEDOSS cohort presents predominantly an “Early” NVC SSc pattern. Notably the prevalence of NVC SSc patterns was higher in the ANA than ANA-stratum. This evidence further reflects the pivotal role of NVC in the very early diagnosis of SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2932

### OP0036 SEROLOGICAL BIOMARKERS OF ECM TURNOVER ARE ASSOCIATED WITH SKIN FIBROSIS AND LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

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**Background:** Extracellular matrix (ECM) unbalance of the skin is a hallmark of systemic sclerosis (SSc). However, currently there is no objective tool to monitor the ECM unbalance in SSc patients allowing for better understanding of the disease stage and activity.

**Objectives:** We investigated the potential of serological biomarkers of ECM turnover (collagen formation and degradation) as biomarkers of skin fibrosis and internal organ involvement in SSc patients.

**Methods:** Peripheral blood obtained from 79 SSc patients and 19 healthy subjects was included in the study. Type I, III, IV, V and VI collagen formation and degradation (P1NP, PRO-C3, P4NP7S, PRO-C5, PRO-C6) and degradation (C3M, C4M, C5M, C6M) biomarkers were detected by ELISA in serum. Modified Rodnan skin score (mRSS) and extent of internal organ involvement (renal, lung, vasculopathy and gastrointestinal) were recorded for SSc patients with a scoring between 0 and 4, with 0 being no involvement and 4 being severe involvement. Mann-Whitney t-test was used to test difference in the biomarker levels between the patient groups and in groups with and without internal organ involvement. Spearman’s correlation coefficient investigated the association between biomarkers and clinical manifestations.

**Results:** SSc patients had a mean age of 63.0 years, mean disease duration of 98.3 months and a mean mRSS of 11.1. SSc patients compared to healthy individuals had higher levels of C5M, C6M and PRO-C6 (p<0.0001, p=0.003, p<0.0001, respectively). The levels of type VI collagen formation and degradation (PRO-C6 and C6M) were twice as that of healthy controls (12.6 vs. 5.4 and 26.0 vs 13.8ng/mL, respectively). C4M2, PRO-C3 and PRO-C6 was associated with skin fibrosis assessed by mRSS (Spearman’s rho=0.24, 0.39 and 0.29, respectively). Patients with signs and manifestation of lower gastrointestinal lesion compared to patients without lesion had higher levels of C3M (median 10.7 vs 13.8ng/mL, p=0.017, figure). C7M was higher in patients with pulmonary hypertension (p=0.04) compared to patients with signs of or no pulmonary hypertension (median 22.1 vs 29.9ng/mL, p=0.026). P1NP was lower in patients with interstitial pneumonia, whereas C6M was higher. There was no difference in the biomarker levels with and without upper gastrointestinal lesions, renal dysfunction or vasculopathy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4855

### OP0037 EVALUATION OF SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS BY USING TWO ULTRASOUND TRANSDUCERS WITH DIFFERENT FREQUENCY

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**Background:** The modified Rodnan skin score (mRSS) is the validated method to evaluate the extension of skin involvement in systemic sclerosis (SSc) and to distinguish between patients with limited cutaneous skin involvement (lCSSc, skin involvement is confined to the extremities) or diffuse (dCSSc) (1,2). Recently several studies have demonstrated that skin high frequency ultrasound (US) is a valid and reproducible technique to measure dermal thickness (DT) in patients with SSc (3–6).

**Objectives:** To compare the values of DT obtained by two ultrasound transducers with different frequency (18 MHz and 22 MHz) in evaluating the DT in lCSSc patients and healthy controls.

**Methods:** Thirty-seven lCSSc patients (mean age 62±13SD years, mean disease duration 5±5SD years) and 37 healthy controls (CNT) sex and age matched were enrolled after informed consent. Both US transducers of 18 and 22 MHz (Esaote, Genova) were used to evaluate DT in the seventeen areas of the skin (zygoma, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, feet) of SSc patients where Rodnan skin score (mRSS) is usually assessed. Skin US was also performed in the same seventeen areas of CNT, looking for DT differences in comparison with lCSSc patients. Statistical analysis was carried out by non-parametric tests.

**Results:** DT evaluated with the 22 MHz probe was found significantly higher in all body areas in comparison with the 18 MHz transducer, both in lCSSc patients and healthy controls (p<0.01) and in CNT (p=0.05). The median difference of DT values between the two probes was of 0.11 millimetres in lCSSc patients (minimum 0.0023, maximum 0.28mm) and 0.01 millimetres in CNT (minimum 0.0029, maximum 0.03 mm). Of interest, in lCSSc DT evaluated by 18 MHz transducer was recognized significantly higher (p<0.001) also in four out of six skin areas where the mRSS was found normal (score=0) (upper-arms, chest and abdomen), with exclusion of thighs (p=0.08), in contrast with the classification of lCSSc. However, by using the 22

<table>
<thead>
<tr>
<th>Healthy</th>
<th>SSc</th>
<th>P-value</th>
<th>Spearman’s correlation to mRSS (rho=p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C5M</td>
<td>12.8</td>
<td>13.4</td>
<td>0.21 (0.06)</td>
</tr>
<tr>
<td>C4M2</td>
<td>31.1</td>
<td>34.0</td>
<td>0.24 (0.03)</td>
</tr>
<tr>
<td>C5M</td>
<td>2.6</td>
<td>3.9</td>
<td>0.0001  (0.03)</td>
</tr>
<tr>
<td>C6M</td>
<td>16.7</td>
<td>26.0</td>
<td>&lt;0.0001 (0.11)</td>
</tr>
<tr>
<td>P1NP</td>
<td>36.9</td>
<td>130.4</td>
<td>0.02 (0.00)</td>
</tr>
<tr>
<td>PRO-C3</td>
<td>14.2</td>
<td>20.8</td>
<td>0.39 (&lt;0.001)</td>
</tr>
<tr>
<td>P4NP7S</td>
<td>286.8</td>
<td>290.3</td>
<td>0.19 (0.10)</td>
</tr>
<tr>
<td>PRO-C5</td>
<td>525.2</td>
<td>484.4</td>
<td>0.07 (0.52)</td>
</tr>
<tr>
<td>PRO-C6</td>
<td>5.4</td>
<td>12.6</td>
<td>-0.0001 (0.29)</td>
</tr>
</tbody>
</table>
Myositis autoantibodies outperform clinical subgroups in predicting muscle weakness in myositis patients

Background: Myositis patients may be classified as belonging to one of four clinical groups: dermatomyositis (DM), polymyositis (PM), clinically amyopathic dermatomyositis (CADM) or necrotizing myositis (NM). Alternatively, myositis patients may be classified according to myositis autoantibody status.

Objective: Our study was to determine whether clinical groups or myositis autoantibodies provide better prognostic categories with regard to muscle involvement in these patients.

Methods: All Johns Hopkins Myositis Center patients from 2002 to 2015 with a myositis-specific autoantibody confirmed by two different immunologic techniques were included. Autoantibody groups accounting for less than 2% of the final sample size were excluded. Strength (analyzed as the average of deltoid and hip flexor strength using Kendall’s scale) and log transformed CK levels were compared between the different autoantibody groups using multilevel regression models adjusted for age, time from disease onset, sex, race and treatments. Models with different combinations of key variables were compared using the likelihood ratio test to ascertain if autoantibody groups and clinical subgroups provided the same amount of information regarding muscle weakness and CK levels over time.

Results: 483 patients with 4181 visits were included and 10 different autoantibody groups were identified. Muscle weakness and CK levels followed a gradient among both antibody and clinical groups. Anti-SRP patients had the greatest weakness, followed by anti-HMGCR, anti-Mi2 and anti-NXP2, and then anti-Jo1. CK levels were highest in anti-HMGCR patients, followed by anti-SRP, anti-PL7, anti-Jo1 and anti-Mi2. Interestingly, strength and CK levels were more consistently associated with disease activity and CK levels in two groups: anti-NXP2 patients had significant weakness with low CK levels and anti-PL7 patients were relatively strong despite high CK levels. Multilevel regression models showed autoantibody groups explained the strength and the CK variability better than the clinical groups (AIC difference >20). Indeed, adding clinical groups to a model using only autoantibodies did not improve the model’s ability to predict strength (p>0.2) and only mildly improved its ability to predict CK (p=0.01). In comparison, adding the autoantibodies to a model using the clinical groups resulted in a marked improvement in predicting both CK and strength (both p<0.001).

Conclusions: In patients with myositis, autoantibody status predicts strength and CK levels better than clinical grouping.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2718
Bacteremia in Systemic Lupus Erythematosus Patients from RELESSER Registry: Risk Factors, Clinical and Microbiological Characteristics and Outcomes

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Background: According to RELESSER (Spanish Society of Rheumatology Lupus Registry) data, bacteremia is the main cause of death by infection in systemic lupus erythematosus (SLE). However, the available information about this severe infection in SLE patients remains scarce.

Methods: Retrospective, nested case-control study of SLE patients (ACR-97 criteria) with at least one bacteremic episode and random controls from RELESSER Registry. Descriptive, bivariate and multivariate analysis (logistic regression).

Results: 114 bacteremic episodes in 83 patients were recorded. Incidence rate: 2.7/1,000 patient-years (n total: 3658). At the time of the bacteremia: median age: 40.5 (8–90) years, 88.6% female, disease duration: 9.7 (IRI6.7), median SELENA-SLEDAI: 4 (IRB), 86% with severe flare (SFI criteria), active nephritis: 16.7%, median SLICC/ACR DI: 3 (IR), any comorbidity: 64% (McCabe-Jackson criteria: 28.1% rapidly or ultimately fatal), more frequent renal failure (15.8%) or diabetes (11.4%). SLE treatment at the time of bacteremia: 88.6% corticosteroids (66.8%>10mg/day), 57% immunosuppressors (mycophenolate 17.5% and cyclophosphamide 12.3%), 27% antimarialials. 44.7% suffered invasive procedures, more frequently intravascular catheterization (24.6%). The bacteremia was nosocomial in 35.1% and the source was more frequently urinary (27.2%). 64% developed systemic inflammatory response syndrome and 35% needed intensive care unit admission, with multorganic failure in 22.8%. The most frequent microorganism was E.lolii (29.8%) followed by Staphylococcus aureus (16.7%) (Cox mathillin-resistant) and Salmonella spp (15.4%). The most frequent enteric bacilli were extended-spectrum b-lactamase positive. 17.5% were multidrug resistant. 68.4% started the antibiotic therapy before blood culture results, resulting finally active in susceptibility testing in 56 cases (71.8%), indicating an appropriate empirical antibiotic therapy in 49%. The bacteremia-related mortality was 14%. The risk of death was higher in patients with severe sepsis (Pitt index >8) (OR: 13 (IC95%: 3.71–45.17), The bacteremia was recurrent in 26.3%.

Associations with bacteremia in bivariate analysis (114 bacteremias vs 688 controls) are shown in Table 1. Antimalarials were protective. In the multivariate analysis (adjusted for disease duration), only elevated creatinine (OR 1.31 (95% CI 1.01–1.70), p=0.045), diabetes (OR 6.01 (95% CI 2.26–15.95), p<0.000), cancer (OR 5.32 (95% CI 2.23–12.70), p<0.000), immunosuppressors (OR 6.35 (95% CI 3.42–11.77), p<0.000), cyclophosphamide (OR 9.37 (95% CI 5.12–17.14), p<0.000), cancer and SLICC/ACR DI (OR 1.65 (95% CI 1.31–2.09), p<0.000) remained statistically significant.

Conclusions: Bacteremia occurred mostly in active SLE, frequently in the context of a severe flare. Gram negative bacilli predominated, with high rate of multidrug resistance. The empiric treatment was inappropriate in a half of the cases. The empiric treatment was inappropriate in a half of the cases.
recurrence and mortality were high. Immunosuppressors use, comorbidity and damage were all associated to bacteremia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4138

OP0043

THE NUMBER OF CIRCULATING REGULATORY T CELLS IS REDUCED AND LOW-DOSE IL-2 SELECTIVELY STIMULATES ITS PROLIFERATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The imbalance of T help 17 cells (Th17)/regulatory T cells (Tregs) is considered to be a pivotal cause of autoimmune diseases 1, including systemic lupus erythematosus (SLE). However, previous reports 2-4 describing the respective changes of Tregs and Th17 cells in SLE patients were controversial because a few samples or diverse markers were used to identify Tregs with little consensus.

Objectives: To clarify the status of Tregs and Th17 in SLE, we investigated the frequencies of Tregs and Th17 cells on a large scale and whether those defects can be corrected by the supplementation of low-dose human recombiant interleukin-2 (IL-2).

Methods: Two hundred and thirty-five SLE patients (219 women and 16 men), with mean age of 37.80±14.00 years, were enrolled. The disease activity using erythrocyte sedimentation rate (ESR) and SLEDAI scores. The frequencies of CD3+CD4+FOXP3+Treg cells and Th17 cells in peripheral blood from these patients were measured by flow cytometry. And low-dose IL-2 was used among 127 patients at a dosage of fifty WIU every day for five days.

Results: As compared to healthy controls (median of Treg cells: 33.09 cells/ul), the frequencies of circulating CD4+CD25+FOXP3+Treg cells were significantly decreased, while CD4+CD25+FOXP3+Treg cells were negatively correlated with ESR and SLEDAI (P<0.01; r=-0.25, P<0.001), tended to balance and had no difference with healthy individual (P>0.25).

Conclusions: Our study assessed for the first time ASCA IgG+IgA with a highly specific immunoblot assay in a large cohort of pSS patients, showing that ASCA positivity identifies a peculiar clinical and serological pSS phenotype. In particular, ASCA+ pSS patients display anti-Ro52, anti-Ro60 and anti-La autoantibodies (p<0.001). No differences concerning T regulatory and Th17 cell proportion could be observed in ASCA+ compared to ASCA- pSS patients. S. cerevisiae mannan displays a consistent similarity with 52kD and 60kD Ro/SSA, La/SSB autoantigens. The highest similarity was observed when aligning the mannan with 60kD Ro/SSA (identities 71/114, 64%; positives 8/11, 72%; E value 2.2).

Disclosures: None declared

DOI: 10.1136/annrheumdis-2017-eular.3163

OP0044

ANTIBODIES ANTI-SACCHAROMYCES CEREVISIAE IN PRIMARY SJÖGREN’S SYNDROME: PREVALENCE, CLINICAL ASSOCIATIONS AND POSSIBLE CROSS-REACTIVITY WITH DISEASE SPECIFIC AUTOANTIGENS

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Background: Saccharomyces cerevisiae is a common yeast used in the food industry. Antibodies against the phosphopeptidomannan part of the cell wall of S. cerevisiae (ASCA) are a well established biomarker of Crohn’s disease and have been assessed in several organ-specific and systemic autoimmune diseases (ADs) (1–2) Although the pathogenic significance of ASCA is not yet fully understood, the molecular mimicry of self-antigens in several associated ADs has been suggested as putative mechanism.

Objectives: Since to date ASCA have not been tested in primary Sjögren’s syndrome (pSS), the purpose of this study was to assess these antibodies in a large cohort of pSS patients and investigate their significance as potentially helpful biomarker in a clinical setting.

Methods: One hundred and four patients with pSS according to the 2002 American European Consensus criteria and 30 healthy donors were enrolled. ASCA IgG+IgA were assessed in serum samples by ASCA screen dot (Alphadia sa/mv). T cell phenotyping was performed in paired peripheral blood samples by flow cytometry. To compare the aminoacid sequence of mannan of Saccharomyces cerevisiae and well characterized auto-antigens peculiar of pSS (52kD and 60kD Ro/SSA, La/SSB) we browsed the protein database of the National Center for Biotechnology Information (NCBI) and run the Basic Local Alignment Search Tool (BLAST).

Results: ASCA were detected in 5 out of 104 pSS patients, therefore the prevalence in our cohort is 4.8%. None of the ASCA+ pSS patients displayed IL-2 or other autoimmune concomitant disease not significant for ASCA positivity. ASCA+ pSS patients displayed more frequency a reduction of C3 and C4 complement fractions as well as pulmonary, articular and cutaneous involvement (all p<0.05).

Binary logistic regression revealed that ASCA+ pSS patients display an odds ratio of 14 (p=0.006) to have cutaneous manifestations of pSS. All ASCA+ patients but only 39% of ASCA- patients displayed anti-Ro52, anti-Ro60 and anti-La autoantibodies together (p=0.01). No differences concerning T regulatory and Th17 cell proportion could be observed in ASCA+ compared to ASCA- pSS patients. S. cerevisiae mannan displays a consistent similarity with 52kD and 60kD Ro/SSA, La/SSB autoantibodies. The highest similarity was observed when aligning the mannan with 60kD Ro/SSA (identities 71/114, 64%; positives 8/11, 72%; E value 2.2).

Conclusions: Our study assessed for the first time ASCA IgG+IgA with a highly specific immunoblot assay in a large cohort of pSS patients, showing that ASCA positivity identifies a peculiar clinical and serological pSS phenotype. In particular, ASCA+ pSS patients display anti-Ro52, anti-Ro60 and anti-La autoantibodies, low complement and cutaneous involvement. The high similarity between S. cerevisiae mannan and Ro60/SSA autoantigen may suggest: i. ASCA may bind Ro52 and Ro60 autoantigens such as anti-Ro, as already postulated for other autoantigens (2); ii. ASCA may bind more likely Ro60 autoantigen rather than the Ro52 or La autoantibodies in pSS. A possible pathogenic/prognostic significance of ASCA in pSS may therefore be speculated.

Disclosures: None declared

DOI: 10.1136/annrheumdis-2017-eular.3163

OP0045

PREDICTORS OF PERSISTENT DISEASE ACTIVITY AND PERISTANT LONG QUESCENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS – RESULTS FROM THE HOPKINS LUPUS COHORT

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Background: Systemic lupus erythematosus (SLE) is characterized by a diversity of disease activity.

Objectives: The aim of this study was to identify prognostic factors of persistent disease activity and persistent long quiescence using baseline demographics and clinical characteristics.

Methods: Patients enrolled in the Hopkins Lupus Cohort from 1987 to 2014, who had at least 3 visits per year during the first 3 years following cohort inclusion and complete information on disease activity were included. Three major patterns of SLE disease activity over time (1 year intervals) based on the modified SLE Disease Activity Index have been previously described: low quiescent (LQ), chronic active (CA) and relapsing-remitting (RR). (1). Based on maintenance of the aforementioned
patterns over 3 consecutive years, patterns have been defined as: Persistent Long Quiescence (pLQ), Persistent Relapsing-Remitting (pRR), Persistent Chronic Active (pCA) and Mixed, at least 2 different pattern types. Predictors of pCA (vs. pLQ, pRR and mixed) and pLQ (vs. pCA, pRR and mixed) were identified by univariate and multivariate logistic regression analyses. Several baseline demographics (age, sex, ethnicity, disease duration, years of education and combined annual family income), disease characteristics at baseline (SLEDAI, PQA) and treatment categories (hydroxychloroquine, prednisone and cytotoxic treatment followed ≥75% of visits vs. <75% of visits) were used as independent variables.

Results: 916 patients were identified. The results of the univariate analyses for pCA are shown on table 1. In the multivariate model, African American ethnicity (OR: 2.43, 95% CI: 1.19–4.94, p = 0.01) and high baseline SLEDAI (OR: 1.09, 95% CI: 1.03–1.16, p = 0.004) remained significant predictors of pCA. Higher education (>12 years: OR: 2.16, 95% CI: 1.11–4.20, p = 0.02) and low baseline SLEDAI (OR: 0.62, 95% CI: 0.52–0.75, p < 0.001) were significant predictors of pLQ in the multivariate analysis while African American ethnicity (OR: 0.36, 95% CI: 0.16–0.78, p = 0.01) and female patients (OR: 0.26, 95% CI: 0.12–0.56, p = 0.001) were less likely to achieve persistent long quiescence.

Table 1. pCA (vs. pLQ, RR and mixed) and pLQ (vs. pCA, pRR and mixed) were identified by univariate and multivariate logistic regression analyses. Several baseline demographics (age, sex, ethnicity, disease duration, years of education and combined annual family income), disease characteristics at baseline (SLEDAI, PQA) and treatment categories (hydroxychloroquine, prednisone and cytotoxic treatment followed ≥75% of visits vs. <75% of visits) were used as independent variables.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female vs. male)</td>
<td>1.6 (0.4–6.7)</td>
<td>0.54</td>
</tr>
<tr>
<td>Age (&gt;40 vs. ≤40 yrs)</td>
<td>1.4 (0.7–2.8)</td>
<td>0.32</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>1.0 (0.8–1.1)</td>
<td>0.17</td>
</tr>
<tr>
<td>African American (vs. other)</td>
<td>2.6 (1.3–5.3)</td>
<td>0.007</td>
</tr>
<tr>
<td>Years of education (&gt;12 vs. ≤12 yrs)</td>
<td>0.7 (0.3–1.4)</td>
<td>0.27</td>
</tr>
<tr>
<td>Income (≥30000$ vs. &lt;30000$)</td>
<td>3.5 (0.7–17)</td>
<td>0.02</td>
</tr>
<tr>
<td>Smoking baseline (yes vs. no)</td>
<td>2.1 (0.9–5.0)</td>
<td>0.13</td>
</tr>
<tr>
<td>SLEDAI baseline (100 vs. &lt;100)</td>
<td>1.1 (0.3–4.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>PGA baseline</td>
<td>1.1 (0.2–5.0)</td>
<td>0.02</td>
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<tr>
<td>Captopril therapy (&gt;75% vs. &lt;75% of visits)</td>
<td>1.0 (0.5–2.3)</td>
<td>0.85</td>
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<tr>
<td>Animalinara therapy (&gt;75% vs. &lt;75% of visits)</td>
<td>0.5 (0.3–0.9)</td>
<td>0.06</td>
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<tr>
<td>Prednisolone therapy (&lt;75% vs. ≥75% of visits)</td>
<td>1.1 (0.6–2.2)</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Conclusions: In this large SLE cohort, African American ethnicity and high disease activity at the time of diagnosis are predictors of chronic activity, regardless of treatment, even after adjustment for education years and income, while higher education and low disease activity at baseline predict long-term quiescence.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2260

Osteoporosis treatment gap, new options and new strategies

OP0047 OSTEOPOROTIC HIP FRACTURE PREVENTION: ARE WE A CRISIS?

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Background: Osteoporotic hip fractures are a significant cause of morbidity and mortality in the elderly. With the aging of the US population, it was expected that there would be a nationwide “epidemic” of osteoporotic fractures; however, Medicare reimbursement for osteoporosis screening and the rapid uptake of bisphosphonate therapy in the late 1990s and early 2000s probably forestalled this epidemic. In fact, osteoporotic hip fractures numbers declined during this time, despite the dramatic growth of the elderly population (1). However, bisphosphonate prescriptions have dropped precipitously by over 50% from their peak in 2008 (2), likely because of concerns about their adverse events. In this era of “crisis” in osteoporosis prevention, has the pendulum swung back on hip fracture numbers?

Objectives: To study the number and prevalence of osteoporotic hip fractures in patients 50 years and older over the last 22 years (1993–2014) in the US?

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary diagnosis of non-traumatic hip fractures, and calculated age-adjusted prevalence rates. We studied the number and prevalence of osteoporotic hip fractures in patients 50 years and older over the last 22 years (1993–2014) in the US.

Results: There were 407 million all-cause hospitalizations in 1.88 billion person-years of observation among people 50 years of older from 1993 to 2014 (21,626 hospitalizations per 100,000 person-years). During this time-period, there were 6.15 million hospitalizations for osteoporotic hip fractures in this population (327 per 100,000 person-years). After an increase in hip fracture rates from 1993 to 1996, there was a decline of 10.6% in total number of hip fractures from 300,154 in 1996 to 286,366 in 2010 even though population of 50 years and older increased from 69.9 million to 99.6 million in the same time. After bottoming out in 2010, the total number of hip fractures increased by 6.2% to 285,050 in 2014 (Figure, blue solid line). However, the age-standardized prevalence rate of hip fractures declined steadily (from 414/100,000 in 1996 to 269/100,000 in 2014, p<0.0001. Figure solid red line), although the rate of decline has ameliorated somewhat from 2010 onwards (not statistically significant).

Conclusions: The total number of osteoporotic hip fractures in 50 years and
older declined since 1996, bottomed out in 2010 but has started increasing again. It is critical to evaluate risks and benefits of preventive treatments for optimal management of this potentially serious problem.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5685

**OP0048 ROMOSOZUMAB RAPIDLY REDUCES CLINICAL VERTEBRAL FRACTURE INCIDENCE: RESULTS FROM THE FRAME STUDY**


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**Background:** Romosozumab (ROMO) inhibits sclerostin and has a dual effect on bone, increasing formation while decreasing resorption, resulting in significant increases in bone mineral density (BMD) at 6 months (m), which at 12m reach 13.3% vs placebo (PBO) at the spine. Using high resolution quantitative computed tomography, BMD increases were observed at both trabecular and cortical compartments of the spine, the spinal planes representing the significant reductions in radiographic vertebral fracture (VFx) risk in women with osteoporosis (OP) enrolled in the FRAME trial (NCT01578534).

**Objectives:** Here, we report the effect of ROMO on clinical (clin) VFx incidence over 12m in women in FRAME with back pain.

**Methods:** FRAME enrolled 7180 postmenopausal women with OP, mean age 70.9 yrs (total hip T-score –2.5 to –3.5) and no severe VFx. Patients received monthly ROMO (n=3589; 210mg) or PBO (n=3591) for 12m. At monthly visits, women with back pain consistent with a clin VFx had a confirmatory spinal X-ray. Clin VFx risk (ROMO vs PBO) was calculated by Cox-proportional hazards model.

**Results:** Of 119 women reporting back pain over 12m, 20 women were diagnosed with a new or worsening VFx. With ROMO, 3 clin VFx (≤0.1%; all at <2m) were identified vs 17 (0.5% at 12m) with PBO (Figure). Clin VFx risk was 83% lower in the ROMO group vs PBO at 12m (hazard ratio 0.17; 95% CI, 0.05–0.58; P<0.001). In women with clin VFx vs no clin VFx, the lumbar spine T-score was numerically lower and the FRAX score higher at baseline; other baseline characteristics were comparable among all women who reported back pain.

**Conclusions:** ROMO treatment for 12m was associated with rapid and large reductions in clin VFx risk vs PBO. In the ROMO group, all clin VFx occurred ≤2m; clin VFx risk was ≥5 times higher with PBO vs ROMO. Monthly study visits in FRAME allowed for timely radiologic confirmation of a suspected clin VFx.

**References:**

**Acknowledgements:** Funded by Amgen Inc. and UCB Pharma.


**DOI:** 10.1136/annrheumdis-2017-eular.5796

**OP0049 SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS EVALUATING BISPHOSPHONATES FOR THE PREVENTION AND TREATMENT OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS**

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**Background:** Glucocorticoid therapy is a major risk factor for osteoporosis related fractures. A previous meta-analysis conducted by Homik et al reported that bisphosphonates therapy increased BMD in glucocorticoid-induced osteoporosis (GIO) when compared to placebo, whereas results for incident vertebral fracture did not reach statistical significance.

**Objectives:** To evaluate the efficacy of bisphosphonates in GIO based on randomized controlled trials (RCTs). Both placebo controlled and active comparator trials were analyzed.

**Methods:** Two authors screened citations from the following electronic databases: Medline (1998–2015), EMBASE (1998–2015), Cochrane Library (1998–2015). A manual search was completed for conference proceedings from the ACR (2010–2015), CRA (2009–2015), and ASBMR (2009–2014). We used the study by Homik et al to identify RCTs published prior to 1998. Only RCTs that had a minimum prednisone dosage of 5 mg/day or equivalent and treatment duration of at least 3 months were included. Primary outcomes were changes in BMD and incident fractures. Two authors abstracted data using a standardized data abstraction form. We used the Cochrane Risk of Bias Tool to evaluate the quality of the selected RCTs and devised a quality score ranging from 0 to 6, where 6 represents the highest quality.

**Results:** A total of 466 citations were identified (239 Medline, 217 EMBASE, and 10 Cochrane Library). Fourteen RCTs met the inclusion criteria. An additional two RCTs were identified from conference proceedings. Eleven RCTs compared bisphosphonates to a placebo, three RCTs compared bisphosphonates to a vitamin D derivative, one RCT compared alendronate to teriparatide, and one RCT compared zoledronic acid to risedronate. The RCTs were of reasonably good quality with a mean quality score of 4.

Overall, of the 11 RCTs that compared bisphosphonates to a placebo, all found that the bisphosphonates were superior. Nine RCTs were pooled for mean percentage change in lumbar spine BMD (bisphosphonates n=687, placebo n=654). The pooled mean percentage change was in favor of bisphosphonates compared to placebo [weighted mean difference (WMD) of 4.03%, 95% CI (1.59–6.47), P<0.001]. Six RCTs were pooled for mean percentage change in femoral neck BMD (bisphosphonates n=481, placebo n=483) and the results favored bisphosphonates compared to placebo [WMD of 2.95%, 95% CI (2.09 –3.82), P<0.04]. Seven RCTs were pooled for outcome of incident fractures (bisphosphonates n=613, placebo n=469) and the results favored bisphosphonates compared to placebo [RR of 0.85, 95% CI (0.48–0.88), P<0.006 (Figure 1)]. Results were pooled using RevMan (version 5.3).

**Figure 1**

**Conclusions:** Bisphosphonates mitigate adverse changes in BMD and lower fracture risk in patients treated with glucocorticoids.
Background: In Sweden, ∼50% of women and ∼25% of men are expected to suffer an osteoporosis (OP)-related fracture (Fx) during their lifetime, and hip Fx incidence in Sweden is one of the highest worldwide. Despite this, nationally only 12% of patients with Fx are prescribed an OP treatment following Fx. 1 Understanding the reasons for the marked under-treatment of patients with Fx may provide insights into how to improve deficiencies in the management of OP.

Objectives: To assess rates of OP treatment initiation within 1 year (<1 yr) following first Fx in treatment-naïve patients with fracture in Sweden and to evaluate the determinants of treatment initiation.

Methods: Patients aged ≥50 yrs with any type of Fx were identified from Swedish national registers between 2006–2012 and followed from time of first Fx. Patients who were treatment-naïve at the time of first Fx were included in the analysis. Here, we report OP treatment initiation <1 yr after Fx in the different baseline subgroups considering gender, age, Fx type, steroid use and comorbidities.

Results: 258,827 treatment-naïve patients with a first Fx (68% female; mean age 72.7 [SD 12.9] yrs) were included. Overall, 6.6% of patients initiated OP treatment <1 yr; the proportion was higher in females (8.5%) than in males (2.3%), and was highest in patients aged 70–80 yrs (10.7%) vs other ten-year age groups (mean 5.5%). Patients with a diagnosed vertebral Fx were more likely to start OP treatment (21.2%) compared with non-vertebral Fx (5.6%). The proportion of patients starting OP treatment was higher in patients receiving glucocorticoid (GC) treatment (17%) compared with those not treated with glucocorticoids (6.1%). In general, comorbidities were not positively associated with treatment initiation, except for those indirectly connected to known contributors of Fx risk, i.e. chronic pulmonary disease (GC use) and rheumatoid arthritis (FRAX-algorithm risk factor), which were associated with increased treatment initiation. Although both dementia and dependency are known to be associated with increased risk of Fx, the tendency to initiate treatment was lower in patients with these conditions compared with those without (1.5% vs 6.9% and 2.3% vs 7.4%, respectively).

Conclusions: This study confirms the large treatment gap in OP treatment initiation following a first Fx in Sweden; rate of OP treatment initiation was below the post-Fx treatment initiation rate goal of 30% and also lower than the 12% published national indicator for treatment exposure (2015). 1 The proportion of patients initiating OP treatment appears to be somehow influenced by gender, age, Fx type, GC use, rheumatic disease, dependency and dementia; nevertheless, treatment initiation rates were low. These data highlight the need for significant efforts to improve OP management post Fx in Sweden.

References:


Acknowledgements: Funded by UCB Pharma.
CORTICAL BONE LOSS IS AN EARLY FEATURE OF AXIAL SPONDYLOARTHRITIS

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Background: Systemic bone loss is a well-known and severe consequence in axial spondyloarthritis (axSpA). To date determination of bone microstructure has only been described in patients with long-standing ankylosing spondylitis while bone microstructure has not been assessed in axSpA.

Objectives: The aim of the present study was to investigate bone microstructure, geometry and bone mineral density (BMD) using high-resolution peripheral quantitative CT (HR-pQCT) in a cohort of axSpA patients at an early stage of disease and to search for potential factors for deterioration of bone microstructure.

Methods: An inception cohort of 101 axSpA patients and 50 healthy controls of similar age and sex was assessed for geometric, volumetric and microstructural parameters of bone using HR-pQCT scanning of the radius. Additionally, demographic and disease specific characteristics of SpA patients were recorded.

Results: SpA patients and controls were comparable in age (median IQR 45.0 (15.0) vs. 44.76 (26.0) years, p=0.917), sex (female 41.6% vs. 40%, p=0.852) and BMI (23.8 (5.2) vs. 23.8 (5.5) kg/m2, p=0.752). Patients showed HLA-B27 positivity. Median disease duration was 6.5 (9.0) years, 58.4% of patients were on biological treatment and 14.9% of patients in disease remission according to ASDAS-CRP. Geometric and microstructural analysis by HR-pQCT revealed a significantly reduced cortical area (p=0.022) and cortical thickness (p=0.006) in SpA patients compared to controls. No differences in cortical porosity (p=0.668), trabecular geometry or microstructure were detected. Total and cortical vBMD were significantly reduced in SpA patients (p=0.042 and p=0.007), while there was no difference in trabecular vBMD (p=0.376). Patients with a short disease duration (<2 years) had a significantly smaller cortical thickness and cortical area (p=0.050 and p=0.032) compared to controls. Patients with a disease duration >2 years (n=55) additionally showed a decrease of cortical and total vBMD (p=0.004 and p=0.036). Multivariate regression models identified male sex to be associated with lower cortical vBMD and female sex with lower trabecular vBMD. History of prednisolone treatment (>5mg >3months) was associated with lower trabecular vBMD, and disease duration with higher trabecular vBMD. Remission status, treatment with TNF inhibitors, HLA-B27 status and presence of peripheral arthritis did not influence bone microstructure independently.

Conclusions: Bone microstructure in SpA patients is primarily characterized by deterioration of cortical bone. Cortical bone loss starts early and is evident within the first 2 years of disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3888

BONE LOSS AND CARDIOVASCULAR RISK IN PATIENTS WITH EROSIve AND NON-EROsive HAND OSTeOARTHRITIS

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Background: Hand osteoarthritis (OA) and its more severe subset erosive hand OA are common causes of pain and morbidity. Some metabolic factors were suggested to be implicated in erosive disease. Furthermore, few studies investigated differences in systemic bone loss and cardiovascular risk factors between erosive and non-erosive hand OA.

Objectives: To compare bone mineral density (BMD) and major cardiovascular risk factors between patients with erosive and non-erosive hand OA in a cross-sectional study.

Methods: Patients with symptomatic disease fulfilling the American College of Rheumatology (ACR) criteria for hand OA were included in this study. Erosive OA was defined by at least one erosive interphalangeal joint. All patients under-2 or more VF were identified. The 5-year incidence of VFs was 1.6%.

Results: Out of these patients, 72 had erosive disease. The disease duration (p<0.01) was significantly higher in patients with erosive compared with non-erosive hand OA (-0.08 SD vs. 0.0750, p<0.01; total 10.92%). The decrease of T-score in femur neck, total femur and the decrease of BMD (g/cm2) in all regions were also higher, although not significantly, in patients with erosive compared with non-erosive hand OA. In addition, more patients with erosive compared with non-erosive hand OA were treated for dyslipidaemia at baseline and after two years (32% vs. 28% and 32% vs.30%, p<0.01 for both comparisons).

Conclusions: These results suggest that patients with erosive hand OA are at risk for development of general bone loss and cardiovascular diseases.

Disclosure of Interest: This work was supported by the project MHCR No. 023728.

DOI: 10.1136/annrheumdis-2017-eular.6064

INCIDENCE OF VERTEBRAL FRACTURES IN EARLY SPONDYLOARTHRITIS: 5-YEAR PROSPECTIVE DATA OF THE DESIR COHORT

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Background: Osteoporosis is a well-recognized feature of axial spondyloarthritis (axSpA) and an increased risk of vertebral fractures (VFs) has been reported in patients with SpA. The prevalence of VFs is highly variable across studies, up to 30%. These data are unexpected in a disease affecting a young population, predominantly males. These results could be related to differences in methods of diagnoses of VFs and in populations with highly variable duration of the disease. We hypothesized that the prevalence and incidence of VFs be lower than the ones previously reported, especially in early spondyloarthritis.

Objectives: Our primary aim was to assess the prevalence of VFs in a cohort of early inflammatory back pain suggestive of early axial SpA and their incidence over 5 years.

Methods: Study population: patients from the DESIR (Devenir des Spondyloarthopathies Indifférenciées Récentes) cohort, which is a french national longitudinal prospective cohort including adults between 18 and 50 years old, and presenting with inflammatory back pain suggestive of axSpA for less than 3 years.

Results: Follow-up is still ongoing, but the data presented here includes the first 5 years of follow-up. All patients had thoracic and lumbar spine X-rays at baseline, 2 years and 5 years. For this particular study, all radiographs of the DESIR cohort were centrally read by one reader, an expert in the field of the diagnosis of VFs according to Genant’s method. Careful assessment was used to distinguish true VFs not to be mistaken with deformities. Using a temporal sequence of reading (i.e. unblinded for chronological order), an incident VF was defined as a change in the score of a vertebra from grade 0 to a subsequent grade 1 or more. All vertebræ between T4 and L4 were evaluated. In doubtful cases, an adjudication by two other senior experts was performed. Prevalence at inclusion and the incidence of VFs over the first 5 years of follow-up were described.

Results: A total of 708 patients with inflammatory back pain were included in the DESIR cohort. Plain dorsolumbar spine X-rays were available for 694 patients, and thoracic and/or lumbar X-rays were available for 843 patients at baseline. Twenty eight VFs were identified in 21 patients (19 grade 1 VFs and 9 Grade 2 or 3 VFs); therefore, the prevalence of VFs was 4.0%. Complete X-ray follow up between baseline and M60 was available for 433 patients. Seven incident VFs were identified in 6 patients: at 2 years grade 1 VFs and 1 grade 2 VF were identified; and at 5 years, grade 1 VF and grade 2 or 3 VFs were identified. The 5-year incidence of VFs was 1.6%.

Conclusions: In this study focused on a population of early spondyloarthropathy, the reported low prevalence of VFs of 4.5% and incidence of 1.6% confirm our hypothesis that the real prevalence and incidence of VF in SpA is probably much lower than what was reported in previous studies. These discrepancies might be explained by the variability in the methods of vertebral fracture’s assessment as vertebral deformations might be inappropriately considered as fracture.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6324

PREFERENCES FOR SELF-MANAGEMENT AND SUPPORT SERVICES IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A DANISH NATIONWIDE CROSS-SECTIONAL STUDY

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Background: During recent years the medical treatment of inflammatory arthritis Rehabilitation and modern drug treatment - needs and challenges
IL-23P19 IS UP-REGULATED IN MONOCYTE-DERIVED FLUORESCENCE OPTICAL IMAGING IN JUVENILE IDIOPATHIC ARTHRITIS

Objectives: To compare levels of the IL23 subunit, IL23p19, produced by monocytes from patients with Enthesitis related arthritis (ERA) to those of healthy controls. Other pro-inflammatory cytokines and markers of the UPR were also studied.

Methods: Adult patients with IA (rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (sSpA)) were invited to participate through The Danish Rheumatism Organization, arthritis networks, and hospitals’ rheumatology departments across the country. MDMs were derived from patients treated with IFN-γ or TNF inhibitors and LPS. IL23p19 expression was higher in MDMs from HLAB27 positive patients with ERA compared to those who were HLAB27 negative. A significant increase in IL23p19 expression was seen in MDMs treated with LPS from male HLAB27 positive patients with ERA compared to those who were HLAB27 negative. This increase was also seen in MDMs treated with LPS from male HLAB27 positive patients with ERA compared to male healthy controls. In this group, the induction of the UPR was observed in 63% of the ERA patients, while it was seen in only 3% of the healthy controls. The results suggest that the UPR is involved in the pathogenesis of ERA, particularly in those who are HLAB27 positive.

Results: IL23p19 expression was higher in MDMs from HLAB27 positive patients with ERA compared to healthy controls treated with LPS [median relative expression 384.7 (IQR 179.2–1340) vs 90.5 (49.9–455.9); p=0.02]. With the addition of the UPR inducer, TM, enhanced IL23p19 mRNA expression was also seen in HLAB27 positive patients compared to those who were HLAB27 negative and MDMs treated with LPS alone. When HLAB27 positive patients were compared to male healthy controls, a significant increase in IL23p19 expression was seen in MDMs treated with LPS from male HLAB27 positive patients with ERA compared to male healthy controls. In this group, the induction of the UPR was observed in 63% of the ERA patients, while it was seen in only 3% of the healthy controls. The results suggest that the UPR is involved in the pathogenesis of ERA, particularly in those who are HLAB27 positive.

Conclusions: IL23p19 expression is a potential biomarker for the diagnosis and treatment of ERA, particularly in those who are HLAB27 positive. Further studies are needed to confirm these findings and to investigate the role of the UPR in the pathogenesis of ERA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5004
Improvement in Patient-Reported Outcomes in Patients with Polyarticular-Course Juvenile Idiopathic Arthritis and Inadequate Response to BioLogic or Non-BioLogic Disease-Modifying AntiRheumatic Drugs Treated with SC Abatacept

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Background: In patients (pts) with polyarticular-course juvenile idiopathic arthritis (pJIA), SC abatacept (ABA) 125 mg weekly has a similar pharmacokinetic profile, therapeutic equivalency efficacy and comparable safety to IV ABA 10 mg/kg every 4 weeks.1 Although some data on paediatric pt-reported outcomes (PRO) are available, few clinical trials have published PRO data following treatment with SC ABA have not.2

Objectives: This analysis evaluated the effect of SC ABA treatment on PROs (activities of daily living [ADL] limitation questionnaire of parent/caregiver, childhood HAQ [CHAQ]-DI, and parent global assessment of overall pt well-being [PaGA]) in 6–17-year pts with active pJIA in a Phase III trial (NCT01844518).

Methods: Pts with pJIA aged 2–17 years with an inadequate response/intolerance to MTX were enrolled in this single-arm, open-label study and received SC ABA weekly for 4 months based on body weight tier (10–25 kg [50 mg ABA], 25–50 kg [87.5 mg ABA] and ≥50 kg [125 mg ABA]). JIA-ACR 30 criteria (ACR Pediatric 30) responders at Month 4 could receive ABA for another 20 months. For the 6–17-year cohort reported here, ADL limitation questionnaire of parent/caregiver (mean [SD]) number of days [D] of parent/caregiver missed activity, paid care and missed school [absolute values per month and percentage of D missed per month relative to an assumed average of 20 school D/month]; CHAQ-DI (0–3 scale across 8 domains of disability component); and PaGA (0–100 mm visual analogue scale) were collected.

Results: Baseline characteristics of the 173 pts with pJIA from the 6–17-year cohort were: median (min, max) age, 13.0 (6.0, 17.0) years; median (min, max) number of active joints, 10.0 (2.0, 42.0); 78.6% of pts used MTX (median dose: 11.6 mg/m²/week); and 26.6% were with prior biologic failure. All ADL limitation components improved from baseline to D113 (Month 4): these improvements were largely maintained at D309 (Figure). Relative percentage D missed from school decreased from 15% (D1) to 5.5% (D309, Figure D). CHAQ-DI and PaGA improved from baseline to D309 (Table). Further 2-year data are pending.

Table 1. CHAQ-DI and PaGA scores over time in the 6–17-year cohort

<table>
<thead>
<tr>
<th>Day</th>
<th>CHAQ-DI</th>
<th>PaGA (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=170)</td>
<td>0.99</td>
<td>45.6</td>
</tr>
<tr>
<td>29 (n=170)</td>
<td>0.82</td>
<td>45.6</td>
</tr>
<tr>
<td>57 (n=170)</td>
<td>0.73</td>
<td>25.97</td>
</tr>
<tr>
<td>85 (n=167)</td>
<td>0.63</td>
<td>24.56</td>
</tr>
<tr>
<td>113 (n=166)</td>
<td>0.61</td>
<td>24.56</td>
</tr>
<tr>
<td>197 (n=144)</td>
<td>0.52</td>
<td>23.59</td>
</tr>
<tr>
<td>309 (n=89)</td>
<td>0.46</td>
<td>23.42</td>
</tr>
</tbody>
</table>

Data are mean (SD). For CHAQ-DI (scale 0–3) and PaGA (0–100 mm visual analogue scale), higher scores indicate greater dysfunction and lower well-being, respectively.

Conclusions: In this analysis of patients with pJIA aged 6–17 years, SC abatacept demonstrated a beneficial effect on PROs including reductions in disability (CHAQ-DI) and improvement in well-being (PaGA) up to D309.

References:

Golimumab Versus Tolizumab for Severe and Refractory Juvenile Idiopathic Arthritis-UVEITIS. Multicenter Study of 33 Patients

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Background: Uveitis is a severe manifestation of Juvenile Idiopathic Arthritis (JIA). Anti-TNFa are recommended in refractory cases, mainly infliximab (IFX) or adalimumab (ADA) (Levy-Clarke et al. Ophthalmology 2014; 121: 785–796). However, they sometimes are ineffective, contraindicated or not tolerated. The next therapeutic step is not defined.

Objectives: To compare the efficacy of Golimumab (GLM) and Tolizumab (TCZ) in related A/J uveitis refractory to conventional immunosuppressive drugs and anti-TNFa.

Methods: Multicenter study of 33 patients with uveitis associated-JIA. They were refractory to conventional treatment with high dose of corticosteroids and at least a) one conventional immunosuppressive drug and b) one anti-TNFa. For this reason it was decided to iniciate TCZ or GLM. TCZ was used in 25 patients: 8 mg/kg/4 w iv (n=21), 8 mg/kg/2 w (n=2); 8 mg/kg/8 w (n=2); 8 mg/kg/8 w (n=2) and 2.9 mg/kg sc (n=1). GLM was used in 8 patients (50 mg/sc/moonth). We assessed visual acuity (VA), degree of intracocular inflammation, vitreous inflammation and macular thickening (with OCT). Quantitative variables were expressed with mean±SD or median [IQR], according to its distribution. They were compared with the Student t or the Mann-Whitney U test, respectively. Dichotomous variables were expressed as percentages and compared by the chi-square test.

Results: We studied 33 patients/61 affected eyes. There were no significant differences between TCZ and GLM at baseline in sex (31/6 vs 20/41; n=0.19), mean age (18.5±8.3 vs 19.9±8.7; p=0.55), positive ANA (95% vs 100%; p=0.71), uveitis duration before TCZ or GLM onset (116.4±93.8 vs 142±37.4).

DOI: 10.1136/annrheumdis-2017-eular.2236

DOI: 10.1136/annrheumdis-2017-eular.2236
Results are expressed as mean±SD.

Conclusions: TCZ and GLM seem to be equally effective and safe for refractory uveitis associated-JIA. The superiority of one or the other should be established with prospective randomized studies “Head to Head”.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3496

OP0060 HEALTH BEHAVIOR IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS- RESULTS OF THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS (ICON)

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Background: Knowledge concerning health behavior in adolescents with juvenile idiopathic arthritis (JIA) is essential for assessing their health risks. Although there is some evidence about a relationship between low socioeconomic status (SES) and health risk behavior in adulthood, it is less clear whether this association is also true for adolescents with JIA.

Objectives: To compare the health behavior between adolescents with JIA and healthy peers and to examine the association with sex and SES.

Methods: Data of adolescents (aged 13 to 17) with JIA and healthy peers enrolled in ICON were considered for this analysis. Health behavior was assessed via questionnaire within the first years of disease. SES- Score (low, moderate, high) was determined by using an established German multidimensional aggregated index and based on the parents’ education level as well as household net income.

Results: A total of 334 adolescents with JIA (61% female, mean age 15.1 (SD 1.1), mean disease duration 1.3 (SD 1.7)) and 181 healthy peers (57% female, mean age 15.3 (SD 1.3)) were included. Adolescents with JIA were less physically active and reported less consumption of alcohol compared with healthy peers (see Table). In both groups, boys were more frequently physically active and spent more time in playing video games than girls. Whereas girls with and without JIA used more often mobile phones than boys. No gender specific differences in both groups were found in consumption of illicit and legal drugs.

After stratification in groups according to the SES- Scores, socioeconomic differences were the same in adolescents with JIA and healthy peers. Teenagers with low social background (n=200) spent significantly more time in consumption of TV, mobile phones and video games than those from families with high SES (n=122). No significant relationship was found between parental SES and alcohol, nicotine and drug consumption by adolescents. The parental SES- Score was strongly associated with the education level of adolescents.

Conclusions: Adolescents with JIA have a similar health behavior as healthy peers, except for alcohol consumption and physical activity level. Gender and socioeconomic status are associated with health behavior of adolescents with and without JIA. Parental SES may affect adolescents’ educational outcomes.

Acknowledgements: ICON is supported by a grant from the Federal Ministry of Education and Research (01IS1112).

Disclosure of Interest: M. Listing: None declared, I. Liedmann: None declared, M. Niewerth: None declared, J. Klotzsche: None declared, K. Mönkemöller: None declared, I. Foeldvari: None declared, J. Kümmerle-Deschner: None declared, T. Hospach: None declared, K. Minder Speakers bureau: Pfizer, Roche, Pharm-

DOI: 10.1136/annrheumdis-2017-eular.4720

OP0061 DIFFUSE ALVEOLAR HEMORRHAGE: A MULTICENTER STUDY IN 847 CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Data of diffuse alveolar hemorrhage (DAH) in childhood-onset systemic lupus erythematosus (cSLE) patients are limited due to the small representation of this complication in previous case series or the focus on the comparison to adult SLE, precluding an accurate analysis of associated factors and outcomes in patients with and without this severe complication.

Objectives: To evaluate prevalence, clinical manifestations, laboratory abnormalities and treatment in a multicenter cohort study including 847 cSLE patients with and without diffuse DAH, as well as concomitant parameters of severity.

Methods: DAH was defined as the presence of at least three respiratory symptoms or signs associated with diffuse interstitial/alveolar infiltrates on chest X-ray or high-resolution computer tomography and sudden drop in hemoglobin levels with no other source of bleeding. Holm-Bonferroni correction for multiple comparison was performed adjusting the significance level (p<0.0022).

Results: DAH was evidenced in 19/847 (2.2%) cSLE patients. Cough/dyspnea/tachycardia/hypoxemia occurred in all cSLE patients with DAH. Concomitant parameters of severity observed were: mechanical ventilation in 14/19 (74%), hemoptysis 12/19 (63%), macrophage activation syndrome 10/19 (53%), sepsis 5/19 (26%) and death 9/19 (47%). Further analysis of cSLE patients at DAH diagnosis compared to 76 cSLE control patients without DAH with same disease duration [3 (1–151) vs. 4 (1–151) months, p=0.335], showed higher frequencies of constitutional involvement (74% vs. 10%, p<0.0001), serositis (63% vs. 6%, p<0.0001) and intravenous cyclophosphamide (47% vs. 8%, p<0.0001) were also significantly higher in DAH patients.

Conclusions: This is the largest study to evaluate DAH. This complication, although not a disease activity score descriptor, occurs in the context of significant moderate/severe cSLE flare. Importantly, we identified that this condition is associated with serious disease flare compounded by sepsis and with high mortality rate.

Acknowledgements: This study was supported by research grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 304180/2013-0 to RMRP, 303752/2015-7 to MT, 301479/2015-1 to CSM, 305068/2014-8 to EB and L.M.A. Campos’ Foundation) and by Núcleo de Apoio à Pesquisa “Saúde da Criança e do Adolescente” da USP (NAP-CriAd) to CAS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4826
ASSESSMENT OF BIOTHERAPIES’ EFFICACY IN BLAU SYNDROME: DATA FROM AN INTERNATIONAL RETROSPECTIVE COHORT OF 23 CASES

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Background: Blau Syndrome (BS) is a rare autosomal dominant inflammatory disorder characterized by recurrent joint mono-arthritis, dermatitis, recurrent uveitis, and bone deformities. Optimal treatments have not been determined yet.

Objectives: To assess the efficacy of several biologic agents in this affection

Methods: We conducted an observational, international, retrospective cohort of BS collecting clinical, biological and histological data.

Results: Among the twenty-three patients included in the cohort, 14 patients were treated by one or several lines of biologic agents, mostly by TNF blockers (80%), IL1 blockers (16%) or treatment targeting CTLA-4 (4%). Fifty-seven percent of patients achieved remission after two lines of treatment (1.75 lines; [0.8–2.7]). Association with csDMARDs did not significantly improve response to biologics. Considering the 3 mains symptoms independently, TNF blockers were associated with a better response in case of articular or skin features but less effective in case of ocular involvement, a clinical situation in which IL-1 targeting should be preferably chosen.

Conclusions: Biologic treatments appeared to be effective in BS but additional data prospectively collected are still needed in order to define their place in the therapeutic strategy in order to minimize functional consequences.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6660

CANA Kininumab Treatment in Patients with Colchicine-Resistant FMF (CRFMF), HIDS/MKD and TRAPS: EFFICACY in the 16 Weeks Randomised Controlled Phase and Maintenance of Disease Control and Safety at Week 40


Background: Canakinumab (CAN) is a fully human monoclonal antibody targeting IL-1β, a key cytokine in the pathogenesis of periodic fever syndromes (PFS) including familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome (TRAPS).

Objectives: The CLUSTER trial (NCT02059291) studied efficacy and safety of CAN in crFMF, HIDS/MKD and TRAPS. The primary objective was to demonstrate that CAN150 mg every 4 weeks (q4w) is superior to placebo (PBO) in resolving the flare by Day 15 with no new flares over 16 weeks (wks). Secondary objectives included the proportion of patients (pts) who maintained optimal control of disease activity (absence of new flares) between Wk 16 and Wk 40 after dose reduction.

Methods: The study comprised 4 epochs (E1-E4). After lead-in E1, in E2 patients at time of an active fever flare were randomised to CAN150 mg q4w or PBO for 16 wks. Responders in E2 were re-randomised to PBO or 150 mg q8w for 24 wks. During E3, pts who escaped to open-label CAN in E2, were similarly down-titrated to open-label CAN q8w to gain additional information on the long-term maintenance dose. In pts with a flare, dose could be escalated up to 300 mg q4w. Safety assessments included adverse events (AEs) and serious AEs.

Results: The proportion of responders at Wk 16 was statistically higher with CAN vs PBO (Table). In E3, among the 41 re-randomised pts (PBO vs CAN 150 mg q4w) the proportion of pts who did not present new flares was numerically higher in the CAN vs PBO group (Table). Overall at Wk 40 (end of E3), including re-randomised pts and pts treated in open-label, 46% of the crFMF pts, 53% of the TRAPS pts and 23% of the HIDS/MKD pts maintained disease control with 150 mg q8w. Conversely, up-titration to 300 mg q4w was required in 28.8% of HIDS/MKD pts, and in 10.2% and 8.3% of pts with crFMF and TRAPS, respectively. In E3, the majority of pts who received CAN had PGA <2, normal CRP and SAA levels in all 3 cohorts. No new safety findings nor death were reported in CAN-treated pts through E3 (Table).

Table. Efficacy results and summary of safety

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>CAN (150 mg q4w)</th>
<th>PBO (N=40)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP ratio≤3</td>
<td>0.8–2.7</td>
<td>≤2</td>
<td>2.5–5.0</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>HIDS/MKD</td>
<td>10.0/10.1</td>
<td>30.0</td>
<td>0.3–1.0</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>TRAPS</td>
<td>10.0/10.1</td>
<td>30.0</td>
<td>0.3–1.0</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

Conclusions: Canakinumab (150 mg q4w) was efficacious in resolving flare at Day 15 and preventing new flares over 16 wks. In the longer term (40 wks), absence of flares was maintained in more than half patients at the extended dosing interval (150 mg q8w) in the crFMF and TRAPS cohorts. A higher dose was needed in HIDS/MKD patients. No unexpected safety issues were reported over 40 wks of canakinumab treatment.

Disclosure of Interest: None declared
Diagnosis of axial spondyloarthritis (axSpA) is often delayed, with many fears and beliefs having been identified, including unpredictability of the disease course and concerns for the future. A survey revealed that 61% of pts want to share such experiences with other pts.

Objectives: The goals were to: 1) create a video program to help pts share experiences and promote coping strategies; 2) establish the program on the internet and social networks; 3) assess the usefulness of the program for pts and healthcare professionals (HCPs).

Methods: Clefs de dos is a national French program initiated in 2015. It is led by a pt organisation, ACS-France (Action Contre les Spondylarthropathies), Catalpa (conducted interviews, made visuals) and UCS Pharma (co-creation and promotion). Pts with axSpA were recruited by ACS on a voluntary basis to participate in focus groups; pts were selected according to their level of disease acceptance (denial [Gp1] or acceptance [Gp2]). 4 steps were planned: 1) Gp1 focus group interviews to collect feelings, words and voices; 2) Gp2 interviews to describe the pt pathway and stages in the process of disease acceptance; 3) face-to-face Gp1+Gp2 meetings for pts to share their own experiences and confront their own views; 4) rheumatologist interviews to evaluate the impact of pt testimonies on their own practice.

Results: 13 axSpA pts (10 Gp1, 3 Gp2) participated, aged 25–65 years (yrs), with 5–17 yrs disease duration; 10 were female. An animated visual was produced using Gp1 pt interviews; analysis revealed feelings of loss prior to diagnosis. Photographs and audio testimonies were used to create 3 documentary portraits of Gp2 pts, illustrating the process of disease acceptance (denial [Gp1] or acceptance [Gp2]). 4 steps were planned: 1) Gp1 focus group interviews to collect feelings, words and voices; 2) Gp2 interviews to describe the pt pathway and stages in the process of disease acceptance; 3) face-to-face Gp1+Gp2 meetings for pts to share their own experiences and confront their own views; 4) rheumatologist interviews to evaluate the impact of pt testimonies on their own practice.

Conclusions: Clefs de dos was developed by and for axSpA pts. The program answers unmet needs by sharing pt experiences, particularly in situations of delayed diagnosis and lack of disease acceptance. Online access reflects good acceptability of the program, which can also be used as an educational tool in self-management. The next step is to involve other HCPs (eg., nurses, physiotherapists, psychologists).

References:

Acknowledgements: The authors acknowledge all patients who participated in the Clefs de dos program, and L. Espivet and A. Martra for contributions in co-building the communication plan. This program was conducted in partnership with ACS-France and Catalpa, and co-created and funded by UCS Pharma.


adherence to treatment recommendation (ATR) and recidivism before the 15th day after the day of consultation (need of further consultation due to the same medical problem). Registries included those generated along the first 12 months after the end of the courses.

Results: The TT group generated 175 registries while PBL generated 219. Both courses were followed by 20 non-rheumatology second-year residents. Proportion of AITR were 73.3 and 60.2% for BLT and TT groups, respectively (P<0.001). Considering only the registries generated in the first trimester after the courses, those proportions were respectively 80.2 and 79.5%. Proportion of ATR were 69.9 and 55.7%, respectively (P<0.001), however when considering only registries generated in the first trimester those proportions were 77.1 and 76.9%, respectively. Global recidivism rate (number of patients who need a further consultation due to the same medical problem or due to the side effects of their treatment among all patients attended) at the first 15th day since the first attendance was 8.7% in the PBL group and 17.5% in the TT group (P<0.001). At the end of both courses a survey to the students were performed. The satisfaction index—measured by a 0–10 progressive ordinal scale—were 9.1 SD 1.3 for the PBL model and 8.2 SD 1.4 for the TT model (P<0.05).

Conclusions: The pedagogical PBL teaching method shows a better academic impact in terms of concept retention and attendance into the medical practice along the time. In our opinion and according to our experience, most programs of

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3984

CP0067 DEVELOPMENT AND VALIDATION OF A MODEL TO FACILITATE RECOGNITION OF ARTHRITIS BY GENERAL PRACTITIONERS

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Background: Early initiation of treatment of rheumatoid arthritis is strongly associated with an improved outcome, but requires the early identification of arthritis. Physical examination of joints is crucial to this end, but is difficult for general practitioners (GPs) who have little experience. Another difficulty is that GPs see many persons with musculoskeletal symptoms per year but only few patients with clinical arthritis. To promote early recognition of arthritis, the Early Arthritis Recognition Clinic (EARC) was initiated in Leiden, the Netherlands in 2010. GPs were instructed to refer to this clinic in case of doubt on the presence of arthritis (and not to wait and see, or to perform additional laboratory tests). At this clinic, patients filled out a form with questions on their symptoms and were seen by a rheumatologist in a short visit that comprised a full joint examination. As reported previously, this clinic importantly improved the early identification of arthritis and RA (1), but this approach may not be easily implemented in other centres or regions.

Objectives: To assess if a combination of symptoms and signs that are easy to assess can differentiate patients with and without clinical arthritis at joint examination.

Methods: 1,288 patients in whom GPs doubted on the presence of arthritis visited the EAR C during 2010 and 2015. Reported symptoms and signs were studied with respect to the presence of synovitis (joint examination). Multivariable logistic regression was used. A model was derived in 644 patients, and validated in the second set of 644 patients.

Results: 41% of the patients who visited the EAR C had arthritis at examination. Age (per year OR 1.02; 95% CI 1.01–1.03), male sex (OR 1.8; 95% CI 1.4–2.2), symptom duration (4–12 weeks OR 3.83; 95% CI 2.22–6.60), morning stiffness >60 min (OR 1.7; 95% CI 0.9–2.9), difficulty with eating a fish (OR 1.6; 95% CI 0.97–2.5), number of tender joints (≥3 tender joints OR 9.7; 95% CI 1.1–81.8) and self-reported swollen joints (OR 2.5; 95% CI 1.8–7.0) were associated with the presence of arthritis in multivariable analysis. The AUC was 0.75 (SE 0.02) in the derivation set and 0.71 (SE 0.02) in the validation set. To facilitate application in practice, a simplified model was made. This consisted of 7 variables and the total score ranged between 0–7. The AUC was 0.73 (SE 0.02). Depending on the cut-off, the PPV of the simplified model ranged between 41% and 74% and the NPV between 100 and 62%. With a cut-off of 4, the NPV was 86%, PPV 49%, specificity 35%, and sensitivity 91%.

Conclusions: A set of clinical characteristics that can be easily assessed by GPs had a reasonable discriminative ability for clinical arthritis, and can be applied by GPs in case of doubt on the presence of arthritis. This model requires further validation in general practices, but may lead to a tool that could assist GPs in their decision making regarding referral or ordering additional tests for patients with suspected early arthritis.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2881

OP0068 PRACTICES PARTICIPATING IN THE ACR’S RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) NATIONAL REGISTRY SHOW IMPROVEMENTS IN QUALITY OF CARE

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Background: The ACR launched the RISE registry in 2014 to facilitate quality improvement on a national scale. The registry passively extracts electronic health record (EHR) data from rheumatology practices, aggregates and analyzes these data centrally, and feeds performance on quality measures back to clinicians using a web-based dashboard.

Objectives: We used data from RISE to 1) examine variation in performance on quality measures across practices and 2) evaluate trends in measure performance over time.

Methods: RISE’s informatics platform continuously collects data from the EHRs of participating practices, allowing centralized aggregation and analysis of quality measures. We analyzed data collected between July 1, 2014-July 1, 2016 on all patients seen by 294 clinicians across 63 practices. Measures in the areas of rheumatoid arthritis, drug safety, preventive care and gout were examined.

Performance on quality measures, defined as the percentage of eligible patients receiving recommended care, was examined at the practice level. To examine trends in performance over time, we took the subset of practices that continuously participated in RISE since its inception (n=44), and developed 1) control charts and 2) logistic regression models, in which the outcome was practice-level performance each month and the predictor was time.

Results: Data from 289,812 patients was examined. Mean (SD) age was 59 (16) years, 75% were female, 21% were racial/ethnic minorities, and 37% had public insurance. Most rheumatologists were in a group practice (73%); 25% were in solo practice and 2% part of a larger health system. Performance on measures varied significantly across practices (Table). The largest gaps were observed for gout and preventive care. For 4 of 5 measures for which the Medicare program has set national benchmarks, average performance of RISE practices exceeded targets. Of 11 measures, performance improved over time on 5 measures (p<0.05 in logistic models; see Figure for example control chart), was at goal on 4 measures, and saw no improvement on 2 measures (BMI screening and urate target).

Conclusions: We found significant variation in performance on quality measures across RISE practices, with the largest gaps seen in gout care and preventive care. Some practices have achieved a very high level of performance. Over time, RISE practices demonstrated improvement in over half of the measures.

Abstract OP0068 – Table 1

<table>
<thead>
<tr>
<th>Electronic Quality Measure (eQOM)</th>
<th>Measure denominator (N)</th>
<th>Average performance across patients (%)</th>
<th>Average practice-level performance (percentile)</th>
<th>CMS benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA: Assessment of Disease Activity</td>
<td>63,472</td>
<td>52.1</td>
<td>56.1</td>
<td>100</td>
</tr>
<tr>
<td>RA: Functional Status Assessment</td>
<td>63,472</td>
<td>50.0</td>
<td>56.1</td>
<td>100</td>
</tr>
<tr>
<td>RA: DMARD</td>
<td>63,472</td>
<td>90.1</td>
<td>91.4</td>
<td>98.2</td>
</tr>
<tr>
<td>Drug Safety: TB screening pre-biologic</td>
<td>7,842</td>
<td>61.1</td>
<td>66.6</td>
<td>95.7</td>
</tr>
<tr>
<td>Drug Safety: ≥1 High-Risk Medication in Elderly*</td>
<td>101,820</td>
<td>4.7</td>
<td>2.8</td>
<td>0</td>
</tr>
<tr>
<td>Drug Safety: ≥2 High-Risk Medications in Elderly*</td>
<td>101,820</td>
<td>4.7</td>
<td>2.8</td>
<td>0</td>
</tr>
<tr>
<td>Preventive Care: Tobacco screening and counseling</td>
<td>219,415</td>
<td>85.3</td>
<td>89.3</td>
<td>99.8</td>
</tr>
<tr>
<td>Preventive Care: BMI documentation, follow-up plan</td>
<td>154,501</td>
<td>26.4</td>
<td>26.7</td>
<td>50.7</td>
</tr>
<tr>
<td>Preventive Care: Blood pressure management</td>
<td>30,607</td>
<td>70.0</td>
<td>63.2</td>
<td>100</td>
</tr>
</tbody>
</table>

*Lower number indicates higher performance.
examined. As rheumatologists aim to improve quality of care, RISE will, by design, allow participants to measure, benchmark, and continuously monitor performance improvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5640

THE BURDEN OF ANKYLOSING SPONDYLITIS: A POPULATION-BASED STUDY
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Background: Ankylosing spondylitis (AS) is an inflammatory rheumatic disease with musculoskeletal and systemic manifestations. Because AS is typically diagnosed before the age of 40 years and follows a chronic progressive course, its impact on the patient is life-long. In addition to the burden on the individual patient, that on the society is also increasing cumulatively every year [1]. The burden of AS is not confined to healthcare cost spent due to back pain and stiffness of the disease itself [2–4], but also encompass extra-articular manifestation (EAM), comorbidities, disability, and mortality contributed from AS [5].

Objectives: This study aimed to evaluate the disability, mortality, and healthcare costs (direct and indirect) for quantifying the burden of AS.

Methods: We conducted a nationwide population-based study based on national health insurance data in Korea. The patients with incident AS (n=1111) were identified with controls (n=5555) who were matched by age, sex, income, and geographic region from the year 2003 to 2013. EAMs, comorbidities, mortality and type and severity of disabilities were presented as incidence rate and compared to the controls as incidence rate ratios (IRRs). Annual health expenditure per patient was analyzed by the year and relation to AS.

Results: During the follow-up, 28% of patients in this cohort experienced any kind of EAM. More comorbidities with Charlson comorbidity index ≥3 (OR 2.18, 95% CI 1.91 to 2.48) were significantly associated. Disability rate was higher than controls regardless of causes and severity (OR 2.94, 95% CI 2.48 to 3.48). Crude IRRs for mortality was not significantly increased, but by multivariate analysis, older age at diagnosis (≥45 years old) (OR 10.53, 95% CI 4.31 to 25.68) was most strongly related to increased disability and mortality rates (Fig.1). Biological agents elevated annual health expenditures of AS but decreased AS unrelated costs (mean 1112 vs 877 USD, p=0.0068) (Fig.2).

Conclusions: Along with demographic factors, systemic consequences such as EAMs and other comorbidities were associated with increased disabilities and healthcare expenditures in AS. Older age at diagnosis was significantly associated with increased mortality rates.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4020

THE ROLE OF INDIVIDUAL AND COUNTRY-LEVEL SOCIO-ECONOMIC FACTORS IN WORK PARTICIPATION IN PATIENTS WITH SPONDYLOARTHRITIS ACROSS 22 COUNTRIES WORLDWIDE: RESULTS FROM THE COMOSPA STUDY
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Background: Spondyloarthropathy (SpA) carries substantial financial costs, including direct costs (use of medical services and treatments) and indirect costs (loss of work productivity). While disease related factors have been repeatedly shown to be associated with work outcomes, information on the role of educational attainment and the economic wealth of the patients’ country of residence is scarce.

Objectives: To explore the role of individual and country level socio-economic (SE) factors on employment, absenteeism and presenteeism across 22 countries.

Methods: Patients with a clinical diagnosis of SpA, fulfilling the ASAS SpA criteria and in working age (<65 years old) from COMOSPA were included. Outcomes explored were employment-status, absenteeism and presenteeism according to the Work Productivity and Activity Impairment Specific Health Problem (WPAI-SHP) questionnaire. Absenteeism and presenteeism were assessed in employed patients. Multilevel logistic (for work status) and linear (for absenteeism and presenteeism) regression models with random intercept for country were explored. Independent contribution of individual (education) and country level socio-economic factors (country healthcare expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) were assessed in models adjusted for clinical factors.

Results: In total 3,114 patients from 22 countries were included (mean (SD) age 40.9 (11.8) years; 66% males; and 63% employed). Of these, 89% had axial SpA and 11% a peripheral SpA. Unadjusted employment rates ranged from 28% (Colombia) to 83% (Canada). After adjustment for relevant socio-demographic and clinical variables, differences between countries in work status persisted (Figure).

Figure – Adjusted estimates of employment rate and (95%CI) by country

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4020

Table – Impact of individual and country SE factors on work outcomes, in two-level models adjusted for socio-demographic and clinical variables

<table>
<thead>
<tr>
<th>Independent predictors</th>
<th>Work status (employed vs not)</th>
<th>Gender (male vs female)</th>
<th>Age (≥50 vs &lt;50)</th>
<th>Employment (employed vs not)</th>
<th>Disability (not vs yes)</th>
<th>Presenteeism (yes vs no)</th>
<th>Absenteeism (yes vs no)</th>
<th>GDP (low vs medium/high)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>2.43 (1.81–3.23)</td>
<td>2.33 (1.94–2.79)</td>
<td>1.21 (0.79–1.84)</td>
<td>2.35 (1.79–3.11)</td>
<td>2.33 (1.79–3.01)</td>
<td>2.33 (1.79–3.01)</td>
<td>2.33 (1.79–3.01)</td>
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</tr>
<tr>
<td>Gender (male)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability (yes)</td>
<td></td>
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<tr>
<td>Presenteeism (yes)</td>
<td></td>
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<tr>
<td>Absenteeism (yes)</td>
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<td>GDP (low)</td>
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</tr>
</tbody>
</table>

References:
1. Rodrigues Manica, A, Sepriano, S, Ramiro, F, Pimentel-Santos, P, Puttkir, E, Nikiphorou, A, Mottu, M, Dougdados, D, van der Heijde, R, Landewé, F, Van den Bosch, A, Boonen, A. Rheumatology Department, Centro Hospitalar de Lisboa Ocidental; 8CEDOC - NOVA Medical School | Faculdade de Ciências Médicas, NOVA University of Lisbon, Lisbon, Portugal; 3Leiden University Medical Center, Leiden; 4Department Internal Medicine, Division of Rheumatology, Maastricht University Medical Center, Maastricht, Netherlands; 5KCL, London, United Kingdom; 7Rheumatology B Department, Paris Descartes University, Cochin Hospital, AP-HP; 7INSERM (U1153), Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France; 6ARC, Amsterdam & Atrium MC Heerlen, Amsterdam, Netherlands; 8Department of Rheumatology, Ghent University Hospital, Ghent, Belgium
High healthcare expenditures were associated with higher employment (OR=2.42; 95% CI=1.53;3.81) and lower presenteeism (β=4.53;CI=−8.90;−0.17). Similarly, higher GDP was associated with higher employment (OR=1.70; 95% CI=1.02;2.83), and in the same direction with presenteeism but without reaching statistical significance (β=3.42;CI=13.07;6.23). No significant association between any outcome and SE factors and absenteeism was found. At individual level, higher education was positively associated with employment-status, presenteeism and absenteeism.

Conclusions: Individual- and country-level SE factors affect work participation in SpA, and this varies significantly across countries. Better socio-economic welfare seems to support SpA patients to stay employed and productive.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3926

Background: Musculoskeletal disorders, including inflammatory arthritis (IA), are among the most common reasons for work disability and sick leave. Early IA patients with risk factors for persistent and/or erosive disease, such as high swollen joint count (SJC), acute-phase reactants, RF- or ACPA-positivity, are treated aggressively to prevent joint damage and disability.

Objectives: To study the rate of sick leave according to clinical diagnosis in an unselected very early IA cohort, and to investigate whether the predictors for sick leave are the same as the known predictors for persistent and/or erosive disease.

Methods: Data from the Norwegian Very Early Arthritis Clinic (NOR-VEAC), a longitudinal observational study of adults with IA of <16 weeks duration, were used. Exclusion criteria were arthritis due to crystal deposits, trauma, osteoarthritis and septic arthritis. For the present study we included patients eligible for work participation, i.e. <65 years with no retirement or disability pension, who had information about work in the baseline and six-month case report forms. Independent tests t-test, Mann-Whitney-U test or chi-square test were used as appropriate to compare patients on sick leave after 6 months with patients not reporting sick leave. Clinically relevant baseline variables with univariate p-value <0.2, as well as age and sex, were included in the multivariable logistic regression analyses with manual backwards selection to find predictors for sick leave after six months.

Results: Of 880 patients eligible for analysis (<65 years, no retirement or disability pension), 664 (75.5%) had complete work participation data. Duration of joint swelling before inclusion (median [25–75 perc.]) was 35 (14–69) days, mean (SD) age 42.1 (12.1) years, 56.0% were females, 27.3% current smokers, and 22.4% anti-CCP and/or RF positive. The most common clinical diagnoses were undifferentiated arthritis (35.2%), rheumatoid arthritis (22.1%) and reactive arthritis (19.7%). The overall rate of sick leave at presentation was 37.7% and after 6 months 23.2%. More than one-third of the patients reported sick leave at first visit, regardless of diagnosis (Figure 1). At six months >20% sick leave was still reported in all groups except sarcoid arthritis and reactive arthritis. Smoking, low education (≤ high school), longer duration of joint swelling, ACPA and RF positivity, joint pain, fatigue, patient's global assessment, SF-36 (physical and mental component summary scores), HAQ-DI and tender joint count at baseline were univariably associated with sick leave after six months, whereas SJC, ESR and CRP were not. Independent predictors were current smoking (OR 2.1 (95% CI 1.1–4.3)), low education (OR 1.7 (95% CI 1.1–2.5)), longer duration of joint swelling and low SF-36 (physical and mental component summary scores).

Conclusions: Sick leave in IA is common, even six months after diagnosis. Predictors for sick leave after six months were associated with lifestyle and level of education rather than factors commonly considered to be predictive for unfavourable arthritis outcomes. In early IA care, health care providers should focus not only on disease activity, but also on work ability and early facilitation efforts at work.

Disclosure of Interest: E. S. Norli: None declared, G. Hetland Brinkmann: None declared, T. K. Kvien Consultant for: Tore K Kvien has received fees for speaking and/or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, GaAs, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Octal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, S. Lillegraven: None declared, O. Bjørneboe: None declared, A. Julsrud Haugen: None declared, H. Nygaard: None declared, C. Thunem: None declared, E. Lie: None declared. M. Mjåvatten: None declared.

Comorbidities: having one RMD is enough - we don’t need anything else
Topic: Osteoporotic Fracture Risk Assessment Using FRAX Following Hematopoietic Stem Cell Transplantation

Methods: We conducted a retrospective cohort study of patients >18 years that received a HSCT at The University of Texas MD Anderson Cancer Center, from January 1, 2001 to December 31, 2010. Patients were considered to have entered the cohort at the time of HSCT. All patients were retrospectively followed until December 31, 2013 for assessment of osteoporotic fracture. Osteoporotic fractures following HSCT were identified using ICD-9 codes, and confirmed by radiology and physician documentation. FRAX probabilities were calculated from baseline information obtained by chart review.

Results: A total of 5,170 patients underwent a HSCT during the 10-year study period. During an average of 3.3 years of follow up, 10% of patients developed a fracture. Fracture rates were higher (14%) in patients that underwent an autologous HSCT in comparison to those that received an allogeneic HSCT (6%). Mean major osteoporotic fracture FRAX scores were significantly higher in individuals who sustained an osteoporotic fracture compared to individuals who did not. The area under the receiver operating characteristic curve at 5 and 10 years following the HSCT were 0.61 and 0.66 respectively (Figure 1). We assessed the ability of the FRAX model for prediction of osteoporotic fracture with and without considering death as a competing risk. The hazard ratios were similar for both models (HR, 2.63, 95% CI, 1.93, 3.59; HR, 2.54, 95% CI, 1.86, 3.47, respectively).

Conclusions: The FRAX model has modest discriminative ability in predicting osteoporotic fractures following HSCT. Further independent validation of our findings is necessary, before routinely using the FRAX model in clinical practice.

Table: Predictive Value of FRAX in Osteoporotic Fracture Risk Assessment Following HSCT

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
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<tbody>
<tr>
<td>Multivariable analysis OR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nontuberculous mycobacteria</td>
<td>2.00 (4.48–89.36)</td>
<td>11.24 (2.37–53.24)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1.86 (1.41–2.45)</td>
<td>1.29 (0.97–1.71)</td>
</tr>
<tr>
<td>CCI ≥1</td>
<td>1.89 (1.77–2.01)</td>
<td>1.83 (1.71–1.94)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>3.19 (2.76–3.69)</td>
<td>2.74 (2.36–3.18)</td>
</tr>
</tbody>
</table>

Figure 1: Predictive Value of FRAX in Osteoporotic Fracture Risk Assessment Following HSCT
**RISK OF DEVELOPING ADDITIONAL IMMUNE MEDIATED MANIFESTATIONS FOR PATIENTS WITH SYSTEMIC ARTHRITIDES**

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1Medical University of Vienna, Vienna, Austria; 2University of Calgary, Calgary, Canada; 3Medicus Economics, LLC, Milton; 4AbbVie Inc., North Chicago, United States

**Background:** Patients with the systemic arthritides ankylosing spondylitis [AS], psoriatic arthritis [PsA], rheumatoid arthritis [RA] may develop additional, non-musculoskeletal immune mediated manifestations (nms-IMMs).

**Objectives:** To compare the risk of developing nms-IMMs between patients with and without an existing AS, PsA, or RA.

**Methods:** Risk for nms-IMMs was estimated in the MarketScan Commercial Claims and Encounters database (1/2006-9/2015) for case patients with AS, PsA, RA, or all three conditions. Unmatched controls were matched by age, sex, state of residence and insurance type to case patients aged 18–64. The systemic arthritides ("cases") were identified by ICD-9 diagnosis codes on ≥ 2 medical claims ≥ 30 days apart. A case patient's earliest nms-IMM claim was designated as the index date for the case and all matched controls. Onset of 6 nms-IMMs was identified by the first post-index claim: celiac disease [CE], hidradenitis suppurativa [HS], inflammatory bowel disease [IBD], lupus [SLE], psoriasis [PsO], uveitis [UV]; some of these are well-known manifestations of seronegative spondyloarthropathies, like PsA and AS; some are not. All subjects had continuous health plan enrollment for ≥ 965 days before and after index date. Cumulative incidence of nms-IMMs was assessed at 5 years. Their risk was analyzed with stratified Cox proportional hazards models. Standard errors were adjusted for clustering by case-control match group.

**Results:** Among 117,794 cases, mean age was 49 years and 71% were female. Mean number of matched controls per case was 664. Across the 3 initial cohorts of patients with AS, PsA, or RA, median follow-up ranged 939–972 days for cases and 931–950 days for controls. Among case patients, 5-year cumulative incidence of any nms-IMM occurrence was 17.5% for AS, 41.8% for PsA, and 14.4% for RA. Patients with nms-IMMs had significantly higher risk than matched controls of developing each, any 1, or any 2 of the 6 manifestations (P<0.002) (Table).

**Conclusion:** The risk of developing non-musculoskeletal manifestations was significantly higher for patients with AS, PsA, and RA than for matched controls. These included not only the well-known manifestations of PsA and AS but also others like manifestations leading to claims for SLE, celiac disease or HS. When managing these systemic arthritides, surveillance for additional immune mediated manifestation is warranted.

**Acknowledgements:** Design, study conduct, and financial support for the study were provided by AbbVie Inc. AbbVie participated in the interpretation of data, review and approval of the abstract; all authors contributed to the development of the abstract and maintained control over the final content. Medical writing services were provided by Andrew Epstein of Medicus Economics and were funded by AbbVie.

**Disclosure of Interest:** D. Aletaha Grant/research support from: AbbVie, AsstraZeneca, BMS, Eli Lilly, Grünenthal, Jansen, Medac, Merck, Mitsubishi Tanabe, Novo Nordisk, Pfizer, and Sanofi/Regeneron, Consultant for: AbbVie, AstraZeneca, BMS, Eli Lilly, Grünenthal, Jansen, Medac, Merck, Mitsubishi Tanabe, Novo Nordisk, Pfizer, and Sanofi/Regeneron. Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, Grünenthal, Jansen, Medac, Merck, Mitsubishi Tanabe, Novo Nordisk, Pfizer, and Sanofi/Regeneron.

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**PRIMARY PROPHYLAXIS FOR PNEUMOCYSTIS PNEUMONIA IN PATIENTS WITH RHEUMATIC DISEASE AND TREATED WITH PROLONGED, HIGH-DOSE STEROID: A RETROSPECTIVE COHORT STUDY WITH 12-YEAR OBSERVATION**

J.W. Park 1, J. Moon 1, J.R. Curtis 2, J.K. Park 1, E.Y. Lee 1, Y.W. Song 1, E.B. Lee 1

1Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic Of; 2Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, United States

**Background:** Pneumocystis pneumonia (PCP) is a significant cause of morbidity and mortality in patients with rheumatic diseases, especially in the case of patients receiving high-dose steroid treatment.

**Objectives:** To investigate the efficacy and safety of PCP prophylaxis using trimethoprim/sulfamethoxazole (TMP-SMX) in patients with rheumatic disease receiving prolonged, high-dose steroids.

**Methods:** This study includes 1522 cases of prolonged (≥4 weeks), high-dose (≥30mg/day predonison or equivalent) steroid treatment from 1092 patients with any rheumatic diseases during a 12-year period in a single tertiary referral center in South Korea. Of them, prophylactic TMP-SMX was administered in 262 cases (prophylaxis group) with a mean (SD) duration of 229.0 (272.7) days whereas other 1260 cases received no prophylaxis (control group). Primary outcome was 1-year incidence of PCP between the two groups. Secondary outcomes included PCP-related mortality, ICU admission rate, all-cause in-hospital mortality and incidence of any adverse drug reactions (ADRs) of TMP-SMX. To minimize the baseline imbalance between the two groups, we introduced propensity-score matching and performed the same analysis in the post-matched population as a sensitivity analysis.

**Results:** Patients in the prophylaxis group were treated more often with secondary immunosuppressive drugs and had a higher proportion of patients with PCP high-risk diseases (ANCA-associated vasculitis and dermatomyositis) and lymphopohia at baseline. Overall, 30 cases of PCP occurred and resulted in death in 11 cases (36.7%). In the prophylaxis group, only one non-fatal case of PCP occurred. One-year PCP incidence was significantly lower in the prophylaxis group (adjusted HRS=0.096 [0.013-0.719]) (Figure). TMP-SMX also significantly reduced the PCP-related mortality (adjusted HR=0.101 [0.001-0.809]) whereas...
ICU admission rate and in-hospital mortality rate were not different between the two groups during the observation. This result was consistent in the sensitivity analysis where same analysis was performed in the post-matched population. Thirty-four cases of ADRs of TMP-SMX occurred, with an incidence rate (95% CI) of 24.2 (17.3–33.0) per 100 person-year. There were two cases of serious ADR (one pancytopenia and one Steven’s Johnson syndrome) but they all recovered shortly after the discontinuation of TMP-SMX. The number needed to harm (NNH) of serious ADR was 109 whereas the number needed to treat (NNT) to prevent one case of PCP in the whole population was 52.

Conclusions: In patients with rheumatic disease receiving prolonged, high-dose steroid treatment, TMP-SMX prophylaxis significantly lower the incidence of PCP with favorable safety.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2803

OP0078 THE LONG TERM PROGNOSTIC SIGNIFICANCE OF PULMONARY HYPERTENSION IN SARCOIDOSIS - A BIG DATA ANALYSIS
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Background: Sarcoidosis is a multisystem, chronic, progressive, granulomatous disease. Sarcoidosis-associated pulmonary hypertension is well described, but not common complication of sarcoidosis. In small scale studies, it has been previously described as a manifestation of advanced disease and was found to be associated with increased morbidity and mortality. Previous studies have shown that treatment may be safe and improve pulmonary hemodynamics in sarcoidosis-associated pulmonary hypertension. However, big data analyses regarding the exact magnitude and prognosis of sarcoidosis-associated pulmonary hypertension are lacking.

Objectives: To assess the long-term prognostic significance of sarcoidosis-associated pulmonary hypertension using a big data registry with a 15-year follow-up period.

Methods: Utilizing the medical records of Clalit Health Services, the largest HMO in Israel, we extracted a cohort consisted of sarcoidosis patients along with their age-and-sex matched controls. Dates of registration in the medical records of sarcoidosis, pulmonary hypertension and death, as well as anthropometric information and medical comorbidities were collected from the database. To compare the distribution of variables across the cohort strata, univariate analysis was performed using Chi-square and student t-test. Multivariate analysis using a logistic regression model was used to find variables associated with pulmonary hypertension. Survival analysis using Cox proportional hazards method and log-rank test was performed to find variables associated with increased risk of all-cause mortality.

Results: The cohort included 3,993 sarcoidosis patients and 19,856 age-and-sex matched controls. The mean age of both groups was 56, and both consisted about 63% females. Pulmonary hypertension was observed among 269 sarcoidosis patients (6.74%) vs. 400 controls (2.01%), p<0.001. In multivariate analysis, sarcoidosis was found to be independently associated with diagnosis of pulmonary hypertension (OR 3.09, 95% CI 2.6–3.67). After more than 15 years of follow-up, 710 (17.8%) of the sarcoidosis patients had died, compared to 2121 (10.7%) of the controls (p<0.001). In multivariate survival analysis, both sarcoidosis and pulmonary hypertension were found to be significantly associated with increased risk to all-cause mortality (HR 1.83, 95% CI 1.66–2.02 and HR 2.32, 95% CI 2.05–2.63, respectively).

Conclusions: Sarcoidosis-associated pulmonary hypertension is associated with poor prognosis. Proper screening methods are recommended to assess whether early identification and treatment may improve life expectancy.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4464

OP0079 BODY FAT PERCENTAGE AND WAIST CIRCUMFERENCE WERE ASSOCIATED WITH THE DEVELOPMENT OF RHEUMATOID ARTHRITIS – A DANISH FOLLOW-UP STUDY
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Background: Several studies have investigated the association between overweight and the development of rheumatoid arthritis (RA) and have come out with conflicting results. Body Mass Index (BMI) has been the preferred surrogate measure for overweight in these studies. However, BMI correlates only modestly with total amount of body fat and does not reflect fat distribution.

Objectives: To investigate the association between BMI, waist circumference, bio-impedance-derived total body fat percentage and risk of RA.

Methods: A population-based cohort study conducted within the Danish Diet, Cancer and Health cohort, which included individuals aged 50 to 64 years at the recruitment in the period between 1993 and 1997. Body fat composition measurements and data on lifestyle factors were collected at the enrolment into the cohort. The participants who subsequently developed RA were identified via linkage to The Danish National Patient Registry. The participants were followed until development of RA, death, loss to follow-up or October 2016, whichever came first. Data were analyzed by Cox proportional hazards regression model with delayed entry and age as the underlying time variable. Analyses were stratified by gender. Cox regression analyses with restricted cubic spline were carried out to elucidate the dose-response association between anthropometric measures and risk of RA. Smoking, socio-economic status, alcohol consumption, physical activity and intake of n-3 fatty acids were included in multivariate analyses as potential confounders.

Table 1. Cox proportional hazard ratios for association between body composition measurements and incidence of RA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio (95% confidence interval)</th>
<th>Multivariable adjusted*</th>
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<tbody>
<tr>
<td>BMI &lt; 18.5 kg/m²</td>
<td>N/A</td>
<td>0.66 (0.21–3.48)</td>
</tr>
<tr>
<td>BMI 18.5–24.99 kg/m²</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>BMI 25–29.99 kg/m²</td>
<td>0.83 (0.55–1.24)</td>
<td>1.48 (1.14 – 1.91)</td>
</tr>
<tr>
<td>BMI &gt; 30 kg/m²</td>
<td>0.69 (0.37–1.30)</td>
<td>1.54 (0.99 – 2.17)</td>
</tr>
<tr>
<td>Abdominal obesity (waist circumference &gt; 102 cm for men, &gt;88 cm for women)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>No</td>
<td>1.16 (0.75–1.80)</td>
<td>1.24 (0.96–1.61)</td>
</tr>
<tr>
<td>Yes</td>
<td>1.54 (0.99–2.17)</td>
<td>1.09 (0.75–1.58)</td>
</tr>
</tbody>
</table>

*Adjusted for age, smoking status, total tobacco consumption (g/day), smoking duration, alcohol consumption (g/day), socio-economic status, physical activity (Mets Equivalent of Task, MET), total intake of n-3 fatty acids.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2803
Results: Data were available on 54,284 subjects (52% female). During follow-up (median 21 years), 283 women and 110 men developed RA. The median (IQR) time to onset of RA was 7 (4–11) years. The adjusted hazard ratio (HR) for developing RA are presented in Table 1. Restricted cubic spline analysis of body fat percentage displayed a positive slope in women (Image). There was no linear association between fat and incidence of RA among men.

Conclusions: Overweight and obesity, defined by BMI, abdominal obesity and higher body fat percentage, especially above 30%, were in women associated with a higher risk for the development of RA. In men the associations were not consistent.

Acknowledgements: The Danish Rheumatism Association, The Danish Heart Foundation, Central Denmark Region, North Denmark Regional Hospital, Scandinavian Rheumatology Research Foundation

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1526

OP0080 RISK OF AUTISM SPECTRUM DISORDER IN CHILDREN BORN TO MOTHERS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS IN TAIWAN

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Background: There is emerging evidence suggesting that offspring born to patients with rheumatic diseases has higher risk of neuropsychiatric diseases. Previous data from Quebec showed children born to women with SLE have an increased risk of autism spectrum disorder (ASD) but data regarding risk of ASD in offspring of mothers with systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) mothers has not been reported in other population.

Objectives: We aimed to examine whether offspring of mothers with SLE and RA in Taiwan has a higher risk of developing ASD using data from a linkage between National Health Insurance (NHI) database and National Birth Registry in Taiwan.

Methods: We established a birth cohort of all live-births between 2001 and 2012 in Taiwan established using the National Health Insurance database and the National Birth Registry. Children born to mothers with SLE or RA were identified and matched up to 8 controls by maternal age, 1-minute Apgar score, 5-minute Apgar score, mode of delivery, sex of child, gestational age, birth weight, socioeconomic status (place of residence, income level, occupation). A marginal Cox proportional hazard models were used to estimate the relative risk (RR; 95% confidence interval [CI]) for ASD in newborns with affected mothers.

Results: Of 1,893,244 newborns, 0.08% (n=1,594) were born to mothers with SLE (mean age 30.43±4.37 years old) and 0.04% (n=673) were born to mothers with RA (mean age 31.97±5.1 years old). Overall, 5 of 673 (0.74%) RA offspring developed ASD, 7 of 1594 (0.44%) SLE offspring developed ASD and 10,631 of 1,893,244 (0.56%) all infants developed ASD. The incidence of ASD was 140.39 (95% CI, 45.58–327.62) per 100,000 person-years for RA group, 76.19 (95% CI, 30.63–156.97) per 100,000 person-years for SLE group, 89.85 (95% CI, 88.15–91.57) per 100,000 person-years for non-RA group and 89.87 (95% CI, 88.17–91.60) per 100,000 person-years for non-SLE group. The children born to RA and SLE mothers did not have higher risk of ASD with a HR (95% CI) of 1.42 (0.60–3.40) and 0.76 (0.58–1.09) for ASD, respectively.

Conclusions: Children born to women with SLE and RA do not have higher risk of developing ASD.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2882

WEDNESDAY, 14 JUNE 2017

Scleroderma, myositis and related ethology

OP0081 PAN-PPAR AGONIST IVA337 IS EFFECTIVE IN THE PREVENTION OF EXPERIMENTAL LUNG FIBROSIS AND PULMONARY HYPERTENSION

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Background: Peroxisome proliferator-activated receptors (PPARs) are nuclear receptors known to modulate fibrosis. The pan-PPAR agonist IVA337 recently demonstrated efficacy in prevention and treatment of experimental skin fibrosis [1].

Objectives: Our objective was to evaluate the antifibrotic effects of IVA337 in preclinical mouse models of pulmonary fibrosis and related pulmonary hypertension (PH).

Methods: IVA337 has been evaluated in the mouse model of bleomycin-induced pulmonary fibrosis and in Fra-2 transgenic mice, this latter being characterized by non-specific interstitial pneumonia and severe vascular remodeling of pulmonary arteries leading to PH. Mice received 2 doses of IVA337 (30 mg/kg or 100 mg/kg) or vehicle administered by daily oral gavage up to 4 weeks.

Results: Both 30 mg/kg and 100 mg/kg doses of IVA337 were well tolerated in all mouse models.

IVA337 demonstrated at a dose of 100 mg/kg a marked protection from the development of lung fibrosis induced by bleomycin compared to mice receiving 30 mg/kg of IVA337 or vehicle. Indeed, IVA337 (100 mg/kg) strongly reduced by 61% and 28% tissue density on histological measurements and total lung hydroxyproline concentrations, respectively, as compared to vehicle. IVA337 at 100 mg/kg also significantly decreased col1, col3 and fibronectin in lesional lungs. Similarly, Fra-2 transgenic mice treated with 100 mg/kg of IVA337 displayed reduced lung density (20% vs. vehicle) and significant increase of functional residual capacity (30% vs. vehicle) when assessed by chest micro-CT imaging. These results were emphasized by a 50% reduction of the Ascroft fibrosis score (Figure 1A) and by a 48% reduction of hydroxyproline concentrations upon IVA337 (100 mg/kg) compared to vehicle treated mice.

Successful targeting of the TGF-b signaling axis was observed in both mouse models upon treatment with 100 mg/kg of IVA337. 100 mg/kg IVA337 also significantly reduced T cell and B cell infiltration in lesional lungs of Fra-2 transgenic mice. Regarding vessel remodeling and related pulmonary hypertension, treatment with 100 mg/kg of IVA337 led to a substantial attenuation of right ventricular systolic pressure and right ventricular hypertrophy compared to mice receiving the vehicle (Figure 1B and 1C). Furthermore, IVA337 given at 100 mg/kg markedly reduced medial wall thickness (Figure 1D) and the number of muscularized distal pulmonary arteries.

In vitro primary human lung fibroblasts, IVA337 inhibited in a dose-dependent manner TGF-ß-mediated fibroblasts to myofibroblasts transition and PDGF-mediated proliferation.

Figure 1

Conclusions: We demonstrate that treatment with 100 mg/kg IVA337 prevents lung fibrosis in two complementary animal models and substantially attenuates PH in the Fra-2 mouse model. These findings confirm that the pan-PPAR agonist IVA337 is an appealing therapeutic candidate for systemic sclerosis both, for skin and key cardiovascular complications.

References:


DOI: 10.1136/annrheumdis-2017-eular.3805
FIBROSIS AND MICROANGIOPATHY ARE THE MAIN HISTOPATHOLOGICAL HALLMARKS OF SCLERODERMA-RELATED MYOPATHY

C. Corallo 1, M. Cutolo 2, S. Soldano 2, N. Volpi 1, D. Franchi 1, A. Montella 1, C. Chirico 1, R. Nuti 1, N. Giordano 1, 1 Medicine, Surgery and Neurosciences, University of Siena, Siena; 2 Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy

Background: Systemic sclerosis (scleroderma, SSc) is an autoimmune connective tissue disease characterized by skin and internal organ fibrosis, coupled with widespread vascular pathology. Skeletal muscle involvement in SSc has often been considered as a minor component of the disease associated with disuse.

Objectives: The goal of this study is to identify specific histopathological hallmarks of skeletal muscle involvement in SSc.

Methods: A total of 50 SSc patients presenting clinical, serological and electromyographic (EMG) features of muscle weakness, were enrolled. Patients underwent vastus lateralis biopsy, assessed for individual pathologic features including fibrosis [type I collagen (Col-I), transforming growth factor β (TGF-β)], microangiopathy [cluster of differentiation 31 (CD31), pro-angiogenic vascular endothelial growth factor (A VEG-F, anti-angiogenic VEGF-A165b), immune/inflammatory response [CD4, CD8, CD20, human leucocyte antigens ABC (HLA-ABC)], and myocardial attack complex (MAC). SSc biopsies were compared to biopsies of (n=50) idiopathic inflammatory myopathies (IIMs) and to (n=50) non-inflammatory myopathies (NIMs). Ultrastructural abnormalities of SSc myopathy were also analyzed by transmission electron microscopy (TEM).

Results: Fibrosis in SSc myopathy (90%) is higher compared to IIM (30%, p<0.05) and to NIM (15%, p<0.05). Vascular involvement is dominant in SSc (90%), and in IIM (75%) compared to NIM (20%, p<0.05). In particular, CD31 shows loss of endomysial vessels in SSc myopathy with respect to IIM (p<0.05) and to NIM (p<0.01). VEGF-A is downregulated in SSc myopathy compared to IIM (p<0.05) and to NIM (p<0.05), while VEGF-A165b is upregulated in SSc myopathy. The SSc immune/inflammatory response signature was also present with major [80%] HLA-ABC fibrin deposits and complement deposits on endomysial capillaries MAC, compared to IIM (p<0.05), characterized by CD4+/CD8+ B-cell infiltration, and to NIM (p<0.05). TEM analysis showed SSc vascular alterations consisting of thickening and lamination of basement membrane and endothelial cell ‘swelling’ coupled to endomyosial/perimysial fibrosis.

Conclusions: The predominant features of SSc-related myopathy are fibrosis, microangiopathy and humoral immunity. However, it is difficult to identify specific histopathological hallmarks of muscle involvement in SSc, since they could be present also in other (IIM/NIM) myopathies.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4070

MOLECULAR TARGETED IMAGING BIOMARKERS FOR PERSONALIZED MEDICINE STRATEGIES IN SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a life-threatening complication in systemic sclerosis (SSc). Substantial research progress has identified distinct genomic and molecular subtypes in SSc-ILD and brought molecular targeted therapies within reach. However, personalized medicine approaches are still lacking, since currently applicable tools for individualized patient stratification are not yet available.

Objectives: To assess the possibility of imaging molecular targets as a biomarker for stage-dependent assessment of ILD in the mouse model of bleomycin-induced lung fibrosis.

Methods: Expression of integrin α v β 3 and folate receptor β (FR-β) was analyzed in lung tissues from patients with idiopathic pulmonary fibrosis (IPF), SSc-ILD, and healthy controls as well as from bleomycin treated mice and saline treated controls using immunohistochemistry and qPCR (n=5–11), SPECT (Single Photon Emission Computed Tomography) or PET (Positron Emission Tomography) was performed at days 3, 7, and 14 after bleomycin instillation using the integrin α v β 3 -specific 177Lu-(RGD)k-ligand and the FR-β-specific 18F-Azafol. Additionally, 18F-FDG-PET and high resolution CT (HRCT) scans were performed. The specific lung uptake of the radiotracers over time was assessed by ex vivo SPECT or PET/CT scans and biodistribution studies.

Results: Expression of FR-β was significantly increased at the mRNA and protein level of SSc-ILD patients as compared to healthy subjects (p<0.05), whereas only its gene expression was upregulated in IPF patients (p<0.01). Integrin α v β 3 was increased in the lesion level of both SSc-ILD and IPF patients (p<0.05), while its mRNA expression was not significantly altered. Similarly, in lungs of bleomycin treated mice, but not of controls, FR-β expression was increased time-dependently at the mRNA and protein level with higher expression at day 3 and day 7, the inflammatory stages of bleomycin-induced lung fibrosis (p<0.05). In contrast, expression of integrin α v β 3 was upregulated at day 7 and day 14 at the protein, but not at the mRNA level in bleomycin treated mice, and thus not in the inflammatory but also in the fibrotic stages (p<0.05).

Conclusions: Our data suggest that stage-dependent visualization of ILD with radiotracers that target key markers of lung inflammation and/or fibrosis shows promise for clinical application to unselective imaging techniques such as 18F-FDG-PET and HRCT, the introduction of specific imaging biomarkers for individualized management of SSc-ILD patients could represent the first step towards precision medicine.

Disclosure of Interest: J. Schniering Grant/research support from: Swiss National Science Foundation (S-85605–02–01), M. Benešová Grant/research support: from: Swiss National Science Foundation (S-85605–02–01), M. Brunner: None declared, C. Feghali-Bostwick: None declared, R. Schibli Grant/research support from: Merck & Cie, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingehelm, Pfizer, Sanofi; Patent/licensing income for the treatment of systemic sclerosis. All authors declared: 4 D Science, Actelion, Actelion, Active Biotech, Bayer, Biogenedic, BMS, Boehringer Ingehelm, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacies, Pfizer, Sanofi, Sorapharm, Sinoxa, Speckers Therapeutics, Takeda, M. Müller Grant/research support from: Merck & Cie, B. Maurer Grant/research support from: AbbVie, Protegen, EMDO, Novartis, Pfizer, Roche, Actelion; Patent licensed: mir-29 for the treatment of systemic sclerosis.

RESCUE FROM THE FAILING HEART IN SYSTEMIC SCLEROSIS, A NOVEL INSIGHT: TARGETING TGF-β/FRA2/BECLIN AUTOFLUORESCENCE

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Background: The majority of Systemic Sclerosis (SSc) patients have subclinical primary cardiac involvement, which resembles the inflammatory dilated cardiomyopathy (IDCM) with inflammation and fibrosis. Firstly, cellular progenitors of pathological myofibroblasts remain undescribed.

Secondly, autophagy may favor fibrosis through enhanced differentiation of fibroblasts into myofibroblasts.

Objectives: To unravel the role of Fas-related antigen 2 (Faz2)autophagy crosstalk in TGF-β-driven myocardial fibrosis in SSc

Methods: Genetically modified mice overexpressing Faz2 were used. Endomyocardial biopsies (EMBs) from SSc/IDCM patients and hearts from Faz2tg and control mice were analysed by immunohistochemistry (IHC) and immunofluorescence (IF). Murine myocardial gp38+ (podoplanin+) stromal cells were sorted and stimulated in vitro with TGF-β. The cellular phenotype was assessed by qPCR, IF, stress fiber staining, SirColC and contraction assay on sorted cells.

Results: Cardiac fibroblasts in myofibroblasts showed higher expression of profibrotic markers: αSMA, vimentin and collagen I compared to control mice (n=5), as well as the expression of the autophagy markers LC3b and Beclin in fibrotic regions. Importantly, the expression of gp38+ cells co-expressed αSMA, vimentin and collagen I together with autophagy markers (LC3B and Beclin, n=3), following in vitro stimulation with TGF-β, gp38+ cells entered fibroblast-to-myofibroblast transition characterized by increased mRNA and protein levels of αSMA, collagen I, fibronectin (n=3–4), αSMA-fiber and stress-fiber formation (n=3), increased cell proliferation (n=4; p<0.04) and contraction capability (n=2; p<0.05) and enhanced collagen secretion (n=3; p<0.04). Importantly, Faz2tg gp38+ cells showed the presence of αSMA and stress fibers even without TGF-β stimulation as well as an increased contraction capability compared to control cells.

Conclusions: TGF-β stimulation of control gp38+ cells induced the expression of LC3B, Beclin and Atg5 at mRNA and protein level (n=3–5). In contrast, TGF-β inhibition caused the downregulation of these markers (n=3). In addition, Faz2 silencing resulted in a decreased differentiation capability of fibroblasts in myofibroblasts. This study thus suggests an autophagy-mediated rescue from the failing heart in SSc.
Conclusions: The TGF-β/Fra2 axis fosters an enhanced autophagy flow, leading in turn to the stromal-to-myofibroblast transition. Therefore, targeting this process might be a therapeutic strategy to abrogate fatal cardiac remodeling in SSc.

Disclosure of Interest: M. Stellato: None declared, M. Rudnik: None declared, F. Renoux: None declared, E. Pachera: None declared, D. Kayalar: None declared, K. Sotfar: None declared, K. Klingel: None declared, J. Henes: None declared, P. Biysczuk: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, Biogenidec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, expereRare foundation, Genentech-Roche, GSK, Inventiva, Lilly, medac, MePha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacycils, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, IQone Healthcare, MePha, G. Kania Grant/research support from: Bayer AG

DOI: 10.1136/annrheumdis-2017-eular.3760

Conclusions: This study is the first to characterize lower G19 microRNA in SSc patients at multiple time points. The findings provide further evidence that lower G19 dysbiosis is a feature of the SSc disease state and that specific genera may contribute to G19 symptoms and serve as potential targets for therapeutic intervention.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2077
pathways with the highest number of significantly enriched genes (n=5; p<0.005). Apoptosis markers like BCL2, IGFBP3 and FAF1 (n=5; p<0.005) were upregulated in H19X-silenced fibroblasts. This indicated that targeting H19X might have a pro-apoptotic effect on fibroblasts thereby protecting from fibrosis. Functional studies showed enhanced fibroblast apoptosis after H19X silencing and TGFβ stimulation (n=5; p<0.005). In addition to decreased apoptosis, increased fibroblast proliferation might also favor fibrosis. Indeed, H19X downregulation led to reduced cell proliferation as measured by BrdU assay (n=5, p<0.05). Scratch assay (n=5) showed that H19X knockdown decreases TGFβ reduced wound healing. H19X expression was significantly increased in SSc interstitial lung disease and IPP patients versus HC (n=11 each, p<0.05). A significant H19X overexpression was also detected in fibrotic tissue from Cohn’s disease patients (n=4–10, p<0.05).

Conclusions: H19X supports TGFβ-driven fibrosis not only by favoring myofibroblast development and extracellular matrix synthesis, but also by inducing proliferation and reducing apoptosis of dermal fibroblasts. These effects are not limited to SSC, but appear operative in a wider range of fibrotic diseases. Our results highlight the IncRNA H19X as a potent new therapeutic target in fibrotic diseases opening thereby new possibilities for the treatment of TGFβ-driven fibrosis.

Disclosure of Interest: E. Pacher: None declared, A. Wunderlin: None declared, S. Assassi Consultant for: Boehringer Ingelheim, Genentech and Biogen IDEC Inc., Bayer HealthCare, Galalagos: None declared, M. Frank-Bertolone: None declared, R. Dobrota: None declared, M. Brock: None declared, C. Feghali-Bowicket: None declared, G. Gerhard Roiger: None declared, G. Dijkstra: None declared, T. van Haaften: None declared, J. Distler: Shareholder of: 4D Science, Grant/research support from: from Anamar, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCIB., G. Kania: Grant/research support from: from Actelion, Active Biotech, Bayer, BMS, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, Medimmune, Mitsubishi Tanabe Pharma, Pharmaceuticals, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha

DOI: 10.1136/annrheumdis-2017-eular.4877

OP0088

THE ROLE AND FUNCTION OF MONOCYTE-DERIVED FIBROBLAST-LIKE CELLS IN MULTIORGAN FIBROSIS IN SYSTEMIC SCLEROSIS


Background: Systemic sclerosis (SSc) is a systemic connective tissue disease characterised by autoimmunity, vascular disorder and fibrosis of skin and other organs (1). Although substantial reports have been hitherto provided upon its pathogenesis in relation to microvascularature, among which are on endothelial and fibroblastic Fli1 deficiencies (1, 2), adequate investigation into hemoxytic involvement is yet to be attained. Platelets are well known for its function in organs (1). Although substantial reports have been hitherto provided upon its involvement is yet to be attained. Platelets are well known for its function in monocytes involvement in SSc might lead to novel treatment strategies.

Methods: In dermal injuries on Fli1 PcKO mice, inflammatory disturbances precipitate myofibroblast formation in the granulation tissue, thus anticipating wound closure by mechanical contraction.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1350

OP0087

PLATELET-SPECIFIC Fli1-KNOCKOUT MICE SHOW ACCELERATED WOUND CLOSURE ASSOCIATED WITH INCREASED MYOFIBROBLAST FORMATION IN THE INFLAMMATORY PHASE


Background: Systemic sclerosis (SSc) is a systemic connective tissue disease characterised by autoimmunity, vascular disorder and fibrosis of skin and other organs (1). Although substantial reports have been hitherto provided upon its pathogenesis in relation to microvascularature, among which are on endothelial and fibroblastic Fli1 deficiencies (1, 2), adequate investigation into hemoxytic involvement is yet to be attained. Platelets are well known for its function in hematosis whereas they also play a part in inflammation, immunity and cellular proliferation (3), thus prompting us to speculate their cardinal role in the development of the disease.

Objectives: Here we aim to unravel the role of platelets in the pathogenesis of SSc, with generation of platelet-specific conditional Fli1 knockout (Fli1 PcKO) mice to scrutinise its dermal wound healing process.

Methods: We generated Fli1 PcKO mice using the Cre-Lox system along with PcCre mice as an appropriate control. We made two excisional wounds on the dorsal skin of each mouse (three months old) using an eight-millimeter-diameter punch and traced the wound surfaces every other day to measure their areas using Image J until all the wounds were epithelised. On a separate experiment, perilesional skin tissues harvested on the day two, from which we extracted mRNA for the measurement of proinflammatory and profibrotic cytokines. An immunostaining for α-SMA was performed on the skin samples.

Results: The areas of the wounds were calculated and shown in ratio to their initial areas (day 0). Fli1 PcKO mice showed a significant decrease in the areas compared to the control on day 2. mRNA measurement revealed a significant increase in Mmp13 and significant decreases in Tgfβ1, Ifng and Il13 for Fli1 PcKO. In histopathology, α-SMA positive fusiform-shaped cells were abundant in the granulation tissue of Fli1 PcKO mice (Figure; left, PcCre +/−; right, Fli1 PcKO; original magnification, ×400).

Conclusions: In dermal injuries on Fli1 PcKO mice, inflammatory disturbances precipitate myofibroblast formation in the granulation tissue, thus anticipating wound closure by mechanical contraction.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3800
COMBINATION THERAPY OF SELECTIVE MMP9 AND TNF INHIBITORS ARE EFFICACIOUS IN THE MOUSE CIA MODEL OF RHEUMATOID ARTHRITIS


Background: Matrix metalloproteinase-9 (MMP9) is highly expressed by infiltrating inflammatory cells, pannus tissue, and multinucleated cells in the synovium and subchondral bone tissue, including osteoclasts. MMP9 is implicated in rheumatoid arthritis (RA) by its involvement in joint destruction, activation of cytokinesis, and promotion of tissue destruction by degrading the basement membrane of epithelia and vasculature. MMP9 knockout mice are protected from collagen-induced arthritis (CIA) disease progression. A potent, allosteric antibody inhibitor of MMP9 is currently being investigated in clinical trials. The ability of a functional murine analog of this antibody to reduce disease signs and symptoms in established, chronic mouse CIA model both as a single agent and in combination with anti-TNF, was investigated.

Objectives: We evaluated the efficacy and safety of selective MMP9 inhibition both alone and in combination with anti-TNF (etanercept), in CIA models of RA.

Methods: CIA was induced in male DBA/1j mice (n=15/group) and treatments were initiated after disease establishment. Efficacy was assessed via metrics of joint injury including clinical score (erythema/ paw swelling, score 0–4) in addition to histopathological assessment of destructive joint remodeling (soft tissue changes: edema, necrosis, inflammatory cell infiltration, and fibroplasia, score 0–4; bone changes: 0–6; bone erosion, periosteal bone formation, synovitis, pannus formation, and joint destruction, sum score 0–24).

Results: All animals were included in the evaluation. In all endpoints assessed, treatment with each therapeutic agent, on its own or in combination, resulted in improvement with respect to body weight change, clinical score, and histopathological signs of joint injury. The combination group provided the best overall trend for therapeutic benefit, although statistical significance as compared to each single agent alone was not met in most parameters. Body weight recovery was superior in combination as compared to single agent therapies (52% vs. 12–34%, relative to sham; p<0.05 combination vs. single agents). Clinical score and histopathology measures in soft tissue and bone changes were most improved in the combination therapy group, although it did not achieve statistical significance as compared to each single agent (26% vs. 17–21%; 1.5 vs. 1.5–1.8; and 7 vs. 7–9, respectively). Importantly, combination therapy resulted in a significant number of limbs with zero or mild disease as compared to single agents (no disease sign: 25% vs. 172–223%; mild disease sign: 178% vs. 138–141%). Analysis of complete blood count at the end of study revealed no abnormalities in any treatment group.

Conclusions: Selective inhibition of MMP9 was active in reducing disease severity in CIA models of RA. The combination of anti-MMP9 with anti-TNF was well tolerated and increased the number of limbs with no or mild disease compared to anti-TNF alone. Further studies are required to examine combination therapy of selective anti-MMP9 and anti-TNF therapies in a clinical setting.


DOI: 10.1136/annrheumdis-2017-eular.1941
Results: Our results demonstrate that early exposure to S100A8 interferes with in-vitro differentiation of moDCs. Compared to controls S100A8-exposed moDCs show dramatically reduced surface expression of co-stimulatory molecules upon LPS-induced maturation. In addition, early treatment of moDCs with S100A8 alters the secretion of immune-regulatory cytokines and chemokines depending on the differentiation state of moDCs. S100A8-induced effects on moDCs and their maturation are not limited to TLR4 stimulation but rather trigger a common state of unresponsiveness. Furthermore, mitochondrial respiration and glycolytic function is diminished in S100A8-treated moDCs. As a consequence, S100A8-exposed moDCs have a reduced potential to induce autologous FcεR1 proliferation. We can show that these differences are mainly caused by reduced surface expression of co-stimulatory molecules on S100A8-treated moDCs. Mechanistically, genome-wide gene expression analysis reveals dramatic differences in the gene expression between S100A8-exposed and conventionally differentiated moDCs. We demonstrate that S100A8 pre-treatment of moDCs significantly blocks LPS-induced gene expression during moDC activation. Interestingly, in-silico analysis of transcription factor networks predicts NFκB and C/EBPs as master regulators of S100A8-induced effects in developing moDCs. C/EBPs on protein level, indeed, shows reduced expression in S100A8-differentiated moDCs prior and after LPS-induced maturation when compared to conventionally differentiated moDCs.

Conclusions: Taken together, our results demonstrate a novel regulatory mechanism of innate immunity to prevent overwhelming immune responses. Dysregulation of type 1 interferon may lead to detrimental immune responses which very well contribute to the disease phenotype in auto-immune disorders with high systemic S100A8/A9 levels. Therefore, S100A8-differentiated immune-suppressive DCs might very well be master regulators of S100A8-induced effects in developing moDCs. C/EBP as well as changes in amino acid and purine metabolism. Oxidative phosphorylation. Metabolomic analyses of plasma and muscles of mice with systemic inflammation induced by LPS injection. We further investigated the effects of IL-37 on exercise tolerance in healthy mice, with specific focus on the metabolic changes induced by IL-37 administration and possibly responsible for a reduction in the metabolic costs of inflammation.

Results: Exogenous administration of IL-37 to healthy mice, not subjected to an inflammatory challenge, also improved exercise performance by 82% compared to vehicle-treated mice (p<0.001). Treatment with 8 daily doses of IL-37 resulted in a further 326% increase in endurance running time compared to the performance level of mice receiving vehicle (p<0.001). These properties required the engagement of the IL-1 decoy receptor 8 (IL-1R8) and the activation of AMPK, a key regulator of intracellular energy homeostasis. Conditioning media from these cells, containing released IL-37, was also able to elicit an anti-inflammatory effect on human macrophages and RA-FLS by reducing their IL-23 (M1) and IL-6 (M1 and RA-FLS) expression.

Conclusions: This study shows for the first time that IL-37 overexpression attenuates the severity of experimental arthritis in two mice arthritis models. IL-37 may exert its anti-inflammatory effects by decreasing the production of pro-inflammatory cytokines by macrophages and fibroblast-like synovocytes. This effect can lead to the development of novel treatment strategies in arthritis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2257
**OBJECTIVES:** To develop biomarkers of progression to systemic autoimmunity, with a view to enabling early intervention for disease prevention.

**Methods:** A prospective observational study was conducted in 125 patients at Risk of CTD defined by (i) ANA; (ii) ≤1 clinical SLE criteria; (iii) symptom duration <12 months and (iv) treatment-naïve. Progression was defined by meeting 2012 ACR/SLICC SLE, 2016 ACR/EULAR Primary Sjogren’s, or other diagnostic criteria. Expression of 30 selected ISGs was measured using Taqman. Factor analysis was used to reduce the gene expression data to a limited set of factors, which were compared between patient groups using Mann Whitney U Test. Two factor scores explained 80% of the data variance; “Score A” (composed of IFN-γ responsive genes) and “Score B” (genes responsive to IFN-γ and γδ T cells) were used to calculate IFN Score A and B.

**Results:** 82 patients with 1-year follow-up data were studied. 71 were female with mean age 48±1.5 years. 16 (20%) patients progressed to CTD (SLE=12, Sjogren’s=4) in the following 12 months. At baseline, only IFN Score A was increased in both At-Risk-CTD and SLE vs healthy controls; p<0.001. IFN Score B was only increased in true established SLE.

**Conclusions:** IFN Score B was low in patients who did not progress and increased in those who did progress; p<0.001. There was no difference in IFN Score A between these two groups; p=0.292 (Figure 1). Although complement levels and lymphocyte counts were lower in SLE, these were not different between the At-Risk progression and non-progression groups. Anti-dsDNA titres were higher in SLE but not different between the progression groups; all p>0.10.

**References:**


Cytokines and chemokines

**OP0097** SYSTEMIC IFN TYPE I AND TYPE II SIGNATURES IN PRIMARY SJÖGREN’S SYNDROME REVEAL DIFFERENCES IN DISEASE SEVERITY

I. Bodewes, S. Al-Ali, C.G. van Helden, N.K. Maria, J. Tarn, D. Lendrem, M.W. Schirurs, E.C. Steenwijk, P.L.A. van Daene, T. Both, S. Bowman, B. Griffiths, W.-F. Ng, M.A. Versnel, Immuno, Erasmus MC, Rotterdam, Netherlands; 2Musculoskeletal Research Group, Newcastle University, Newcastle upon Tyne, United Kingdom; 3University of Basrah, Basrah, Iraq; 4Internal Medicine, Erasmus MC, Rotterdam, Netherlands; 5Rheumatology, University Hospital Birmingham, Birmingham; 6Newcastle upon Tyne Hospitals NHS Foundation Trust; 7National Institute for Health Research, Newcastle Biomedical Research Centre, Newcastle upon Tyne, United Kingdom

**Background:** Local and systemic activation of interferons (IFNs) has been demonstrated in primary Sjögren’s syndrome (pSS).[1–4] Type I IFNs are associated with higher disease activity and autoantibody levels.[5] Recent findings also show activation of interferon type II (IFNγ) induced gene expression in salivary glands of pSS patients.[6, 7] Although IFN type I and II bind to different receptors they induce partially overlapping gene expression patterns. Understanding the relative contribution of IFN type I and type II may deepen our knowledge in pSS pathogenesis and promote a stratified approach to therapeutic development.

**Objectives:** Determine IFN type I and II inducible gene expression in patients with pSS and correlate this to disease manifestations.

**Methods:** In whole blood of 50 pSS patients modular IFN scores were determined using real-time quantitative PCR followed by principal component analysis. Subsequently, five indicator genes per module were analysed in two independent European cohorts with a total of 141 patients.

**Results:** Three groups were distinguished: without IFN activation (19–47%), with IFN type I (53–81%) and with IFN type I and II activation (35–55%). Patients with IFN activation (I or II) have a higher presence of auto-antibodies, IgG levels and lower lymphocyte counts compared to IFN negative patients. The biological domain of the EULAR Sjögren’s Syndrome Disease Activity Index (biological-ESSDAI) was higher in patients with IFN activation, while total-ESSDAI scores were not significantly different.

66–67% of the IFN type I positive patients had an additional IFN type II inducible gene expression. Patients with IFN type II induction have significantly higher IgG levels and lower lymphocyte counts compared to patients with only IFN type I activation. There were no differences in fatigue or dryness, but pain scores were lower.

**Conclusions:** pSS patients can be stratified according to their systemic IFN activation patterns. IFN activation (I or II) is present in patients with the highest activity of the biological-ESSDAI. These data raise the possibility that the biological-ESSDAI rather than total-ESSDAI score may be a more sensitive endpoint for trials targeting either type I or type II IFN pathways.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3688

**THURSDAY, 15 JUNE 2017**

**Progress in biological treatment of RA**

**OP0098** REMISSION AND MAINTENANCE OF EFFICACY IN A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN 6 RECEPTOR NANOBODY, IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS DURING TREATMENT WITH METHOTREXATE

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**Background:** Vobarilizumab is a Nanobody® consisting of an anti-IL-6R domain and an anti-human serum albumin domain in development for treatment of RA. The efficacy and safety were assessed in a 24-week double-blind global phase 2b study in patients with active RA on a stable background of MTX. Main efficacy and safety results were previously reported.[1]

**Objectives:** To report the impact of treatment with vobarilizumab on secondary efficacy endpoints including SDAI and CDAI remission and the sustained response at 4 consecutive visits based on ACR50, ACR70 and DAS28<2.6.

**Methods:** Patients were randomized to receive subcutaneously administered placebo or 1 or 4 dose regimens of vobarilizumab in addition to MTX. SDAI and CDAI remission at Week 24 was evaluated, as was maintenance of efficacy as defined by sustained DAS28<2.6 responses at 4 consecutive visits (i.e., at Weeks 12, 16, 20 and 24). In addition, a post-hoc analysis was performed on sustained ACR50 and ACR70 responses from Week 12 through Week 24. Proportions of patients achieving response for these endpoints were summarized by treatment group. Subjects with missing values were analyzed as non-responders.

**Results:** A total of 345 patients were randomized. Demographics and baseline characteristics were similar across groups with mean baseline DAS28CRP between 5.8 and 6.2. At Week 24, up to 19% and 20% in the vobarilizumab groups reached CDAI remission, respectively, vs. 10% and 9% who received placebo (Table 1).

At Week 24, up to 61% and 45% of the patients in the vobarilizumab groups achieved an ACR50 or ACR70 response, respectively (39% and 17% on placebo). Approximately one third of the randomized patients in the 3 highest treatment groups had a sustained ACR50 response from Week 12 through Week 24 (Table 2). Sustained remission defined by DAS28<2.6 at 4 consecutive visits, i.e. at weeks 12, 16, 20 and 24, was observed in 20% to 25% of the patients in the 3 highest dosing arms compared with 3% of those receiving placebo.

**Table 1. Percentage of patients with CDAI and SDAI remission at Week 24**

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Vobarilizumab (N=69)</th>
<th>Vobarilizumab (N=70)</th>
<th>Vobarilizumab (N=68)</th>
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<tr>
<td>CDAI remission</td>
<td>(n=2.8)</td>
<td>10</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>SDAI remission</td>
<td>(n=3.3)</td>
<td>9</td>
<td>10</td>
<td>19</td>
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</tbody>
</table>

**Table 2. Percentage of patients with sustained efficacy response at 4 consecutive visits (Weeks 12, 16, 20 and 24)**

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Vobarilizumab (N=69)</th>
<th>Vobarilizumab (N=70)</th>
<th>Vobarilizumab (N=68)</th>
<th>Vobarilizumab (N=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR50</td>
<td>16</td>
<td>14</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>ACR70</td>
<td>4</td>
<td>7</td>
<td>11</td>
<td>13</td>
</tr>
</tbody>
</table>

**Conclusions:** In patients with active RA, treatment with vobarilizumab at the 3 highest dose regimens in addition to MTX had a positive and sustained impact on disease activity through Week 24 as defined by clinically relevant efficacy endpoints.

**References:**


**THURSDAY, 15 JUNE 2017**

**OP0099** SAFETY, TOLERABILITY AND INITIAL SIGNS OF EFFICACY OF THE FULLY HUMAN IMMUNOCYTOKINE DEKAVIL (FBL10): A NOVEL THERAPEUTIC APPROACH FOR RHEUMATOID ARTHRITIS

M. Galeazzi, T. K. R. G. Sebastiani, R. Völz, J. Wollenhaupt, O. Viapiana, J. Dudler, E. Selvi, C. Baldi, M. Bardelli, B. Bannert, S. Finzel, C. Specker, P. Sarzi Puttini, F. Bootz, Neri, on behalf of the DEKAVIL Study Group. 1University Hospital, Siena; 2San Camillo-Forlanini Hospital, Rome, Italy; 3University Medical Center, Freiburg; 4Schooss-Klinik, Hamburg Eilbek, Germany; 5University Hospital, Verona, Italy; 6Cantonal Hospital, Fribourg, Switzerland; 7University Hospital, Essen, Germany; 8Luigi Sacco Hospital, Milan, Italy; 9Philochem AG, Otelfingen, Switzerland; 10Philogen SpA, Siena, Italy

**Background:** The antibody-based targeted pharmacodelivery of cytokines by means of immunocytokines has the potential to enhance therapeutic activity at the site of disease while sparing healthy tissues. Dekavil (F8IL10) is a fully human immunocytokine composed of the vascular targeting antibody F8 (specific to
EDA) fused to the cytokine interleukin-10. Dekavil is currently in phase II clinical development for the treatment of rheumatoid arthritis (RA).

Objectives: In the phase Ib dose escalation study, the primary objective was to explore safety, tolerability and the maximum tolerated dose of Dekavil when administered in combination with methotrexate (MTX). The aim of the currently ongoing phase II study is to assess the therapeutic activity of Dekavil plus MTX over MTX alone by measuring the mean change from baseline of DAS28-2CRP. Immunogenicity of F8IL10 and its PK and PD profile will also be explored.

Methods: Patients with active RA despite MTX therapy and who failed anti-TNF treatment are the target population of both studies. In the phase Ib trial, cohorts of 3–6 patients were treated with escalating doses of Dekavil (6, 15, 30, 60, 110, 160, 210, 300, 450 and 600 μg/kg) in combination with a fixed dose of MTX (10–15 mg). In the multicenter, double-blind, placebo-controlled phase 2 study, patients are randomized into two treatment groups (Dekavil 30 or 160 μg/kg plus MTX) and one placebo group (placebo plus MTX). Dekavil is administered once weekly by s.c. injection for a maximum of 8 weeks in both studies.

Results: Dekavil has been shown to be well tolerated up to the highest investigated dose (600 μg/kg) and an MTD was not reached. In 33 out of 34 patients treated in the phase 1 study, no DLTs, no SAES and no SUSARS have been reported. One patient in cohort 9 (450 μg/kg) experienced a DLT (G2 purpura) and a SAE (G2 dyspnea, not drug related). The patient received corticosteroids and fully recovered within one week. Mild injection site reactions were the most frequently observed adverse events and occurred in 62% of the patients. Furthermore, two cases of drug related anemia (G2 and G3) were reported in this study. All adverse reactions resolved completely. At the first efficacy assessment after 4 cycles of treatment, 48% of evaluable patients (16/33) revealed ACR and/or EULAR responses. At the last assessment after 8 cycles of treatment, 2 patients benefited from ACR20 responses for more than 12 months after last drug administration. As of January 2017, 22 out of 83 patients have been treated in the phase 2 clinical study and neither SUSAR nor treatment-related deaths were recorded.

Conclusions: The currently available data suggest that Dekavil is a safe and potentially novel therapeutic for the treatment of RA.

Disclosure of Interest: M. Galeazzi: None declared, G. Sebastiani: None declared, R. Völl: None declared, J. Wollenhaupt: None declared, O. Viapiana: None declared, J. Dudler: None declared, E. Selvi: None declared, C. Baldi: None declared, M. Bardelli: None declared, B. Barrient: None declared, S. Finzel: None declared, C. Specker: None declared, P. Sacchi Puttini: None declared, F. Bootz: Employee of: Philochem AG, D. Neri Shareholder of: Philogen SpA

DOI: 10.1136/annrheumdis-2017-eular.4840

OP0101

OVERALL CANCER RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TNF INHIBITORS, TOCILIZUMAB, ABATACEPT, OR RITUXIMAB

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Background: Immune incompetence may lower host surveillance against incipient tumours. Conversely, immune therapies have emerged as a promising therapeutic approach to cancer. Malignancies thus constitute an important aspect of the treatment of patients with rheumatoid arthritis (RA), which is a chronic inflammatory disease of unknown cause with a predilection for the joints. Through linkage with the Swedish national and population-based registers (see Additional file 1), and educational level, there were no statistically significant differences in the overall risk of malignancies among RA patients initiating, tocilizumab, abatacept, rituximab, or a first - or second TNFi, and RA patients treated with csDMARDs.

Objectives: To present the overall incidence rates of OI and herpes infections observed in patients (pts) receiving ABA using combined clinical trial data.

Methods: All adverse events were summarized from 16 clinical trials (both placebo-controlled and cumulative abatacept exposure): all pts randomized to placebo were on a non-biologic DMARD. Incidence rates (per 100 person-years (p-y)) were calculated by the number of pts experiencing the first event divided by the total number of p-y of exposure. The p-y of exposure was censored at the time of the first event, death, discontinuation or end of study. Random effects meta-regression was performed across the trials to estimate the frequency of OI after adjusting for study heterogeneity. OI were identified using a pre-specified list in the setting of biologic therapy for patients with RA. Criteria for consideration were based on type, location of the infection and causing organism. Excluded from the list were non-specific infections caused by organisms considered to be opportunistic, but common in the general population.

Results: A total of 7044 pts with RA with >21,330 p-y of ABA exposure were included in the cumulative randomized trial data (Table). The frequency of OI

Abstract OP0101 – Table 1

<table>
<thead>
<tr>
<th>Infection Outcome</th>
<th>Abatacept (N=2653) p-y=1255</th>
<th>Placbeo (N=1485) p-y=1255</th>
<th>Cumulative abatacept (N=7044) p-y=21,330</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>IR/100 p-y (95% CI)</td>
<td>N (%)</td>
<td>IR/100 p-y (95% CI)</td>
</tr>
<tr>
<td>Opportunisitc infections*</td>
<td>4 (0.2)</td>
<td>0.17 (0.05, 0.43)</td>
<td>0.5 (0.5)</td>
</tr>
<tr>
<td>Bronchopulmonary aspergillosis</td>
<td>1 (0.01)</td>
<td>0.04 (0.00, 0.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Eye infection fungal</td>
<td>1 (0.01)</td>
<td>0.04 (0.00, 0.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gastronintestinal candidiasis</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fungal oesophagitis</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Meningitis cryptococcal</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Oesophagal candidiasis</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pneumocystis jirovecii pneumonia</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pneumonia pseudomonal</td>
<td>1 (0.01)</td>
<td>0.04 (0.00, 0.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Respiratory moniliasis</td>
<td>0 (0)</td>
<td>0.08 (0.0, 0.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0 (0)</td>
<td>0.08 (0.0, 0.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Herpes</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>57 (2.1)</td>
<td>2.5 (1.9, 3.2)</td>
<td>22 (1.5)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>44 (1.7)</td>
<td>1.9 (1.4, 2.5)</td>
<td>21 (1.4)</td>
</tr>
<tr>
<td>Herpes virus infection</td>
<td>5 (0.2)</td>
<td>0.2 (0.1, 0.5)</td>
<td>4 (0.3)</td>
</tr>
</tbody>
</table>

*Except herpes; †n (%) for SAE was 19 and IR/100 p-y was 0.1 (95% CI 0.05, 0.14); ‡n (%) for SAE was 11 and IR/100 p-y was 0.05 (95% CI 0.03, 0.09); – indicates value is not available. SAE = serious AE.
was 64% lower among pts treated with ABA vs placebo. After adjusting for heterogeneity across studies, the frequency (95% CI) of OI remained lower for the ABA group (0.15% [0.06, 0.42] vs the placebo group (0.48% [0.22, 0.94]).

Conclusions: Abatacept-treated pts had a lower incidence rate of OI compared with placebo. The OI and herpes infection incidence rates in the cumulative data are similar or lower to those reported in the literature.1,3

References:


DOI: 10.1136/annrheumdis-2017-eular.2306

The Effect of Sirukumab Plus Methotrexate on Circulating Biomarkers of Joint Destruction in Moderate to Severe Rheumatoid Arthritis Patients from the Sirround-D Phase 3 Study


DOI: 10.1136/annrheumdis-2017-eular.2955

Patient Reported Benefits of Sarilumab in Adult Patients with Active Rheumatoid Arthritis

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Background: The phase 3 MONARCH superiority study (NCT02332590) compared efficacy and safety of sarilumab (a human anti-IL-6R monoclonal antibody [mAb]) 200 mg administered subcutaneously every 2 weeks (q2w), with adalimumab from MONARCH.

Methods: To compare patient-reported outcomes (PROs) with sarilumab vs adalimumab from MONARCH.

Objectives: Consistent with IL-6R or TNF blockade.

Results: Baseline demographics, disease characteristics and PROs assessed at baseline, weeks 12 and 24 included ACR components, SF-36 physical component summary [PCS], Morning Stiffness VAS, Health Assessment Questionnaire Disability Index [HAQ-DI]), Short Form-36 Physical Component Summary (SF-36 PCS), quality of life (QoL) and health domain summary (RAD), physical function (physical function [PHI], Physical Function [VAS]), role limitations due to physical problems (role limitations due to physical problems [VSA], role limitations due to emotional problems (role limitations due to emotional problems [VSS]), vitality (vitality [VSA], vitality [VSS]), mental health (mental health [VSA], mental health [VSS]), pain (pain [VSS], pain [VAS]), social functioning (social functioning [VSA], social functioning [VSS]), and general health (general health [VSA], general health [VSS]).

Conclusions: Sarilumab monotherapy compared with adalimumab monotherapy resulted in greater and clinically meaningful improvements in many PROs, including patient-reported disease activity, pain, physical function, morning stiffness, productivity, health related quality of life and health status.

Acknowledgements: This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.


Disclosure of Interest:

DOI: 10.1136/annrheumdis-2017-eular.2306

Circulating Biomarkers of Joint Destruction in Moderate to Severe Rheumatoid Arthritis Patients from the Sirround-D Phase 3 Study

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and <0.5 (n=51). BL or Wk 4 changes in levels of individual analytes were not associated with Wk 24 ACR50 or DAS28-CRP responses.

Conclusions: SIR 50mg q4w + MTX, vs pbo + MTX, inhibited radiographic progression in RA pts in SIRROUND-D and strongly inhibited biomarkers of joint and tissue destruction while enhancing markers of bone formation. These data suggest SIR may actively suppress inflammatory pathways implicated in joint destruction in RA pts.


DOI: 10.1136/annrheumdis-2017-eular.3588

OP1014 TOCILIZUMAB: DOSE REDUCTION OR INTERVAL SPACING – WHICH PROVES A BETTER TAPERING STRATEGY FOR RHEUMATOID ARTHRITIS IN CLINICAL REMISSION?

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1Department of Rheumatology, Taisho General Hospital, Goyougawara; 2Marketing Department; 3Marketing Department, Diagnostics Division, Sekisui Medical Co., Ltd., Tokyo; 4Departments of Orthopaedic Surgery; 5Departments of Dermatology, Taisho General Hospital, Goyougawara; 6Department of Pharmacology, Hiroakis University Graduate School of Medicine, Hiroakis, Japan

Background: A number of studies have revealed that reduction of biological disease-modifying anti-rheumatic drugs (bDMARDs) is possible for some rheumatoid arthritis (RA) patients in whom bDMARD treatment has induced clinical remission or low disease activity. For tocilizumab (TCZ), while there have been studies concerning tapering, there have been no studies regarding which tapering option is better in RA after clinical remission has been achieved: a dose reduction strategy (DRS) or an interval spacing strategy (ISS).

We previously demonstrated that a twin target strategy [targeting both a simplified disease activity index (SDAI) score of less than 3.3 and normalization of matrix metalloproteinase (MMP) 3 levels] can achieve effects non-inferior to standard care with regard to maintaining clinical remission in the r-4study.

Objectives: To evaluate any significant differences that may be present between the two strategies (DRS and ISS) while tapering TCZ in RA patients who satisfied the SDAI remission and MMP-3 normalization targets under the twin target scheme.

Methods: DRS was used in patients treated with intravenous (IV) TCZ, whereas ISS was used for those treated by subcutaneous injection (SC). 57 RA patients who demonstrated SDAI remission and MMP-3 normalization using TCZ (IV, n=42; SC, n=15) participated. Dose reduction methodology (every 3 months): DRS- 80 mg every 4 weeks; ISS-162 mg every 4 weeks. After DRS was used in patients treated with intravenous (IV) TCZ, whereas ISS was used for those treated by subcutaneous injection (SC). 57 RA patients who demonstrated SDAI remission and MMP-3 normalization using TCZ (IV, n=42; SC, n=15) participated. Dose reduction methodology (every 3 months): 5.76
target was re-achieved. The primary outcome was the difference in the number of times when a patient’s SDAI exceeded 3.3 across the four time points.

Results: Fifty-five patients completed the observation period of 12 months and were analyzed (ITT). There were differences in the number of the times which SDAI scores exceeded the target over the 12 months in the DRS group vs the ISS group: 2.4±1.7 and 0.9±1.2, respectively (p=0.0027). DRS had a duration (months) of maintained SDAI remission significantly shorter than that of ISS (3.9±15.0 vs 7.4±5.1, p=0.0213). At month 12, the proportions for DRS and ISS, (months) of maintained SDAI remission significantly shorter than that of ISS (3.9±15.0 vs 7.4±5.1, p=0.0213). At month 12, the proportions for DRS and ISS, respectively, for ΔMTS =-0.5 were 71.4 and 66.7% (p=0.729); for maintained HAD(0-10) were 83.8 and 66.7% (p=0.4227) and for AE were 81.0 and 46.7 (p=0.0112). The total dose for TCZ in DRS tended to be lower than that for ISS (1367±840 vs 1626±583mg, p=0.0824). The rate of total TCZ reduction showed a significant difference between DRS and ISS (29.3±15.2% vs 41.8±15.0%, p=0.037). Comparing three groups consisting of 400mg-, 401-<500mg and 500mg- across the DRS with ISS groups, there were significantly greater number of times when SDAI exceeded 3.3 in the DRS vs the ISS group; 2.3±1.6, 2.7±1.8 and 2.4±1.9, p=0.0395.

Conclusions: ISS using the twin targets as defined by the r-4 study is an excellent strategy that is both safe and cost-effective for RA patients who are both being treated with TCZ and have reached said targets.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2501

OP1015 LONG-TERM SAFETY OF TOCILIZUMAB FROM LARGE CLINICAL TRIAL AND POSTMARKETING POPULATIONS

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Background: Tocilizumab (TCZ) is a recombinant humanized monoclonal anti-body targeted against the interleukin-6 receptor that was approved to treat rheumatoid arthritis (RA) in the EU in 2009 and in the US in 2010. TCZ has now completed long-term extension (LTE) follow-ups in a number of intravenous and subcutaneous RA trials.

Objectives: To provide an updated report on the incidence of safety events during TCZ treatment in patients with RA using data from multiple completed clinical trials and their LTEs, as well as to provide an update from the global TCZ postmarketing safety database.

Methods: Incidence and reporting rates of adverse events (AEs) of special interest, including infections, malignancies, anaphylaxis, bleeding events, myocardi al infarctions, gastrointestinal perforations, strokes, hepatic events and demyelination, were estimated from 2 distinct patient data sets. Incidence rates were calculated from 12 completed TCZ RA clinical trials and their LTE periods and are reported as events per 100 patient-years (PY). Reporting rates were also estimated from the global TCZ postmarketing safety database (Oct 2008 to Oct 2015), which includes information from all spontaneously reported cases and postmarketing regulatory programs as well as literature cases, and are reported as cases per 100 patients.

Results: The clinical trial all-exposure population consisted of 7647 TCZ-treated patients with RA (81.6% female; mean [SD] age, 52 [12.6] years, constituting 22,394 PY (mean follow-up, 2.93 years) of exposure. The overall rate (95% CI) of serious AEs in the clinical trial population was 14.16 (13.67–14.66) per 100 PY. Overall incidence rates for individual events for the clinical trial population are reported in the Table and were consistent in each 6-month period over the 5-year duration. The global postmarketing population included 606,937 patients. The overall spontaneous reporting rate (range) of AEs of special interest in the postmarketing population was 8.97 (7.35–10.56) cases per 100 patients. Reporting rates of individual safety events of interest in the global postmarketing population are shown in the Table and were consistent in each 6-month period over the 7-year duration.

Conclusions: The safety profile of TCZ in the current analysis, which includes information about safety events from 12 clinical trials and their LTEs and across >10 years of real-world postmarketing reports encompassing >600,000 patients, was consistent with previous safety reports. These findings are consistent with the previously reported profile of TCZ and indicate that there is no evidence of increased safety risk with increasing exposure to TCZ.

Acknowledgements: This study was funded by F. Hoffmann-La Roche/Genentech, Inc.


DOI: 10.1136/annrheumdis-2017-eular.3573
Background: Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with several severe comorbidities such as cardiovascular diseases, diabetes, and depression. Tumour necrosis factor inhibitor (TNFi) therapy fails among half of patients with PsA treated in routine care.

Methods: Data on patient characteristics, disease activity and treatment adherence was obtained from the DANBIO register. Information on comorbidities according to the Charlson Comorbidity Index (CCI) and psychiatric comorbidities was obtained through linkage with the Danish National Patient Register. We performed Kaplan-Meier plots and multivariate Cox proportional hazard regression analyses adjusted for sex, age, disease duration, DAS28-CRP, obesity, smoking, concurrent methotrexate treatment, calendar period, and diagnosis with depression and/or anxiety. Percentages of patients achieving relevant clinical response rates were calculated.

Results: We identified 1750 patients eligible for analyses. Patients with higher CCI scores had statistically significantly higher disease activity measures at baseline compared with patients without comorbidities (Table 1). Kaplan–Meier curves showed shorter adherence to treatment for patients with CCI >2 compared with patients with lower CCI scores (CCI =0: 2.6 years [2.2 to 2.9], CCI =1: 2.2 years [1.7 to 2.8], CCI ≥2: 1.3 years [1.0 to 1.6], p<0.001) (Figure). Also, for patients with depression and/or anxiety the adherence to treatment was shorter compared with patients without depression and/or anxiety (absence of depression and/or anxiety: 2.4 years [2.1 to 2.6], presence of depression and/or anxiety: 1.7 years [0.26 to 3.0], p=0.027). In the multivariate Cox regression analysis a CCI score ≥2 was associated with increased risk of TNFi treatment discontinuation compared with patients without comorbidities (HR 1.72, [95% CI 1.26 to 2.37], p=0.001). A statistically significantly smaller proportion of patients with a CCI score ≥2 achieved EULAR good response (CCI =0: 41%; CCI ≥2: 23%) and EULAR good-or-moderate response (CCI =0: 54%; CCI ≥2: 47%) at 6 months compared with patients without comorbidities.

Table 1. Baseline characteristics according to Charlson Comorbidity Index (CCI)

<table>
<thead>
<tr>
<th>CCI</th>
<th>n (no.1666)</th>
<th>CCI =1 (n=490)</th>
<th>CCI ≥2 (n=1191)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tender joint count (28) (no.)</td>
<td>6 (2–11)</td>
<td>6 (3–12)</td>
<td>8 (3–15)</td>
<td>0.001</td>
</tr>
<tr>
<td>Swollen joint count (28) (no.)</td>
<td>2 (0–6)</td>
<td>3 (0–6)</td>
<td>2 (0–6)</td>
<td>0.016</td>
</tr>
<tr>
<td>DAS28-CRP (0–10)</td>
<td>4.4 (3.5–5.2)</td>
<td>4.6 (3.8–5.4)</td>
<td>4.9 (3.9–5.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ score (0–3)</td>
<td>0.88 (0.5–1.4)</td>
<td>1.1 (0.6–1.5)</td>
<td>1.4 (0.88–2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAS patient global (0–100)</td>
<td>68 (40–84)</td>
<td>69 (52–84)</td>
<td>75 (58–88)</td>
<td>0.021</td>
</tr>
<tr>
<td>Depression and/or anxiety, n (%)</td>
<td>46 (4.3)</td>
<td>33 (6.7)</td>
<td>15 (7.9)</td>
<td>0.042</td>
</tr>
</tbody>
</table>

Values are the median/interquartile range except where stated otherwise. Comparisons were assessed by y2/Kruskal-Wallis test.

Conclusions: Presence of comorbidities was associated with higher baseline disease activity, increased risk of TNFi treatment discontinuation and reduced clinical response rates in a cohort of Danish patients with PsA.
INHIBITION OF RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS BY ADALIMUMAB INDEPENDENT OF THE CONTROL OF CLINICAL DISEASE ACTIVITY

P. Landewé 1, C.T. Ritchlin 2, L.C. Coates 3, D. Aletaha 4, B. Guerette 5, T. Zhang 6, T. Ganz 6, C. Van de Putte 7, L. Huneault 8, G. van Vollenhoven 9, R. Landewé 1

1University of Amsterdam, Amsterdam, Netherlands; 2University of Rochester Medical Center, Rochester, United States; 3and remission/low disease activity status across all the outcome measures.


DOI: 10.1136/annrheumdis-2017-eular.2881

OP0108

INHIBITION OF RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS BY ADALIMUMAB INDEPENDENT OF THE CONTROL OF CLINICAL DISEASE ACTIVITY

P. Landewé 1, C.T. Ritchlin 2, L.C. Coates 3, D. Aletaha 4, B. Guerette 5, T. Zhang 6, T. Ganz 6, C. Van de Putte 7, L. Huneault 8, G. van Vollenhoven 9, R. Landewé 1

1University of Amsterdam, Amsterdam, Netherlands; 2University of Rochester Medical Center, Rochester, United States; 3University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; 4Medical University of Vienna, Vienna, Austria; 5AbbVie Inc, N Chicago, United States; 6AbbVie AG, Baar, Switzerland; 7AbbVie, Ljubljana, Slovenia

Background: Patients (pts) with psoriatic arthritis (PsA) may experience structural damage and irreversible functional impairment if not treated appropriately. Treatment with TNF inhibitors in rheumatoid arthritis (RA) pts showed inhibition of radiographic progression larger than expected based on the control of clinical disease activity. Preliminary results showed that such a disconnect phenomenon may also be observed in PsA pts following treatment with adalimumab (ADA).

Objectives: The objective of this analysis was to further examine the relationship between inhibition of radiographic progression and control of clinical disease activity using different disease activity measures following treatment with originator ADA than placebo (PBO) in pts with active PsA.

Methods: ADEPT was a 24-week (wks), randomized, double-blind trial comparing the safety and efficacy of ADA with PBO in pts with active PsA. In this post hoc analysis, radiographic progression, defined as change from baseline (BL) to wk 24 in modified total Sharp score (ΔmTSS) ≤ 0.5, was calculated in pts with evaluable radiographs at both time points. Pts were classified based on achieving minimal disease activity (MDA) and different subcategories of disease activity (remission, low, moderate, or high) based on time-averaged (TA) ΔmTSS and PASSAS. The associations between ΔmTSS and disease activity were assessed by Pearson’s correlation coefficient (r) and Spearman’s rank correlation coefficient (r).

Results: Of the 296 pts (ADA, N=144; PBO, N=152) included in this analysis, higher proportions of pts receiving ADA compared with PBO achieved MDA and remission/low disease activity status across all the outcome measures.

There was a significant interaction between treatment and disease activity status with respect to radiographic progression (P<0.001 for all outcome measures). In addition, treatment with ADA for 24 wks resulted in significantly lower mean ΔmTSS even in pts with moderate or high disease activity (TA-DAPSA or TA-PASDAS) or not achieving MDA (Table). Radiographic progression showed a weak but significant correlation in pts treated with PBO (r<0.3, P<0.001 for TA-DAS(CRP), TA-DAPSA, and TA-PASDAS; r=-0.14 95% CI[0.20 to -0.09]) for MDA and remission/low disease activity status across all the outcome measures.

References:


DOI: 10.1136/annrheumdis-2017-eular.2881

OP0109

IS MENTAL HEALTH COMPARABLE IN RHEUMATOID AND PSORIATIC ARTHRITIS PATIENTS? A COMPARATIVE ANALYSIS OF REAL LIFE LONGITUDINAL DATA FROM THE NOR-DMARD STUDY

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Background: Only few studies have compared health related quality of life (HRQoL) between rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients.

Methods: We included RA and PsA patients from the prospective observational multicenter Norwegian-Disease-Modifying Antirheumatic Drug (Nor-DMARD) study, who started first-time tumour necrosis factor inhibitors or DMARD naïve patients starting methotrexate between year 2000 and 2012. Continuous variables were compared using independent t-test (normally distributed data), and using ANOVA for skewed data. Logistic regression analyses were performed to compare SF-36 PCS and MCS between the RA and PsA patients at baseline and after 3 and 6 months follow-up.

Results: A total of 2735 RA and 1236 PsA patients were included. Mean (SD) age was 55.0 (13.5)/ 48.3 (12.4) years, median (25th-75th percentile) years since diagnosis was 7.9/ 6.2 years. HRQoL was better in PsA patients than in RA patients at all time points, in spite of slightly worse physical HRQoL supports the disconnect phenomenon in PsA following ADA treatment.

References:

Acknowledgements: AbbVie funded the study (NCT00646386), contributed to its design, and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD.

Disclosure of Interest: R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, Consultant for: Abbott/AbbVie, AbbVie, BMS, Celgene, Astra-Zeneca, BMS, Janssen (formerly Centocor), GSK, Merck, Nord, Novartis, Pfizer, Roche, Schering-Plough, TiGenics, UCB, and Wyeth; is Director of Rheumatology Consultancy BV, Speakers bureau: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, C. Ritchlin Grant/research support from: Amgen, Janssen (formerly Centocor), and UCB, Consultant for: AbbVie, Amgen, Janssen, Lilly, Pfizer, Schering-Plough, and UCB, L. Coates Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, D. Aletaha Grant/research support from: AbbVie, BMS, Janssen, Lilly, Merck, Medac, Mitsubishi/Tanabe, Pfizer, Roche, and UCB, Consultant for: AbbVie, BMS, Janssen, Lilly, Medac, Mitsubishi/Tanabe, Pfizer, Roche, and UCB, E. Guerette Shareholder of: AbbVie, Employee of: AbbVie, F. Ganz Shareholder of: AbbVie, Employee of: AbbVie, M. Hoijnik Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.1337
The severity of sonographic enthesitis is a marker of radiographic damage in PsA.

Objectives: Enthesitis and the severity of radiographic features of damage in the peripheral and axial joints in PsA.

Methods: A cross-sectional study was conducted in consecutive patients with PsA. The Modified Sonographic Enthesitis Index (MASEI) scoring system was used to quantify the extent of sonographic enthesal abnormalities in 12 enthesal sites. Total MASEI was further categorized into: bone scores (enthophyses, erosions) and soft tissue scores (structural changes, vascularization, bursitis). Radiographic joint damage in the peripheral and spine was assessed independently of the ultrasound results using the modified Steinbrocker score.

Results: 75 patients were available from the Outcomes of Treatment in PsA Study Syndicate (OUTPASS) [n=49 adalimumab; n=26 etanercept]. Mean age was 51±12 years; 61% were female; 20% (n=10/50) of adalimumab-treated patients were positive for ADAbs, but none were detected in etanercept-treated patients. Median BMI 28.9 (IQR 26.0–34.9). 20% (n=10/49) of adalimumab-treated patients were positive for ADAbs, but none were detected in etanercept-treated patients. Median BMI 28.9 (IQR 26.0–34.9).

Conclusions: The severity of sonographic enthesitis is a marker of radiographic peripheral and axial joint damage in PsA. The association was found with both erosive and bone formation lesions. These findings highlight the potential role of enthesitis in the pathogenesis of articular damage in PsA.

Disclosure of Interest: None declared


OP1011

THE ASSOCIATION BETWEEN SONOGRAPHIC ENTHESITIS AND RADIOGRAPHIC JOINT DAMAGE IN PSORIATIC ARTHRITIS

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Background: Enthesitis is a common clinical finding and a key pathogenic feature in psoriatic arthritis (PsA). Ultrasound is emerging as a preferred method to assess enthesitis. Little is known about the relation between the presence of enthesitis and the severity of joint damage in patients with PsA.

Objectives: Our objective was to examine the association between sonographic enthesitis and the severity of radiographic features of damage in the peripheral and axial joints in PsA.

Methods: A cross-sectional study was conducted in consecutive patients with PsA. The Modified Sonographic Enthesitis Index (MASEI) scoring system was used to quantify the extent of sonographic enthesal abnormalities in 12 enthesal sites. Total MASEI was further categorized into: bone scores (enthophyses, erosions) and soft tissue scores (structural changes, vascularization, bursitis). Radiographic joint damage in the peripheral and spine was assessed independently of the ultrasound results using the modified Steinbrocker score.

Results: 222 patients were included (58% men) with mean (s.d.) age of 55.9 (12.3) years and PsA duration of 17 (12.4) years. The modified Steinbrocker score was 15.6 (12.6). The mean modified Steinbrocker score was 18.1 (32.3), mSASSS was 1.7 (3.7) and 37% had sacroiliitis. Multivariate regression analysis found associations between higher MASEI scores and peripheral joint damage: modified Steinbrocker score (β 0.92, p < 0.0001), joint ankylosis (Odd’s Ratio (OR) 2.09, p = 0.0001) and arthritis mutilans (OR 1.73, p = 0.005). The association between MASEI scores and periostitis was of borderline statistical significance (OR 1.29, p = 0.06). Similarly, an association was found in multivariate analyses between higher MASEI scores and axial damage as measured by mSASSS (β 1.55, p = 0.0001) and sacroiliitis (OR 1.36, p = 0.02). Sub-analysis showed that the bone score was more strongly associated with radiographic damage outcomes than the MASEI soft tissue score.

Conclusions: The severity of sonographic enthesitis is a marker of radiographic peripheral and axial joint damage in PsA. The association was found with both erosive and bone formation lesions. These findings highlight the potential role of enthesitis in the pathogenesis of articular damage in PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5007

OP1012

IN PSORIATIC ARTHRITIS FATIGUE IS DRIVEN BY INFLAMMATION, DISEASE DURATION, AND CHRONIC PAIN: AN OBSERVATIONAL DANBIO REGISTRY STUDY

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Background: Fatigue has been identified as one of the most significant symptoms and an outcome of great importance to patients with psoriatic arthritis (PsA), but the association between underlying components of experienced fatigue and the disease activity and bone formation markers has been sparsely studied (1).

Objectives: To describe the degree of fatigue in a PsA population. Secondly, to explore which components of inflammation and non-inflammatory factors contribute to experienced fatigue.

Methods: The study was designed as a cross-sectional survey including patients...
Metabolic Syndrome and Liver stiffness in Psoriatic Arthritis and Psoriasis Patients: A Case-Control Study

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Background: Psoriatic arthritis (PsA) and psoriasis (PsO) are commonly associated to various comorbidities, among which metabolic syndrome (MetS) has been demonstrated to be more prevalent in these groups with respect to the general population. However, few data are available regarding the comparison between PsA/PsO. Besides, a possible consequence of MetS is the development of a non-alcoholic fatty liver disease (NAFLD), which can progress to fibrosis, the latter rarely assessed in PsA/PsO.

Objectives: The aim of this case-control study was: 1) to compare prevalence of MetS in PsA and PsO 2) to evaluate the presence of liver fibrosis in these two groups using hepatic elastography.

Methods: Forty-three consecutive PsA patients classified according to CIASanillo criteria for Psoriatic Arthritis (CASPRI), and 33 consecutive PsO patients without history/manifestations of arthritis, attending the Rheumatology and Dermatology Units of University of Padua, were studied. Exclusion criteria were: conditions which may cause liver fibrosis other than NAFLD (eg viral hepatitis, autoimmune or genetic liver disease), alcohol consumption >20 grams/day, active smoking, daily use of non-steroidal anti-inflammatory drugs. Anamnestic, laboratory (cholesterol, triglycerides, uric acid, fasting glucose, insulin, albumin, transaminase) and metrological (blood pressure, waist circumference, height, weight) data were collected. MetS was defined according to the criteria of National Cholesterol Education Program's Adult Treatment Panel III report. Insuline resistance was quantified through HOMA (Homeostatic Model Assessment). All patients underwent hepatic elastography to evaluate liver stiffness; values >7 kPa were taken as indicator of liver fibrosis. PsO severity was assessed through Psoriasis area severity index (PASI). Differences in variables between PsA/PsO were compared through non parametric Mann-Whitney test, and Chi-square test for categorical variables. Correlations between variables were evaluated through Spearman test.

Results: PsA and PsO patients showed similar characteristics (mean age 60.2±8.4 vs 54.5±19.6 years, 74.4% vs 63% males, arthritis/PsO duration 12.6±8.5 vs 18.2±14.2 years). The only variables which differ in PsA/PsO groups were Body Mass Index (BMI) (25.7±5.4 vs 29.1±6.3), PASI (5.4±6.1 vs 15.2±5.2) and serum uric acid (4.9±1.5 vs 5.7±1.4 mg/dL), all higher in PsO (p-values 0.0092, 0.0355 and 0.0001 respectively). Prevalence of MetS and liver fibrosis in the 2 groups were similar: 34.9% and 30.8% in PsA vs 33.3% and 27.6% in PsO (p=ns).

Among all correlation studied, only serum uric acid, liver stiffness and PASI correlated with other variables (Table). Most interestingly, liver stiffness very well correlated with serum uric acid in PsO (p<0.0001 r=0.73).

Table. Correlations found between serum uric acid, liver stiffness and PASI with other variables studied

Conclusions: We observed a similar prevalence of MetS and hepatic stiffness in PsA and PsO. The correlation found between uric acid level and hepatic stiffness could lie on the fact that uric acid seems to favour insulin resistance, hypertension, dyslipidemia and other MetS risk factors. MetS could be therefore one of the major determinants to liver fibrosis in PsA and PsO, thus highlighting how comorbidities are not only coexisting conditions, but are strongly linked to each other and need to be treated as well as the skin and joint aspect.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5520

References:

Acknowledgements: This study was supported by the Oak Foundation. Data was extracted from the DANBIO Registry.

Disclosure of Interest: M. Skougaard: None declared, T. Jørgensen Speakers bureau: AstraZeneca, Novo Nordisk, MSD; L. Dreyer: None declared, P. Højgaard Consultant for: Biogen IDEC, Amgen, Pfizer, Boehringer Ingelheim, Consultant for: Biogen IDEC, Eli Lilly, Novartis, Momenta, UCB, Kiniksa, AbbVie, Amgen, Pfizer, Janssen Pharmaceuticals, Jannsen, Abbvie, Roche, UCB, Novartis, Biogen, S. Rifbjerg-Madsen: None declared, T. Jørgensen: None declared, T. Jørgensen: None declared, T. Jørgensen: None declared, T. Jørgensen: None declared.
LOW DOSE COMPUTED TOMOGRAPHY DETECTS MORE STRUCTURAL DAMAGE IN AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE SIAS COHORT

Background: Recently we presented the good interreader reliability and sensitivity to detect changes in a newly developed scoring system of bone formation on low dose computed tomography (LD-CT) of the whole spine in patients (pts) with Ankylosing Spondylitis (AS). Next step in the validation is the comparison with conventional radiographs (CR).

Objectives: To compare the assessment of syndesmophyte formation and growth on CR and LD-CT in pts with AS.

Methods: Pts from the SIAS (Sensitive Imaging of Axial Spondyloarthritis) cohort from Leiden and Herne were analysed. Inclusion criteria were modified NY criteria, ≥ 1 syndesmophytes on either the cervical or/and lumbar spine on CR, and ≥ 1 inflammatory lesion on MRI-spine. Pts had CR of the lateral cervical and lumbar spine and LD-CT (approximately 2–3mSv) of the entire spine at baseline and two years. Two readers independently assessed both CR and CT in separate sessions. Images were paired per patient, blinded to time order, patient information, and result of the other imaging technique. CR was assessed using the mSASSS scoring method. On CT, syndesmophytes were scored in the coronal and sagittal planes for all “corners” per view, thus scoring 8 “corners” per vertebral unit. Syndesmophytes were scored as absent (score 0), <50% of the intervertebral disc height (IVDH) (score 1), ≥50% of the IVDH but no bridging (score 2) or as bridging the IVDH (score 3). The formation of new syndesmophytes (score changes 0–1 or 2–3) and growth of existing syndesmophytes (CR score 2–3, CT 1–2 or 2–3, and growth of both combined) was calculated per vertebral corner. Consensus about each of these outcomes was defined by agreement of both readers on the same vertebral level. Data of CR and CT was compared per reader and for the consensus score.

Results: 50 patients (mean age 48.6 years; 84% male; 80% HLA-B27) were included in the analysis. The number (%) of pts with newly formed, growth or combined newly formed and growth of syndesmophytes for separate readers and consensus score are presented in table 1. In all comparisons, CT detected more patients with progression. This is especially aparent in case of growth and for cut-offs of a higher number of (newly formed or growth of) syndesmophytes per patient. E.g. with the strictest comparison the consensus score for both CR and CT, 30% of the patients show bony proliferation (newly formed and growth) at ≥ 3 sites on CT compared with only 6% on CR.

Conclusions: LD-CT covering the whole spine, is a more sensitive method for assessing the formation and growth of syndesmophytes than CR which is limited to cervical and lumbar spine in pts with AS and is a promising method for assessment for clinical research.
BONE MARROW OEDEMA IN SACROILIAC JOINTS OF YOUNG ATHLETES SHOWS MOST FREQUENTLY IN THE POSTERIOR INFERIOR ILIUM

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Background: Low grade bone marrow oedema (BMO) was reported in the sacroiliac joints (SIJ) of up to 25% of healthy individuals and mechanical back pain patients, challenging the imaging discrimination from early spondyloarthritides (SpA) [1]. Potential explanations range from mechanical stress lesions to vascular pain patients, challenging the imaging discrimination from early spondyloarthritis.

Objectives: To determine BMO frequency and anatomical distribution in 8 SIJ (SpA) regions in young athletes. The sample consisted of 2 cohorts of 20 healthy hobby runners (HR) and 22 professional ice hockey players (IP). The sample consisted of 2 cohorts of 20 healthy hobby runners (HR) and 22 professional ice hockey players (IP).

Methods: MRI scans were assessed for BMO independently by 3 blinded readers (AGJ, AZ, 1/3) of readers indicating ≥2/3 of readers.

Results: In the 2 cohorts of young athletes, the presence of BMO was highly predictive of radiographic progression (OR=4.85 [95% CI: 2.95–7.97]) together with a younger age (OR=0.97 [95% CI: 0.94–0.99]) and longer symptom duration (OR=1.40 [95% CI: 1.04–1.89]). Of the 365 patients with complete data, the net % patients who switched from nr-axSpA to r-axSpA after 5 years ranged from 2.0% to 13.5% according to the modified New York criteria (grade 0 to 4 per joint). A mean of two readers score for each joint was used.

Conclusions: In young male professional and amateur athletes, BMO showed on average in 3–4 SIJ quadrants. The posterior lower ilium was the SIJ region most frequently affected by BMO. These findings in healthy controls may help refine thresholds for a positive SIJ MRI in early SpA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1637

IMPACT OF RADIOGRAPHIC DAMAGE IN THE SACROILIAC JOINTS ON FUNCTION AND SPINAL MOBILITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: It has been shown in the past that the spinal mobility in patients with axial spondyloarthritis (axSpA) is associated with spinal structural damage, disease activity parameters and spinal inflammation [1]. The impact of radiographic damage in the sacroiliac joints on functional parameters in patients with axial spondyloarthritis has not been investigated so far.

Objectives: To analyze the association between radiographic sacroiliitis and parameters of the functional status and spinal mobility in patients with axSpA.

Methods: Altogether 210 patients with definite axSpA (115 with radiographic and 96 with non-radiographic axSpA) from the German Spondyloarthritides Inception Cohort (GESPiC) were included in the current study. Radiographs of sacroiliac joints were obtained at baseline and after 2 years of the follow up and were scored by two trained readers according to the conventional grading system of the modified New York criteria (grade 0 to 4 per joint). A mean of two readers score for each joint and a sum score for both SIJ were calculated for each patient, giving a total sacroiliac damage score between 0 and 8.

Results: In the longitudinal mixed model analysis that was corrected for the dependencies between the two time-point values of each individual and adjusted for the structural damage in the spine (modified Stoke Ankylosing Spondylitis Spine Score - mSASSS), disease activity (the Bath Ankylosing Spondylitis Disease Activity Index – BASDAI) and level of C-reactive protein – CRP, and sex, the BMD in the sacroiliac joints associated with a decrease in the BASDAI by 0.10 (95% CI 0.01–0.19) and the BASMI: β=0.12 (95% CI 0.03–0.21), respectively – table. These data indicate that change by one radiographic sacroilitis grade in one sacroiliac joint is associated with a BASFI/BASMI worsening by 0.10/0.12 points independently of structural damage in the spine and disease activity. Assuming linear association, progression of radiographic sacroilitis from grade 0 bilaterally to grade 4 bilaterally would result in a worsening by 0.8 points in BASFI and 0.96 points in BASMI. Sensitivity analysis performed in radiographic and non-radiographic axSpA subgroups provided similar results for both outcomes.

Conclusions: Radiographic damage in the sacroiliac joints may have an impact,
Although small, on spinal mobility and physical function in patients with axial SpA independently of structural damage in the spine and disease activity.

References:

Acknowledgements: The DESIR cohort is financially supported by unrestricted grants from the French Society of Rheumatology and Pfizer France.

Disclosure of Interest: B. Meghnathi Grant/research support from: ASAS Society (ASAS FELLOW), A. Etcheto: None declared, A. Saraux: None declared, M. Dougados: None declared, A. Molto: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3490

OP0119 EVALUATION OF THE PREDICTIVE VALIDITY OF THE ASAS AXIAL SPONDYLOARTHRITIS CRITERIA IN THE DESIR COHORT

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Background: The face validity1 and cross-sectional external validity2 of the Assessment of SpondyloArthritis International Society (ASAS) criteria for axial spondyloarthritis (axSpA) and its arms has been already confirmed in previous studies. However, so far, only one study3 has reported data regarding the predictive validity of such criteria after 4 years of follow-up.

Objectives: To evaluate the predictive validity of the ASAS criteria and its arms after 5 years of follow-up. The predictive validity of the other axSpA sets of criteria (Amor, ESSG and mNY) was also evaluated.

Methods: Patients: This analysis was performed on the DESIR cohort. A total of 708 adult (≥18 and <50 years) patients presented with inflammatory back pain suggestive of axSpA (according to the rheumatologist’s conviction of ≥5/10) for >3 months but <3 years duration. They were followed up every 6 months for the first 2 years and then yearly up to 5 years. Starting from month 24, as per protocol, patients could be excluded from the cohort in case another diagnosis (different from SpA) was made.

Methods: The gold standard for this analysis was the diagnosis of axSpA according to the rheumatologist at 5 years of follow-up. For this analysis, patients were considered as axSpA, if the rheumatologist at 5 years with a conviction of ≥7/10 for an axSpA diagnosis. Conversely, patients excluded as per protocol due to another diagnosis or patients with a rheumatologist conviction at 5 years of ≤3/10 for axSpA were considered as Non-axSpA. The set of criteria collected at baseline (ASAS, and its arms, Amor, ESSG and mNY: fulfilled/not fulfilled) were tested against the Rheumatologist’s axSpA diagnosis (fulfilled/not fulfilled) after 5 years of follow-up. Predictive validity of all sets of criteria at baseline was evaluated by the positive predictive value (PPV).

Results: In total, among the 708 patients included in the DESIR cohort at baseline, data on Rheumatologists diagnosis at 5 years was available in 454 patients; amongst them, 352 (77.5%) had an axSpA diagnosis according to the rheumatologist. Among these 352 patients, 245, 300, 291 and 88 patients fulfilled the ASAS criteria for axSpA, Amor, ESSG and modified NY criteria’s respectively. Figure 1 shows the PPV (95% CI) of the different sets of criteria below.

Conclusions: Predictive validity of the ASAS criteria for axSpA (including both arms) at 5 years was excellent; it is worth noting that the performances of the other criteria were also very good.

References:

Acknowledgements: The DESIR cohort is financially supported by unrestricted grants from the French Society of Rheumatology and Pfizer France.

Disclosure of Interest: B. Meghnathi Grant/research support from: ASAS Society (ASAS FELLOW), A. Etcheto: None declared, A. Saraux: None declared, M. Dougados: None declared, A. Molto: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3490

OP0120 THE ROLE OF SMOKING IN THE DEVELOPMENT AND PROGRESSION OF STRUCTURAL DAMAGE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: THE PRELIMINARY RESULTS OF A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Smoking may constitute a major risk factor for not only disease susceptibility but also disease severity in patients with ankylosing spondylitis (AS). Some previous cross-sectional and longitudinal studies suggested that smoking may be associated with cumulative spinal radiographic damage and regarded it as an independent predictor of spinal radiographic progression.

Objectives: The objective of this study is to determine whether smoking is associated with the cumulative radiographic spinal structural damage and radiographic progression in AS patients. In order to reach this objective, we conducted a systematic review and meta-analysis of the available studies to-date.

Methods: An electronic search was conducted from inception to June 21 2016 in EMBASE, MEDLINE, PubMed, Cochrane Central Register of Controlled Trials databases. Cross-sectional and longitudinal cohort studies investigating the association between smoking and cumulative spinal structural damage or radiographic progression were included. The outcome of interest were the presence of syndesmophytes in cross-sectional studies and radiographic progression in longitudinal studies. Two independent reviewers carried out the screening process. The Quality assessment was done using The Agency for Healthcare Research and Quality (ARHQ) checklist and Newcastle-Ottawa scale. Authors of potential relevant studies were contacted for the unpublished data. Data from eligible cross-sectional studies were extracted and arranged in a 2x2 table. The odds ratios (ORs) and 95% confidence intervals (CIs) for the dichotomous outcome of interest were computed. Random-effects method was used to combine the outcome data in Comprehensive Meta Analysis Software Version 3.3.070.

Results: The combined data of eight eligible cross-sectional studies for the assessment of association between smoking and cumulative spinal structural damage suggested a significant association (OR, 2.02; 95% CI 1.51–2.70)

Table. Association between the sum radiographic syndesmophytes score and functional status / spinal mobility in patients with axial spondyloarthritis.

<table>
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<tr>
<th>Parameters</th>
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<th>Adjusted mixed model</th>
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<td>90 (86-93)</td>
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<tr>
<td>ASAS [axSpA]: IMAGING ARM</td>
<td>97 (93-99)</td>
<td>97 (82-94)</td>
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<td>ASAS [axSpA] – BOTH ARMS COMBINED</td>
<td>91 (95-95)</td>
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Figure 1. Bar diagram representing Positive Predictive Value (95% Confidence interval) of various axSpA criteria.

References:

Acknowledgements: The DESIR cohort is financially supported by unrestricted grants from the French Society of Rheumatology and Pfizer France.

Disclosure of Interest: B. Meghnathi Grant/research support from: ASAS Society (ASAS FELLOW), A. Etcheto: None declared, A. Saraux: None declared, M. Dougados: None declared, A. Molto: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3490
VALIDATION OF MRI STRUCTURAL LESIONS USING COMPUTED TOMOGRAPHY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: MRI can detect both inflammatory and structural lesions in the sacroiliac joints (SIJ) of patients with axial SpA. However, standard MRI sequences do not directly depict bone and the appearance of erosion may vary according to the presence/absence of inflammation. Consequently, further validation using an accepted gold standard, namely, computed tomography (CT), is essential.

Objective: We aimed to assess the detection of structural lesions in the SIJ by MRI using CT as the gold standard.

Methods: CT scans from 44 patients (26 females, mean age 49.4 years, mean symptom duration 9.1 years) were reconstructed in the semicoronal plane parallel to the superior border of the sacrum, as for conventional MRI evaluation of the SIJ, and scoring of lesions by CT was confined to this plane. Structural lesions were scored in consecutive slices in SIJ quadrants (erosion, sclerosis) or SIJ halves (ankylosis) on a dichotomous basis (present/absent) using the same anatomical principles for scoring SIJ quadrants as developed for the SPARCC MRI SIJ inflammatory and structural scores. T1W MRI scans of the SIJ from the same cases conducted at the same time as CT were assessed independently for structural lesions (erosion, fat, backfill, ankylosis, sclerosis) blinded to CT assessments using the SPARCC method. Agreement between CT and MRI was assessed by kappa statistics. Sensitivity/specificity of MRI for CT lesions was calculated. The primary analysis was based on lesions detected concordantly by both readers at the level of the individual iliac/sacral joint surface (erosion, sclerosis) or the individual joint (ankylosis, backfill).

Results: With CT as gold standard and a lesion defined as being present when recorded in the same location on at least 1 coronal slice by both readers, MRI-defined ankylosis had 56.3% sensitivity and 100% specificity for CT ankylosis (Table). For erosion, sensitivity and specificity of MRI was 81.3% and 96.2%, and for sclerosis, sensitivity and specificity of MRI was 50% and 97%, respectively. Agreement between CT and MRI for erosion increased when the cut-off for presence of a lesion was set at 2 slices but only marginally for sclerosis, even when the cut-off for presence of a lesion was set at 3 slices. Lesions observed on CT corresponding to backfill on MRI were ankylosis, erosion, and sclerosis, in 66.7%, 66.7%, and 80% of backfill lesions, respectively.

Conclusions: Ankylosis and erosion on MRI correspond closely with the same type of lesion observed on CT. Both new bone formation and erosion are frequently evident on CT at locations where backfill is observed on MRI supporting the hypothesis that backfill is an intermediary tissue between erosion and ankylosis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4859

VENOUS THROMBOEMBOLISM IN SYSTEMIC SCLEROSIS: PREVALENCE, RISK FACTORS AND IMPACT ON SURVIVAL

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Background: Systemic sclerosis (SSc) is characterized endothelial dysfunction and vasculopathy, which may result in thrombosis. Venous thromboembolism (VTE) is a vascular phenomenon that includes deep vein thrombosis (DVT) and pulmonary embolism (PE).

Objectives: To evaluate the epidemiology of VTE in SSc, specifically cumulative incidence, risk factors and impact of VTE on survival.

Methods: We conducted a cohort study of patients who fulfilled the ACR–EULAR classification criteria for SSc attending the Toronto Scleroderma Program 1970–2017. DVT was defined as the presence of thrombus on doppler ultrasound of either upper or lower extremity. PE was defined as the presence of thrombus on CT angiogram of the thorax. Time to all-cause mortality was evaluated in Kaplan Meier and Cox models.

Results: 1181 subjects (971 (82%) female, 210 (18%) male) were included. There were 40 (3.4%) VTE events. The cumulative incidence of VTE was 2.7 (95% CI 1.9, 3.7) per 1000 patient years. The presence of ILD, PAH, Scl70 antibody, anticardiolipin antibody, coronary artery disease, diabetes mellitus and PVD occurred more frequently in subjects who developed VTE.

Table 1. Venous Thromboembolism in SSc

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>VTE (N=40)</th>
<th>No VTE (N=1141)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scl 70 antibody</td>
<td>11 (28%)</td>
<td>186 (16%)</td>
<td>1.73 (1.03, 2.91)*</td>
</tr>
<tr>
<td>Anticentromere antibody</td>
<td>5 (13%)</td>
<td>215 (19%)</td>
<td>0.68 (0.30, 1.56)</td>
</tr>
<tr>
<td>Anticardiolipin</td>
<td>3 (8%)</td>
<td>14 (1%)</td>
<td>6.27 (1.88, 20.9)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (15%)</td>
<td>65 (5%)</td>
<td>2.69 (1.47, 4.92)*</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>9 (23%)</td>
<td>98 (9%)</td>
<td>4.23 (1.66, 10.7)*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (28%)</td>
<td>237 (21%)</td>
<td>1.32 (0.79, 2.22)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>8 (20%)</td>
<td>41 (4%)</td>
<td>5.57 (2.79, 11.08)*</td>
</tr>
<tr>
<td>Cancer</td>
<td>7 (18%)</td>
<td>127 (11%)</td>
<td>1.57 (0.79, 3.14)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6 (15%)</td>
<td>45 (4%)</td>
<td>3.80 (1.72, 8.39)*</td>
</tr>
</tbody>
</table>

*Denotes statistical significance.

On multivariable logistic regression PAH (OR 3.77 (95% CI 1.83, 8.17), Scl70 antibodies (OR 2.45 (95% CI 1.07, 5.30), anticardiolipin antibodies (OR 5.70 (95% CI 1.16, 21.2) and PVD (OR 5.31 (95% CI 1.99, 12.92) were independent predictors of VTE. Subjects with ILD more frequently experienced DVT (RR 2.85 (95% CI 1.08, 7.54) but not PE (RR 1.82 (95% CI 0.89, 3.70). There were 440 deaths. There was no significant difference in survival between those with and without VTE (HR 1.6 (95% CI 0.70, 1.92). Only the presence of ILD (HR 1.54 (95% CI 1.27, 1.88) or PAH (HR 1.35 (95% CI 1.10, 1.65) remained independent predictors of mortality.

Acknowledgements: Dr. Johnson is supported by the Canadian Institutes of Health Research.

Disclosure of Interest: None declared

Figure 1. Kaplan Meier survival curves of SSc subjects with and without venous thromboembolism. Log rank test p=0.54

Conclusions: The risk of VTE in SSc is not increased, as the incidence of VTE in SSc is comparable to the general population. The presence of PAH, PVD, Scl70 and anticardiolipin antibodies are risk factors for VTE in SSc. VTE does not independently affect SSc survival.

ACKNOWLEDGEMENTS:

Dr. Johnson is supported by the Canadian Institutes of Health Research.

Disclosure of Interest: None declared

Scientific Abstracts

Thursday, 15 June 2017

Clinical and therapeutic news in systemic sclerosis
PREDICTION OF PROGRESSIVE SKIN THICKENING IN EARLY DIFFUSE SYSTEMIC SCLERODERMA OBSERVATIONAL STUDY (ESOS)

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Background: ESOS (European Scleroderma Observational Study) was a prospective observational study of early diffuse cutaneous systemic sclerosis, recruiting from 50 centres in 19 countries and thus providing a unique opportunity to study parameters of disease progression at regular intervals.

Objectives: To describe the characteristics of patients with progressive skin thickening and derive prediction models for progression over 12 months.

Methods: Duration of skin thickening and autoantibody status (anti-topoisomerase-1[anti-Scl-70], TOPO, anti-RNA polymerase III[Pol3], antitromere[ACA]) were documented. The modified Rodnan skin score (mRSS) was recorded 3-monthly for up to 2 years after baseline. The main outcome was the progression of mRSS. Progressive patients (“progressors”) had to meet a 5-unit and 25% increase in their mRSS within the first 12 months of follow-up. Features of progressors vs. non-progressors were compared using the Fisher or Kruskal-Wallis test (for categorical and continuous variables), as were progression parameters between autoantibody groups. Logistic models were fitted to predict progression and, using ROC curves, were compared based on AUC, accuracy, and positive predictive value (PPV).

Results: 326 patients were recruited, with median disease duration of 11.9 months. During the first 12 months, 66 patients (20.3%) progressed, 227 (69.6%) did not and 33 (10.1%) could not have their status assessed. At baseline, progressors had shorter disease duration than non-progressors: 8.1 months vs. 12.6 months (p<0.001). Progressors started with a lower mRSS, median 19 units vs. 21 for non-progressors (p=0.030). 124 patients were TOPO+, 50 were Pol3+, 20 were ACA+, 2 were TOPO+/ACA+ and 68 had none. Pol3+ patients had a higher mRSS peak (35 units vs. 12.6 months (p=0.001). Progressors started with a lower mRSS, median 19 units vs. 21 for non-progressors (p=0.030). 124 patients were TOPO+, 50 were Pol3+, 20 were ACA+, 2 were TOPO+/ACA+ and 68 had none. Pol3+ patients had a higher mRSS peak (35 units vs. 21.4) and did so earlier (median 17.9 months vs. 23.1 months overall [p=0.214]).

Using an mRSS 22 cutoff point to predict progression in the ESOS cohort (as suggested in the literature) would yield a PPV of 24.3%, a weak improvement from the observed 20.3% share of progressors. A first model (Model A, with mRSS, duration of skin thickening and their interaction) had an accuracy of 60.9%, AUC of 0.71 and PPV of 41%. Model B, the model reached an accuracy of 71%, AUC of 0.71 and PPV of 41%.

Conclusions: 1. Patients with shorter disease duration and a lower mRSS have a higher likelihood of being progressors, with a trade-off between the two. 2. Pol3+ patients experience higher mRSS peaks and tend to reach them earlier. 3. Two prediction models for progressive thickening were derived. The advantage of having two is that Model B, while more accurate and useful in identifying high-risk patients in clinical practice, risks being too restrictive for patient selection into trials and may over-represent Pol3+ patients.


TREATMENT WITH CYCLOPHOSPHAMIDE FOR SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE DOES NOT IMPROVE SURVIVAL AFTER 12 YEARS OF FOLLOW UP

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Background: Treatment with cyclophosphamide (CYC) is associated with short-term improvements in lung function, dyspnea, and radiographic fibrosis in patients with systemic sclerosis-related interstitial lung disease (SSc-ILD). However, the effects of CYC therapy on long-term morbidity and mortality outcomes are unknown.

Objectives: To determine whether 1 year of treatment with CYC for SSc-ILD affects long-term morbidity and mortality in patients who participated in the Scleroderma Lung Study (SLS) 1.1

Methods: SLS I randomized 158 SSc-ILD patients from 13 US SSc centers to 1 year of oral CYC versus placebo. The primary endpoint was the change in FVC% predicted over 1 year. Twelve years after the study commenced, each study center contacted enrolled patients or designated surrogates to assess the following: mortality, cause of mortality, development of organ failure, need for transplant and functional status. We used counting process cox proportional hazard modeling to determine the variables associated with survival. The model findings were validated using a joint model of longitudinal and survival data. We also tested the model using long-term follow-up data from SLS II (CYC vs. Mycophenolate).

Results: Nearly half of all SLS I patients (43%) died during the follow-up period, and only 24% remained alive in the absence of organ failure. The median follow up period for all patients was 8 years. Where known, the cause of death was attributable most often to SSc. Among patients who developed malignancy (N=13), a similar proportion were treated with CYC compared with placebo. The most common type of organ failure was respiratory failure (N=31 of 33 organ failures) defined as the need for supplemental oxygen therapy (N=29) and/or lung transplantation (N=3). There was no difference in the time to death (Figure 1), or time to organ failure, or time to malignancy in patients randomized to CYC versus placebo. The Cox model identified the following variables as the most important predictors of mortality: baseline skin score (HR 1.033; P=0.0038), age at randomization (HR 1.056; P=0.0001), and the course of the FVC from baseline to 24 months (HR 0.975; P=0.0215). The course of the FVC was a better predictor of mortality than the baseline FVC. The joint model identified the same variables associated with mortality.

Conclusions: Treatment with 1-year of oral CYC for SSc-ILD does not decrease long-term mortality, organ failure or malignancy compared with placebo. In addition to standard traditional mortality risk factors in SSc-ILD (increased skin score and advanced age), this study found that progression of the FVC over 2 years was a more important predictor of mortality than the baseline FVC. These findings suggest that early changes in surrogate measures of SSc-ILD progression may have important effects on long-term outcomes.


Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2488

MORTALITY IN PATIENTS WITH DERMATOMYOSITIS/POLYMYSITIS IN A CHINESE MEDICAL CENTRE

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Objectives: To investigate the mortality and the causes of death in Chinese patients with dermatomyositis (DM) or polymyositis (PM).

Methods: We collected the clinical data of all DM/PM patients in Rheumatology CENTRE

Conclusions: Treatment with 1-year of oral CYC for SSc-ILD does not decrease long-term mortality, organ failure or malignancy compared with placebo. In addition to standard traditional mortality risk factors in SSc-ILD (increased skin score and advanced age), this study found that progression of the FVC over 2 years was a more important predictor of mortality than the baseline FVC. These findings suggest that early changes in surrogate measures of SSc-ILD progression may have important effects on long-term outcomes.


Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2488
Results: A total of 226 DM and 54 PM cases were included and the mean age of onset was 49.9±14.8 years for DM and 48.1±17.1 years for PM. The median follow-up duration was 40.6 (11.6–77.6) months. Among 267 patients who were successfully traced, 66 patients died. Infection (50.0%) was the leading cause of death followed by malignancy (15.7%), and interstitial lung disease (ILD) (9.1%). The overall age and sex adjusted SMR was 9.0 (95% CI: 6.8–11.2) for DM, and 5.0 (95% CI: 2.4–7.5) for PM. The overall age and sex adjusted SMR of DM/PM patients with ILD was 8.4 (95% CI: 5.8–11.0), and the SMR of the patients with malignancy was 14.9 (95% CI: 8.5–21.2). The YLL of women and men were 37.5 and 28.4 years respectively for DM, and 24.3 and 12.0 years respectively for PM (Table1). The 10-year survival of patients with ILD or malignancy was significantly worse than those without ILD or malignancy respectively (Figure 1 and 2). The independent predictors of mortality for DM were age of disease onset, respiratory muscle involvement and malignancy; and the independent predictor of mortality for PM was age at disease onset (Table2).

Table 1. The standardized mortality ratio (SMR), life expectancy (LE) and years of life lost (YLL).

<table>
<thead>
<tr>
<th>Disease</th>
<th>Overall (n=280)</th>
<th>Females (n=201)</th>
<th>Males (n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death number</td>
<td>55</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>SMR (95% CI)</td>
<td>9.0 (6.8–11.2)</td>
<td>12.0 (6.8–11.2)</td>
<td>6.0 (3.2–8.7)</td>
</tr>
<tr>
<td>LE of general population (years)</td>
<td>–</td>
<td>80.8</td>
<td>75.8</td>
</tr>
<tr>
<td>LE of DM patients (years)</td>
<td>–</td>
<td>43.3</td>
<td>47.4</td>
</tr>
<tr>
<td>YLL (years)</td>
<td>37.5</td>
<td>28.4</td>
<td></td>
</tr>
<tr>
<td>Polymyositis</td>
<td>54</td>
<td>38</td>
<td>16</td>
</tr>
<tr>
<td>Death number</td>
<td>11</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>SMR (95% CI)</td>
<td>5.0 (2.4–7.5)</td>
<td>4.2 (1.3–7.2)</td>
<td>9.3 (1.2–19.8)</td>
</tr>
<tr>
<td>LE of general population (years)</td>
<td>–</td>
<td>80.8</td>
<td>75.8</td>
</tr>
<tr>
<td>LE of PM patients (years)</td>
<td>–</td>
<td>56.5</td>
<td>63.8</td>
</tr>
<tr>
<td>YLL (years)</td>
<td>24.3</td>
<td>12.0</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DM: dermatomyositis; PM: polymyositis; LD: life expectancy; YLL: years of life lost; PBO: placebo.

Table 2. Multivariable cox regression analyses of risk factors in the DM/PM patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatomyositis</td>
<td>1.04</td>
<td>0.99–1.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.35</td>
<td>0.74–2.48</td>
<td>0.319</td>
</tr>
<tr>
<td>ILD</td>
<td>2.58</td>
<td>1.19–5.58</td>
<td>0.016</td>
</tr>
<tr>
<td>Respiratory muscle involvement</td>
<td>3.12</td>
<td>1.49–6.58</td>
<td>0.003</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1.08</td>
<td>1.00–1.16</td>
<td>0.044</td>
</tr>
<tr>
<td>ILD</td>
<td>2.47</td>
<td>0.18–34.00</td>
<td>0.500</td>
</tr>
<tr>
<td>ESR</td>
<td>1.92</td>
<td>0.99–1.04</td>
<td>0.74</td>
</tr>
</tbody>
</table>

*Age: Age at disease onset. Abbreviations: HR: Hazard Ratio; CI: confidence interval; ILD: interstitial lung disease; ESR: erythrocyte sedimentation rate.

Conclusions: Mortality of DM/PM patients in China is substantial, especially in females, and those with ILD or malignancy. Infection was the leading cause of death. Patients with older age at onset, respiratory muscle involvement, ILD, and malignancy need to be paid more attention.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2873

OP0126 A PHASE 2 STUDY OF SAFETY AND EFFICACY OF ANABASUM (JBT-101) IN SYSTEMIC SCLEROSIS

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Background: Anabasum (JBT-101) is a synthetic, oral, non-immunosuppressive, preferential CB2 agonist. It inhibits onset and activates resolution of innate immune responses in animal models of systemic sclerosis (SSc).

Objectives: Evaluate safety and efficacy of anabasum in SSc.

Methods: A double-blind, randomized, placebo (PBO)-controlled Phase 2 trial dosed 42 diffuse cutaneous SSCs with disease duration <6 years on stable medication including immunosuppressive drugs. Subjects received anabasum 5 mg OD, 20 mg OD, or 20 mg BID on Days 1–28, then 20 mg BID on Days 29–84, or PBO on days 1–84. Subjects were followed off study drug on Days 85–113. The primary safety outcome was treatment-emergent adverse events (TEAEs). The primary efficacy outcome was improvement in ACR Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRIS) score, combined anabasum group vs PBO, Days 29–113 (end of weeks 4–16). The five domains of the ACR CRIS are the modified Rodnan skin score, HAQ-DI, patient and physician global assessments, and FVC % predicted.

Results: Of 42 dosed subjects, 27 (64%) received anabasum and 15 (36%) received PBO. Three anabasum subjects withdrew; 1 (3.7%) for a TEAE of moderate bone pain; 1 withdrew consent; and 1 by physician decision. One PBO subject withdrew consent. Baseline demographic and CRIS domain scores were similar except slightly more anabasum subjects used background immunosuppressive drugs (93% versus 80%, anabasum vs PBO). Seventeen (63%) anabasum subjects had 66 TEAEs, and 9 (60%) PBO subjects had 35 TEAEs. There were no serious, severe, or unexpected TEAEs related to anabasum. Severity and relationship of TEAEs to study drug were similar in both groups. The most frequent TEAEs by MedDRA system (% anabasum vs % PBO) were: nervous system (37% vs 27%); general disorders (30% vs 7%); gastrointestinal (22% vs 20%); infections (22% vs 20%); musculoskeletal (22% vs 13%); and investigations (0% vs 20%). The most frequent TEAEs in anabasum subjects were dizziness (22%) and fatigue (19%) which were usually mild. Anabasum subjects had greater improvement in ACR CRIS scores than PBO subjects (mixed model repeated measures analysis, p=0.044, 1-sided). The median ACR CRIS scores at the end of Weeks 4, 8, 12, and 16 (anabasum vs PBO) were 3.0% vs 1.0%, 19.0% vs 1.0%, 27.5% vs 1.0%, and 33.0% vs 1.0%, respectively. Among anabasum subjects, 50% had ACR CRIS >20% after 8 weeks of dosing. The individual domains of the ACR CRIS score showed greater improvement, with improvement that reached minimal important differences in several domains, and less worsening in anabasum vs PBO groups. Anabasum subjects had greater improvement in SSC skin symptoms and itch. Plasma metabololipidic profiles showed anabasum, not PBO, shifted lipid mediator production to increase pro-resolving vs pro-inflammatory lipid mediators.

Conclusions: Anabasum provided significant and medically meaningful efficacy in SSc as assessed by the ACR CRIS score and its individual domains and had acceptable safety and tolerability in this Phase 2 trial. These data support continued clinical development of anabasum for the treatment of SSc.

Disclosure of Interest: R. Spiera: None declared, L. Hummers: None declared, L. Chung: None declared, T. Frech: None declared, R. Domsic: None declared, D. Furst: None declared, J. Gordon: None declared, M. Mayes: None declared, B. White: None declared, N. Hashimoto: None declared, K. Itano: None declared, T. Nakazawa: None declared, T. Ishiaki: None declared, T. Hashimoto: None declared, 1Hashimoto Rheumatology Clinic, Osaka; 2Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya; 3Osaka Saiseikai Nakatsu Hospital, Osaka; 4Department of Pharmacy, Hyogo University of Health Sciences, Kobe, Japan

Background: Systemic sclerosis (SSc) is an inflammatory autoimmune disease characterized by fibrosis and small vascular involvement in the skin, lungs, heart and gastrointestinal (GI) tract. The esophagus is the most frequently involved GI tract disorder. Although the small intestinal involvement such as malabsorption and pseudo-obstruction is less common, it has been related to morbidity and mortality of SSc patients. We previously reported a close correlation between the...
esophageal diameter and the small intestinal clearance (SIC) (EULAR 2011). We also suggested that anti-centromere antibodies (ACA) are an important factor of esophageal dilatation in SSC patients (EULAR 2010). However, changes of small intestinal involvement during long-term follow-up have not yet been defined.

**Objectives:** The aim of this study was to evaluate a correlation between the small intestinal involvement and clinical features in SSC patients during ten years follow-up.

**Methods:** Fifty-five patients with a definite diagnosis of SSC (52 females and 3 males with an age range of 59.4 years (range 29–77 years) were included in the study. Thirteen (23.6%) patients were classified as diffuse SSC and 42 (76.4%) as limited SSC. The SSC was classified according to barium meal reach at 30 min after intake; grade 1 (∼2/3 of the whole small intestine), grade 2 (1/3–2/3), grade 3 (∼1/3), grade 4 (the duodenum). The SSC grade was classified as follows; grade 1 and 2 grade or grade non-increase during follow-up was classified as “no progressive”, and grade 3 and 4 grade or increase as “progressive”. All SSC patients were evaluated the items as used for 2013 ACR/EULAR criteria.

**Results:** The mean durations of follow-up period were 9.5±6.0 years. The number of SSC patients in each SIC grade at the initial evaluation and the end of follow-up were as follows; grade 1: initial vs end; 23 vs 24, grade 2: 20 vs 9, grade 3: 10 vs 16, grade 4: 2 vs 6. The SIC change “progressive” was 40.0% of SSC patients. Positive correlation between the esophageal diameters and the SIC grade was observed in SSC patients at the initial evaluation (r=0.61 p<0.01) and the end of follow-up (r=0.71 p<0.01). The esophageal diameters at the initial evaluation were significantly wider in SIC “progressive” group than in “non-progressive” group (non-progressive vs progressive; 21.8±6.5 vs 30.9±8.6 mm, p<0.0001). The frequencies of SSC patients with ACA-positive and scleroderma were higher but with puffy fingers were lower in SIC “progressive” group than in “non-progressive” group (progressive vs non-progressive; 24.2 vs 59.1%, p=0.009; 33.3 vs 63.6%, p=0.03; 73.8 vs 95.6%, p=0.003). The prevalence of pitting scarring and Interstitial lung disease were tended to be higher in SIC “progressive” compared to SIC “non-progressive” group (non-progressive vs progressive; 15.6 vs 36.4%, p<0.07; 21.1 at 46.5%, p=0.06).

**Conclusions:** The present study demonstrated that the progression of small intestinal involvement was associated with esophageal dilatation at the initial evaluation during long-term follow-up of SSC patients. Our findings also suggested that ACA and skin thickening of the fingers were important factors of small intestinal involvement in SSC patients. The SIC may be a useful tool for the assessment of GI tract involvement in SSC patients during long-term follow-up.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2353
MEPOLIZUMAB FOR THE TREATMENT OF PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGITIS: A PHASE III RANDOMISED, PLACEBO-CONTROLLED TRIAL

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Background: Mepolizumab reduces blood eosinophils with concomitant clinical improvement in some hypereosinophilic syndromes and eosinophilic asthma.

Objectives: To investigate the efficacy and safety of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss).

Methods: We conducted a Phase III, randomised, placebo-controlled, double-blind, parallel group, multi-centre study (NCT02020889) in patients with EGPA and a history of relapsing or refractory disease on stable therapy with prednisolone/prednisone >7.5–50mg/day or with additional immunosuppressive therapy for >4 weeks. Patients were randomised 1:1 to receive mepolizumab 300mg or placebo subcutaneously, in addition to standard of care, every 4 weeks for 52 weeks. After Week 4, glucocorticoid dose could be tapered, per physician judgment, according to a suggested standard of care protocol. Co-primary endpoints (intent-to-treat [ITT] analysis) were accrued duration of remission (Birmingham Vasculitis Activity Score [BVAS]=0, prednisolone/prednisone dose <4mg/day) over 52 weeks; and the proportion of patients in remission at both Weeks 36 and 48. Secondary endpoints included average glucocorticoid dose during Weeks 49–52 and time to first EGPA relapse. Safety was also assessed.

Results: The ITT population included 136 randomised patients (mepolizumab n=68, placebo n=68). Baseline characteristics were similar between groups. Duration of remission accrued over 52 weeks was significantly prolonged with mepolizumab vs placebo (odds ratio: 5.91 [95% confidence interval [CI]: 2.68,13.03]; p<0.001); a significantly higher proportion of patients were in remission at Weeks 36 and 48 (32% vs 3%, odds ratio: 16.74 [95% CI: 3.61,77.56]; p<0.001). Significant reductions in average daily prednisolone/prednisone dose during Weeks 49–52 were seen with mepolizumab vs placebo (odds ratio: 0.2095% CI: 0.09,0.41]; p<0.001). Median (range) prednisolone/prednisone dose during Weeks 49–52 was 5.0 (0.0–113.4)mg/day in the mepolizumab group and 10.0 (0.0–223.8)mg/day in the placebo group. Time to first EGPA relapse was significantly longer with mepolizumab vs placebo (hazard ratio: 0.32 [95% CI: 0.21,0.50]; p<0.001). Rates of adverse events (AEs) and serious AEs were similar for mepolizumab and placebo.

Conclusions: Treatment with mepolizumab significantly increased the likelihood and duration of remission, while reducing glucocorticoid use, in patients with EGPA, with a safety profile consistent with previous studies in severe asthma and EGPA. This demonstrates consistent and meaningful clinical benefits of mepolizumab in patients with EGPA.


DOI: 10.1136/annrheumdis-2017-eular.5610

OPTIMAL DOSE OF TOCILIZUMAB FOR THE TREATMENT OF GIANT CELL ARTERITIS: EFFICACY, SAFETY, AND EXPOSURE-EFFICACY ANALYSIS FROM GIACTA


Background: GIACTA, a randomized, double-blind, placebo-controlled trial, evaluated the efficacy and safety of tocilizumab (TCZ), an IL-6 receptor-a inhibitor, in patients with giant cell arteritis (GCA).1,2 Objectives: Secondary analyses to evaluate the differential efficacy and safety of TCZ between patients with new-onset and relapsing GCA and to evaluate the TCZ exposure-efficacy relationship at week 52 of the trial.

Methods: Patients aged >50 years with active GCA were randomly assigned 1:1:2:1 to short-course prednisone (PBO+26), long-course prednisone (PBO+52) (26-week or 52-week prednisone taper + weekly subcutaneous [SC] placebo, respectively), weekly (TCZ-QW) or every-other-week (TCZ-Q2W) SC TCZ 162 mg + 26-week prednisone taper. Subgroup analysis was performed by disease-onset status (new-onset vs relapsing) to evaluate the proportions of patients in sustained remission at week 52 and time to flare. The impact of TCZ exposure, categorized into high, medium and low tertiles, on time to flare was evaluated across all patients in all treatment arms.

Results: Randomization included 251 patients, 119 (47%) with new-onset and 132 (53%) with relapsing GCA, distributed evenly across groups. Higher proportions of patients achieved sustained remission in the TCZ vs placebo groups regardless of disease onset (new-onset, relapsing–TCZ-QW: 59.6%, 52.8%; TCZ-Q2W: 57.7%, 47.6%; PBO+26: 21.7%, 7.4%; PBO+52: 21.7%, 14.3%, respectively). Patients with relapsing disease at baseline were in relapse-free remission longer and thus had lower risk for flare (hazard ratio) when treated with TCZ-QW than TCZ-Q2W. Hazard ratio (99% CI) for flare vs PBO+26 was 0.23 (0.09–0.61) for TCZ-QW and 0.42 (0.14–1.26) for TCZ-Q2W; vs PBO+52 it was 0.36 (0.13–1.00) for TCZ-Q2W and 0.67 (0.21–2.10) for TCZ-Q2W. TCZ exposure-efficacy analysis showed that most patients in the low exposure tertile had been treated with TCZ-Q2W (80%) whereas those with medium and high exposure primarily received TCZ-QW (84% and 98%, respectively). Kaplan-Meier analysis demonstrated that patients with higher exposure benefited from a longer time to flare (Figure). Adverse events (AEs) were similar across groups. Serious AEs were reported in 15.0% TCZ-QW, 14.3% TCZ-Q2W, 22.0% PBO+26 and 25.5% PBO+52 patients; rates were similar between new-onset and relapsing patients.

Conclusions: The compelling treatment effect of TCZ in GCA patients as measured by sustained remission to 52 weeks was consistent regardless of disease-onset status. Duration of relapse-free remission until flare was longer in patients with higher TCZ exposure, most notably in relapsing patients treated with TCZ-QW.

References:
LOW-DOSE INTERLEUKIN-2 SELECTIVELY RESTORE REGULATORY T CELL NUMBERS IN PATIENTS WITH BEHÇET’S DISEASE

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Background: The lack of CD4+CD25+Foxp3+ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as Behçet’s disease (BD). IL-2, an essential growth and survival factor for Treg cells.However, the significance of Treg cells in the pathogenesis and the effect of low dose of IL-2 on BD are remain to investigate.

Objectives: The lack of CD4+CD25+Foxp3+ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as Behçet’s disease (BD). IL-2, an essential growth and survival factor for Treg cells.However, the significance of Treg cells in the pathogenesis and the effect of low dose of IL-2 on BD are remain to investigate.

Methods: Eighty patients with BD and seventy healthy donors were enrolled. CD4+ T cell subsets were analysed before and after treatment by flow cytometry. Twenty-six patients were treated daily with subcutaneous injections of 0.5 million IU of human IL-2 for five consecutive days.

Results: Compared to control, the absolute counts of circulating Treg cells were significantly decreased in patients with BD (median:29.93 cell/μL, VS median:33.18 cell/μL, p=0.039) and it is negative correlation with disease activity. While the ratios of Th17/Treg in patients with BD (median:0.29%n=80=0.034) were significantly higher than those of healthy control (median:0.2:n=70). No difference in the absolute counts of circulating Th17 cells (CD4+IL-17+) between patients with BD and health control. Treatment of patients with BD with a low-dose of IL-2 regimen selectively increased the absolute counts of Treg cells, from a median of 18.97 cell/μL to 74.68 cell/μL (at 5 days) (p=0.000). No significant difference was observed in the absolute counts of circulating Th17, Th1 and Th2 cells after IL-2 treatment.

Conclusions: Th17/Treg cells may play a role in the pathogenesis of Patients with BD, low-dose of IL-2 proposes a selective biological treatment strategy by restoring immune tolerance. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4047

TOCOLIZUMAB IN GIANT CELL ARTERITIS: GIAC TA TRIAL VERSUS A SERIES OF PATIENTS FROM CLINICAL PRACTICE

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Objectives: To assess long term outcome and to elaborate a prognostic score for vascular complications in patients with Takayasu arteritis (TA).

Methods: Prospective multicenter study of characteristics and outcome of 318 TA patients [86% of females; median age 36 [25–47] years; median follow-up of 6 [1–70] years]. TA fulfilling ACR criteria or for Takayasu criteria. Factors associated with event free survival (EFS), relapse free survival (RFS) and incidence of vascular complications were assessed. A prognostic score for vascular complications was elaborated based on a multivariate model.

Results: The 5- and 10-years event free survival (EFS), relapse free survival (RFS) and complication free survival were 48.2% (42.5;54.9) and 36.4% (30.3;43.9), 58.6% (52.7;65.1) and 47.7% (41.2;55.1), and 69.9% (63.7;76) and 53.7% (46.8;61.7), respectively. Progressive disease course (p=0.018) and carotidopathy (p=0.003) were independently associated with EFS. Male gender (p=0.048), elevated C-reactive protein level (p=0.013), and carotidopathy (p=0.003) were associated with RFS. Progressive disease course (p=0.017), thoracic aorta involvement (p=0.009), and retinopathy (p=0.002) were associated with complication free survival. We define high risk patients for vascular complications according to the presence of two of the following factors (i.e a progressive clinical course, thoracic aorta involvement and/or retinopathy). The probability of complication free survival at five years was 78.4% (69.4;88.6) and 51.5% (38.3;69.2) in the low risk and high risk group, respectively.

Conclusions: This nationwide study shows that 50% of TA patients will relapse and experience a vascular complication at 10 years. We could define high risk TA patients for vascular complications. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3579
Conclusions: Patients receiving TCZ in the clinical practice study have several baseline clinical and laboratory differences with regard to those included in the GIACTA trial, and therefore, data of this trial should be taken cautiously when applied in a real-world scenario.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3489

Table 1. miR-223–3p expression in IgAV

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of cases</th>
<th>ΔACT miR223–3p</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>General symptoms</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Arthritis</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Generalized purpura</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Skin necroses</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>GIT involvement</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Severe renal involvement</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
</tr>
<tr>
<td>Elevated serum IgA level</td>
<td>20</td>
<td>3.71</td>
<td>0.001</td>
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</table>

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2250

OP0137 AUTO-REACTIVE B CELLS ESCAPE PERIPHERAL TOLERANCE CHECKPOINTS IN PATIENTS WITH PR3-ANCA ASSOCIATED VASCULITIS

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Background: While extensive studies have been performed to characterize ANCA, little is known about the auto-reactive B cells that produce these autoantibodies. Indirect evidence previously suggested the presence of circulating PR3-specific B cells in patients with PR3-ANCA-associated vasculitis (AAV).

Objectives: To develop a method to detect circulating PR3-specific B cells in patients with PR3-AAV, to study their proportion among the different B-cell subsets and to assess their relationship with disease activity.

Methods: An enzymatically inactive, conformationally mature, recombinant PR3 (rPR3) was tagged using FIC or bioitin. To study the ability of this rPR3 to bind specifically to cells expressing PR3-specific immunoglobulins on their surface, we used two hybridoma cell lines, MCPR3–2 (producing an anti-human PR3 monoclonal antibody) and MCPR3–13 (producing an anti-mouse PR3 monoclonal antibody, with no cross-reactivity with human PR3). We measured the proportion of PR3-FITC positive B cells among PBMCs in 13 patients with PR3-AAV and 14 healthy controls (HCs) by flow cytometry. We then developed a multi-color flow cytometry including CD19, IgD, CD27, CD38, CD24 and biotylated rPR3 to measure the proportion of PR3-specific B cells among different B-cell subsets in an independent group of 13 patients with PR3-AAV and 11 HCs.

Results: PR3 efficiently bound MCPR3–2 hybridoma cells but not MCPR3–13. Specificity of the staining was confirmed by competition experiments: pre-incubation of MCPR3–2 cells with untagged human rPR3 totally abrogated rPR3 efficiently bound MCPR3–2 hybridoma cells but not MCPR3–13. Specificity of the staining was confirmed by competition experiments: pre-incubation of MCPR3–2 cells with untagged human rPR3 totally abrogated rPR3 efficiently bound MCPR3–2 hybridoma cells but not MCPR3–13. Specificity of the staining was confirmed by competition experiments: pre-incubation of MCPR3–2 cells with untagged human rPR3 totally abrogated rPR3 efficiently bound MCPR3–2 hybridoma cells but not MCPR3–13. Specificity of the staining was confirmed by competition experiments: pre-incubation of MCPR3–2 cells with untagged human rPR3 totally abrogated.

Conclusions: To detect circulating PR3-specific B cells in patients with PR3-AAV, we used a novel approach that measures the proportion of PR3-specific B cells among different B-cell subsets and to assess their relationship with disease activity.

OP0136 MICRORNA-223-3P EXPRESSION IN AFFECTED SKIN OF ADULT IGA VASCULITIS CORRELATES WITH THE SEVERITY OF SKIN INVOLVEMENT

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Background: Iga vasculitis (IgAV) represents a common systemic vasculitis in paediatric and adult population. Our current knowledge of disease pathogenesis is still very limited and there is no information on miRNAs profile in IgAV.

Objectives: The aim of our study was to determine the expression of three miRNAs (miR-148–3p, miR-155–5p and miR-223–3p) in the affected skin of adult IgAV patients.

Methods: The study included 65 skin samples from consecutive, untreated IgAV patients. miRNAs expression was then correlated to clinical characteristics of adult IgAV patients. To present relative miRNA expression the ΔACT method was used.

Results: We found significantly higher expression levels of miR-223–3p in the affected skin compared to controls (14-fold; p < 0.001). The expression of the 148b–3p and miR-155–5p was near normal levels (1.05-fold and 1.13-fold increase, respectively). The differences in the expression of miR-223–3p depending on clinical parameters of IgAV are presented in Table 1. Patients with necrotic skin lesions had significantly higher miR-223 tissue expression than those with non-necrotic purpura (p=0.020). Gastrointestinal tract (GIT) involvement inversely correlated with the level of skin miR-223 expression (p=0.024). No significant relationship between renal involvement and skin miR-223 was found.

Conclusions: miR-223 expression was increased in the affected skin of IgAV in comparison to normal skin. Levels of miR-223 expression correlated with severity of skin involvement and inversely with GIT involvement.
circuiting auto-reactive B cells in patients with PRS-AAV, and suggests that PRS-specific B cells are associated with disease activity and may represent a promising biomarker to predict relapse risk in patients in clinical remission. The progressive enrichment in PRS-specific B cells during the B-cell maturation steps in patients suggest that auto-reactive B cells are actively selected and escape peripheral tolerance checkpoints.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6505

THURSDAY, 15 JUNE 2017
HPR mind over matter - patients perspectives

OP0138-HPR
DO PATIENTS' TREATMENT BELIEFS AFFECT TREATMENT CHOICES IN KNEE AND HIP OSTEOARTHRITIS?

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Background: Patients' beliefs about treatment modalities for knee/hip osteoarthritis (OA) might influence their treatment choices. The Theory of Planned Behavior predicts that patients' beliefs, the norms and values of one's social environment (subjective norm) and one's perceived self-efficacy influence behaviour1. Moreover, symptom severity may influence treatment choices2. However, these relationships have not been studied yet in the context of treatment decision-making.

Objectives: To test whether treatment beliefs, subjective norm, perceived self-efficacy and symptom severity were associated with intended treatment choices in OA.

Methods: Patients with knee/hip OA who visited the Sint Maartenskliniek in 2015 and 2016 (N=700) were invited to fill out a booklet. The Treatment beliefs in OsteoArthritis questionnaire was used to assess positive and negative treatment beliefs regarding five treatment modalities: physical activities, pain medication, psychotherapy, injections and arthroplasty. Other measures were demographic and clinical variables, self-efficacy (ASES), and symptom severity (WOMAC). Associations between variables were assessed in three models (Figure 1): 1) whether treatment beliefs are associated with intended treatment choice (model 1); 2) whether treatment beliefs, subjective norm and perceived self-efficacy are associated with intended treatment choice (model 2); 3) whether treatment beliefs, subjective norm, perceived self-efficacy and symptom severity are associated with intended treatment choice (model 3).

Path analyses were conducted to examine the hypothesized associations.

Results: 289 patients filled out the booklet. Model 2 had the highest explained variance for each of the treatment modalities (range 32–45%). Positive treatment beliefs and subjective norm were consistently associated with intended treatment choice across all treatment modalities. Negative treatment beliefs were associated with intended treatment choices for pain medication and arthroplasty. Perceived symptom severity was not related to intended treatment choices. No other associations were found.

Conclusions: This is the first study that found empirical support for the relationship between treatment beliefs and treatment choices. The findings suggest that positive beliefs about treatment modalities and the norms and values of one's social environment are related to a specific treatment choice for knee/hip OA and should be addressed in the clinician's consulting room.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4834

OP0139-HPR
REDUCING ARTHRITIS FATIGUE - CLINICAL TEAMS (RAFT) USING COGNITIVE-BEHAVIOURAL APPROACHES: AN RCT

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Background: RA fatigue is common. Group Cognitive Behavioural Therapy by CBT therapists is effective1 but few rheumatology teams have psychologists, thus we trained rheumatology teams to deliver RAFT, a cognitive behavioural approach (CBA).

Objectives: To test if usual care plus a group CBA course for RA fatigue delivered by rheumatology teams reduces fatigue impact more than usual care alone, in a randomised controlled trial.

Methods: A pair of rheumatology nurses/OTs in each of 7 UK hospitals were trained in RAFT. RAFT is 6, weekly 2hr group sessions and a consolidation session (wk 14). Links between thoughts, feelings and behaviours (pacing, communication, sleep, stress) are addressed, with daily diaries of energy expenditure and weekly goal-setting. Usual care was a 5min discussion of the Arthritis Research UK fatigue booklet. Entry criteria were RA, Bristol RA Fatigue (BRAF-NRS) severity ≥6/10 and no recent major medication change.

Results: 308/333 randomized patients completed 26 wks. The 25 who withdrew had similar (10yr) disease duration but were older (69 vs 62.4 yrs). Baseline fatigue impact was similar for RAFT (n=156, BRAF-NRS 7.10, SD 2.4) and controls (n=152, 7.23, SD 1.6), as were all clinical variables. At 26 wks the RAFT arm had similar (10yr) disease duration but were older (69 vs 62.4 yrs). Baseline fatigue impact (BRAF-Multi-Dimensional Questionnaire), pain, disability, sleep, quality of life, mood, self-efficacy, patient global opinion, valued life activities & disease activity.

Conclusion: Intention-to-treatment regression analysis involved adjustment for baseline scores and centre.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1877

OP0140-HPR
ACCEPTANCE AND COMMITMENT THERAPY: A RETROSPECTIVE STUDY OF OUTCOMES FROM A HOSPITAL-BASED, GROUP, PAIN REHABILITATION PROGRAMME IN RHEUMATOLOGY SERVICES IN THE SOUTH EAST OF IRELAND

N. Nealon Lennox1,2, S. O'Neill1, A. Hannigan1, 1GEMS, University Limerick, Limerick; 2Psychology, Ulster University, Derry, Ireland

Background: Acceptance and Commitment Therapy (ACT) is a form of cognitive...
behavioural therapy (CBT), which focuses on psychological flexibility and behavior change. ACT has been advocated for the treatment of Persistent Pain. A systematic review concluded that ACT is efficacious for enhancing physical functioning and decreasing distress amongst adults with chronic pain attending Pain Rehabilitation Programmes (Hann & McCracken 2014). A call was made for further studies to examine the construct validity of the AAQ2.

**Objectives:** To assess the effects of an eight-week group ACT, Rheumatology based programme, for people with persistent pain, on pain acceptance, activity engagement, psychological distress and self-efficacy.

**Methods:** Patients were referred to the programme by three Consultant Rheumatologists over a five-year period. Over one hundred patients' outcome measures were available for this retrospective study from a convenience sample. Consent had been sought routinely from patients who attended the ACT programme and ethical approval was granted from the Hospital Research Ethics Committee (REC) and Ulster University. Participants were asked to complete baseline measures were taken at assessment, on the final day of the programme and at the follow up six-month review. Data was analysed with One Way Repeated Measures ANOVA using SPSSv20. Effect sizes were calculated using Partial Eta Squared and interpreted using the guidelines proposed by Cohen (1998).

**Results:** For those with scores at all three time points, mean depression scores, anxiety scores and self-efficacy scores were statistically significantly different over time. In addition, for those with activity engagement and pain willingness scores at all three time points, scores were statistically significantly different over time.

Table 1. Change from assessment to the 6-month review

<table>
<thead>
<tr>
<th>Measure (n)</th>
<th>Mean (SD) at assessment</th>
<th>Mean (SD) at 6-month review</th>
<th>Mean change</th>
<th>P-value Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression (n=91)</td>
<td>8.6 (3.62)</td>
<td>5.9 (3.62)</td>
<td>-2.7 (3.47, -1.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety (n=91)</td>
<td>11.0 (3.91)</td>
<td>8.1 (3.96)</td>
<td>-2.9 (3.66, -2.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Self-efficacy (n=89)</td>
<td>37.0 (12.72)</td>
<td>49.6 (12.30)</td>
<td>12.6 (9.48, 15.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Activity engagement (n=78)</td>
<td>32.5 (12.27)</td>
<td>43.8 (10.26)</td>
<td>11.3 (8.59, 14.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain willingness (n=16)</td>
<td>18.6 (7.46)</td>
<td>23.8 (8.52)</td>
<td>6.8 (4.84, 8.73)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** The ACT Pain Rehabilitation Programme at University Hospital Waterford in Ireland has provided significant outcomes for reducing depression and anxiety amongst its participants as measured by the Hospital Anxiety and Depression Scale (HADS). Increases in self-efficacy were also found to be statistically significant. Increases in activity engagement & pain acceptance, as measured by the Chronic Pain Acceptance Questionnaire (CPAQ) also showed statistically significant increases. A number of limitations should be noted i.e. this was a retrospective study and depended on self report measures only. However, positive outcomes suggest ACT is a helpful intervention for people with persistent pain.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7008

**OP0142-HPR**

AN INNOVATIVE MEASUREMENT INSTRUMENT TO ASSESS ACTIVITY LIMITATIONS IN HIP AND KNEE OSTEOARTHRITIS: THE COMPUTERIZED ANIMATED ACTIVITY QUESTIONNAIRE (AAQ) AND ITS PSYCHOMETRIC PROPERTIES

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**Background:** The Animated Activity Questionnaire (AAQ) measures activity limitations in hip and knee osteoarthritis (HOA), and was developed in close collaboration with patients. Previously we showed an adequate construct- and cross-cultural validity of the AAQ2.

**Objectives:** To determine the reliability, responsiveness and interpretability of the AAQ.

**Methods:** In 6 European countries the AAQ was completed twice on a computer with a 7 days interval by 238 patients (DK (36), FR (37), IT (51), NL (39), SP (36), UK (39)). Reliability was assessed by calculating internal consistency (Cronbach’s alpha), the intra-class correlation coefficient (ICC), the Standard Error of Measurement (SEM) and the Smallest Detectable Change (SDC). In the Netherlands an additional group of 92 patients were followed for 6 months to evaluate responsiveness. Data from the AAQ, a PROM (the Hip disability or Knee injury Osteoarthritis Outcome Score, ADL subscore), and performance-based tests (the Timed Up and Go test, Stair Climbing Test and 30 seconds Chair Stands Test) were collected. To estimate the Minimal Important Change (MIC) of the AAQ an anchor-based MIC distribution method was used with a Global Rating of Change (GRC) as anchor. The Receiver Operating Characteristic (ROC) method was used to find the AAQ change score that best discriminates between patients who improved in activity limitations and who are not. The MIC was compared to the SDC in order to facilitate the interpretation of change scores.

**Results:** Cronbach’s alpha was 0.94. ICC for test-retest reliability was 0.93 (95% CI: 0.91–0.95). SEM and SDC were 4.9% and 13.5%, respectively. With regard to responsiveness the change scores of the AAQ after 6 months correlated 0.58 with the PROM, 0.42–0.55 with the performance based tests, and 0.46 with GRC. The ROC curve showed an area under the curve of 0.72 with a sensitivity of 63% and a specificity of 81% for the optimal MIC of 9.1 for discrimination. The MIC was smaller than the SDC meaning that the change is important but cannot be distinguished from measurement error in individual patients.

**Conclusions:** The AAQ, measuring a new construct in the domain physical activity limitation, showed good construct validity, cross-cultural validity, internal consistency and test-retest reliability. A change in AAQ score over 13.5% indicates a real improvement in activity limitations in HOA patients. The AAQ seems to have great potential for international use in research but the application in clinical practice needs caution.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4050
DISABILITY IN THE FEET RELATED TO PARTICIPATION IN DAILY LIFE IN PATIENTS WITH EARLY RA – AN INTERVIEW STUDY IN THE SWEDISH TIRA PROJECT

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Background: Pain, stiffness and deformity of the feet are related to reduced mobility and participation restrictions in daily activities in patients with established rheumatoid arthritis (RA). The new biological medications are effective and reduce disease activity, but not disability to the same extent. Foot problems are assumed to be related to participation restrictions also in patients with early RA, diagnosed after the introduction of biological medications, hindering for example physical activity. Hence, there is a need for more knowledge about foot problems in order to identify possible needs for rehabilitative interventions.

Objectives: To explore disability related to foot problems in women and men with early rheumatoid arthritis and its relation to participation in daily life.

Methods: 59 patients (58% women, 20–63 years) with early RA were interviewed about participation dilemmas in daily life related to RA, using Critical Incident Technique. The interviews were audio-recorded and transcribed. Data related to foot problems were extracted and analysed thematically. A research partner with RA validated the retrieved categories. The study was approved by the Regional Ethics Committee.

Results: More than 2/3 of the patients mentioned that they had participation restrictions related to foot problems. The analysis revealed 5 categories concerning foot problems and the relation to participation restrictions: 1) foot problems as an early indicator of the disease, 2) hindrance in managing the daily routine and house hold activities, 3) struggling to be mobile, 4) difficulties in doing a good job at work and 5) difficulties in participating in recreation and leisure activities. Both women and men shared many experiences, as difficulties to be physically active. Several women expressed difficulties to use the shoes they wanted. Being able to move on uneven ground in, for example, the forest was something that many men expressed as difficult.

Conclusions: Patients with early RA with access to effective medications and multi professional interventions based on their individual needs still experience a wide range of foot related disability in major life arenas as work, in the household and during leisure time. This indicates a need to pay attention also in today’s early RA patients to foot problems in the multi professional rehabilitation to prevent further disabilities and enable physical activity for men and women with RA.

DISABILITY IN THE FEET RELATED TO PARTICIPATION IN DAILY LIFE IN PATIENTS WITH EARLY RA – AN INTERVIEW STUDY IN THE SWEDISH TIRA PROJECT


RHEUMATOID ARTHRITIS PATIENTS’ SUPPORT NEEDS REGARDING MEDICATION USE AND THEIR PERSPECTIVES ON THE APPLICABILITY OF EHEALTH INTERVENTIONS TO ADDRESS THOSE NEEDS: A FOCUS GROUP STUDY

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Background: Patients with rheumatoid arthritis (RA) encounter various problems with their medication use, including poor knowledge about disease-modifying antirheumatic drugs (DMARDs), concerns about potential adverse consequences of their medication use8 and struggles with opening the medication’s packaging9. Additional support might decrease those problems by targeting RA patients with (eHealth) interventions that address their needs. To date, no studies have explored RA patients’ support needs regarding medication use from their own perspectives and it remains largely unknown if, and to what extent, they perceive eHealth interventions as enabling RA patients to better cope with their medication use. Their perspectives on the applicability of eHealth interventions to address those needs were also identified. RA patients recognized potential advantages of eHealth interventions, such as being less time consuming and easily accessible. However, concerns patients did not know whether PGA affects their treatment decisions in the same way as the objective measures do: “if the answer is not in somehow according to the exams we make (…) obviously they might ignore me”. Some believed that PGA was only used for research purposes. (2) The meaning of PGA. Pain was by far the main meaning of PGA, but also fatigue, function and other dimensions contributed to the perceptions. (3) Global Perspective. Many of these difficulties arose from the presentation of the three different PGA formulations, anchor points and their presentations: “I always think that 100 is great: you feel 100%”, “Usually the scale is 0 to 10, here I can see 0 to 100”, “Usually it has the numbers, I answer 2, it’s not like a straight line like this one”; “Today is different (…) when they ask the last week, we have to go back in time and the pain isn’t the same anymore”. Also cultural issues and the subjectivity of the concept were expressed: “We, the patients, can’t really assess the intensity of the pain, what could be a 9 for her, for me it might be a 5”; “I can never answer 0, because I always have something that affects me”. (4) Clarification from a HCP as a key factor for global understanding: “[Sometimes I just give a random number. (…) now maybe I will think more carefully and try to be as accurate as possible”.

Figure 1. Main themes of Patients’ perspective of PGA

Conclusion: Our results suggest that patients’ interpretation of PGA is diverse and may reflect different symptoms such as pain or psychological well-being and comorbidities. Standardization of PGA is warranted and dedicated patient debriefing is likely to improve the reliability of this assessment.

DISABILITY IN THE FEET RELATED TO PARTICIPATION IN DAILY LIFE IN PATIENTS WITH EARLY RA – AN INTERVIEW STUDY IN THE SWEDISH TIRA PROJECT


IT CAN’T BE ZERO: A QUALITATIVE STUDY OF PATIENTS’ PERSPECTIVE ON PATIENT GLOBAL ASSESSMENT IN RHEUMATOID ARTHRITIS

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Background: Patient Global Assessment (PGA) plays an important role in disease activity assessment and treatment decisions in rheumatoid arthritis (RA). However, it is open to patient interpretation and this may affect the validity and reliability of clinical assessments.

Objectives: We aimed to explore: (i) patients’ perspective on PGA and its different formulations (ii) how patients’ perspective may be improved by a brief explanation from a health care professional (HCP).

Methods: This was a qualitative study including consecutive patients with RA attending a day hospital and an outpatient department of a university hospital in Portugal. Data collection included 4 focus-groups (FGD) and 3 individual interviews to determine patients’ perspectives. To help the discussions, patients completed 3 different PGA formulations consecutively and then a HCP explained what information was expected to inform their PGA. The 3 PGA formulations and their implications were then discussed between the patient and the HCP. Data from the FGDs and the interviews were transcribed verbatim and inductive content analysis was undertaken by two independent researchers. Data were coded and categorized into themes, which were agreed upon with patients, HCP and patient research partners.

Results: Fourteen patients (12 women) with RA participated. Their age ranged from 49 to 72 years, disease duration 4 to 30 years and 11 were on biologic DMARDs. Four main themes emerged (Figure 1): (1) The purpose of PGA. Some
on matters such as privacy, the quality and trustworthiness of information and personal interaction with healthcare providers prevailed.

**Conclusions:** For most RA patients, informational support regarding medication use is the most important (unmet) need. High-quality, unambiguous information about their medication use was emphasised. Moreover, this information should be provided by healthcare providers on an ongoing basis and tailored to their personal situation. Eliminating RA patients’ concerns regarding eHealth interventions should be a first priority before such interventions are applicable to address these informational needs. These findings need to be confirmed in a sample of younger RA patients.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6344

**THURSDAY, 15 JUNE 2017**

**RA: really a systemic disease?**

**OP0146** DECREASE IN CARDIOVASCULAR EVENT EXCESS RISK IN RHEUMATOID ARTHRITIS SINCE 2000: A META-ANALYSIS OF CONTROLLED STUDIES

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**Background:** Compared with the general population, patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease or events (CE): stroke, Myocardial Infarction (MI), Congestive Heart Failure (CHF) and Cardiovascular Mortality (CVM). Systemic inflammation is the cornerstone of both RA and atherosclerosis. Over the past fifteen years, new treatment strategies such as tight control, treat to target, methotrexate optimization, biologic DMARDs use has allowed a better control of this inflammation.

**Objectives:** The aim of this systematic review was to assess the excess risk of presenting a CE in RA patients as compared to general population, before and after the 2000s.

**Methods:** We systematically searched literature (via Pubmed, Cochrane and abstracts from recent ACR and EULAR congresses) up to March 2016 for observational studies providing data about the occurrence of a CE (among stroke, MI, CHF, CVM) in patients with RA and in a control group. A meta-analysis of the relative risk (RR) concerning patients with RA in relation to the control group was performed for each cardiovascular event and for each period (before and after the 2000s).

**Results:** Out of 5714 screened references, 28 studies were included. For studies published before 2000, an increased risk of CEs was observed in RA patients: RR=1.12 [95% CI 1.04; 1.21], p=0.002 for stroke RR=1.25 [1.14; 1.37], p=0.00001 for CHF RR=1.21 [1.15; 1.28], p=0.00001 for CVM RR=1.32 [1.24; 1.41], p=0.00001 for MI. For all studies published after the year 2000, the increased risk was not retrieved for CHF (RR=0.58 [0.11; 3.55], p=0.52) and CVM (RR=1.07 [0.74; 1.56], p=0.71). The excess risk of MI was reduced in comparison with the period before 2000: RR=1.18 [1.14; 1.23], p=0.00001. The excess risk of stroke was stable: RR=1.23 [1.06; 1.43], p=0.006.

**Discussion:** This meta-analysis confirms an increased risk of CEs among people with RA relative to the general population. It also appears that this excess risk is less prevalent than prior to 2000s. This might have two explanations: a better management of the cardiovascular risk in patients with RA and a better control of chronic systemic inflammation thanks to new therapeutic strategies.

**Conclusions:** The cardiovascular excess risk of RA patients relative to the general population has decreased since 2000s. This suggests that the recent improvements in RA management may have a positive impact on cardiovascular comorbidities.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4415

**TRENDS IN MORTALITY, CO-MORBIDITY AND TREATMENT AFTER ACUTE MYOCARDIAL INFARCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS 1998-2013**

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**Background:** Rheumatoid arthritis (RA) patients have increased mortality due to cardiovascular disease (CVD). Case fatality after an acute myocardial infarction (AMI) has been reported to be increased. Whether the prognosis after AMI has changed over time in RA is unknown.

**Objectives:** To study the one-year mortality after a first AMI in RA versus non-RA patients during the time period 1998–2013. To identify time trends in mortality, co-morbidities and secondary preventive treatments and to explore any characteristics associated with mortality.

**Methods:** We identified all patients with a first time AMI in the Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA) between 1998–2013. We used the National Patient Register (NPR) to identify AMI patients with RA (RA defined as ≥2 visits to a Rheumatology or Internal Medicine department with a diagnosis of RA). In total 245376 AMI patients were identified, 4268 of them had RA. To study trends over time, the study period was divided into five consecutive time periods. Multivariate Cox regression analysis was used to identify variables associated with mortality.

**Results:** The one-year mortality in RA patients was stable and lower compared to non-RA patients during the first time periods but thereafter increased above the non-RA patients. In non-RA patients, mortality decreased over time and stabilised during the last time period (Figure). In RA patients the mean age at admission increased from 69 to 73 years, whilst in non-RA patients it was unchanged, 71 years. Atrial fibrillation (AF) was initially more common in non-RA patients but the prevalence decreased over time (from 19.2% to 17.5%). In RA patients, AF increased over time from 15.6% to 21.4%. The prevalence of congestive heart failure (CHF) during hospitalisation decreased markedly more in non-RA (from 41.5% to 22.7%) than in RA patients (from 36.0% to 29.2%). The most important secondary preventive treatments were similar in RA and non-RA patients. In a multivariate Cox model including data from the last time period, 2011–2013, age, CHF during hospitalisation, ST-elevation AMI (STEMI), AF, prior diabetes mellitus, a diagnosis of RA and oral anticoagulation were significantly associated with higher one-year mortality (Table).

**Conclusions:** The marked decrease in one-year mortality after AMI seen over time in non-RA patients was not applicable in RA patients. Our finding might to some extent be explained by an increased age at AMI onset and unfavourable trends for AF and CHF in RA. However, RA per se was significantly associated with a worse prognosis during the last years of the study period. Secondary preventive treatment was similar in RA and non-RA patients. Further analyses including RA treatments are necessary to gain further insight into reasons behind the discrepant prognosis in RA vs. non-RA patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4481
OP0148  IMPACT OF A CARDIOVASCULAR EVENT ON DMARD TREATMENT AMONG PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR PSORIASIS

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Background: Chronic inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (PsO) increase the risk of cardiovascular (CV) disease. However, a gap in knowledge exists regarding detailed information on changes in immunomodulatory (DMARD) treatments after a CV event.

Objectives: We describe treatment patterns among patients with RA, PsA, or PsO who were being treated with DMARDs prior to a CV event.

Methods: Patients with RA, PsA, or PsO, who experienced a CV event (acute myocardial infarction, stroke, or cardiac rehospitalisation) between 1/1/2006 and 6/30/2015 were identified in an administrative claims database. Index date was defined as the hospital discharge date for the first CV event during the study period. Patients required to be continuously enrolled for 12 months prior to index date; have ≥1 TNFi claim, or a conventional synthetic (cs)DMARD claim, or another biologic DMARD claim within 6 months prior to the index date; and have ≥30 days of follow-up after index date. Treatment patterns were assessed after index date and patients were classified as remaining on (“persistent”), switching, or discontinuing pre-index DMARD medication.

Results: We identified 9,529 patients with RA, PsA, or PsO prior to the index date. 3,274 (34.4%) patients were on TNFi, 5,177 (54.3%) were on only csDMARDs as monotherapy or combination, and 1,078 (11.3%) were on non-TNFi biologics. Patients on csDMARDs at index date were older (69.4 yrs) than those on TNFi (64.1 yrs) or other biologic DMARDs (66.0 yrs). Approximately 73% of patients were on TNFi on their pre-CV event treatment, with higher persistence among csDMARD alone (70.6%) and TNFi + csDMARD combo (76.7%) groups and lower in the non-TNFi biologic + csDMARD combo group (60.8%, Table 1). Across all treatment groups, 95% of persistent patients resumed treatment within 90 days after the index CV event. Combination therapy users switched their pre-CV event treatment more often than monotherapy users, with non-TNFi biologic users more likely to discontinue all therapy after index CV event. Patients that discontinued all therapy after an index CV event tended to be slightly older females (68.7 yrs vs 67.1 yrs), with a history of PsO (24.4% vs 16.1%), and stroke as index event (49.3% vs 41.3%) compared to those that continued therapy.

Conclusions: In a large US database reflective of typical clinical practice, nearly one-quarter of patients with RA, PsA, or PsO discontinued or switched their pre-index DMARD treatment after index CV event. Further research is needed on whether these DMARD treatment patterns after initial CV event affect risk of repeat CV event.


DOI: 10.1136/annrheumdis-2017-eular.2324

OP0149  MORTALITY IN NEW-ONSET RHEUMATOID ARTHRITIS - HAS MODERN RHEumatology HAD AN IMPACT?

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Background: A wealth of studies have linked rheumatoid arthritis (RA) with an excess mortality compared to the general population. With increasingly effective anti-rheumatic treatment strategies there is, however, considerable uncertainty whether this mortality gap still exists and, if so, how soon after RA onset it occurs.

Objectives: To assess the mortality in RA compared to the general population with specific focus on whether during the course of the disease the risk is increased and if it also applies to patients diagnosed in recent years.

Methods: We performed a population-based cohort study of 17,512 patients with new-onset RA (identified from the Swedish Rheumatology Quality Register) 1997 through 2015, and 78,847 individually matched general population comparator subjects. We followed all individuals using nationwide census registers with full coverage to identify all deaths through 2015. We calculated mortality rates with 95% confidence intervals (CI) and compared the mortality in RA to that in the general population using Cox proportional hazards models adjusted for age, sex, year of diagnosis, and residential area.

Results: During a mean follow-up from RA diagnosis of 7 years, 2,386 RA patients and 9,850 population comparator subjects died (crude incidence: 19 per 1000 in RA and 18 per 1000 in the general population), with only a marginal decline (in the RA and in the general population cohort) during the study period. The overall HR was 0.99 (0.95–1.04), but whereas there was no increase in mortality during the first five years after RA diagnosis; the HR >10 years after RA onset was 40% increased. The overall pattern of HRs was similar for patients diagnosed 1997–2001, 2002–2006, and 2007–2011 (table).

Conclusions: Higher 10-year mortality in RA is not increased, neither for patients diagnosed in the past nor for those diagnosed during the most recent five years. By contrast, at least in the most recent inception cohort for which ten-year mortality currently can be calculated (those diagnosed up to 2006), RA is still associated with an increased risk of death.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2580

OP0150  PARADOXICAL EFFECT OF BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH OVERWEIGHT AND OBESITY: LESS OFTEN CLINICAL REMISSION, BUT ALSO LESS RADIOLOGICAL DAMAGE

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Background: The relationship between treatment with biological disease-modifying antirheumatic drugs (DMARDs), including TNF-blocking agents, and disease activity in overweight and obese rheumatoid arthritis (RA) patients has not been clarified yet.

Objectives: The aim of this review is to assess the effect of overweight/obesity on the therapeutic efficacy of these drugs. Secondly, we aimed to assess the influence of overweight/obesity on the occurrence of joint destruction.

Methods: A systematic review of all articles published on these subjects using PubMed and EMBASE was executed. For the first research question, studies were eligible when focused on the clinical efficacy of biological DMARDs only in overweight/obese RA patients versus normal weight patients. For the second research question studies were eligible when questioning the relation between overweight and joint destruction in patients with RA. Overweight and obesity were defined according to the following body mass index (BMI) categories; BMI >20 kg/m² for overweight, BMI >25 kg/m² and BMI >30 kg/m² for obesity.

Results: A total of 6782 articles were found, of which 12 were eligible for this review. A total of 3647 RA patients were treated with adalimumab, etanercept, infliximab, golimumab, or certolizumab pegol, or TNF blockers, rituximab, or tocilizumab.

Ten studies used disease activity as outcome. In general, these studies showed that higher BMI was associated with poor response, based on either outcome or percentages on remission or improvement defined according to EULAR guidelines. In addition, four studies showed that higher BMI is also associated with higher Health Assessment Questionnaire (HAQ)-scores. Two articles (of which one article described the results of studies in two different RA cohorts) focused on the association between BMI and joint destruction. These articles showed that higher BMI values were associated with lower odds for having joint destruction. One study also showed that having a BMI <20 kg/m² was associated with a higher odds ratio (OR =4.12) for joint destruction.

Conclusions: Higher BMI levels in RA patients treated with biological DMARDs...
are associated with reduced therapeutic efficacy as compared to RA patients with normal body composition. The unfavourable effect of body weight on disease activity was paralleled by a favourable, protective effect on joint destruction. This uncoupling is not fully elucidated yet, and should be further investigated.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4694

OP0151 DOCOSAHEXAENOIC ACID TREATMENT OF RHEUMATOID ARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSS-OVER STUDY

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Background: Epidemiological studies and clinical investigations indicate a beneficial impact of long-chain n-3 polyunsaturated fatty acids (n-3 PUFA) on the inflammatory activity of rheumatoid arthritis (RA). However, the knowledge about the physiological effects of the individual compounds eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is limited.

Objectives: In our pilot study presented here, we investigated the clinical benefit of daily intake of foods enriched with microalgae oil as source of DHA in RA patients. In particular, we focused on disease activity and changes in the profile of pro-inflammatory/non-resolving and anti-inflammatory/pro-resolving lipid mediators as expected.

Methods: This is a randomized, double-blind, cross-over study on 38 patients (32 females/6 males) with active RA (DAS28≥2.4). They were allocated to consume foods enriched with microalgae oil from Schizochytrium sp. (2.1 g DHA/day) or sunflower oil (placebo) for 10 weeks while maintaining stable immunosuppressive treatment.

Results: Thirty-two patients finished the study but seven patients were excluded from analysis because their DHA increase in erythrocyte lipids (EL) was less than 25% after 10 weeks of intervention indicating insufficient adherence to the intervention. Supplementation of DHA led to a decline in tender joints (TJ68) 8.4±5.6 to 6.0±5.0 (p=0.03), swollen joints (SJ66) 5.6±3.5 to 3.9±3.5 (p=0.07) and DAS28 4.3±1.0 to 3.9±1.2 (p=0.07). Joint counts in the placebo arm remained stable (TJ68) 6.7±4.9 to 8.2±8.0 (p=0.12), swollen joints (SJ66) 3.5±3.0 to 4.2±3.7 (p=0.40) and DAS28 4.0±0.9 to 4.1±1.2 (p=0.45). Ultrasound score (US-7) remained stable (15±9.5 to 12±4.7; p=0.160) while it increased in the placebo arm (11.4±7.0 to 14.0±8.8; p=0.03). The amount of n-3 PUFA in erythrocyte increased in supplemented patients (7.0±1.2% to 10.6±1.4%; p<0.001) and the ratios of arachidonic acid (AA) /EPA (BSRBR-RA).2. To establish whether the organ class of index infection predicted to infection.

Objectives: To identify the effects of disease activity on renal function in RA in a multi-center cohort study.

Methods: RA patients with a sampling interval of less than 150 days were enrolled because wide sampling intervals could not take into consideration changes in disease activity and medications during their follow-up. An estimated glomerular filtration rate (eGFR) was calculated using an equation approved by the Japanese Society of Nephrology and used as an outcome variable. Linear mixed effect models were used to evaluate the renal trajectories of patients. Time from baseline (months), disease activity, and their interaction were included as fixed effects while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, NSAIDs, and DMARDs that were known as a cause of renal impairment, such as tacrolimus, igrutamid, and tofacitinib, were included as covariates.

Results: A total of 25661 samples (mean sampling interval: 2.0 months) from 2104 patients was included. Patients with lower DAS28-CRP had worse renal function at inclusion, but a significantly better longitudinal trajectory on eGFR (0.0079 ml/min/1.73m² per month, P=0.025). Although all RA patients had naturally progressive renal impairment as they got older, patients who achieved remission or low disease activity had slower renal impairment rate of -0.068 ml/min/1.73m² per month compared to patients with moderate or high disease activity (-0.084 ml/min/1.73m² per month; P=0.037). These results were also similar using SDAI or CDAI.

Conclusions: Lower disease activity results in slower renal impairment. Because the effects of disease activity on renal function are mild, additional measures to protect renal function, such as avoiding nephrotic medications and treating cardiovascular risk factors are important.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4544

OP0153 RECURRENT INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS, RESULTS FROM THE BSRBR

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Background: Rheumatoid arthritis (RA) patients have an increased susceptibility to infection.

Objectives: 1.To establish the rate of recurrent infection in RA patients recruited to the British Society of Rheumatology Biologics Registry Rheumatoid Arthritis (BSRBR-RA).2.To establish whether the organ class of index infection predicted future serious infection.

Methods: The BSRBR-RA is a prospective observational cohort, previously described. Patients with at least one episode of serious infection requiring hospitalisation were included if they occurred whilst on anti-rheumatic drug therapy or within 5 drug half-lives of stopping. Infections were coded by MedDRA classification in to 7 categories. Infections occurring over 14 days after the first index infection were considered as new events. Event rates were calculated and compared using a Cox proportional hazards model with adjustments made for age, gender, disease duration, baseline DAS28 score, smoking status and seropositivity.

Results: See Table 1.

In total, 21,943 subjects with 115,423 patient-years follow up were studied, 5365 subjects reported at least one serious infection. Comparing organ classes of prior infection at baseline, each group had comparable age, disease duration, baseline DAS28 and HAQ scores. The cohort characteristics are tabulated. The baseline annual rate of first serious infection was 4.6% (95% CI 4.5–4.7). Following an
Abstract OP0153 – Table 1

<table>
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<tr>
<th>Overall</th>
<th>Patients with infection</th>
<th>Respiratory</th>
<th>Gastrointestinal</th>
<th>Genitourinary</th>
<th>Musculoskeletal</th>
<th>Sepsis</th>
<th>Skin/Soft Tissue</th>
<th>Other</th>
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<td>Age, years (SD)</td>
<td>57.3 (12.5)</td>
<td>61.5 (11.7)</td>
<td>60.0 (11.5)</td>
<td>61.7 (11.1)</td>
<td>59.8 (11.9)</td>
<td>58.7 (10.5)</td>
<td>63.5 (11.2)</td>
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<td>Female (%)</td>
<td>75.7</td>
<td>72.6</td>
<td>74.8</td>
<td>77.4</td>
<td>89.2</td>
<td>70.2</td>
<td>76.6</td>
<td>79.5</td>
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<td>Baseline DAS28 (SD)</td>
<td>6.2 (1.2)</td>
<td>6.4 (1.2)</td>
<td>6.3 (1.2)</td>
<td>6.3 (1.1)</td>
<td>6.3 (1.2)</td>
<td>6.5 (1.2)</td>
<td>6.4 (1.1)</td>
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<td>Baseline ESR (SD)</td>
<td>1.9 (0.7)</td>
<td>2.1 (0.6)</td>
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<td>2.2 (0.5)</td>
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<td>Steroid use,n (%)</td>
<td>8346 (38.2)</td>
<td>2632 (49.4)</td>
<td>2832 (43.8)</td>
<td>493 (51.5)</td>
<td>1226 (44.5)</td>
<td>390 (51.6)</td>
<td>316 (57.3)</td>
<td>1583 (45.2)</td>
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<td>Current smoker, n (%)</td>
<td>4682 (21.7)</td>
<td>1159 (21.9)</td>
<td>1422 (22.1)</td>
<td>165 (17.3)</td>
<td>452 (16.4)</td>
<td>186 (24.8)</td>
<td>122 (22.4)</td>
<td>692 (19.9)</td>
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<tr>
<td>Recurrent infection rate, % per annum (95% CI)</td>
<td>13.340 (62.2)</td>
<td>3533 (67.5)</td>
<td>4176 (66.1)</td>
<td>626 (66.2)</td>
<td>1737 (64.6)</td>
<td>527 (71.4)</td>
<td>361 (66.1)</td>
<td>2241 (65.6)</td>
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THURSDAY, 15 JUNE 2017

Advances in RA and SpA pathophysiology

OP0154 ALTERED LYMPH NODE STROMAL CELLS DURING THE EARLIEST PHASES OF RHEUMATOID ARTHRITIS

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Background: Lymph node stromal cells (LNSC) have a crucial role in shaping the immune response and maintaining peripheral tolerance. We developed an experimental model for studying the functional capacities of human LNSC during the earliest phases of RA and compared their cellular and molecular characteristics to LNSC from healthy volunteers.

Methods: ACPA+ RA patients (n=24), ACPA+ RA-risk individuals (n=23) and seronegative healthy controls (n=14;HC) were enrolled. LNSCs were isolated and expanded in vitro from healthy volunteers. ACPA+ RA-risk and ACPA+ RA patients were more similar to each other compared with HC. Pathway analysis of commonly increased genes in RA (-risk) and associated with antigen processing and presentation (HLA-DRB1), immune destruction in the development of Rheumatoid arthritis (RA). However, the precise molecular mechanisms by which this pathogenic process is regulated are not clearly defined.

Objectives: Increasing evidence indicates that p53 plays a critical role in the invasion and metastasis of cancer cells. This study aims to investigate the role of MDM2-mediated sumoylation of p53 in regulating the migration and invasion of fibroblast-like synoviocytes (FLSs) from patients with RA.

Methods: Synovial tissues were obtained from OA and RA patients, and then FLSs were isolated from synovial tissue. Protein expression was measured by Western blotting or IHC staining. The sumoylation of p53 in cells was determined by immunoprecipitation. A specific inhibitor of MDM2-p53 interaction was used to inhibit the sumoylation of p53. Migration and invasion of FLSs in vitro were measured by Boyden chamber assay.

Results: MDM2, SUMO1, and SUMO2 expression was significantly increased in the synovial tissue and FLSs of RA patients. Stimulation with TNF-α increased MDM2 expression and p53 sumoylation in RA FLSs. MDM2 shRNA inhibited p53 sumoylation, pro-inflammatory cytokines and MMPs expression, and capacity of in vitro migration and invasion in RA FLSs. Inhibition of p53 sumoylation by MDM2 shRNA promoted apoptosis and reduced proliferation of RA FLSs. p38 MAPK signal pathway was involved in the downstream signal transduction in RA FLSs. Administration of MDM2 shRNA expression lentivirus attenuated the severity of rats with collagen-induced arthritis (CIA).

Conclusions: Increased MDM2-mediated p53 sumoylation contributes to aberrant invasive behaviors of RA FLSs. Our findings suggest inhibition of MDM2 or p53 sumoylation might be a novel therapeutic strategy to prevent synovial invasiveness and joint destruction in RA.

References:
[1] Bottini N, Firestein GS. Duality of fibroblast-like synoviocytes in RA: passive...
OP0156 METHOTREXATE INCREASES EXPRESSION OF THE CELL CYCLE REGULATORS LBH AND P21 AND REDUCES FIBROBLAST-LIKE SYNOVIOTYCE PROLIFERATION AFTER MITOGEN STIMULATION

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Background: Activated fibroblast-like synoviocytes (FLS) are key effector cells in the joint in rheumatoid arthritis (RA). Local FLS proliferation is responsible for synovial hyperplasia, a key feature of the RA synovium correlating with disease activity. PDGF and IL-1β are known FLS mitogens, LBH is a transcription regulator and tumor suppressor, recently identified as a RA risk gene. We have demonstrated that LBH regulates FLS proliferation and that LBH expression is regulated by growth factors and by epigenetic mechanisms[1]. Methotrexate (MTX) is still the first-line treatment of RA and to identify novel markers for drug response.

Methods: Primary FLS from RA patients and from patients with osteoarthritis (OA) were plated on day 0 in DMEM complete, pre-treated 24 hours with MTX or control medium day 1, and stimulated with 20ng/ml PDGF+2 ng/ml IL-1β with or without 1μM MTX in DMEM with 1% FBS for 24–48 hours starting day 2. Cells were then harvested for qPCR for gene expression and flowcytometry for cell cycle analysis.

Results: Stimulating RA-FLS cultures (n=3) with PDGF+IL-1β for 24 hours, pushed 24±3±3% cells into G2/M phase compared to 3.4±0.8% in unstimulated controls. Interestingly, treating PDGF+IL1β stimulated FLS with MTX, significantly inhibited cell cycle progression (4.6±1.1% in G2/M phase, p=0.02). PDGF+IL-1β stimulation of FLS for 24 hours reduced LBH mRNA expression. However, in the presence of 1μM MTX the LBH mRNA expression was significantly higher in RA-FLS (3.2±0.5 fold, p=0.002, n=5) and in OA-FLS (2.2±0.5 fold, p=0.02, n=5) after PDGF+IL-1β stimulation compared to untreated controls. In addition, MTX treatment strikingly increased the CDKN1A expression 14.3±4.4 fold (p=0.006) of treated vs untreated stimulated FLS. Furthermore, we found that 1 μM MTX restored and increased a lowered DNMT1 mRNA expression to 144±12% after PDGF+IL-1β stimulation. There were no significant effects of MTX on CCND1 or DNM1A expression at investigated time points.

Conclusions: Therapeutic doses of MTX reduce mitogen induced FLS prolifera tion and significantly revert mitogen-induced reduction of LBH and p21 expression in RA FLS. MTX restores expression of DNMT1 suggesting that MTX might regulate gene expression and proliferation by affecting the epigenome.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1554

OP0157 APOTOPSIS RESISTANCE OF SYNOVIAL FIBROBLASTS OF PATIENTS WITH RHEUMATOID ARTHRITIS IS REGULATED BY THE LONG NON-CODING RNA FAS-AS1

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Background: Apoptosis resistance is thought to contribute to the accumulation of synoviocytes in the affected joints of patients with rheumatoid arthritis (RA). Of particular interest, the Fas receptor (FasR) - Fas ligand (Fasl) apoptotic pathway is altered in RA. Long non-coding (lnc) RNAs are emerging as key regulators of gene expression. Their role in disease, however, is still poorly understood. The recently described IncRNA FAS-AS1 has been implicated in alternative splicing of FasR. This results in increased amounts of soluble FasR (sFasR) and thereby prevents FasL-induced cell death[2]. Whether IncRNA FAS-AS1 is involved in the apoptosis resistance of synovial fibroblasts in RA is unknown.

Objectives: To assess the regulatory role of IncRNA FAS-AS1 in the apoptosis resistance of synovial fibroblasts from patients with RA (RASF).

Methods: Levels of expression of IncRNA FAS-AS1 were measured in RASF and synovial fibroblasts from patients with osteoarthritis (OASF) by qPCR using SYBRGreen detection. Cells were treated with TNFα (10ng/ml, 24h) and/or with Fasl (50ng/ml, 18h) to assess the secreted amount of sFasR by ELISA and the induction of apoptosis by Annexin V staining followed by flow cytometry. LncRNA FAS-AS1 was silenced using locked nucleic acid antisense oligonucleotides (GapmeR).

Results: There was no significant difference in basal levels of IncRNA FAS-AS1 expression between RASF and OASF (n=4 each). TNFα stimulation of synovial fibroblasts, regardless of the disease context (RA or OA), resulted in higher than 6-fold induction of IncRNA FAS-AS1 expression (6.45±1.39; p<0.05; n=4 for RAF and 6.26±1.47; p=0.05; n=4 for OASF). In addition, TNFα induction of secreted sFasR in RASF from 107±74 to 390±274 pg/ml (p<0.05; n=6) and OASF from 69±53 to 249±134 pg/ml (p<0.05; n=6). Fasl induced apoptosis in both RASF and OASF (55–75±11%). However, treatment with TNFα reduced the FasL-induced apoptosis in RASF by 25±19% and in OASF by 15±10%. Silencing with GapmeR successfully decreased the expression of IncRNA FAS-AS1 by 40±22% SEM. Most interestingly, silencing of IncRNA FAS-AS1 reverted the TNFα inhibitory effect on Fasl-induced apoptosis by 37×11% (n=4).

Conclusions: Our data revealed a novel mechanism, which may underlie apoptosis resistance in RASF. We showed that a pro-inflammatory cytokine mimicking IncRNA FAS-AS1 up-regulation in the release of sFasR and thereby may lower the responsiveness of cells to death signals. Thus, targeting IncRNA FAS-AS1 might prevent apoptosis resistance and synovial hyperplasia in RA.

References:
[1] Hong et al., Life Sciences, 2015; Feb 1; 122-37-41.

Disclosure of Interest: A. Pajak: None declared, E. Horai: None declared, E. Pachera: None declared, M. Brock: None declared, S. Gay Grant/research support from: EJ Sanofi, Adalimumab, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Active Biotec, Bayer, BiogenIdec, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, Epipharma, esparé Foundation, Genentech/Roche. GMC, Inventiva. Lilly, medad, Mepha, MedImmune, Mitsubsihi, CyclinB1/CDK1-Phosphorylated Pachera: None declared, M. Brock: None declared, S. Gay Grant/research support from: EJ Sanofi, Adalimumab, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, Epipharma, esparé Foundation, Genentech/Roche. GMC, Inventiva. Lilly, medad, Mepha, MedImmune, Mitsubsihi, CyclinB1/CDK1-Phosphorylated

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2677

OP0158 PREVALENCE OF IMMUNIZATION OF PATIENTS WITH AUTOIMMUNE DISEASE IN MEXICO


Background: Current guidelines recommend immunization in patients with autoimmune diseases and use of immunosuppressants including biological treatment. Despite the above, the frequency of immunization is unknown in our population.

Objectives: To identify the prevalence of immunization in patients with autoimmune disease in a Rheumatology Service of a third level hospital in Mexico.

Methods: Observational, descriptive, cross-sectional, retrospective. Among consecutive patients with autoimmune diseases who attended the Rheumatology Service of the Hospital Civil of Guadalajara during a period of 2 months (Dec. and Jan.) were included. A questionnaire was carried out to obtain demographic and immunization data. Descriptive statistical analysis was performed.

Results: 1398 patients were surveyed, 484 (40%) had a diagnosis of autoimmune disease; of whom 286 (59%) were on immunosuppressant therapy. 321 patients had a complete immunization during childhood. None of the patients knew what vaccines should be received by their diagnosis. When asked if they had been invited for immunization and from whom, 24 reported that their

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5079
general practitioner, 126 immunization campaign, 19 nurse, 9 rheumatologist, 4 pulmonologist, 1 infectious disease specialist, 1 family doctor and 1 internist. 260 (54%) reported having their immunization records. Only 37 had been vaccinated with influenza, 27 pneumococcus, 4 human papilloma virus and 2 Hepatitis B in the past. 372 (77%) accepted the invitation to be vaccinated on the day of their interview. Of these, only 19 (41%) went to get the immunization: 41 of whom were given anti-influenza vaccines and 34 Pneumococcus (PPSV 23). The main causes for which the patient considers not to be vaccinated are: 85% “Because my treating doctor has not recommended me to get vaccinated”, 36% “They often do not have the vaccine to apply”, 36% “I forget to get the vaccine on time”, 31% “I think the application of the vaccine can make me sick”, 14% “A vaccination center is not accessible”, 7% “I think it is not useful to get vaccinated”, and 5% “My doctor recommended me not to get vaccinated”. These patients presented a total of 172 recurrent infections that included: upper airway infection 55, pneumonia 4 and others; 90 hospitalizations were reported due to infection of which the main were due to: pneumonia 29, pulmonary tuberculosis 4, kidney 3, bone 1 and meningitis 1.

Conclusions: Immunization in this group of patients is low and rarely accepted mainly because their rheumatologist does not provide them with this information and due in general to a lack of information. This action is extremely important as it might reduce some serious infectious processes that lead to hospitalizations and increase the mortality in these immunosuppressed patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6721

OP0159 THE INITIATION, BUT NOT THE PERSISTENCE, OF EXPERIMENTAL SPONDYLOARTHRITIS IN HLA-B27/Hu2m TRANSGENIC RATS IS CRUCIALLY DEPENDENT ON THE IL-23 AXIS

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Background: The pro-inflammatory cytokine IL-17A is a central driver of pathologic changes in the gut and joint compartments in a mouse-model over-expressing human TNF in the ileum. These mice, together with wild type littermates, were evaluated for the development of arthritis up until the age of 13 weeks after which they were euthanized and ankle and sacroiliac joints as well as ileum were processed for histology.

Results: The differential effect of IL-23R targeting in the initiation versus control animals. The upregulation of TNFR1 on intestinal epithelium and TNFR2 in lamina propria node expression data in samples from the therapeutic experiment indicate a twofold increase in IL-17A expression and no difference in IL-22 expression in the anti-IL23R treated rats compared to controls.

Conclusions: IL-17A expression and production is dependent on the IL-23 axis in the initiation phase of experimental SpA but not in established disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5248

OP0160 GUT-DERIVED TNF AS RISK FACTOR FOR THE DEVELOPMENT OF SACROILIAC INFLAMMATION

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Background: An intriguing link exists between gut and joint inflammation in spondyloarthritides (SpA). About 50% of patients has subclinical (eg. microscopic) gut inflammation, which represents a risk factor for development of Crohn's disease, sacroiliac inflammation and evolution in to Ankylosing Spondylitis. However, the underlying mechanisms are still relatively poorly understood.

Objectives: Our goal was to examine the relationship between TNF, microscopic gut inflammation and axial inflammation using human samples and a novel mouse model.

Methods: We examined in situ expression of TNF, TNFR1 and TNFR2 using triple in situ hybridisation in gut biopsies of human SpA patients. Furthermore, we generated intestinal specific human TNF transgenic mice, in which hTNF is under control of a rat IFABP (fatty acid binding protein) promoter, generating a mouse-model over-expressing human TNF in the ileum. These mice, together with wild type littermates, were evaluated for the development of arthritis up until the age of 13 weeks after which they were euthanized and ankle and sacroiliac joints as well as ileum were processed for histology.

Results: There was a marked upregulation of TNF in inflamed versus non-inflamed gut biopsies of human SpA patients. We also noted a predominant upregulation of TNFR1 on intestinal epithelium and TNFR2 in lamina propia respectively. Of interest, IL-17 and IL-23 were also markedly increased while IL-22 was most abundant in chronically inflamed samples. In line with this, we found that patients with gut inflammation had a higher need for anti-TNF therapy and their degree of clinical response after anti-TNF was also markedly higher.

Our transgenic mice exhibited a runt phenotype and hallmarks of inflammatory bowel disease, including increased intestinal permeability and inflammation compared to their wild-type littermates. While in peripheral joints no clear signs of arthritis were observed, the sacroiliac joints in transgenic mice, by contrast, showed marked signs of inflammation as well as bone erosion and destruction.

Conclusions: These data propose a new paradigm that gut-derived TNF is sufficient to trigger sacroiliitis and provide an alternate explanation on the relationship between gut inflammation, evolution to inflammatory bowel disease and axial inflammation in SpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4999

OP0161 THE JAK1 SELECTIVE INHIBITOR FILGOTINIB REGULATES BOTH ENTHESIS AND COLON INFLAMMATION IN A MOUSE MODEL OF PSORIATIC ARTHRITIS


Background: Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease characterized by the association of musculoskeletal involvement and extra-skeletal symptoms such as psoriasis and Inflammatory Bowel Disease

Objectives: and clinical evidence from SpA-related diseases suggest, however, that IL-17A and IL-23 have a partially overlapping but distinct biology. In contrast, we showed previously to be crucially dependent on the IL-23 pathway for exposure to anti-IL23R.

Methods: HLA-B27/Hu2m tg rats were immunized with low dose heat-inactivated M. tuberculosis/IFA. Rats were treated with a depleting anti-mouse/rat chimeric anti-IL23R antibody or PBS in a prophylactic (treatment initiation after immunization, before disease onset) or therapeutic (treatment initiation after disease onset) experiment. Clinical measurements included spondylitis and arthritis scores and hind paw swelling (plethysmometry). At the end of the study spleen and lymph nodes were used for cytokine expression, serum samples were analyzed for exposure to anti-IL23R.

Results: In the prophylactic treatment strategy, 58% and 67% of the rats in the control group developed spondylitis and arthritis, respectively. The average arthritis scores at the end of the study was 0.9 ± 1.1 and the average hind paw swelling was 0.35 ± 0.09 cm³. Prophylactic treatment with anti-IL23R completely protected the rats against the development of spondylitis as well as arthritis. In the therapeutic treatment strategy, however, anti-IL23R treatment failed to reduce the incidence or decrease the severity of experimental SpA (fig. 1). With an average increase in arthritis scores after the start of treatment of 1.62 ± 2.8 versus 2.1 ± 2.5 and an increase in paw swelling of 0.6 ± 0.7 compared to 0.3 ± 0.06 cm³ in anti-IL23R treated versus control animals. The differential effect of IL-23R targeting in the initiation phase versus established disease could not be explained by pharmacokinetic differences as serum analyses revealed similar exposure levels. Mechanistically, the expression of presumably downstream effector cytokines such as IL-17A (p < 0.05) and IL-22 (p < 0.01) was reduced in the popliteal lymph node of rats treated prophylactically with anti-IL23R versus controls, with a similar trend in spleen. Accordingly, IL-17A production upon ex vivo re-stimulation was reduced in samples from anti-IL23R treated rats compared to controls, similar popliteal lymph node expression data in samples from the therapeutic experiment indicate a twofold increase in IL-17A expression and no difference in IL-22 expression in the anti-IL23R treated rats compared to controls.

Conclusions: IL-17A expression and production is dependent on the IL-23 pathway for exposure to anti-IL23R.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5476
(IBD) with a variable clinical course. Common findings include enthesis and dactylitis. Current treatments include anti-TNFα and anti-IL-12/IL-23 antibodies with varying success rates but the involvement of several pro-inflammatory cytokines suggests that other targeted therapies may be effective. Notably, the JAKs (a family of 4 non-receptor tyrosine kinases) are crucial for the signaling of many pro-inflammatory cytokines. In this regard, the JAK1-selective inhibitor filgotinib (GLPG0634, GS-6034) demonstrated clinical efficacy in patients with rheumatoid arthritis, a disease that shares some hallmarks with PsA and Crohn’s disease, making this molecule a potential therapeutic tool for the treatment of PsA.

Objectives: Filgotinib was evaluated at the dose of 30 mg/kg (per os) in a mouse model of PsA induced by overexpression of IL-23.

Methods: Overexpression of IL-23 was induced by hydrodynamic delivery of pMIG-23 enhanced Episomal Expression Vector (SBi) to male B10.RIII mice. Evolution of inflammation of hindlimbs and forepaws with fluorescent signal using ProSense™ imaging was associated with inflammation of the paws and forepaws and filgotinib reduced the target-related gene expression. High levels of IL-23 were maintained during the time-course of the study.

Results: High levels of IL-23 were maintained during the time-course of the study and were correlated with severity of finger and paw swelling. Localization of the inflammatory and target-related biomarker gene expression.

Conclusions: The role of IL-23 in the development of inflammation of hindlimbs and forepaws was demonstrated. Target engagement both in hindlimbs and colon was also demonstrated. This data support the evaluation of filgotinib in patients with PsA.

References:

THURSDAY, 15 JUNE 2017
Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design

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Background: Online technology has revolutionised the way in which people connect and share their experiences. It also brings new opportunities to engage patients in health and social care research through the use of an online research community platform (ORCP). For example, it can improve the accuracy and utility of information gathered about research priorities, and it can be used to understand behaviours and preferences. Given an increasing prevalence of long-term conditions including rheumatoid arthritis, online technology represents a novel route for participation and engagement in research.

Objectives: To explore the benefits and limitations of an ORCP through understanding how ORCP can support engagement of adults with rheumatoid arthritis.

Methods: We used a purposive sampling approach to ensure variation of key attributes amongst people with rheumatoid arthritis. A total of eight individuals used the ORCP during the pilot study. Qualitative data were collected through online focus groups, conducted as semi-structured interviews and asynchronous threaded discussions. The study was conducted in line with fieldwork guidelines, and written informed consent was obtained.

Results: The closed ORCP enabled a physically disconnected group to share their experiences of living with rheumatoid arthritis, describing the symptoms, diagnostic experience and support they received. In addition, participants shared their experiences and opinions about treatment delivery and adherence, the impact of rheumatoid arthritis, and the experiences of transitional care from paediatric to adult health services, where appropriate. Reasons and feeling about research participants and drug development processes were also discussed.

Conclusions: Our pilot study provided important accounts from people living with rheumatoid arthritis, highlighting the substantial impact of the disease on their daily lives. The ORCP removed physical contact between the researcher and participants, the absence of which may enable a richer data collection. However, it also has its limitations, primarily because the researcher is less able to establish clinical rapport. ORCPs represent a novel route of data collection, enabling researchers to immerse themselves into a community of individuals, whether they be patients, carers or professionals.

Acknowledgements: The authors would like to thank the individuals who contributed their thoughts and experiences to the pilot study.


DOI: 10.1136/annrheumdis-2017-eular.1029

THURSDAY, 15 JUNE 2017
Osteoarthritis: new horizons for treatment

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Background: The design of clinical trials for osteoarthritis is challenging; structural changes in tissues are quantitatively small and proceed very slowly. No clear guidance exists on how to optimise recruitment: KL grade is a poor recruitment criterion as centres interpret KL differently. Quantitative measures should be

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1923
better, and metric radiographic joint space width (rJSW) is related to subsequent risk of radiographic progression. Although new MRI measures provide increased responsiveness in DMOAD trials, it is unknown whether selecting for recruitment based on radiographic criteria are well suited for responsiveness of these new measures.

Objectives: (1) To determine which baseline rJSW values are associated with most subsequent progression for rJSW, MRI cartilage and bone outcomes (2) Explore baseline covariates that influence progression rates (3) Estimate the trial numbers needed using the criteria determined by steps (1) and (2).

Methods: We used all knees from the Osteoarthritis Initiative which had all 3 measures recorded (rJSW – Duyrea method; MRI cartilage thickness & bone area, Imorphics) at baseline, 1 and 2 years. We categorised knees into bins of 1mm rJSW, and assessed the 2 year changes of each bin, and characterised the distribution of rJSW in KL 0 knees. We used ANCOVA models to consider which covariates (including gender, height, weight, alignment, age, pain severity) affected 2-year slope of change, and responsiveness using SRMs. For the final optimised recruitment groups, we calculated SRMs (Cls assessed using the bootstrap method of Efron) and derived the number of patients per arm in a putative trial.

Results: 4796 knees were included (2789 females, mean age 61.45). The lower 95th percentile values for rJSW in women and men were 3.9 and 4.5mm respectively. The mean changes at 2-years for all 3 outcomes were greatest for the categories of 2–3 and 3–4mm baseline rJSW (Figure 1A) with notably little change in knees with rJSW >2mm. Of the covariates, only pain improved responsiveness. Using a total WOMAC pain criterion; ≥10.1136/annrheumdis-2017-eular.6860 DOI: Employee of: Imorphics Ltd, P. Conaghan: None declared


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Background: There are two major needs in clinical development of DMOADs: 1) Identifying a suitable population with an active and progressive disease in order to demonstrate significant improvements by an efficacious intervention; and 2) Phenotyping patients and linking them to a corresponding treatment mode-of-action (e.g. anti-inflammatory). The biochemical marker CRPM is a neoepitope of C-reactive protein (CRP) and is released from the local inflamed tissue when CRP is degraded by proteases such as matrix metalloproteinases.

Objectives: The purpose of this study was to translate the CRPM, from rheumatoid arthritis (RA), where it has been extensively tested, to OA, and to test whether it is predictive of radiographic OA.

Methods: The placebo arms of two phase III OA trial (clinicaltrial.gov: NCT00486434 and NCT00704847), a phase III RA study (the LITHE study, N=490), which included patients with active, moderate-severe RA (NCT00106535), as well as in an early RA cohort (N=92) were used. Subjects with symptomatic and radiographic knee OA: WOMAC pain ≥150mm and/or WOMAC function ≥510mm, and Kellgren-Lawrence grade (KLG) 2 or 3. KLG were scored for both knees at baseline and year 2 (Y2). Serum CRPM and hsCRP were measured at baseline. The association between serum CRPM levels and disease activity score (DAS28) and hsCRP was investigated by Spearman’s correlations. Quartile ranges of CRPM in the early RA cohort were used to define the cut-off between inflammatory OA and non-inflammatory OA. OA knees were divided into cases and controls based on a terminology proposed by the FNHI-OAI consortium (1) (knees with KLG>2 at BL were excluded, and incidence OA at Y2 was defined KLG>2). Logistic regression was used to compare cases and controls.

Results: There was a significant correlation between disease activity measures and CRPM in both RA studies. Seventy-five percent of the LITHE patients had high or very high levels of CRPM at BL, which was changed to a pattern similar to early RA after treatment. The mean CRPM levels were significantly lower in OA (8.5 [95% CI 8.3–8.8] ng/mL) compared to the RA patients (15.6 [9.5–21.6] ng/mL); however, a significant subset of OA patients (41% and 31% in SMC2301 and SMC2202) had CRPM levels ≥9ng/mL as 75% of patients with early RA. Patients with BL or Y2 CRPM levels ≥9ng/mL were more likely to develop knee OA than patients with low level of CRPM. Overall, moderate to very high levels of CRPM at BL and Y2 were predictive of incidence OA with odds ratio of 4.6 [1.2–17] and 2.5 [1.2–4.8].

Conclusions: A subset of OA patients, up to 41%, appear to have tissue inflammation comparable to that of RA, reflected by the level of CRPM. Further, high CRPM levels at BL was prognostic of incident knee OA. These data suggest that CRPM is blood-based biochemical marker for finding OA patients with an inflammatory phenotype.

References:


DOI: 10.1136/annrheumdis-2017-eular.6290
Conclusions: Radiographic outcomes from this interim analysis demonstrated that treatment with SM04690 maintained or increased JSW compared to placebo. This supports the development of SM04690 as a potential DMOAD for the treatment of knee OA. Further studies are ongoing.


A PHASE 2A, PLACEBO-CONTROLLED, RANDOMIZED STUDY OF ABT-981, AN ANTI-INTERLEUKIN-1ALPHA AND -INTERLEUKIN-1BETA DUAL VARIABLE DOMAIN IMMUNOGLOBULIN, TO TREAT EROSIIVE HAND OSTEOARTHRITIS (EHOA)

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Background: No approved OA therapies reduce pain and slow joint damage. Mouse data suggested that inhibiting IL-1α and IL-1β with ABT-981 would reduce pain and slow structural progression in EHOA.

Objectives: To test the efficacy and safety of ABT-981 in EHOA.

Methods: Subjects with HOA per ACR criteria, ≥3 inflamed IP joints (tender, swollen, or both), hand pain ≥5 (scale 0–10), and ≥1 erosive IP joint on X-ray (Verbruggen-Veys) were randomized to placebo (PBO) or ABT-981 200 mg SC every 2 wk for 26 wk. The primary outcome was AUSCAN hand pain at 16 wk. Subjects had radiographs of both hands and MRI of the index hand at baseline and 26 wk. Both radiographs (Verbruggen-Veys, GUSS™, OARSI, Kelgren-Lawrence [KL] and MRIs [HOAMRIS] with read by 2 independent central readers. A modified intent-to-treat population (ie, randomized and treated) was analyzed. Continuous efficacy endpoints were assessed using ANCOVA models with treatment and country as main factors and baseline measurements as covariates with LOCF imputation for the primary endpoint.

Results: Of 131 treated subjects (85% women; mean age 68 y), 61/67 randomized to PBO and 49/64 to ABT-981 completed the study; subject characteristics were well matched. AUSCAN pain was not significantly different vs PBO at wk 16 (P=0.39; Table 1, Figure); X-ray data and other endpoints also were not statistically different vs PBO (Table 1). ABT-981 significantly decreased hsCRP, neutrophils, IL-1α, and IL-1β. Immunogenicity had no impact on ABT-981 pharmacokinetics. Besides injection site reactions and neutropenia, ABT-981 was well tolerated and safety was similar vs PBO, with no serious infections (Table 2).

Table 1. Longitudinal associations of OP phenotype status and WOMAC knee pain changes

Table 2. Adverse AEs and serious AEs

Conclusions: Despite adequate pharmacodynamics results, targeting IL-1 may be ineffective in EHOA, as ABT-981 did not improve outcomes.

Acknowledgements: AbbVie funded the study (NCT02384538); participated in study design, data collection, analysis, and interpretation and in abstract writing, review, and approval; and funded writing support by M. Theisen of CPS.


References:
LEPTIN AND ADIPONECTIN MEDIATE THE ASSOCIATION BETWEEN BODY MASS INDEX AND HAND AND KNEE OSTEOARTHRITIS

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Background: Associations between adiposity and osteoarthritis (OA) in non-weight-bearing joints suggest that besides mechanical factors also systemic influences contribute to OA. Systemically active substances secreted by adipose tissue, including leptin and adiponectin, are hypothesized to play a role in OA.

Objectives: To examine whether leptin and adiponectin mediate the association between body mass index (BMI) and hand and knee OA.

Methods: Cross-sectional data of a population-based study were used. Participants completed questionnaires and underwent standardized physical examination of hands and knees to define OA according to clinical American College of Rheumatology criteria. Fasting serum leptin and adiponectin were measured with immunoassays. Potential mediation was investigated using the Baron and Kenny framework. Four assumptions were investigated: associations between (1) BMI and OA (pathway C), (2) BMI and adipokines (pathway A), (3) adipokines and OA (pathway B), and (4) attenuation of the total association between BMI and OA after including adipokines (pathway C').

Results: In 6462 participants (56% women, median age 56 years (range 45–65), filled. Models were adjusted for age, ethnicity and education, and stratified by sex. Confidence intervals (CIs) was estimated, only when all four assumptions were fully met. Percentage mediation with 95% confidence intervals was estimated, only when all four assumptions were fulfilled. Models were adjusted for age, ethnicity, and education, and stratified by sex.

For the association of BMI and knee OA was defined in women. These findings suggest that systemic mediators contribute to hand OA, and to a lesser extent to knee OA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1060

OP0170 LEPTIN AND ADIPONECTIN MEDIATE THE ASSOCIATION BETWEEN BODY MASS INDEX AND HAND AND KNEE OSTEOARTHRITIS

OP0193 SIGNAL INTENSITY ALTERATION WITHIN INFRAPATELLAR FAT PAD PREDICTS TOTAL KNEE ARTHROPLASTY WITHIN FOUR YEARS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: Osteoarthritis (OA) is a common joint disease that frequently affects the knee and is the leading cause of total knee arthroplasty (TKA) for knee OA. The most common reason for taking TKA is to ease pain and disability. Identification of prognostic factors associated with TKA could be a possible way to find therapeutic targets to slow disease progression and delay the time for knee replacement.

Objectives: To investigate whether infrapatellar fat pad (IPFP) signal intensity (SI) alteration predicts the occurrence of TKA in patients with knee OA over 4 years.

Methods: Participants with symptomatic knee OA were selected from the Osteoarthritis Initiative (OAI) study. Case knees (n=127) were defined as those that received TKA during 4 years follow-up visit. They were matched by gender, age and radiographic status assessed at baseline with a control knee. We used T2 weighted MR images to measure IPFP SI alteration using a newly developed algorithm in MATLAB. The measurements were assessed at OAI baseline (BL), T0 (the visit when TKA was reported), 1 year prior to T0 (T1). Conditional logistic regression was used to assess the relationship between cases and control knees and assess the risk of TKA in relation to SI alteration.

Results: Participants (n=237) were mostly female (57%), with average age of 63.7±8.5 years old and mean BMI of 29.5±4.7 kg/m2. In a multivariable analysis, standard deviation of IPFP SI [sd (IPFP)] and the ratio of high SI region volume to whole IPFP volume [Percentage (H)] measured at BL were significantly associated with TKA after adjustment for BMI, knee bending activities, self-reported knee injury and surgery history (HR: 3.5, 95% CI 1.1 to 11.4; HR: 8.9, 95% CI 1.2 to 67.2). IPFP SI alterations measured at T1 including sd (IPFP), Percentage (H) and clustering effect of high SI [Clustering factor (H)] were significantly associated with TKA (HR: 4.0, 95% CI 1.2 to 13.2; HR: 10.9, 95% CI 1.9, 63.6; HR: 1.8, 95% CI 1.1 to 2.9). All measurements including mean value of IPFP SI [Mean (IPFP)], sd (IPFP), mean value of IPFP high SI [Mean (H)], standard deviation of IPFP high SI [sd (H)], median value of IPFP high SI [Median (H)], upper quartile value of IPFP high SI [IQ (H)], Percentage (H), Clustering factor (H) were significantly associated with TKA at T0.

Conclusions: IPFP SI is an important predictor for TKA in knee OA patients. Targeting IPFP SI could be a potential way to reduce the need for future TKA.

Acknowledgements: Special thanks go to the participants who made this study possible, the OAI investigators, staff, participants and the funding of POMA study.

Disclosure of Interest: None declared

THURSDAY, 15 JUNE 2017

Cellular drivers of inflammation in rheumatic disease

OP0172 EXPANDED T-CELL CLONES PRESENT IN SYNOVIAL FLUID AT ONSET OF RHEUMATOID ARTHRITIS ARE ALREADY PRESENT IN THE SYNOVIUM IN THE SEROPOSITIVE “AT RISK” STAGE

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Background: T-cells are thought to be key players in the initiation and progression for the association of BMI and knee OA was defined in women. These findings suggest that systemic mediators contribute to hand OA, and to a lesser extent to knee OA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3394

OP0171 SIGNAL INTENSITY ALTERATION WITHIN INFRAPATELLAR FAT PAD PREDICTS TOTAL KNEE ARTHROPLASTY WITHIN FOUR YEARS: DATA FROM THE OSTEOARTHRITIS INITIATIVE
of rheumatoid arthritis (RA). Earlier we showed that already at the seropositive ‘at risk’ stage uninfamed synovial tissue contains T-cell infiltrates. In another study we showed that inflamed synovium selectively harbours expanded T-cell clones that are hardly present in paired blood samples.

**Objectives:** Following up on these observations, we longitudinally investigated whether the same expanded T-cell clones found in the inflamed synovial tissue at onset of RA are already present in the synovium in the seropositive ‘at risk’ stage.

**Methods:** Fifty-five individuals without arthritis but seropositive for IgM rheumatoid factor and/or anti-citrullinated protein antibody (ACPA) were prospectively followed. In five aCCP+ individuals synovial biopsies and paired blood samples at inclusion (‘at risk’ stage) and after development of RA (ACR2010 criteria; mean time to arthritis 27 months (range 11.7-47.3)) were available for analysis. T-cell clones were identified by their unique TCRβ sequence using RNA-based next generation sequencing. For each sample, 3570 TCRβ sequences were analysed. Clones with a frequency of >0.5% were arbitrarily considered as highly expanded clones (HECs). ANOVA and t-test were used for statistical analysis.

**Results:** T-cell repertoires in ‘at risk’ and RA synovium were similar (mean ± SD) number of clones 488±70 vs 567±204 respectively, p=0.46). Number of HECs of aCCP+ individuals at inclusion (‘at risk’ stage) and after development of RA (ACR2010 criteria; mean time to arthritis 27 months (range 11.7-47.3)) were available for analysis. T-cell clones were identified by their unique TCRβ sequences using RNA-based next generation sequencing. For each sample, 3570 TCRβ sequences were analysed. Clones with a frequency of >0.5% were arbitrarily considered as highly expanded clones (HECs). ANOVA and t-test were used for statistical analysis.

**Conclusions:** Many T-cell clones found in early RA synovial tissue are already present in the pre-clinical ‘at risk’ phase. The resemblance in TCR repertoires indicates that the process leading to disease – at least at the T-cell level – constitutes a smooth development. These clones, being already present in the very early stage of this disease and persisting as dominant clones during contraction of active arthritis, form attractive candidates for further characterization.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6318

**OP0174 NEW PROTEIN ARRAY TECHNOLOGY IDENTIFIES RITUXIMAB TREATED NON RESPONDER RHEUMATOID ARTHRITIS PATIENTS ARE GENERATING A NEW AUTOANTIBODY REPertoire**

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**Objectives:** Rituximab (RTX) has shown clinical efficacy but up to 40% of RTX treated rheumatoid arthritis (RA) patients are poor responders (Ann-Rheum-Dis. 2005 Feb;64(2):246-52) and the commonly used RA biomarkers (RF/ACPA) are poor predictors for therapy response. In this study the autoantibody repertoire analysed on protein macorarrays from RA patients under RTX treatment was correlated to clinical DAS28 response.

**Methods:** Screening of RA sera was conducted on 37.830 unique human proteins correlated to clinical DAS28 response. The autoantibody repertoire in all patients or associated with response. However, RTX reduced the repertoire of autotagnostin-in-silico and by hierarchical clustering.

**Results:** In the cohort of 26 patients 1292 different autoantigens (IgD, IgA, IgG) were detected. Using protein array we investigated clusters of autoantigenic responses that disappeared or developed during RTX treatment of RA patients. RA autoantigenic patterns before and 6 months after RTX were patient-specific and no relevant autoantigenic cluster was found that was shared between patients or associated with response. However, RTX reduced the repertoire of autoantibodies after 24 weeks of treatment in the tested RA patient cohort on average by 60%. RA patients which do not respond are generating on average 63% new autoantibodies. In good responders to RTX only 5.5% (+/-3%) new autoantibodies can be detected. The IgA and IgG autoantibody repertoire. The IgA and IgG autoantibody repertoire. The serum after 24 weeks of RTX treatment is reduced (IgA: 41%, IgG: 31%) in good responders whereas it is increased (IgA: 1.3%, IgG: 24%) in non responders to RTX.

**Conclusions:** After 6 month of RTX treatment the autoantibody repertoire in all good responding RA patients is reduced and non responders to RTX change their autoantibody repertoire directed against new but patient specific antigens. The fast rebuilding of functional B cells is only detected in non-responders to rituximab.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6978
Characterization of Novel Stromal-Derived Autoantigens Recognized by Ra Synovial Monoclonal Antibodies

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Background: We previously showed that up to 40% of RA synovial recombinant monoclonal antibodies (Ra-mAbs) generated from germinal center-like structure (GC-LS+) RA synovium recognize citrullinated antigens contained in neutrophils extracellular traps (NET) (1). The cellular source of other potential autoantigens targeted by the majority of locally differentiated B cells remains undefined. Recently, RA-fibroblast-like synovocytes (RA-FLS) have been implicated in the release of citrullinated antigens (2, 3). However, whether these cells are targeted by Ra-mAbs is still to be determined.

Objectives: Here, we aimed to define the Ra-mAbs immunoreactivity towards i) RA-FLS and ii) identify potential stromal-derived autoantigens.

Methods: 67 Ra-mAbs were generated from single CD19+ B cells FACs-sorted from fresh synovial cell suspensions following IgV H+VL genes cloning (1). Ra-mAbs were tested by means of i) cell-based immunofluorescence assays with FLS of RA patients and controls (sarcoid arthritis (OA)-FLS and RA-dermal fibroblast (RA-DF)), ii) co-localization with stromal specific markers and iii) immunoenzymatic tests with co-localizing antigens. Control rmAbs were also used (Sjögren’s syndrome/healthy donors).

Results: Immunofluorescence on RA-FLS demonstrated reactivity of 21% of Ra-mAbs (14/67 rmAbs) towards cytoplasmic components of FLS. Only 4 mAbs out of 14 were binding both FLS and NET components. For some Ra-mAbs this reactivity was not specific to RA-FLS since it was also observed for OA-FLS and RA-DF. Interestingly, co-localization was observed with calreticulin (CRT) which in its citrullinated (cit-CRT) form has been previously shown to recognize the RA “shared epitope” HLA domain sequence (3). When tested in ELISA for native and cit-CRT with 4 out of 8 rmAbs displaying increased immunoreactivity towards cit-CRT. Controls rmAbs showed reactivity to either FLS or CRT. Preliminary data suggest that RA patient serum preferentially recognize the lectin-like N-terminal domain of CRT (4).

Conclusions: Here, we provide new evidence that a subset of locally differentiated B cells within RA synovial GC-LS can react towards RA-FLS derived antigens. Preliminary data suggest that part of this reactivity is directed towards CRT. Identification of immunodominant epitopes within CRT is under investigations.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3870

Paracaspase MALT1 Plays a Central Role in the Pathogenesis of Rheumatoid Arthritis

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Background: One of the hallmarks of many inflammatory arthritides is their strong linkage with MHC-signalling, which is mirrored by the marked role for adaptive immunity. Accordingly, rheumatoid arthritis (RA) is characterized by the activation of auto-reactive T-cells and the development of auto-antibodies. T-cells may additionally respond to non-TCR mediated signals, which are essential in developing effector functions. Pathways leading to the modulation of both innate and adaptive signals are therefore of marked interest to study in arthritic diseases.

Objectives: The paracaspase MALT1 is a key player in the activation and proliferation of immune and non-immune cells. These cells include the lymphoid, myeloid and mast cells, indicating MALT1’s crucial role in both innate and adaptive signalling (1). Therefore, MALT1 is regarded a promising target for the treatment of autoimmune diseases and defining its role in the pathogenesis of inflammatory arthritis is a critical first step.

Methods: To unravel MALT1’s role in inflammatory arthritis, we initially assessed MALT1-activation in mice that were challenged with collagen-induced arthritis (CIA), the prototype model for antigen-induced RA. We then addressed the role of MALT1 in the pathogenesis of inflammatory arthritis by challenging MALT1-deficient mice to distinct models of arthritis (CIA and CAIA) or by backcrossing MALT1-deficient mice to TNFÎ²-/- mice, representing a Spâ-like model. Additionally, CIA was induced in CD4-specific MALT1-deficient mice to determine the importance of MALT1 in T-cells.

Results: We provide evidence that MALT1 plays a crucial role in the pathogenesis of RA as MALT1-deficient mice were completely protected against CIA. This complete protection was additionally observed in CD4-specific MALT1-deficient mice, indicating that the selective ablation of MALT1 in CD4-positive cells is sufficient for the observed resistance against CIA. CAIA on the other hand, which is a T- and B-cell independent model of RA, did not depend on the presence of MALT1, since both MALT1-/- and MALT1-/- mice showed comparable symptoms of RA. Interestingly, TNFÎ²-/- mice that were deficient for MALT1 also showed a reduced arthritis and ileitis phenotype, although TNF-concentration in the serum of these mice was higher compared to MALT1-/-xTNFÎ²-/- mice.

Conclusions: Overall, our data highlight that MALT1 plays a crucial role in the pathogenesis of inflammatory arthritides and represents an interesting candidate to target therapeutically.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5904

N-Glycosylation Sites in the Variable Domain of B Cell Receptors Specific for Citrullinated Antigens

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Background: Recent structural analysis of anti citrullinated protein antibodies (ACPA) in serum and synovial fluid of patients with rheumatoid arthritis (RA) revealed that the vast majority (~90%) of secreted ACPA IgM molecules carry N-glycans in the variable (Fab) domain. This remarkable degree of Fab-glycosylation is absent from ACPA-depleted control IgGs and from autoantibodies in other tissue extracts. So far, it is unclear why ACPA carry this feature and which biological effects these glycans mediate in the context of RA. Of note, however, N-glycosylation requires a specific amino acid consensus sequence in the protein backbone, which is very rare in germline-encoded variable region genes.

Objectives: To study the B cell receptor (BCR) repertoire of ACPA-expressing B cells to determine the frequency, origin and localisation of N-glycosylation sites in ACPA Fab domains.

Methods: Citrullinated antigen-specific and non citrulline-reactive control B cells were identified in peripheral blood of ACPA-positive RA patients by antigen-specific tetramer staining and isolated by fluorescence activated cell sorting. Cells were either sorted in pools and directly lysed, or sorted as single cells and cultured for two weeks followed by the detection of ACPA-positive culture wells by ELISA. Full-length immunoglobulin (Ig) rearrangements were identified by anchoring reverse transcription of Ig sequences, amplification by nested PCR and either next generation sequencing (NGS, PacBio platform) or, for single cell transcripts, Sanger sequencing (scSeq). Sequence reads were analysed using IMGT V-QUEST tools.

Results: The mean number of nucleotide mutations in heavy chains (HC) of IgG BCRs derived from ACPA-expressing B cells was high (33 in NGS, 48 in scSeq samples; similarity to germline: 88% in NGS, 84% in scSeq). NGS identified 12 unique IgG clones derived from 4 donors, of which 10 (83%) had at least one N-glycosylation site in the HC or light chain (LC). scSeq identified 86 unique IgG clones derived from 6 donors, of which 68 (79%) had N-glycosylation sites. For 57/86 IgG clones, we could determine the combination of HC and LC sequences. In these, only 7 (12%) clones had no sites, while 19 (33%) had one, 23 (41%) had two, 5 (9%) had three and 3 (4%) clones had four sites. 57 sites were found in the HC and 34 in the LC. All N-glycosylation sites were created by somatic mutations and not encoded in the germline sequence. Several sites were located in antigen-engaging regions. No correlation was found between the number of N-glycosylation sites and the number of somatic mutations.

Conclusions: We demonstrate that B cell surface-expressed ACPA-IgG molecules display a remarkable frequency of N-glycosylation sites in the Fab domain, all of which are generated by somatic mutation. This could indicate that ACPA-expressing B cells acquire a selective survival advantage by introducing N-glycosylation consensus sequences in the Fab domain, a process that is likely to occur under the influence of T cell help and that could facilitate the break of tolerance to citrullinated antigens.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5904

Fibroblast Priming is Common to Many Sites, and Psoriatic Skin Fibroblasts May Acquire Inflammatory Memory

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Background: Rheumatoid arthritis (RA) is a common chronic inflammatory
BRAFV600E PROMOTES MYELOID SKEWING IN PHARMACOLOGICAL CHARACTERIZATION OF THE ADAMTS-5 DELETION OF THE PROSTAGLANDIN D2 RECEPTOR DP1

Disclosure of Interest: None declared

RESULTS:

we isolated HSPC from human cord blood and transduced them at two different levels (50% and 20%) with lentiviral vectors that ubiquitously express BRAFV600E, BRAFWT or GFP.

METHODS:

We wished to assess whether fibroblasts from sites other than the joint, skin, lung, tonsil, bone marrow and gum removed and the cells were washed free of stimulus. Cells were rested for 24h before once again being washed and stimulated with 10ng/ml TNFα for a further 24h. The conditioned medium was removed and secreted mediators compared between first and second response to stimulus. Transcription and intracellular signalling at time points within each challenge were also determined.

RESULTS:

Priming occurs in fibroblasts from a variety of anatomical sites with diverse functions. Its prevalence is a shared phenomenon, but the variation between sites suggests a specific role required in some tissues and not others. We have shown that inflammatory memory in the form of IL6 production, fibroblasts from the skin of psoriasis (Ps) patients mounted a primed response that was significantly augmented compared to their first response to TNFα, and signficantly higher than the second response of healthy skin. This augmented response matches that of FLS, as IL6 but not IL8 was increased. This pattern was also matched both for fibroblasts from periodontitis.

In conclusion:

3.1 Priming fails to occur in fibroblasts from other sites, providing support to the hypothesis that this phenomenon is a site-specific feature.

4.126 Thursday, 15 June 2017

Joint health & joint damage: a tale of three tissues —

Disclosure of Interest: None declared


OP0179

BRAFV600E PROMOTES MYELOID SKEWING IN MULTISYSTEMIC LANGERHANS CELL HISTIOCYTOSIS HUMANIZED MOUSE MODELS

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Background: Multisystem Langerhans cell histiocytosis (mLCH) is an aggressive disease characterized by the accumulation of mononuclear phagocytes with immunohistochemical features of dendritic cell (histiocytes). Histiocytes infiltrate multiple tissues, including lung and spleen, and produce high levels of proinflammatory cytokines/chemokines, leading to organ dysfunction. In patients, around 10% of cells in lesions carries an oncogenic mutation in the MAPK pathway, mostly BRAFV600E (70% of cases). BRAFV600E can be detected also in non-malignant reactive histiocytes in patients, whereas only a fraction of them carries a mutation in B cells and none in T cells.

Objectives: To study the role of BRAFV600E in the pathogenesis of mLCH, we set up a humanized mouse model of mLCH based on the transplantation into immunodeficient mice (NSG) of human HSPC expressing BRAFV600E, BRAFWT or GFP.

Methods:

In this report we describe the in vitro and in vivo characterization of the small molecule GLPG1972, an inhibitor of ADAMTS-5. GLPG1972 anti-catabolic activity was evaluated in murine and human cartilage explants and DMOAD activity was investigated in the destabilization of the medial meniscus (DMM) model. In conclusion:

Background: Degradation of articular cartilage and alterations of the underlying subchondral bone are hallmarks of osteoarthritis (OA). A disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5) is a key aggercan-cleaving enzyme involved in this pathogenic process from the earliest stages of cartilage degradation and as such, is an attractive drug target for the development of a disease-modifying OA drug (DMOAD). Objectives: In this report we describe the in vitro and in vivo characterization of the small molecule GLPG1972, an inhibitor of ADAMTS-5. GLPG1972 anti-catabolic activity was evaluated in murine and human cartilage explants and DMOAD activity was investigated in the destabilization of the medial meniscus (DMM) model.

Methods: The ADAMTS-5 biochemical assay is based on the cleavage of a fluorescent substrate by recombinant ADAMTS-5. Mouse femoral head cartilage explants were stimulated by interleukin-1α (IL-1α) for 3 days and GAG release quantified. Human articular cartilage explants were stimulated with IL-1α for 12 or 19 days and the NITEGE epitope quantified using the AGNx1 assay. Unilateral OA was induced in C57BL6 mice by DMM. Mice were treated with vehicle or GLPG1972 at 30, 60 or 120 mg/kg, b.i.d. for 8 weeks. Medial femoral joint sections were scored by an evaluator blinded to treatment.

RESULTS:

GLPG1972 showed potent inhibition of human ADAMTS-5 (IC50=20 nM). In murine cartilage explants, GLPG1972 demonstrated DMOAD activity, as shown by significant reduction of catabolic activity, collagen breakdown and aggrecanase activity.

Conclusions: GLPG1972 is an orally bioavailable, potent and selective ADAMTS-5 inhibitor showing significant anti-catabolic activity in cartilage explants. In the DMM model, treatment with GLPG1972 resulted in significant protective effects on both cartilage and subchondral bone pathology. Taken together these results provide support to progress GLPG1972 into the clinic as an oral treatment for OA.

References:

4) GLPG1972 demonstrated DMOAD activity, as shown by significant reduction of catabolic activity, collagen breakdown and aggrecanase activity.
5) Disclosure of Interest: None declared


OP0181

DELETION OF THE PROSTAGLANDIN D2 RECEPTOR DP1 EXACERBATES AGING-ASSOCIATED AND INSTABILITY-INDUCED OSTEOARTHRITIS

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Background: The D prostaglandin receptor 1 (DP1), a receptor for prostaglandin D2 (PGD2) plays important roles in inflammation and cartilage metabolism. However, its role in the pathogenesis of osteoarthritis (OA) remains unknown.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5179
CONVERGENCE OF JOINT REPAIR AND PAIN PATHWAYS VIA CORDYCEPIN, A NOVEL COMPOUND, REDUCES KNEE JOINT DAMAGE IN RATS

Objectives: We undertook this study to explore the roles of DP1 in the development of OA and to evaluate the efficacy of a DP1 selective agonist in the treatment of OA.

Methods: We compared the development of aging-associated OA and destabili- zation of the medial meniscus (DMM)-induced OA in DP1-deficient (DP1-/-) and wild-type (WT) mice. The progression of OA was assessed by histology, immunohistochemistry, and microcomputed tomography (micro-CT). Cartilage explants from DP1-/- and WT mice were treated with interleukin-1α (IL-1α) ex vivo, to evaluate proteoglycan degradation. The effect of intra-peritoneal administration of the DP1 selective agonist BW245C on OA progression was evaluated in WT mice.

Results: Compared to WT mice, DP1-/- mice had exacerbated cartilage degradation in both models of OA and this was associated with increased expression of MMP-13, and ADAMTS-5. In addition, DP1-/- mice demonstrated enhanced subchondral bone changes. Cartilage explants from DP1-/- mice showed enhanced proteoglycan degradation following treatment with IL-1α. Intraportal injection of BW245C attenuated the severity of DMM-induced cartilage degeneration and bony changes in WT mice.

Conclusions: These findings indicate a critical role for DP1 signaling in OA pathogenesis. Modulation of DP1 functions may constitute a potential therapeutic target for the development of novel OA treatments.

Acknowledgements: This work was supported by the Canadian Institutes of Health Research (CIHR) Grant MOP-130929, the Arthritis Society, and the Fonds de la Recherche Du Centre de Recherche Du Centre Hospitalier de l’Université de Montréal (CRCHUM).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6132

OP0182 CONVERGENCE OF JOINT REPAIR AND PAIN PATHWAYS VIA NERVE GROWTH FACTOR AND P75 EXPRESSING MESENCHYAL STEM CELLS—A NOVEL EXPLANATION FOR OSTEOARTHRITIS PROGRESSION WITH ANTI-NGF IN OSTEOARTHRITIS

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Background: Nerve growth factor (NGF) is a key regulator of pain and anti-NGF therapy reduces osteoarthritis (OA) associated pain. However, anti-NGF therapy is associated with rapidly progressive OA (RPOA) [1]. In hip OA there is a 5-fold increase in mesenchymal stem cells (MSCs) from MRI bone marrow (BM) lesions, areas associated with OA progression [2], MSCS in such lesions are uniformly positive for the NGF receptor, p75, which is also linked to chemotaxis and proliferation in other stromal cell compartments [3].

Objectives: Evaluate anti-NGF treatment in monoiodoacetate (MIA) induced OA and test whether NGF influences human BM-MSC function.

Methods: Human tibial plateau (TP) bone was isolated from patients undergoing total knee replacement. OA was induced in male Sprague Dawley rats by intra-articular injection of mono-sodium iodoacetate (MIA; 1mg/50μl) on day 0. Cordycepin was administered orally (2mg/rat mixed in 1g of wet mash) every other day for 2 weeks.

Results: The MIA rodent model of OA pain exhibited significant pain behaviour, synovial inflammation and angiogenesis, cartilage damage, osteophyte formation and subchondral bone changes, compared with non-arthritic controls. A two week pre-emptive and therapeutic treatment with cordycepin reduced MIA-induced pain behaviour and synovial changes (inflammation and angiogenesis). Pre-emptive cordycepin treatment reduced cartilage damage and the level of ADAMTS-5 and MMP13 from the chondrocytes. Pre-emptive and therapeutic cordycepin treatment reduced the number of channels crossing the OCJ and TRAP positive osteoclasts in the subchondral bone, but had no effect on numbers of osteophytes. Therapeutic cordycepin treatment did not alter cartilage damage score or the level of ADAMTS-5 and MMP13 positive chondrocytes.

Conclusions: Our data show that the analgesic effects of orally administered cordycepin in a pre-emptive and therapeutic protocol are associated with synovial changes (inflammation and angiogenesis) and bone remodelling. Administration of cordycepin before the onset of MIA-induced OA reduced cartilage damage and had a chondroprotective effect. Whereas therapeutically administered cordycepin did not alter cartilage damage. Further studies will investigate whether cordycepin mediated reduction in MIA-induced pathology and pain behaviour is as a result of its direct action on polyadenylation inhibition. Polyadenylation inhibitors could therefore be a novel class of drugs for treating OA.

Disclosure of Interest: None declared

OP0183 CORDYCEPIN, A NOVEL COMPOUND, REDUCES KNEE JOINT PATHOLOGY AND PAIN IN THE MIA RAT MODEL OF OSTEOARTHRITIS

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Background: Cordycepin (3’ deoxyadenosine) is a popular traditional medicine in Asia, taken for conditions associated with ageing. Osteoarthritis (OA) is a common cause of pain and disability in the ageing population. Inflammation is a key component of osteoarthritis pain. Cordycepin is thought to act by inhibiting polyadenylation, the last step of mRNA synthesis, and can potentially have increased therapeutic benefit in OA (anti-inflammatory and analgesic) with fewer side effects than currently available therapies.

Objectives: The aim of this study was to determine whether cordycepin treatment alters osteoarthritic pain and pathology, and to decipher the mechanisms of action by which cordycepin exerts any potential beneficial actions.

Methods: OA was induced in male Sprague Dawley rats by intra-articular injection of mono-sodium iodoacetate (MIA; 1mg/50μl) on day 0. Cordycepin was administered orally (2mg/rat mixed in 1g of wet mash) every other day for 2 weeks (pre-emptive study: day 0, day 2 and day 14 to day 28; Pain behaviour was measured as hind-limb weight-bearing asymmetry and mechanical paw withdrawal thresholds. Joint tissues were collected at days 14 and 28. Joint changes were quantified using histology and immunohistochemistry techniques. Synovial inflammation was quantified as extent of CD68 positive macrophage and cellular infiltration. Synovial angiogenesis was measured as endothelial cells positive for proliferating cell nuclear antigen (PCNA). Safranin-O staining was used to score cartilage damage and bone changes (osteophytes and channels crossing the osteochondral junction [OCJ]). Tartrate-resistant acid phosphatase (TRAP) positive osteoclasts and ADAMTS-5 and MMP13 positive chondrocytes were quantified as additional markers to detect bone and cartilage changes.

Results: The MIA rat model of OA pain exhibited significant pain behaviour, synovial inflammation and angiogenesis, cartilage damage, osteophyte formation and subchondral bone changes, compared with non-arthritic controls. A two week pre-emptive and therapeutic treatment with cordycepin reduced MIA-induced pain behaviour and synovial changes (inflammation and angiogenesis). Pre-emptive cordycepin treatment reduced cartilage damage and the level of ADAMTS-5 and MMP13 from the chondrocytes. Pre-emptive and therapeutic cordycepin treatment reduced the number of channels crossing the OCJ and TRAP positive osteoclasts in the subchondral bone, but had no effect on numbers of osteophytes. Therapeutic cordycepin treatment did not alter cartilage damage score or the level of ADAMTS-5 and MMP13 positive chondrocytes.

Conclusions: Our data show that the analgesic effects of orally administered cordycepin in a pre-emptive and therapeutic protocol are associated with synovial changes (inflammation and angiogenesis) and bone remodelling. Administration of cordycepin before the onset of MIA-induced OA reduced cartilage damage and had a chondroprotective effect. Whereas therapeutically administered cordycepin did not alter cartilage damage. Further studies will investigate whether cordycepin mediated reduction in MIA-induced pathology and pain behaviour is as a result of its direct action on polyadenylation inhibition. Polyadenylation inhibitors could therefore be a novel class of drugs for treating OA.

Disclosure of Interest: None declared

Thursday, 15 June 2017

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Background: General synovitis score (GSS) has been developed by Krenn et al. in order to discriminate inflammatory arthritis (IA) and non-inflammatory arthritis (NIA) (1). This score assesses 3 major components of synovitis: lining layer hyperplasia, activation of resident cells (stroma) and inflammatory infiltrate. All components are graded semi-quantitatively from 0 to 3 and the total score is on 9. High-grade synovitis is highly associated with IA and is defined by a score above 5 with a sensitivity of 61.7% and a specificity of 96.1%. As immunohistochemistry (IHC) is frequently used to better characterize synovitis, we propose to create a new IMmunologic SYnovitis SCore (IMSYC) adding 5 additional components: the GSS: CD68, CD3, CD20, CD163 and Ki67 immunostaining.

Objectives: Our work aimed to evaluate the diagnostic performance of this new score including IHC, to define the best cut-off for inflammatory arthritis recognition, and to compare its diagnostic performance and the one of GSS.

Methods: 53 synovial samples from patients were obtained during surgery (arthroplasty or synovecctomy). All patients gave written consent prior surgery. Samples were cut and Hematoxylin and eosin stained. CD68, CD3, CD20, CD163 and Ki67 immunostaining were performed. GSS was assessed for each slide and semi-quantitative 4 score scales (0-3) were given for each immunostaining, in a blind manner. The score is calculated on 24 (GSS 0–9 points, and 0–3 score for each of the 5 immunostaining). A representative amount of slides was read by 2 observers with a good interobserver variability (spearman correlation coefficient of 0.95, p<0.0005). They defined a consensus and revised the data.

Results: 53 patients were included. 25 were females (47.2%), mean age was 62.1 years [Standard deviation (SD) 13.2 years], 36 had inflammatory arthritis reaped as follows: 28 Rheumatoid arthritis (RA), 5 Psoriatic arthritis, 3 Undifferentiated arthritis. “Non inflammatory” arthritis group included 10 patients with Osteoarthritis and 7 with ligaments or meniscus injuries. Mean GSS was significantly higher in the IA group 5.70 [SD 0.32] vs.3.51 [SD 0.35]; p<0.001. Mean IMSYC was significantly superior in the IA group 14.94 [SD 8.77] vs. 8.50 [SD 6.39]; p<0.001. In univariate analysis by logistic regression, GSS (Odd Ratio (OR) 2.27; p<0.001), CD3 (OR 4.3; p=0.002), CD68 (OR 4.5; p=0.002), Ki67 (OR 11.8; p<0.001), and CD31 scores (OR 6.5; p=0.001) were significantly associated with IA, however CD20 score was not (OR 0.9; p=0.34). ROC curve analysis determined the score of 10.5 out of 24 as the best cut off for discrimination between IA and non-IA with a sensitivity of 74.3% and specificity of 100%. The area under ROC curves was statistically superior with IMSYC (0.93) compared to GSS (0.81) (p=0.05).

Conclusions: We hereby propose a new synovitis score including IHC. This score has a better sensitivity and specificity than the global synovitis score discriminative between IA versus non-IA. Moreover, this score accurately describes any synovial membrane immunophenotype and could therefore give a basis for tissue driven therapies in rheumatic diseases, especially in RA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2547

OP0186 TENOFOVIR, A NUCLEOSIDE ANALOG REVERSE TRANSCRIPTASE INHIBITOR FOR TREATMENT OF HIV, PROMOTES OSTEOCLAST DIFFERENTIATION AND BONE LOST IN A MECHANISM DEPENDING ON ATP RELEASE AND ADENOSINE, AND DIPYRIDAMOLE MAY BE A USEFUL TREATMENT TO REVERT THE EFFECTS

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Background: HIV infection devastates the immune system but also affects other tissues and organs. Bone alterations have been observed in HIV disease for nearly two decades, in particular a higher risk of low bone mineral density (BMD) and fragility fractures. Treatment with Tenofovir alone or as part of HAART, leads to changes in bone catabolism markers and significant reductions in BMD in children and young adults. Tenofovir is taken up by cells and phosphorylated in cells inhibits HIV reverse transcriptase by mimicking AMP. We have recently found that Tenofovir inhibits BMD by blocking osteoclastic differentiation and bone loss in murine models. Inhibition of osteoclast formation via adenosine A2A receptor stimulation or increasing local adenosine concentration stimulates new bone formation as well as rhBMP-2.

Objectives: As adenosine and ATP are key regulators of bone homeostasis, we determined whether Tenofovir directly affects bone by an adenosine- or ATP-dependent mechanism and if treatment with Dipyridamole, an agent that decreases extracellular adenosine by blocking cellular adenosine uptake, may be a useful treatment to counteract Tenofovir effects.

Methods: M-CSF/RANKL-induced osteoclast (OC) was studied in primary murine bone marrow cultures as the number of TRAP-positive cells after challenge with Tenofovir (1nM-100uM) alone or in combination with Dipyridamole (1nM-100uM). OC markers were measured by RT-PCR. Pannexin-1 and Connexin-43 expression were determined by Western-blot on bone marrow samples. Tenofovir 75mg/kg/day alone or in combination with Dipyridamole 1mg/kg/day for 4 weeks. Double labelling of bone with calcein/Alizarin Red to analyzed bone formation was performed and long bones were prepared for microCT and histology.

Results: Tenofovir produced a dose-dependent increase in OC differentia-
tion (EC50=44.95mM) that was reversed by Dipyridamole (IC50=0.3μM). When Pannexin-1 and Connexin-43 were absent, Tenofor did not increase OC number. Tenofor increases Cathepsin K and NFATc1 mRNA levels during OC differentiation, and the effect was reversed by Dipyridamole. Tenofor reduced bone formation in vivo (192±5m bone apposition vs 35±4μm untreated p<0.05) and this effect was reversed in the presence of Dipyridamole (30±5μm vs 0.05μm vs Tenofor alone). microCT revealed decreased BMD and altered trabecular bone in Tenofor-treated mice, treated in the presence of Dipyridamole. TRAP-staining showed increased OC in vivo in Tenofor-treated mice (217±1 vs 16±1 OC/hip in untreated, p<0.005) that was reversed with Dipyridamole. Similar results were obtained for Cathepsin K.

Conclusions: These results indicate that Tenofor enhances OC differentiation and inhibits osteoblast differentiation by an adenosine-dependent mechanism and suggests that treatment with agents that increase local adenohamine concentrations, like Dipyridamole, might prevent bone loss following Tenofor treatment.

Disclosure of Interest: F. Conesa: None declared, P. Llamas: None declared, T. Wilder: None declared, P. Atencio: None declared, A. Cabello: None declared, M. Görgolas: None declared, B. Cronstein: None declared, R. Largo: None declared, G. Herrero-Beaumont: None declared, A. Mediero Grant/research support from: Instituto de Salud Carlos III, Fondos FEDER

DOI: 10.1136/annrheumdis-2017-eular.3207

OP0187 TRANSGENIC DISRUPTION OF GLUCOCORTICOID-SIGNALING IN MATURE OSTEOBLASTS AND OSTEOCYTES ATTENUATES STRUCTURAL BONE DAMAGE IN A LONG-TERM MURINE K/BXN SERUM-INDUCED ARTHRITIS MODEL

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Background: The role of endogenous glucocorticoids (GC) in bone metabolism in chronic inflammatory arthritis remains unclear. We have previously shown that disruption of osteoblastic GC-signaling in a murine arthritis model.

Methods: Intracellular GC-signalizing in osteoblasts was disrupted by transgenic overexpression of 11beta-hydroxysteroid dehydrogenase type 2 (11HSD type 2) under the control of a type 1 collagen promoter. Arthritis was induced in 5-week old male transgenic (tg) mice and their wild-type (WT) littermates. In order to maintain a chronically active arthritis, mice were boosted on day 14 and 28 by subcutaneous injection of K/BxN serum, controls (CTR) received PBS, respectively. Severity of arthritis was assessed daily by clinical scoring and ankle size measurements until the endpoint (day 42). Ankle joints were assessed by a histopathologic score and microfocal computed tomography (micro-CT). Systemic effects of inflammation on bone metabolism were quantified by histomorphometry and micro-CT of the tibia.

Results: Acute Arthritis developed in both tg and WT mice and remained active over the period of 42 days with a reduced, yet non-significant, severity in tg compared to WT mice. Histological indices of inflammation, cartilage damage and especially bone erosion, additionally assessed by micro-CT, tended to be overall reduced in tg mice, yet not reaching a level of significance. Bone volume and bone turnover did not differ between tg and WT arthritic mice.

Conclusions: The modulating effect of disrupted GC-signalizing in osteoblasts in serum-induced autoimmune-arthritis prevails in a chronic inflammatory setting, leading to less severe local inflammation and bone destruction. This supports the important role of endogenous GCs for an intact bone metabolism in inflammatory bone disease.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5806

THURSDAY, 15 JUNE 2017
Treat-to-target in axSpA: reality or utopy? }

OP0188 DEFINING CLINICALLY IMPORTANT WORSENING BASED ON ASDAS-CRP FOR AXIAL SPONDYLOARTHROPSIS: A DATA-BASED CONSENSUS BY THE ASSESSMENT IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS)

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Background: Disease flares are increasingly used as outcomes in axial spondyloarthritis (axSpA) trials or observational studies.

Objectives: The objective of this initiative was to define a cutoff for the ASDAS score that best defines the concept of “worsening in axSpA”, to be used in the context of clinical trials and longitudinal observational studies.

Methods: Various steps were followed between 2014 and 2017. (a) Initial expert opinion within the steering group to define the scope of the project; (b) systematic literature review to collect cutoffs used for worsening in published studies; (c) vignette-exercise among ASAS members: a theoretical ‘paper’ patient-vignette, in whom an initial and a final value of an outcome was provided, was judged by the physicians on whether or not the patient had worsened (definingphy-worsening) (ref); (d) real-life multicenter international study: data necessary to calculate different outcomes were collected from real patients at 2 consecutive visits (spaced 7 days to 6 months); external standard was defined as a patient’s report that he/she had worsened and he/she felt there was a need for treatment intensification. (e) Testing of different changes in the outcomes against both external standards for worsening (phy-worsening and pt-worsening) followed by a consensus and voting procedure among ASAS members in January 2017.

Results: (a) There was consensus about worsening being an absolute change between 2 time-points (without defining time between the 2 time-points) and about exploring cutoffs for 3 outcomes: ASDAS-CRP, BASDAI and pain. (b) The literature review had yielded 27 different cutoffs in 38 studies indicating important heterogeneity (c) The vignette-exercise yielded 12 preliminary definitions for worsening to be tested (as previously reported); (d) In the prospective study the sensitivity and specificity of each cutoff was tested against pt-worsening and judged by the ASAS-community. (e) No consensus was reached for a BASDAI-based definition due to limited performance of all cut-offs, and it was decided to not define a value for a pain-based definition for worsening. Based on aggregated data (Table), a consensus was reached among the ASAS-members to define worsening as a deterioration in ASDAS of at least 0.9 points. While this cutoff led to only moderate sensitivity when tested against pt-worsening, the overall balance of sensitivity and specificity as well as the overall face validity of this cut-off value for ASDAS was deemed most acceptable.

Table: Sensitivity and specificity of different ASDAS cutoffs to define worsening, compared to external standard and vignette-exercise.

<table>
<thead>
<tr>
<th>Cutoff values for change in ASDAS</th>
<th>Vignette exercise study (N=1100 patients)</th>
<th>Prospective real-life study (N=1105 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASDAS- CPR</td>
<td>Against the external standard vs vignette</td>
<td>Against the external standard vs vignette</td>
</tr>
<tr>
<td>ASDAS&lt;0.9</td>
<td>Sensitivity (75%)</td>
<td>Sensitivity (75%)</td>
</tr>
<tr>
<td>ASDAS&lt;1.2</td>
<td>Specificity (75%)</td>
<td>Specificity (75%)</td>
</tr>
<tr>
<td>ASDAS&lt;1.5</td>
<td>Sensitivity (75%)</td>
<td>Specificity (75%)</td>
</tr>
<tr>
<td>ASDAS&lt;1.8</td>
<td>Specificity (75%)</td>
<td>Specificity (75%)</td>
</tr>
</tbody>
</table>

Conclusions: This data-driven ASAS consensus process has allowed to propose an ASDAS-based cutoff value defining worsening in axSpA. As has been observed in other settings, the change defining worsening (at least 0.9) is smaller than the change defining improvement which is 1.2 for ASDAS. This definition should now be applied in trials.

References:

Acknowledgements: This study was supported by ASAS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4786
TP0199 TUMOR NECROSIS FACTOR INHIBITOR TREATMENT REDUCES SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS BY DECREASING DISEASE ACTIVITY: A LONGITUDINAL ANALYSIS IN A LARGE PROSPECTIVE COHORT

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Background: Whether tumor necrosis factor inhibitors (TNFi) have an influence on radiographic progression in ankylosing spondylitis (AS) remains controversial. Objectives: To investigate the impact of TNFi use on spinal radiographic progression in AS. Methods: Patients fulfilling the modified NY Criteria for AS (as assessed by central reading) in the Swiss Clinical Quality Management Cohort with at least 2 years of clinical and radiographic follow-up were included. Spinal X-rays were taken every 2 years and scored independently by 2 blinded readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) in chronological time order. Average score of the readers was used. Radiographic progression was defined as an increase by >2 mSASSS units over 2 years. The relationship between TNFi use before or after a 2-year X-ray interval and progression in the interval was investigated using binomial generalized estimating equation models with adjustment for potential confounding and multiple imputation of missing covariate data. Ankylosing Spondylitis Disease Activity Score (ASDAS) was regarded as a potential intermediate variable mediating the effect of TNFi on radiographic progression. It was added to the model as a time-varying variable in a sensitivity analysis.

Results: A total of 420 patients with AS contributed to data for 597 X-ray intervals in adjusted analyses (1–5 intervals per patient); BL characteristics: male sex 66%, HLA-B27 81%, mean (SD) age 40.4 (10.9) years, disease duration 13.9 (9.8) years, mSASSS 6.4 (12.4), ASDAS 2.8 (1.1). 39% of the patients were already on TNFi at first X-ray. Mean mSASSS progression in 2 years was 0.9 (2.7) units. The multivariable model (Table) shows that prior use of TNFi reduced the odds of progression in the next 2 year interval by 49% (odds ratio (OR) 0.51, 95% confidence interval (CI) 0.28–0.92, p=0.03). BL mSASSS and male sex also significantly affected progression. Adding ASDAS as a covariate to the model decreased the estimated effect of TNFi on progression: OR 0.65, 95% CI 0.39–1.17, p=0.15. In this model, a decrease in ASDAS by 1 unit would lower the odds for progression by 0.62 (p<0.001).

Table 1. Longitudinal multivariable analysis of radiographic progression

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFi use prior X-ray interval</td>
<td>0.51 (0.28–0.92)</td>
<td>0.03</td>
</tr>
<tr>
<td>NSAID use at start X-ray interval</td>
<td>0.81 (0.43–1.63)</td>
<td>0.55</td>
</tr>
<tr>
<td>mSASSS at start X-ray interval</td>
<td>1.06 (1.04–1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>3.01 (1.56–5.77)</td>
<td>0.001</td>
</tr>
<tr>
<td>Disease duration</td>
<td>1.01 (0.99–1.04)</td>
<td>0.38</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.94 (0.55–1.61)</td>
<td>0.83</td>
</tr>
<tr>
<td>HLAs27</td>
<td>0.99 (0.46–2.12)</td>
<td>0.98</td>
</tr>
<tr>
<td>Nb of exercise sessions per week</td>
<td>0.93 (0.85–1.08)</td>
<td>0.35</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>1.00 (0.56–1.79)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusions: TNFi seem to reduce radiographic progression in patients with AS and this effect is mediated, at least in part, by a decrease in disease activity. Acknowledgements: Supported by the Stiftung für Rheumaforchung and a research grant from the investigator initiated studies program of MSD.

Disclosure of Interest: C. Molnar: None declared, A. Scherer: None declared, X. Baraliakos: None declared, M. de Hooge: None declared, R. Michoril: None declared, P. Exer: None declared, R. Kissling: None declared, G. Tamborrini: None declared, L. Wildi: None declared, M. Nissen: None declared, P. Zufferey: None declared, J. Bernhard: Consultant for: Merck Sharp & Dohme, Pfizer, Roche, U. Weber Consultant for: Abbvie, R. Landewe: None declared, D. van der Heijde: None declared, A. Ciurea Consultant for: Abbvie, Cellgene, Eli Lilly, Janssen-Cilag, Merck Sharp & Dohme, Novartis, Pfizer, UCB

DOI: 10.1136/annrheumdis-2017-eular.2571

THURSDAY, 15 JUNE 2017

Calcium crystal deposition in rheumatic diseases —

OP0190 HISTOLOGICAL CHARACTERIZATION OF ROTATOR CUFF CALCIFIC TENDINOPATHY

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Background: Calcific tendinopathy is one of the most frequent causes of shoulder pain. Calcific deposits lead to chronic discomfort in daily and professional activity. These deposits are composed of carbonated apatite. Although the disease is frequent, its origin stays still largely unknown. Molecular and cellular mechanisms involved in this pathological mineralization process are not clearly identified. Objectives: The objective of the study was to analyze calcified tendinous samples to understand the organization of the deposits and to characterize the cells partially involved in this process.

Methods: Samples were collected from cadaveric subjects. Ultrasound was first used to detect calcified tendons. Then, tendons were collected and fixed in formalin 4% during 48h. They were first analyzed with micro-CT to know the distribution of the calcific deposits. Samples were then decalcified in EDTA, dehydrated and embedded in paraffin. Some samples were then stained to allow a better characterization of the calcific deposits. Several histological staining were performed: hematoxylin and eosin (HE), Safranin O/Fast Green (SO/FG) and Von Kossa (no decalcified samples). Immunohistochemistry using anti-Runn2, anti-Sox9, anti-Caspase II and anti-casparase III antibody has been performed to characterize the cells and tissue around the calcifications.

Results: Six samples were collected (1 normal and 5 calcified). On HE staining, three different histological patterns were observed. Little calcifications disseminated between tendon fibers (N=2), voluminous ones encapsulated by a fibrous tissue (N=2) and in one sample an intra-tendinous osseous metaplasia. In the fibrous peripheral area of larger calcifications, we observed cells with round nuclei, different from tenocytes. These cells expressed Runx2 and Sox9 suggesting a chondrocyte phenotype. On SO/FG staining, this peripheral area presented a red coloration (proteoglycan specific) as the fibrocartilage at the tendon insertion. Moreover, in the central part of the calcification, no or very little cartilage was present in this areas. As pathological calcification in cartilage can be associated with chondrocytes apoptosis, we sought for anti-Casparase III expression in the cells of the peripheral area. None of the chondrocyte-like cells located around the larger calcifications expressed Casparase III. Finally, one sample had an osseous metaplasia within the tendon with Runx2 positive cells.

Conclusions: Histological analyses of whole calcified tendon tissues showed three different patterns of calcific deposits. We can hypothesize that these patterns correspond to different stages of the disease. Chondrocyte-like cells were observed around larger deposits and could be involved in the mineralization process. Interestingly, they differ from the cells of the fibrocartilage as they did not express collagen II. Further analyses are necessary to characterize their phenotype and understand the steps leading to these deposits within the tendon.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4682

OP0191 COMPARISON OF ULTRASONOGRAPHY AND RADIOGRAPHY OF THE WRIST FOR DIAGNOSIS OF CALCIFIED PYROPHOSPHATE DEPOSITION

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Background: The gold standard for diagnosis of calcium pyrophosphate (CPP) deposition (CPPD) is the identification of CPP crystals in synovial fluid. However, aspiration of synovial fluid can be challenging in small joints such as the wrist, a usual location of arthritis in CPPD. Despite its low sensitivity, the most widely used imaging modality is conventional radiography but ultrasound (US) seems a useful tool for diagnosis of CPPD.

Objectives: We aimed to compare the performance of US and conventional radiography of the wrist for diagnosis of CPPD.

Methods: Patients with joint effusion (knee, hip, shoulder, ankle or wrist) were consecutively included. CPPD was diagnosed by CPP crystals identified in synovial fluid. Patients without CPP crystals in synovial fluid were controls. As recommended, we used the term chondrocalcinosis (CC) to assess imaging features suggesting CPPD. Two blinded operators assessed CC in all patients by US and conventional radiography of the wrist. The presence of CC (either or specificity) (Sp) of US for the diagnosis of CPPD were 94% and 85%, respectively; the positive likelihood ratio was 6.1. When analyzing US features of CC separately, US Se was higher at the TFC than RC joint, 81% and 50% respectively. The sensitivity (Sp) of radiography was 25% (US) and 100% (CC) and the discrepancy reliabilities for US and radiographic CC were almost perfect: χ coefficient 0.832 [95% confidence interval 0.651–1.0] and 0.880 [0.314–0.880]. In all 58 patients, 113 joints were analyzed (3 patients had radiography of only one wrist). The χ coefficient between US and radiography for CC was moderate: 0.33 [0.171–0.49].

Conclusions: Our study suggests that wrist US should be considered a relevant tool for the diagnosis of CPPD, with higher sensitivity than radiography.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3987
OP0092

ADDING ULTRASOUND TO THE TREAT-TO-TARGET STRATEGY SHOWS NO BENEFIT IN ACHIEVEMENT OF REMISSION: RESULTS FROM THE BIOMAD COHORT

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Background: While, a Treat-to-Target strategy (T2T), treating patients with rheumatoid arthritis (RA) towards a certain target (eg. clinical remission; T2T-REM), is highly recommended, several patients in clinical remission often have residual synovitis on ultrasound-imaging (US). This may result in silent progression and clinical flare. It is argued whether targeting US-synovitis may result in deeper* remission in clinical practice.

Objectives: To assess whether using US in a T2T strategy leads to more patients meeting clinical remission than using only clinical information.

Methods: Patients with RA who started or changed csDMARD and/or anti-TNF treatment followed in centers with expertise in US and participating in BIODAM (2-year multicenter prospective observational cohort) were included. Clinical and US data [by the US-score that includes 7 joints of the clinically dominant hand and foot for synovitis and tenosynovitis on gray-scale US (GSUS) and power-doppler US (PDUS) and erosions on GSUS] were collected every 3 months. Per visit was decided whether the patient was treated according to the clinical definition of T2T with remission as benchmark (T2T-CLIN-REM). Though not mandatory, US-data could also be used for this purpose. T2T-CLIN-REM was considered correctly applied if: either i) a patient already had a disease activity score below the remission target (i.e. ACR/EULAR boolean remission) or ii) if not, treatment was intensified. A T2T strategy taking also US-data into account (T2T-CLIN-US-REM) was considered correctly applied if: either i) both clinical and US remission (all joints included in the US7-score with GSUS synovitis <2 and PDUS synovitis=0) were present; or ii) if not, the treatment was intensified.

Results: In total 963 visits of 130 patients were included. T2T-CLIN-US-REM was correctly followed in 93% of the visits, T2T-CLIN-REM in 14%, and any of these in 52%. Remission according to the ACR/EULAR-boolean definition was achieved in 19.6% of the visits. Compared to the conventional T2T-CLIN-REM strategy, using a combined clinical and US benchmark for T2T led to a lower — instead of higher — likelihood of ACR/EULAR-boolean remission 3 months later compared to a clinical remission benchmark only (T2T-CLIN-REM) was analyzed using generalized estimating equations with auto-regression.

Conclusions: Our results, from a non-randomized study, did not suggest an advantage of using US 7 joints in addition to clinical examination as a T2T benchmark as compared to clinical examination alone in getting RA patients into clinical remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1613

Thursday, 15 June 2017

OP0093

INFLAMMATION OF ADVENTITIAL NERVES OCCURS IN GIANT CELL ARTERITIS PATIENTS AND IT IS CHARACTERIZED BY INFLAMMASOMES, UPR AND AUTOPHAGY ACTIVATION

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Background: Vascular adventitia is a major site of immune surveillance and inflammatory cell trafficking and is the most complex compartment of the vessel wall comprising fibroblasts, dendritic cells and macrophages, progenitor cells, vasa vasorum, pericytes and adventitial nerves. It has been proposed that activation of adventitial nerves and release of sensory neuropetides from their peripheral terminals may lead to neurogenic inflammation. Giant cell arteritis (GCA) is an immune-mediated disease of unknown etiology in which the inflammatory process seems to start from the adventitia of affected arteries.

Objectives: of the aim was to evaluate the occurrence of adventitial nerves inflammation and to immunologically characterize the adventitial neuritis occurring in GCA patients.

Methods: Immunohistochemistry and RT-PCR were used to study the presence of neuritis in temporal artery samples obtained from 30 patients with temporal arthritis (TAB) positive GCA, 20 TAB negative GCA and 20 controls. Laser capture microdissection (LCM) was used to isolate adventitial nerves and nerve expression of pro-inflammatory cytokines involved in the pathogenesis of GCA such as IL-6, IL-17, IL-2, IL-9, IL-33 was assessed by RT-PCR. Expression of pro-inflammatory cytokines on chondroitin sulfate was evaluated by immunochemistry and confocal microscopy. Autophagy, unfolded protein response (UPR) and inflammasome pathways were also studied by RT-PCR and immunohistochemistry.

Results: Adventitial nerves showed infiltration of CD3+ T cells in all the TAB positive and in 12 out of 20 TAB negative arteries but were never observed in control arteries. RT-PCR expression analysis of different pro-inflammatory cytokines clearly demonstrated specific over-expression of IL-33 in LCM isolated inflamed nerves. Immunohistochemical and confocal microscopy analysis confirmed nerve IL-33 expression, RT-PCR and immunohistochemistry demonstrated that AIM2 and NLPR3, but not NLCR4, inflammasomes were activated in inflamed nerves of GCA patients. According to inflammasome activation, increased IL-18 expression was observed. Autophagy-related genes such as ATG16L1 and LC3 and UPR-related genes such as XBP-1 and CHOP were also over-expressed in GCA adventitial nerves as demonstrated by RT-PCR and immunohistochemistry. Finally, increased expression of AIM2 and NLRP3 inflammasomes, autophagy and UPR was also observed outside the nerves, in the context of infiltrated artery wall.

Conclusions: here we demonstrated that adventitial neuritis is present in both inflamed and non-inflamed arteries of GCA patients. GCA inflamed nerves specifically produce IL-33 a cytokine of the innate immunity that has been demonstrated to be involved in the pathogenesis of GCA. AIM2 and NLRP3 inflammasomes activation was also observed in GCA arteries and in particular in the inflamed adventitial nerves being accompanied by the increased expression of IL-18. Specific activation of autophagy and UPR pathways was also observed in the inflamed GCA nerves. Altogether these findings seem to suggest a complex immune activation of adventitial nerves in GCA, suggesting a possible role of arterial neuritis in the initiation and perpetuation of GCA artery innervation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4345

Thursday, 15 June 2017

OP0094

IN-VITRO ACTIVATION OF TOLL-LIKE RECEPTOR 9 IN THE PATHOGENESIS OF EROSIIVE AUTOIMMUNE ARTHRITIS AND DURING OSTEOCLASTGENESIS

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Background: Release and insufficient removal of endogenous nucleic acids may be involved in triggering harmful autoimmune reactions important in the initiation of systemic autoimmune diseases including rheumatoid arthritis (RA). Nucleic acid sensing molecules, such as the endosomal Toll-like receptors (TLRs) 7 and 9, have been linked to pathogenic autoimmune processes, particularly in systemic lupus erythematosus, but their role in RA is less clear. Results previously obtained in rats with pristane-induced arthritis (PIA) suggested involvement of TLR9 in the pathogenesis of this arthritis model (1). Interestingly, rats with PIA develop autoantibodies associated with RA including rheumatoid factor, anti-RA33 and antibodies to carbamylated proteins (2).

Objectives: To gain more insight into the role of TLR9 in the pathogenesis of autoimmune arthritis by investigating the effects of TLR9 inhibition in rats with PIA.

Methods: Arthritis was induced in DA rats with the mineral oil pristane. Rats were treated with a TLR9 antagonist every other day, starting one before disease induction. Arthritis was scored using established scoring systems, inflammation and bone erosion were quantified by histological analysis. Expression of TLR9...
and other nucleic acid sensing TLRs was quantified by RT-PCR and Western blotting; activation (phosphorylation) of various signal transduction molecules was determined by Western blotting. Furthermore, the role of TLR9 in osteoclast differentiation and activation was investigated in vitro.

**Results:** The TLR9 antagonist significantly reduced clinical signs of arthritis by approximately 50%. Histological analyses revealed diminished inflammatory cartilage degradation, bone erosion and significantly reduced numbers of osteoclasts in animals treated with the TLR9 antagonist. However, when treatment was started after onset of arthritis TLR9 inhibition had no effect on arthritis development and severity. IL-6 serum levels were greatly diminished in animals treated with the TLR9 antagonist and expression and activation of NF-κB in lymph nodes was reduced. Remarkably, mRNA levels of TLR7 and TLR9 strongly differed in the course of in vitro osteoclastogenesis. Whereas TLR7 expression did not change throughout osteoclastogenesis, expression of TLR9 was higher in precursor cells than in mature osteoclasts and stimulation with a TLR9 agonist (CpG) completely inhibited osteoclastogenesis.

**Conclusions:** Taken together, the results suggest an important role for TLR9 in the T cell-dependent initiation phase of PIA and thus important involvement of endogenous DNA released during apoptosis, necrosis or netosis in the initiation of autoimmune arthritis and during osteoclastogenesis. The possible relevance of these findings for human RA needs to be further elucidated in future experiments.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5260

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**Table 1**

|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------
| Disease duration (y) | 6.1±4.0 | 5.1±4.0 | 4.2±3.7 | 3.7±3.0 | 3.3±2.1 | 3.4±3.0 | 3.4±3.0 |
| JIA category (%) | 20.6 | 22.2 | 4.3 | 3 | 1.4 | 0.6 | 0.6 |
| Syn JIA | 25.8 | 31.8 | 32.9 | 36.6 | 33 | 33.7 | 33.7 |
| RFpos PA | 12.5 | 11.0 | 8.1 | 9 | 8 | 8 | 8 |
| RFpos PA | 2.4 | 4.5 | 6.1 | 6.1 | 3.4 | 5.1 | 5.1 |
| PersOA | 18.1 | 13.1 | 21.4 | 22.3 | 21.3 | 21.3 | 21.3 |
| Ext OA | 9.7 | 14.7 | 16.4 | 13.6 | 26.1 | 22.5 | 22.5 |
| ERA | 4.8 | 8.9 | 7.7 | 7.8 | 8 | 4.5 | 4.5 |
| PsA unclass JIA | 6 | 3.6 | 3.2 | 3.2 | 3.2 | 2.8 | 2.8 |
| Uveitis | 2.1 | 5.7 | 5.7 | 5.7 | 5.7 | 5.7 | 5.7 |

**Abstract OP0196 – Table 1**

**THURSDAY, 15 JUNE 2017**

**To be and to become: transition from paediatric to adult care**

**OP0195 WHAT IS THE IMPACT OF JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD? THE MONOCENTRIC EXPERIENCE OF 240 PATIENTS FOLLOWED IN A TRANSITION TERTIARY CLINIC OF RHEUMATOLOGY**

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**Background:** There are many different clinical manifestations, assessment and management of Juvenile Idiopathic Arthritis (JIA) between childhood and adults' arthritis onset. The transition from pediatric to the adult care emphasizes a lot of aspects that need to be addressed.

**Objectives:** To describe the long-term outcome of JIA.

**Methods:** Two-hundred and forty patients affected by JIA and referred to a tertiary transition clinic were considered. The data were collected at the last follow up visit.

**Results:** Seventy-four (30.8%) males and 166 (69.2%) females were included; 53 (22.1%) patients were lost in follow up. Subtypes of JIA at disease onset included 101 oligoarthritis (42.1%), 67 polyarthritis (27.9%), 43 systemic arthritis (17.9%), 28 arthritis with enthesitis (11.6%), 7 psoriatic arthritis (2.9%). 22 enthesitis related arthritis (9.2%). Forty-eight (20%) patients had persistent uveitis. Ninety-three implant prosthesis and 14 arthodesis were recorded. The average disease duration was 20 years, the median age of the patients was 27 (18–57) years. Five deaths (2.1%) occurred in this cohort. At follow up 117 (48.7%) had low active disease activity, 70 (29.2%) had moderate disease activity, 14 (5.8%) had a high disease activity, 24 (10%) were on remission OR on medication and 15 (6.3%) OFF medication. Among patients still on medication, 59 (24.6%) were treated with oral steroids, 18 (7.5%) with csDMARDs and 169 (70.4%) with bDMARDs. Seventy-five (31.3%) patients had a higher educational level (university), 195 (61.3%) had an employment, 128 (53.3%) had a driving license. Twenty-one (8.9%) pregnancies were registered. The transition age was considered after age of sixteen years old. In this context, it was important the multidisciplinary approach of each patient that was realized with the collaboration of other specialists (ophthalmologist, orthopedic, dermatologist, psychologist, psychosomatic).

**Conclusions:** In the era of biologic therapy there was an important improvement in a lot of variables of the long-term outcome of JIA. One-hundred-eighty-seven (77.9%) patients were still in tight control, not only because of the continuation of the biological therapy but also because of the multidisciplinary care carried out even during remission. JIA often persists over the adulthood. The long term follow up and care of these patients has to be conducted by a rheumatologist expertized in JIA in collaboration with other specialists.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5797

**THURSDAY, 15 JUNE 2017**

**Heterogeneity in JIA**

**OP0196 CHANGING PATTERNS OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS TREATED WITH ETALENPETIC FROM 2000 TO 2016 IN THE GERMAN BIKER REGISTRY POPULATION**

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**Background:** There is increasing experience with Etanercept (ETA) in juvenile idiopathic arthritis in the BIKER Registry.

**Objectives:** To report on practice changes ETA utilization and outcome over a period of 16 years.

**Methods:** 6 cohorts of pts were created according to inclusion period. Patients’ and disease characteristics, the utilization of DMARDs, steroids, NSAIDs were analysed. Efficacy was judged by PedACR30/50/70/90, JADAS and ACR-remission.

**Results:** Records from 2105 JIA pts treated with Etanercept with at least a baseline and one follow up form were analysed. Most pts were females (67%). The median age of disease onset increased from 5.9 years in the early to 9.3 years in the later cohorts while age at start of treatment remained stable (about 13 years). Median disease duration markedly decreased from 5.3 to about 2 years. Most pts had RF-neg. JIA followed by extended oligoarthritis. In the more recent cohorts the rate of enthesitis related arthritis increased and the rate of systemic JIA decreased (table). At registry start, 20% of newly enrolled pts belonged to the systemic JIA category compared to < 1% in 2016. During the study period, the overall utilization of glucocorticoids at baseline decreased from 54% to 16% (P < 0.001), MTX from 78% to 64% (P < 0.001), ACR30/50/70/ 90 response rates at month 12 were 80%/74%/59%/40% and did not vary over time while the rate of patients reaching no active joint/CHAI DI=0/JADAS-Remission/AACR-Remission increased from 43%/35%/44%/19% to 69%/48%/55%/85%.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5797

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**Changes in all parameters were significant (p < 0.001) in Kruskal-Wallis Test/Chi-square.**
Conclusions: In recent years, children have been treated earlier, received less concomitant treatment with NSAIDs, corticosteroids as well as DMARDs. More recent cohort of patients had less severe disease at baseline, but also showed a markedly better outcome already at one year of treatment reflected by higher rates of patients with no active joint, a CHAQ DI of 0, a JADAS-MDA, ESR levels were 59.40±27.47 mm/h and 2.00±1.00 mm/h, respectively. Mean±SD receptor levels were 47.65±16.40 ng/mL at baseline and 927.83±148.07 ng/mL at [109–382] to 54.3 \text{[10.9–117]} \text{μg/mL}. Peak and trough exposures were within the exposure range in older children (244 μg/mL). The third has been developed for health professionals to update them on current guidance around RMDs and ongoing employment issues that face these three groups. The second lesson is aimed at employers who have a staff member who is living with an RMD. The first lesson is aimed at employees who are living with an RMD - an eLearning programme which focuses on the tripartite relationship between the employee, employer and healthcare professional. Seven million working days are lost each year in Ireland due to RMDs, such as back & neck pain or stiffness, arthritis, and limb pain. This is therefore a significant problem which obviously impacts on both employers, employees and healthcare professionals. That is why Arthritis Ireland has developed Fit for Work Online - an eLearning programme which focuses on the issues that face these three groups.

Objectives: The objective of the project was to develop an online educational programme to provide information, guidance and support to employees, employers and healthcare professionals on working with RMDs. Methods: In 2015 Arthritis Ireland began its developments of an online education programme ‘Fit for Work Online’ which focuses on the tripartite relationship between the employee, employer and healthcare professional. 3 video lessons were developed as part of this eLearning programme.

- The first lesson is aimed at employees who are living with an RMD
- The second lesson is aimed at employers who have a staff member who is living with an RMD (and finally)
- The third has been developed for health professionals to update them on current guidance around RMDs and ongoing employment

A key message in all 3 videos is that working is good for your health. Since employment has been shown to boost health and happiness, it is crucial, whenever possible, that people who are living with an RMD, remain in employment, or return to work, as soon as they can. That is the central message of this eLearning programme.

A number of issues were addressed in the development of this programme in order to convey these important issues:

- Firstly, employees who are living with an RMD are encouraged to take control of their condition. People living with an RMD are encouraged to consider practical adaptations, supports, flexibility and so on that people who are living with an RMD, remain in employment, or return to work.
- Secondly, from an employer's perspective, in addition to concerns about the welfare of their employees, there are other issues to consider, and it is natural for instance to be concerned about the possible impact of any health condition on their employees' performance & reliability, and consequently on their business. Adaptations, supports, flexibility and so on need to be considered.
- Finally, health professionals need to encourage, advise and facilitate people who are living with RMDs to remain in, or return to work.

Results: The Fit for Work Online programme will go live in February 2015. It is planned that a report on the first four months of the programme's delivery and implementation will be available at EULAR 2017 in Madrid.

Conclusions: The direct cost of RMDs at work in Ireland is estimated to be...
Results: Of 44 countries, 31 (70%) and 30 (68%) have provided data for patients and rheumatologists, respectively. In total, 646 patients (mean age SD) 53 (12), 76% female, 519 (78%) ever worked and 500 rheumatologists filled in the questionnaires. Overall, positive weak to no relationships were present between the GDP per capita and perceptions from rheumatologists or patients about SS arrangements. However, significant differences were observed across the systems type with the Scandinavian type (Finland, Norway, Sweden) consistently scoring higher than the others on most domains (table). Remarkably, rheumatologists in less wealthy and non-EU countries felt more confident in their role related to WD pension.

Conclusions: Patients’ and rheumatologists’ perceptions of systems to support persons with RA encountering work restrictions varied mostly according to the type of the social welfare system, while remarkably little differences were related to country’s wealth and membership in EU. Scandinavian employment support and social security system appeared to most adequately meet the expectations of patients and rheumatologists in questions of remaining at work and application to WD pension.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4319

THURSDAY, 15 JUNE 2017

Epidemiology of rheumatic and musculoskeletal diseases - a critical appraisal

OP0200

CONFounding BY INDICATION WILL MAKE NON-TNFi BDmARDS APPEAR MORE HARMFUL THAN TNFi BDmARDS - A NATIONWiDE STUDY OF CHANNELING IN SWEDEN 2010-2014

T Frisell, E. Baecklund, K. Bengtsson, D. Di Giuseppe, H. Forsblad-d’Elia, J. Askling, on behalf of the ARTIS Study Group.

Background: Confounding by indication occurs when factors associated with the choice of therapy are also predictors of the studied outcome, and is generally considered the major limitation of non-randomized comparisons of different therapies. In RA, age, sociodemographic factors, disease activity, and medical history may influence the choice of e.g. a non-TNFi over a TNFi bDMARD. The degree of bias is difficult to assess since most studies have limited data on potential confounders, and residual confounding cannot be separated from true treatment effects.

Objectives: To quantify the expected confounding by indication caused by baseline differences in patient characteristics at initiation of different bDMARDs in RA.

Methods: All RA patients in the Swedish Rheumatology Register (SRQ) were linked to nationwide registers to assess whether a comprehensive list of covariates predicted the choice of bDMARD to such a degree that different rates of adverse events (AEs) would be expected. Among considered confounders were demographic variables, RA related factors (including RF, disease duration, HAQ, DAS28 w. components) and medical history (health care utilization and 20 specific conditions).

We used historical data on the 5 year risk of several AEs among RA patients starting any bDMARD 2005–2009 to predict the risk among RA patients (bionaire and switching from a first TNFi) starting specific bDMARDs 2010–2014. Risk was modelled in logistic regressions, as a function of baseline characteristics but assuming no effect from the therapy itself.

Results: Patients starting non-TNFi were older than those starting a TNFi, had lower socioeconomic status, higher disease activity and more often a history of diseases including malignancy, serious infections, and diabetes. These factors were in general also significant predictors of AEs, and the predicted proportions of all AEs were substantially higher for non-TNFi compared to TNFi bDMARDs, highest for rituximab. Within the TNFi-group, only minor differences were seen. Age was a strong confounder, and standardizing to the age-sex-distribution of the TNFi group reduced the group difference dramatically.

Predicted percentage with AE within 5 years, based on observed baseline characteristics. Crude and standardized to age-sex distribution of TNFi as first bDMARD.

Conclusions: Even if there are no true differences in risk by bDMARD,
confounding by indication will make the non-TNFi drugs appear less safe than IXE, numerically higher with Q2W vs placebo. No deaths or cases of inflammatory bowel disease, uveitis, TB reactivation, or grade ≥3 neutropenia were reported.

Conclusions: IXE improved arthritis, physical function, and psoriasis\(^1\) vs placebo with no unexpected safety findings in patients with active PsA and prior or intolerance to TNF-inhibitor(s).

References:

OP0202 A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITOR(S)

P. Nash\(^1\), B. Kirkham\(^2\), M. Okada\(^3\), P. Rahman\(^4\), B. Combe\(^5\), D. Adams\(^6\), B. Combe\(^5\), D. H. Adams\(^6\), T. Frisell\(^7\), E. Baecklund\(^7\), A. Kaszuba\(^6\), E. Kudlacz\(^7\), C. Wang\(^7\), S. Menon\(^7\), T. Hendrikx\(^8\), K. S. Kanik\(^7\).

Objectives: To compare efficacy and safety of IXE with placebo in pts with active PsA who are TNFi-IR.

Methods: In the 24 week (wk), double-blind, placebo-controlled period of a Phase 3 PsA study (SPIRIT-P; NCT02349295), pts with prior or intolerance to 1 or 2 TNFi were randomised to SC placebo or IXE 80 mg every 2 (Q2W) or 4 wks (Q4W), following a 160 mg initial dose at Wk 0. Pts with IR to treatment (protocol defined) received rescue therapy at Wk 16. Primary endpoint was ACR20 at Wk 24. Continuous data were analyzed using mixed-effects model for repeated measures; categorical data, using a logistic regression model with missing values imputed by non-responder imputation, which treats IR as non-responders.

Results: 363 pts were randomized: ∼52 yrs old on average, female (53%), white (85%), and reductions in functional disability (HAQ-DI) (Table). A significantly higher proportion of IXE-treated pts reported infection and a significantly higher proportion reported injection site reactions (the majority were mild) (Table). Serious infection (0, 3 [2.4%], 0, Q4W, Q2W, placebo respectively), serious AE, and oral candidiasis were numerically higher with Q2W vs placebo. No deaths or cases of inflammatory bowel disease, uveitis, TB reactivation, or grade ≥3 neutropenia were reported.

Conclusions: IXE improved arthritis\(^1\), physical function, and psoriasis\(^2\) vs placebo with no unexpected safety findings in patients with active PsA and prior or intolerance to TNF-inhibitor(s).

References:
28.8% [p<0.05] vs 13.0%). Secondary endpoints at M3 for tofacitinib 5 mg and 10 mg respectively were: ACR20 response, 29.8% [p<0.05], 28.0% [p<0.05]; ACR70 response, 16.8% (not significant [NS]), 14.4% (NS) ≥75% improvement of PASI in pts with baseline BSA ≥3% and PASI >0; 21.3% (NS), 43.2% (p<0.0001); ΔLEI and ΔDSS in pts with baseline score >0; ΔLEI, -1.3 [p<0.05] and -1.3 [p<0.05] (least squares mean [LSM]); ΔDSS, -5.2 (p<0.05) and -5.4 (p<0.05) (LSM). Effects were maintained to M6. Frequency of serious AEs and discontinuations due to AEs was low and similar across treatment groups (Fig 1E). The most common AEs were upper respiratory tract infection (5.3–10.8%), nasopharyngitis (1.5–10.7%) and headache (4.5–9.1%).

Conclusions: In this study restricted to PsA pts with TNFi-IR, both tofacitinib doses appeared efficacious on musculoskeletal endpoints for treatment of PsA. No new safety risks were identified vs previous studies in other indications.


DOI: 10.1136/annrheumdis-2017-eular.2443

IMPACT OF ADALIMUMAB SERUM CONCENTRATION ON EFFICACY AND ASSOCIATION BETWEEN ANTI-DUAG ANTIBODIES AND SERUM CONCENTRATION: 24 WEEK RESULTS FROM A PHASE III STUDY COMPARING SBS (AN ADALIMUMAB BIOSIMILAR) WITH REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: SBS has been developed as a biosimilar of reference adalimumab (ADL). The 24-week efficacy and safety results comparing SBS and ADL were reported previously.1 Here we report results of subgroup analyses of efficacy by adalimumab serum trough concentration (C_{trough}) and association between anti-drug antibodies (ADA) and C_{trough}.

Objectives: To investigate the impact of C_{trough} on efficacy and the association between ADA and C_{trough} in patients with rheumatoid arthritis (RA) treated with SBS or ADL.

Methods: Patients with moderate to severe RA despite methotrexate treatment were randomly assigned to receive 40 mg of either SBS or ADL administered subcutaneously every other week up to week 24. Blood samples were taken prior to study drug administration at weeks 0, 4, 8, 12, 16, and 24 to measure C_{trough}. The optimal C_{trough} cut-off point of adalimumab for good EULAR response at week 24 is reported to be 1.274 μg/mL.2 Efficacy and immunogenicity were analysed in patients with C_{trough} ≥1.274 μg/mL and ≥1.274 μg/mL.

Results: C_{trough} was measured in 178 patients each from SBS and ADL group. The post-dose mean C_{trough} was comparable up to week 24 for SBS (range: 3.850 to 6.761 μg/mL) and ADL (range: 3.892 to 6.773 μg/mL). Generally efficacy was comparable between SBS and ADL regardless of C_{trough} level. At week 24, the proportion of patients achieving good EULAR response, remission or low disease activity based on DAS28 was higher in patients with C_{trough} ≥1.274 μg/mL than in those with C_{trough} <1.274 μg/mL for both treatment groups (Figure). Other efficacy parameters, including ACR responses, DAS28, simplified disease activity index, and clinical disease activity index, showed similar results.

C_{trough} was higher for patients without detectable ADA, compared to those with ADA. Among patients with ADA, the proportion of patients with C_{trough} ≥1.274 μg/mL was 58.0% (29/50) for SBS and 52.1% (25/48) for ADL. Among patients without detectable ADA, the proportion of patients with C_{trough} ≥1.274 μg/mL was 100.0% (121/121) for SBS and 97.4% (114/117) for ADL.

References:


DOI: 10.1136/annrheumdis-2017-eular.3348
IMPACT OF ANTI-DRUG ANTIBODY AND INJECTION SITE PERFORMANCE OF SLEDAI-2K TO DETECT A CLINICALLY ASSOCIATION BETWEEN T FOLLICULAR HELPER CELL AND REFERENCE ETANERCEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: SB4 is approved by the European Commission as a biosimilar of the reference etanercept (ETN). The phase III clinical study results have been reported previously.1,2 Data to date shows no correlation between the development of anti-drug antibody (ADA) and clinical response or adverse events with etanercept treatment.

Objectives: To investigate the impact of the presence of ADA or injection site reaction (ISR) on efficacy in patients with rheumatoid arthritis (RA) treated with SB4 or ETN up to week 24.

Methods: In this phase III randomised, double blind study, patients with moderate to severe RA received 50 mg/week of either SB4 or ETN with background methotrexate (MTX) for 52 weeks. Efficacy, safety and immunogenicity were assessed.

Results: Up to week 24, the incidence of ADA (2 patients [0.4%] in SB4 vs 39 patients [13.1%] in ETN, p < 0.001) and the incidence of ISR (9 patients [3.0%] in SB4 vs 48 patients [16.2%] in ETN, p < 0.001) were significantly lower in SB4 compared to ETN. Due to the low incidence of ADA in the SB4 treatment group, the impact of ADA on efficacy could not be evaluated. Within the ETN treatment group at week 24, there was a trend towards increased efficacy (ACR, ACR-N, Change in DAS28, remission and low disease activity based on DAS28, SDAI, or CDAI) in patients without detectable ADA compared to patients with ADA (Table). In regards to ISR, efficacy tended to be higher in patients who did not experience ISR compared to those who did within each treatment group. There was no correlation between the presence of ADA and incidence of ISR. In patients without detectable ADA and patients with ADA, respectively, 3.0% (9/297) vs. 0.0% (0/2) of patients from SB4 group and 16.3% (42/248) vs. 15.4% (37/242) of patients from the ETN group experienced ISR.

Conclusions: Significantly fewer patients from SB4 developed ADA or experienced ISR compared to ETN, however the efficacy was still comparable between SB4 and ETN in patients without detectable ADA and in patients who did not experience ISR. Within the ETN group, there was a trend towards increased efficacy in patients without detectable ADA compared to patients with ADA. In both SB4 and ETN group, patients with ISR tended to have higher efficacy than patients without ISR. There was no correlation between the presence of ADA and ISR.


DISCLOSURE OF INTEREST: J. Vencovsky Consultant for; Samsung Bioepis Co., Ltd., Bohen, P. Emery Grant/research support from; Abbvie, BMS, Pfizer, USB, MSD, Novartis, Lilly, Consultant for; Samsung Bioepis Co., Ltd., Keystone Grant/research support from; Abbott, Amgen, AstraZeneca, BMS, Janssen, Lilly, Novartis, Pfizer. Speaker for; Abbott, AstraZeneca, Biostem, Bios, Genentech, Janssen, Lilly, Merck, Pfizer, Samsung Bioepis, Speakers bureau; Abbott, AstraZeneca, BMS Canada, Jansen, J. Ghil Employee of; Samsung Bioepis Co., Ltd., S. Y. Cheong Employee of; Samsung Bioepis Co., Ltd., E. Hong Employee of; Samsung Bioepis Co., Ltd.

DOI: 10.1136/annrheumdis-2017-eular.3043

THURSDAY, 15 JUNE 2017

Which target/outcome is more relevant in the management of SLE?

ASSOCIATION BETWEEN T FOLLICULAR HELPER CELL AND PLASMAFAB CORRELATES WITH DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Various immunological abnormalities contribute to the development and perpetuation of systemic lupus erythematosus (SLE). Since SLE is a molecularly heterogeneous disease, targeted therapy has not yet been fully established. It seems to be important to explore the characteristic and interaction among the immune cell phenotypes in this disease.

Objectives: The aim of this study was to assess the relationship between the peripheral immune cell phenotypes with clinical manifestations and responsiveness to immunosuppressive therapy in patients with SLE.

Methods: Peripheral blood mononuclear cells were obtained from 143 SLE patients and 26 healthy donors (HD). The blood samples were taken at baseline and week 24 after treatment. The subset of circulating B, T and dendritic cells was defined based on comprehensive 8-color flow cytometry analysis for human immune system termed “the Human Immunology Project” proposed by the National Institutes of Health (NIH) and the Federation of Clinical Immunology Societies (FOCIS). The proportion of immune cell phenotypes with clinical characteristics and responsiveness to immunosuppressive therapies, such as cyclophosphamide, mycophenolate mofetil, or calcineurin, in addition to high-dose glucocorticoids, were evaluated. Patients who were required more than two different immunosuppressants therapies in addition to glucocorticoids were considered treatment resistant.

Results: The proportion of CD3+CD4+CXCR5+ICOS+ T follicular helper cell (Thf) cell, but not CD3+CD4+CXCR3+CCR6 Th1 cell and CD3+CD4+CXCR3 CCR6+ Th17 cell, were higher in SLE than that in HD (mean 1.1 vs 0.8, p<0.01). The frequency of CD10+CD20+lgD+CD27+ central memory B cell and CD19+CD10+CD27+ effector B cell were higher in SLE than that in HD (mean 23.6 vs 15.1 and 10.7 vs 5.2, p<0.001 and p<0.001, respectively). The largest difference relative to the HD was observed in the proportion of CD19+CD20+CD27+CD38+ plasmablast, which was higher in SLE (mean 16.2 vs 3.7, p<0.001) and correlated with BILAG index (r=0.7, p<0.01). The proportion of Thf cell only showed positive correlation with that of plasmablast (r=0.24, p=0.02). Treatment resulted in marked improvement in disease activity scores, such as SLEDAI and BILAG and resulted in significant decreased proportions of plasmablast and T cell (plasmablast; mean 17.6 to 10.1, p<0.001, T cell; mean 1.1 to 0.7, p<0.01). The percentage of patients who showed treatment resistance was highest among patients with high Tfh cell plasma-blast axis as a potential therapeutic target for SLE. The peripheral immunophenotyping might be useful in evaluating the pathogenesis and in determining the therapeutic target of each patient.

Disclosure of Interest: S. Nakayama: None declared, S. Kubo Speakers bureau: Bristol-Myers, M. Yoshikawa. None declared, Y. Miyazaki: None declared, S. Iwata: None declared, I. Miyagawa: None declared, K. Nakano: None declared, K. Saito: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Astellas, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Bansu, Lilly, GlaxoSmithKline

DOI: 10.1136/annrheumdis-2017-eular.4165

PERFORMANCE OF SLEDAI-2K TO DETECT A CLINICALLY MEANINGFUL CHANGE IN SLE DISEASE ACTIVITY: A 36-MONTH PROSPECTIVE COHORT STUDY OF 334 PATIENTS

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Background: The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is the core determinant of response in the SLE Responder Index (SRI), a primary efficacy outcome in SLE clinical trials. However, SLEDAI is unable to discriminate partial improvement/worsening, as it scores each item...
categorically. Furthermore, potentially severe lupus manifestations, such as hemolytic anemia, are not scored in SLEDAI.

**Objectives:** To evaluate the performance of SLEDAI-2K to detect a clinically meaningful change in SLE disease activity.

**Methods:** Prospective cohort study of SLE patients followed at a tertiary care lupus clinic from January 2014 to December 2016. Consecutive patients fulfilling the ACR’97 and/or the SLICC’12 classification criteria were included. At each outpatient visit, disease activity from the last 30 days was scored in the Physician Global Assessment (PGA) (0–3 cm scale) and in SLEDAI-2K. The association between PGA and SLEDAI-2K at each visit was tested with Spearman’s Correlation. A clinically meaningful change in SLE disease activity, was defined as difference in PGA ≥0.3 cm at follow-up compared to the baseline visit. Performance of change in SLEDAI-2K was tested in two models: against worsening and improvement in PGA ≥0.3 cm from baseline using Receiver Operating Characteristic (ROC) curve analysis. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) of SLEDAI-2K to change in PGA was calculated. Statistical significance was set at 0.05.

**Results:** We included 334 patients (87.1% female, mean age at baseline - 44.8±14.5 years). At baseline, median PGA and SLEDAI-2K score was 0.2 points (range –0.2–5.2) and 2 points (range 0–19), respectively. Eighty-three patients (24.8%) had a PGA >0.4 points at baseline. During follow-up of 36 months, 2129 visits were performed. PGA and SLEDAI-2K scores presented a high correlation (rho=0.82, p<0.0001) (fig. 1). Reductions in PGA ≥0.3, and worsening were significantly associated with SLEDAI-2K ≥0.3. A scatter plot showing linear positive correlation between PGA and SLEDAI-2K scores (Spearman’s correlation coefficient (r) =0.82, p<0.0001).

**Conclusions:** SLEDAI-2K presents a limited performance in detecting a clinically meaningful change in SLE disease activity, failing to identify more than a quarter of cases with clinically meaningful improvement or worsening. There is a need to optimize SLE disease activity measures.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3895

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**OP0207 B CELL DEPLETION INCREASES REGULATORY T CELLS AND AMELIORATES SKIN AND LUNG FIBROSIS IN A BLEOMYCIN-INDUCED SYSTEMIC FIBROSIS MODEL MOUSE**

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**Background:** B cells play a critical role in systemic autoimmunity and disease expression through various functions such as cytokine production and induction of other immune cell activation. Recently, some clinical studies have shown that the efficacy of B cell depletion therapy with rituximab, a chimeric monoclonal antibody against human CD20, in systemic sclerosis (SSc) patients. However, it still remains unclear why B cell depletion can be an effective treatment for SSc.

**Objectives:** The purpose of this study is to assess the role of B cell depletion in SSc. We evaluated the skin and lung fibrosis of bleomycin (BLM)-induced SSc model mice treated with B cell depletion. Furthermore, we investigated the effect of B cell depletion on T cell cytolytic profile.

**Methods:** To generate BLM-induced SSc model mice, 300 μg of BLM was injected subcutaneously into the shaved backs of the C57BL/6 mice every other day for 4 weeks. Anti-mouse CD20 monoclonal antibodies, which can deplete mouse B cells, were also injected every 2 weeks from 2 weeks later starting BLM treatment. After 4 weeks of BLM treatment, skin and lung fibrosis were assessed histopathologically. T cells and B cells were isolated from spleen using magnetic cell sorting system. Purified T cells (5x10⁶ cells) were cultured with naive T cells. Frequencies of IL-10 producing regulatory T cell frequencies in BLM-treated mice were significantly decreased in BLM-treated mice compared with PBS-treated mice, while IL-6 producing B cell frequencies increased. Moreover, interferon (IFN)-γ-, IL-4, or IL-17 producing T cell frequencies were significantly decreased in BLM-treated mice compared with PBS-treated mice.

**Results:** Derma thickness and lung fibrosis score increased in BLM-treated mice compared with PBS-treated mice, while IL-6 producing B cell frequencies increased. Moreover, interferon (IFN)-γ-, IL-4, or IL-17 producing T cell frequencies were significantly decreased in BLM-treated mice compared with PBS-treated mice. By contrast, frequencies of IFN-γ-, IL-4, or IL-17 producing T cells were significantly decreased by B cell depletion in BLM-treated mice. In addition, fibrogenic cytokine mRNA expression levels of collagen and lung fibrosis decreased in BLM-treated mice after B cell depletion. To assess the role of B cells on T cell cytokine production, purified splenic B cells from BLM- or PBS-treated mice were cultured with naive T cells. T cells which were cultured with B cells from BLM-treated mouse produced greater amounts of INF-γ-, IL-4, and IL-17 than those cultured with PBS-treated mouse B cells. By contrast, B cells from PBS-treated mice induced a higher amount of IL-10 production from T cells than those from BLM-treated mice.

**Conclusions:** B cell depletion inhibited skin and lung fibrosis in BLM-treated mouse further. Moreover, B cell depletion increased regulatory T cell frequencies in BLM-treated mice, through INF-γ-, IL-4, and IL-17 producing T cell frequencies were decreased by B cell depletion. These results suggest that B cell depletion alters T cell cytokine profile, which results in inhibition of fibrosis in this model.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4189

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**OP0208 SYNOVIAL TISSUE OF RA PATIENTS IN REMISSION CONTAINS A UNIQUE POPULATION OF REGULATORY MACROPHAGES**

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**Background:** The majority of RA treatments target inflammation or the adaptive immune response. Partial- or non-response is common and only a minority have sustained remission. There is a knowledge gap in understanding the mechanisms that could reinstate synovial homeostasis in RA. Tissue macrophages may have a role in this process; they are present in healthy synovium and aid resolution of the inflammation in experimental models of RA. However, little is known about the regulatory properties of human synovial tissue macrophages.

**Objectives:** Our hypothesis is that healthy and RA synovium in remission contain macrophages with anti-inflammatory/reparatory properties and identifying the effector pathways that drive their function could facilitate therapeutic restoration of synovial homeostasis in RA.

**Methods:** We developed a flow cytometry sorting strategy for harvesting tissue-resident macrophages obtained from digested synovial biopsy from reponding RA patients (n=21, including in remission n=5; and active RA n=16). Cells were labelled with cell lineage-specific antibodies; then macrophages were gated based on CD14/CD64 expression levels. CD11c+CD64+CD14++ macrophages were sorted using a MSD FACS Aria III and RNaseq performed to characterise their functional signature. In some experiment, macrophages were seeded on collagen-coated plates and production of TNFα assessed.

**Results:** All synovial tissue macrophages from RA in remission were CD206εpos whereas a substantial number of synovial macrophages from active RA tissue were CD206εneg. Gene expression analyses and functional assays suggest that these populations represent distinct subpopulations in the activation spectrum. CD206εpos macrophages have high expression of microRNA-155, which drives production of inflammatory mediators e.g. TNFα. In contrast, CD206εneg macrophages showed regulatory properties characterised by increased expression of soluble e.g. IL10, TGFβ, IL4/10, TGFβRII/1 and 2 cell population (e.g. SHIP1, TAK1, SMAD2, SMAD3, SMAD7) inhibitors of inflammatory activation, and increased expression of repair markers (e.g. ARG2 and CCL18).

**Conclusions:** We propose therefore that anti-inflammatory/reparatory macrophages may be present in human synovial tissue in remission representing a hitherto unnoticed regulatory tissue mechanism.
To determine the incidence and risk factors implicated in the development of cardiovascular events (CVD) in patients with chronic inflammatory diseases (CIRD) attending rheumatology clinics after 2.5 years of follow-up. The total number patient who completed the follow-up visit at 2.5 years and their causes were also analyzed.

Methods: Analysis of data after 2.5 years of follow-up in an observational prospective study [CARdiovascular in rheuMatology (CARMA) project] that includes a cohort of patients with CIRD [rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA)] and another cohort of matched individuals without CIRD attending outpatient rheumatology clinics from 61 hospitals in Spain. The cumulative incidence per 1000 patients and the incidence density per 1000 patient-months of non-fatal CVE were estimated in both cohorts at 2.5 years from the start of the project. Weibull proportional hazard model was fitted to the data.

Results: The total number patient who completed the follow-up visit at 2.5 years was 2,598 (89.2% of those who started the study). Seven patients had died due to CVE and 23 because of non-CVE. The higher number of losses to follow-up was in patients with AS (HR: 4.11; 95% CI: 1.18–13.76, p<0.01), higher systolic blood pressure (HR: 1.02; 95% CI: 1.00–1.04, p=0.01) and longer duration of the rheumatic disease (HR: 1.07; 95% CI: 1.03–1.12, p<0.01). In contrast, woman gender was a protective factor (HR: 0.43; 95% CI: 0.19–1.00, p=0.05).

Conclusions: Patients with AS prospectively followed-up at rheumatology outpatient clinics show higher risk of developing a first CVE than those with RA or PsA. Besides traditional CVD risk factors a longer time course of the disease is a risk factor for the development of CVD in patients with CIRD.

Acknowledgements: This project has been supported by an unrestricted grant from Abbvie, Spain. The design, analysis, interpretation of results and preparation of the manuscript has been done independently of Abbvie.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3338
WHO CARES? AN INVESTIGATION OF THE HEALTH AND PERCEIVED SOCIAL CARE NEEDS OF PEOPLE WITH RHEUMATOID ARTHRITIS LIVING IN SCOTLAND

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Background: Effective and sufficient levels of care and support for individuals newly diagnosed and those with established Rheumatoid Arthritis (RA) are needed to ensure optimal physical and mental health, as well as health-related quality of life. The aim of this study was to explore the extent of care needs among individuals with RA living in Scotland, UK and the factors that contribute to them, such as co-morbidities, perceived caregiver burden and complex care needs.

Objectives: To establish whether the health and social care needs of people with RA in Scotland were being met, if there was regional variation and what other factors impacted such as wealth and age.

Methods: A cross-sectional study of individuals with RA who responded to an online survey (available 11 Nov 2015 to 22 Jan 2016) who were aged ≥16 years, lived in Scotland and reported they had received a clinical diagnosis of RA. Respondents were allowed to skip questions they wished not to answer; standardised instruments were used (e.g., the Self-Administered Comorbidity Questionnaire and the Self-Perceived Burden Scale). Descriptive analyses of quantitative data and thematic analyses of free text responses were conducted.

Results: Overall, 387 individuals participated. The majority were female, of White Scottish or White British background, 45–64 years, and lived in a household with ≥2 people. The majority, 83%, reported well established RA (diagnosis ≥2 years ago) and at least one other comorbidity (78%) – most commonly depression (78%) and fibrotic diseases ≥40% reported taking 3 medications in total. Of those receiving care, the majority (97/101) named family or friends/neighbours as caregivers and 76% (80/97) had an elevated level of self-perceived burden on their caregiver. Respondents who reported anxiety or depression had significantly higher average self-perceived burden scores when compared to those without, 33.0 versus 27.3.

89% responded that they did not know what types of circumstances might make them eligible for care and support from their local Council, and only 10% reported receiving information about care and support from their local council. Very few (n=40) had an assessment, with half being deemed eligible for support from their local council.

Conclusions: Survey responses suggest individuals with RA lack fundamental information about qualifying for and accessing formal resources and services provided by their local Council. This is especially crucial for reasons: 1) respondents indicated they do not want to rely heavily on others, like family or friends who are often the primary caregivers; 2) depression and anxiety are highly prevalent in this population. It is important to ensure those with RA do not have unmet needs at any stage, from being newly diagnosed to having established RA, so that they can flourish at home, at work and in their leisure time. Local councils should make access to information about help with formal social care easily accessible and ensure that health professionals know how best to sign-post people.

Acknowledgements: A partnership between the National Rheumatoid Arthritis Society (UK) and the University of Aberdeen

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1858

THURSDAY, 15 JUNE 2017

Macrophage M2 polarization: implications in fibrotizing diseases

ENDOTHELIN-1 INDUCES A PROFIBROTIC PHENOTYPE IN CULTURED HUMAN MICROVASCULAR ENDOTHelial AND CIRCULATING MONOCYTE/MACROPHAGE CELLS

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Background: The alteration of microvascular endothelial cell (EC) functions and the presence of macrophages in the immune inflammatory infiltrate, followed by the transition of these cell types into a profibrotic phenotype, represent early and crucial pathophysiological features of the fibrotic process in systemic sclerosis (SSc) (1). The alternatively activated macrophage subset M2a was found in several diseases characterized by extensive fibrosis (1). Herein, we investigated the expression specific phenotype markers, CD206 (mannose receptor), CD204 and CD163 (scavenger receptors) as well as profibrotic molecules, primarily transforming growth factor-β1 (TGFβ1) (1). Endothelin-1 (ET1) and/or TGFβ1 are known to induce the transition of fibroblasts into profibrotic myofibroblasts, which are key mediators of fibrosis in SSc.

Objectives: To investigate the effects of ET1 in inducing a profibrotic phenotype in cultured human microvascular ECs (HMVECs) and macrophages.

Methods: HMVECs, at 3rd culture passage, were grown in endothelial cell medium (EMEM) and treated for 6 days with ET1 (100 nM) or treated for 1 hr with ET1 receptor antagonist (ETAB-R, bosentan 10 μM) before stimulation with ET1.

Human monocytes were isolated from peripheral blood mononuclear cells of healthy subjects using a monocye isolation kit. The cells were maintained in RPMI growth medium for 24 hrs and then treated for 6 days with ET1 or treated for 1 hr with bosentan before stimulation with ET1.

Cultured HMVECs and monocytes maintained in EGM2MV and RPMI growth medium, respectively, were used as untreated cells. Gene and protein expression of profibrotic myofibroblast markers—smooth muscle actin (α-SMA), fibroblast specific protein-1 (S100A4), type 1 collagen (COL1) and fibroconnectin (FN)—were evaluated by quantitative real time polymerase chain reaction (qRT-PCR), Western blotting (WB) and immunocytochemistry (ICC) in cultured HMVECs. Gene and protein expression of M2a phenotype markers (CD206, CD204, CD163) and TGFβ1 were investigated by qRT-PCR and WB in cultured human macrophages. Statistical analysis was carried out by Mann-Whitney non-parametric test.

Results: In cultured HMVECs, ET1 induced the significant upregulation of the gene expression of α-SMA, S100A4 (myofibroblast markers), COL1 and FN, compared to untreated cells (p<0.01, p<0.05, p<0.01). ETAB-R significantly contrasted the ET1-mediated transition of HMVECs into a profibrotic phenotype (p<0.05 for α-SMA, COL1 and FN; p<0.01 for S100A4 vs. ET1-treated cells).

In cultured human macrophages, ET1 induced the significant overexpression of M2a markers (p<0.05 for CD204 and CD163 and p<0.01 for CD206 and TGFβ1) compared to untreated cells. ETAB-R significantly contrasted the ET1-mediated transition of cultured macrophages into profibrotic M2a (p<0.05 vs. ET1-treated cells, for all investigated proteins). Data were confirmed by WB and ICC on both cultured cell types.

Conclusions: ET1 seems to be involved in the early phases of the fibrotic process by inducing the transition of both cultured HMVECs and macrophages into a profibrotic phenotype, myofibroblast and M2a respectively (observed in SSc), a process which is apparently contrasted by ETAB-R treatment.

References:

Disclosure of Interest: S. Soldano: None declared. P. Montagna: None declared. R. Brizzolara: None declared. A. Trombetta: None declared, A. Sulli: None declared, C. Pizzorni: None declared, M. Ghio: None declared, S. Paolino: None declared, V. Smith: None declared, M. Cutolo Grant/research support from: Actelion.

DOI: 10.1136/annrheumdis-2017-eular.4317

MACROPHAGES FROM A SCLERODERMA SUBGROUP WITH HIGHER SKIN SCORES EXPRESS ACTIVATION MARKERS AND INDUCE FIBROBLASTS IN CO-CULTURE

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Background: Scleroderma (SSc) is characterized by pathological fibrosis. The mechanisms by which fibrosis occurs in SSc are not fully understood. Alternatively activated M2-like macrophages are associated with fibrosis and have been found to have an important role in pathological fibrosis in humans. Therefore, there is interest in elucidating their role in SSc. M2 macrophages express mannose receptor CD206 and are known to secrete a number of soluble factors to establish a pro-fibrotic milieu when present in damaged tissues. Furthermore, we have shown adenosine tri-phosphate (ATP) concentration is increased in the skin of patients with SSc. Within the extra-cellular environment, ATP is a Damage-Associated Molecular Pattern (DAMP), binding the P2X class of purinergic receptors. Such mechanisms may contribute to SSc pathology.

Objectives: In this study, we explore the relationship of macrophage CD206 and P2X expression to Rodnan Skin Score. The role of these cells in establishing fibrosis was also examined in vitro.

Methods: 17 SSc patients and 9 controls were consented and their skin score recorded. Macrophages were derived from peripheral blood mononuclear cells (PBMCs) and identified through CD14 expression by FACS. CD206 and P2X
co-expression was quantified. CD206 immunofluorescence of skin biopsies was also performed.

Macrophages were co-cultured with 8x10^4 and 2x10^4 fibroblasts in a collagen matrix and within a monolayer respectively. Collagen gel contraction was quantified as a measure of fibrotic activity. CTGF and collagen mRNA expression from gel matrices and cellular monolayers was quantified by qPCR.

Results: CD206 and P2X7 expression is higher on SSc PBMC-derived macrophages (mean fluorescence 776.1 SD=409, 724.4 SD=455.3) compared to healthy controls (mean fluorescence 632.2 SD=73.7, 472.9 SD=25.4). There is a significant correlation of CD206 expression to P2X7 expression (p<0.001, r=0.76) and CD206 expression is significantly correlated to Rodnan skin score (p<0.05, r=0.26). P2X7 expression is positively correlated to skin score. Double positive P2X7 and CD206 were seen in a subgroup with higher skin scores, however MAIT/CD206+ fibroblasts co-cultured with scleroderma macrophages showed stronger collagen mRNA by qPCR compared to co-culture with healthy macrophages (p<0.01), CTGF mRNA was positively correlated with macrophage P2X7 (r=0.23) and CD206 (r=0.81) expression. Preliminary work suggests contraction of collagen discs in fibroblast and macrophage co-culture is increased with SSc macrophages compared to healthy controls.

Conclusions: Data indicates a correlation between disease severity and CD206 expression by macrophages. Upregulation of CTGF and collagen expression in fibroblasts co-cultured with macrophages expressing high CD206 suggests a role for MAIT cells in pathogenic fibrosis. The co-expression of high levels of P2X7 with CD206 may indicate the role of the purinergic pathway in SSc fibrosis. Future work will examine the mechanism of macrophage-fibroblast cross-talk and investigate the effect of inhibitors of CD206.

Acknowledgements: Rosetrees Trust

Arthritis Research UK

Scleroderma and Raynaud’s UK

Royal Free Charity

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2743
USTEKINUMAB IS SUPERIOR TO TNF INHIBITOR TREATMENT IN RESOLVING ENTHESIS IN PSA PATIENTS WITH ACTIVE ENTHETISIS-RESULTS FROM THE ENTHETISAL CLEARSANCE IN PSORIATIC ARTHRITIS (ECLIPSA) STUDY

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Background: IL-23 is considered to play an important role in the development of enthesitis. Ustekinumab (UST), a combined inhibitor of IL-12/IL-23 shows efficacy in psoriatic arthritis (PsA) driven by enthesial disease, while it has no therapeutic role in diseases driven by synovitis alone, such as rheumatoid arthritis. We therefore speculated that inhibition of IL-23 is particularly effective in enthesitis-driven PsA patients.

Objectives: To compare the efficacy of UST with tumor necrosis factor inhibitor (TNFi) treatment in clearing enthesis in PsA patients.

Methods: ECLIPSA is a prospective randomized-controlled open study. Patients with PsA with active enthesitis were randomized 1:1, receiving either standard doses of UST (arm 1) or TNFi (arm 2). At baseline the following parameters were assessed: age, gender, BMI, disease duration, previous DMARDs, use of corticosteroids, use of NSAIDs, swollen and tender joint count, VAS-pain, VAS-global, NAPSI, PASI, MASES, SPARCC, LDI, BASDAI, BASFI, HAQ-DI, SF-36, FACIT-F, ESR and CRP. Primary endpoint was a SPARCC of 0 after 6 months. Patients were seen every 3 months and followed for a total of 6 months. In order to investigate the effect of study treatment over time, individual time- and dose-dependent ANCOVA models were used for both physician’s and patient’s reported outcomes. Furthermore, exploratory logistic regression was used to predict a SPARCC of 0 at month 6 from baseline SPARCC, PASI, NAPSI, FACIT-F and BASDAI while additionally accounting for age, gender, BMI, gender, PsA duration and study treatment.

Results: 51 patients (UST=25; TNFi=26) were screened and 47 patients (UST=23; TNFi=24) were enrolled with 4 patients not presenting signs of active enthesitis at baseline. Mean ± SD age was 59.1±12.16 years and mean ± SD disease duration was 6.4±7.79 years. Mean SPARCC at baseline was 4.87±2.69 in the UST group and 4.45±2.69 in the TNFi group. Patient-reported disease activity (BASDAI and BASFI), physical well-being (SF-36 physical component summary scale), and PASI all p<0.044 with superiority of UST. However, TNFi was superior to UST with respect to improvement of fatigue (FACIT-F), p=0.001. After 6 months, 17 out of 24 UST patients (70.8%) and 10 out of 26 TNFi patients (38.4%) reached the primary endpoint (SPARCC<0). Logistic regression predicting enthesitis-free state of disease was significantly related to study treatment only, with patients receiving UST being more likely to show no signs of enthesitis at month 6 (OR=0.037; p=0.005).

Conclusions: These results show that UST is superior to TNFi in resolving the enthesis component of disease in PsA patients with active enthesial disease. Based on these data more stratified treatment approaches can be designed in PsA patients, where enthesitis-driven patients are targeted by IL-23/IL-17 pathway inhibitors, while more systemic disease manifestations of PsA, such as patients with polyarticular disease or those with high-level fatigue are targeted by TNFi.

Disclosure of Interest: None declared


EFFECTIVICY AND SAFETY RESULTS OF GUSELKUMAB, AN ANTI-IL23 MONOCLONAL ANTIBODY, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS OVER 24 WEEKS: A PHASE 2A, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY


Objectives: To evaluate the efficacy, safety, and tolerability of guselkumab (GUS), a fully human monoclonal antibody against the p19 subunit of IL-23, in patients (pts) with active psoriatic arthritis (PsA).

Methods: Designed as a double-blind, placebo-controlled, multicenter study, pts with active PsA and ≥3% body surface area (BSA) of plaque psoriasis despite current or previous treatment with standard-of-care therapies, including those previously exposed to anti-TNFα agents, were randomized 2:1 to receive GUS 100 mg subcutaneously (SC) or placebo (PBO) at wks 0, 4, and every 8 wks (q8w) through wk44. Pts were then randomized either group with ≥5% improvement from baseline in both swollen and tender joint counts were eligible for early escape to open-label ustekinumab. At wk24, all remaining PBO pts crossed-over to receive GUS 100 mg, and then received GUS at wk28, and q8w thereafter through wk44. The primary endpoint was ACR 20 response at wk24. Major

Conclusions: In TNFi-naive pts with active PsA, tofacitinib was superior to PBO in ACR20 response rates and ΔHAQ-DI at M3, with superiority vs PBO as early as Week 2 for ACR20, which was maintained to M12. No new safety risks were noted. The most common adverse events were upper respiratory tract infection (7.5–10.6%), nasopharyngitis (7.5–11.5%) and headache (3.8–10.6%).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1416

Stable treatment with 1 csDMARD was required. Primary endpoints comparing tofacitinib vs PBO were ACR20 response rate and change from baseline in Health Assessment Questionnaire Disability Index (ΔHAQ-DI) at M3. Secondary endpoints included: ACR20 response rates and ΔHAQ-DI through M12; pts achieving ACR50, ACR70, ≥75% improvement of PASI and PsARC at all time points; and changes from baseline in LUM, Dactylitis Severity Score and SPARCC Enthesis Index. Radiographic progression was assessed by van der Heijde-modified Total Sharp score (mTSS).

Results: 96.9% of pts were white and 53.3% were female; mean age was 47.9 years. 96.2% and 66.4% of pts completed M3 and M12, respectively. At M3, tofacitinib 5 and 10 mg Bd significantly improved ACR20 response rates (50.5% [p<0.05] and 66.6% [p<0.0001] vs 33.3%; Fig 1A) and ΔHAQ-DI (Δ0.35 [p<0.05] and Δ0.40 [p<0.01] vs 0.18; Fig 1B) vs PBO, with responses maintained to M12 (Fig 1C&D). Greater efficacy was also seen for adalimumab vs PBO. Tofacitinib 5 & 10 mg Bd were superior to PBO for ACR20 response rates at Week 2 (22.4% [p<0.001] and 31.7% [p<0.001] vs 5.7%; Fig 1C). Secondary endpoints supported primary findings (data not shown). >91% of pts were radiographic non-progressors at M12 (defined as an increase from baseline in mTSS <0.5). M12 safety findings were similar between groups (Fig 1E).

Conclusions: In TNFi-naive pts with active PsA, tofacitinib was superior to PBO for ACR20 response rate and ΔHAQ-DI at M3, with superiority vs PBO as early as Week 2 for ACR20, which was maintained to M12. No new safety risks were identified vs previous studies in other indications.

Acknowledgements: Previously presented at ACR 2016, to be presented at AAD 2017 and reproduced with permissions. This study was sponsored by Pfizer Inc. Editorial support was provided by AG McCluskey of CMC and was funded by Pfizer Inc.
Conclusions: In pts with active PsA and ≥3% BSA of psoriasis, GUS demonstrated significant improvement on joint symptoms, physical function, psoriasis, enthesitis, dactylitis and quality of life. GUS was well tolerated with no unexpected safety findings in this population.

Disclosure of Interest: A. Deodhar Grant/research support from: Janssen, Abbvie, Pfizer, Novartis, UCB, Eli Lilly, Glaxo, Consultant for: Janssen, Eli Lilly, Pfizer, Novartis, UC, A. Gottlieb Grant/research support from: Janssen, Abbvie, Pfizer, Novartis, UCB, Eli Lilly, Glaxo, Abbvie, Pfizer, Novartis. A. Deodhar Consultant for: Amgen Inc., Astellas, Abbvie, Janssen, Pfizer, Baxalta, Celgene Corporation, J. Gomez-Reino Grant/research support from: Celgene Corporation, D. Nguyen Employee of: Celgene Corporation, L. Teng Consultant for: Celgene Corporation and Novartis, N. Delev Employee of: Celgene Corporation, D. Nguyen Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, J. Gomez-Reino Grant/research support from: Roche and Schering-Plough, Consultant for: BMS, Pfizer, Roche, Schering-Plough, UCB, J. Aelion Grant/research support from: AbbVie, Arena Bioscience, AstraZeneca, BMS, Celgene Corporation, Centocor, Celgene Corporation, Genentech, GlaxoSmithKline, Human Genome Sciences, Janssen, Eli Lilly, Merck, Mesoblast, Novartis, Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, Vertex Pharmaceuticals.


Background: ACTIVe is the first apremilast (APR) trial to evaluate time to onset of efficacy beginning at Wk 2 in a biologic-naïve psoriatic arthritis (PsA) patients (pts) who may have had exposure to 1 prior conventional DMARD.

Objectives: Report the study results through Wk 52.

Methods: Pts were randomized (1:1) to APR 30 mg bid or placebo (PBO). Pts were eligible for early escape (investigator discretion) if ≥40% of ACR20 responders entered active treatment with APR. The primary endpoint was ACR20 response at Wk 16. Other assessments included changes in DAS-28 (CRP), SJC, TJC, HAQ-DI, morning stiffness severity and enthesitis, as measured by the Gladman Enthesitis Index (GEn; 0=no enthesitis, 6=all 6 sites active). Along with collection of safety data, tolerability adverse events (AEs) of diarrhea were further characterized.

Results: 219 pts were randomized (APR: n=110; PBO: n=109); overall, 160/180 (88.9%) pts receiving APR completed Wk 52. Separation in the proportion of ACR20 responders to APR vs PBO was noted at Wk 2 (16.4% vs 6.4%; P=0.0052), the first post-baseline (BL) visit. Early onset of response to APR was observed across clinical assessments, with improvements in DAS-28 (CRP), SJC, HAQ-DI, and morning stiffness severity (Table). At Wk 16, significant ACR20 response rates were observed with APR vs PBO (38.2% vs 20.2%; P<0.005), with similar rates for the subset of pts with use of 1 prior non-biologic DMARD (39.2% vs 20.5%; P<0.005), which comprises 69% of study pts. Significant reductions in PsA disease activity/manifestations vs PBO were also demonstrated by changes in DAS-28 (CRP) (P=0.0001), SJC, and HAQ-DI (P<0.001); improvement in morning stiffness severity and GEn score (P<0.0014). With continued APR exposure, the Wk 52 ACR20/ACR50/ACR70 response rates were 63.3%/32.4%/14.0%, respectively, and percent change in SJC was 75.4%. Among APR pts with BL enthesitis, 62.8% reached a GEn score of 0. Overall incidence of AEs in the PBO-controlled period was generally similar between APR and PBO. The most commonly reported AEs (≥5% of pts) with APR vs PBO were nasopharyngitis (8.3% vs 6.4%), nausea (8.3% vs 1.8%), headache (7.3% vs 3.7%), hypertension (6.4% vs 6.4%) and, diabetes (pt or investigator reported) (14.7% vs 11.0%); using a protocol-defined characterization of diarrhea (≥2 watery/liquid stools/day), overall incidence was lower for APR and PBO (11.0% and 8.3%). Serious AEs were lower with APR and PBO (2.8% vs 4.6%). No opportunistic infections, reactivations of TB, or cases of marked depression were seen. In general, no increase was seen in AE incidence/severity with longer-term exposure to APR.
Randomized, Double-Blind, Global Clinical Trial to Evaluate Equivalence of CHS-1420 to Adalimumab in Patients with Psoriatic Arthritis

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Background: CHS-1420 is being developed as a proposed biosimilar to adalimumab for the treatment of rheumatoid arthritis, plaque psoriasis (PsO), and other auto-immune diseases.

Objectives: This phase 3, randomized, double-blind, active-controlled, multicenter study evaluated the equivalence of CHS-1420 to adalimumab in patients with active, moderate-severe, chronic plaque PsO, including patients with psoriatic arthritis (PsA).

Methods: Male and female patients (aged ≥18 years) were randomized to CHS-1420 or adalimumab. Patients received 40 mg x 2 on Day 0 and then 40 mg every other week (QOW) by subcutaneous injection. To establish the equivalence of CHS-1420 to adalimumab, the 95% CI of the treatment difference for the primary endpoint, PASI75 at Week 12, had to be within pre-specified equivalence margins of ±15%.

Results: The full analysis population for the primary efficacy endpoint consisted of 545 patients (mean age 43.9 years), with 274 and 271 in Group A and Group B, respectively. The mean BMI was 29.6 kg/m², and 72.3% were male. At Week 12, the proportion of patients achieving a PASI75 from Baseline was 77.7% in Group A and 74.5% in Group B. The 95% CI of the treatment difference [-3.63, 10.28] was within the pre-specified equivalence margin [-15.0, 15.0]. Sensitivity analyses supported equivalence of the two treatments.

Conclusions: In the safety population (n=545), adverse events were reported in 48.5% and 50.0% of patients with PsA in Group A and Group B, respectively. A PASI75 was achieved by 81.5% and 77.0% of patients with PsA in Group A and Group B, respectively. A PASI90 was achieved by 47.2% and 44.7% of patients with PsA in Group A and Group B, respectively. A PASI120 was achieved by 15.2% and 14.2% of patients with PsA in Group A and Group B, respectively. A PASI140 was achieved by 10.0% and 9.2% of patients with PsA in Group A and Group B, respectively. A PASI160 was achieved by 3.9% and 2.8% of patients with PsA in Group A and Group B, respectively.

Radiographic Progression of Structural Joint Damage in Patients with Active Psoriatic Arthritis Treated with Ixekizumab over 52 Weeks

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Background: Ixekizumab (IXE), an anti-interleukin-17A monoclonal antibody, was shown to be superior to placebo (PBO) in clinical responses and inhibiting the progression of structural joint damage in patients (pts) with psoriatic arthritis (PsA) treated for 24 weeks (wks). 1

Objectives: To assess progression of structural joint damage in PsA pts with IXE for up to 52 wks.

Methods: Biologic DMARD-naïve pts with active PsA (N=417) entered into SPIRIT-P1 (NCT01695239), a double-blind phase 3 trial. Pts must have had ≥1 x-rays of the hand and foot and x-rays confirmed by central reader. 350 pts had a C-reactive protein level > 6 mg/L at screening. 417 pts were randomized to IXE 80 mg every 2 wks (Q2W; N=103) or 4 wks (Q4W; N=107) following a 160 mg initial dose, PBO (N=106), or adalimumab 40 mg every 2 wks (ADA; active reference arm; N=101) for 24 wks. In the Extension Period (EXT: Wks 24–52), PBO and ADA pts were re-randomized (1:1) to IXE2QW or IXE4QW at Wk 16 (inadequate responders) or Wk 24; ADA pts underwent a washout prior to IXE treatment. All pts were assessed for structural joint damage using the van der Heijde modified PsA Total Sharp Score (mTSS, 0–528 scale). X-rays at Wks 0, 24 and 52 were scored independently by 2 readers blinded to timepoint and clinical data (average of readers). mTSS was excluded from the pre-specified analysis if the radiograph was taken after the scheduled visit date. In a post-hoc analysis, mTSS from a radiograph taken after the scheduled visit date was interpolated and considered as observed data. Any missing data at Wk 52, in either presentation, were imputed using a linear extrapolation if they had at least 1 post-baseline value.

Results: Pts had active PsA at Week 0 (Table). 381 pts (91.3%) entered the EXT, with 374 (96.2%) having radiographs collected during the EXT. Wk 52 mean (SD) mTSS change from baseline were 0.54 (2.11) and 0.09 (1.0) for pts randomized to IXE4QW and IXE2QW at baseline, respectively. Similar changes at Wk 52 were obtained with the post-hoc analysis (Table). The majority of IXE2QW or IXE4QW pts exhibited no structural progression through 1 year of IXE treatment (Figure).

Conclusions: Over a 52 wk period, minimal changes in mTSS were observed in PsA pts entering the EXT and treated with IXE2QW or IXE4QW. 1

References:


Abstract OP0221 – Table 1. Radiographic Progression of Structural Joint Damage for EXT Pts

<table>
<thead>
<tr>
<th>PBO/IXE4QW (N=45)</th>
<th>PBO/IXE2QW (N=46)</th>
<th>ADA/IXE4QW (N=49)</th>
<th>ADA/IXE2QW (N=48)</th>
<th>IXE4QW/IXE4QW (N=97)</th>
<th>IXE2QW/IXE2QW (N=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mTSS (Mean (SD))</td>
<td>24.0 (2.3)</td>
<td>24.0 (2.3)</td>
<td>15.4 (3.2)</td>
<td>19.6 (3.3)</td>
<td>15.2 (2.9)</td>
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<tr>
<td>Tender Joint Count</td>
<td>19.2 (14.0)</td>
<td>20.8 (13.6)</td>
<td>18.8 (12.8)</td>
<td>21.3 (13.8)</td>
<td>21.5 (13.8)</td>
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<td>Swollen Joint Count</td>
<td>10.7 (7.1)</td>
<td>11.0 (7.4)</td>
<td>9.6 (5.5)</td>
<td>12.2 (7.3)</td>
<td>12.2 (7.3)</td>
</tr>
<tr>
<td>mTSS, Pre-Specified (Mean (SD))</td>
<td>15.6 (24.3)</td>
<td>15.4 (30.2)</td>
<td>15.2 (29.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 52 Change from Baseline</td>
<td>n=31</td>
<td>n=37</td>
<td>n=36</td>
<td>n=34</td>
<td>n=50</td>
</tr>
<tr>
<td>mTSS</td>
<td>0.27 (0.8)</td>
<td>0.41 (0.8)</td>
<td>0.32 (1.0)</td>
<td>-0.03 (0.4)</td>
<td>0.54 (2.1)</td>
</tr>
<tr>
<td>Week 52 Change from Baseline</td>
<td>n=44</td>
<td>n=45</td>
<td>n=47</td>
<td>n=45</td>
<td>n=97</td>
</tr>
<tr>
<td>mTSS</td>
<td>0.25 (0.8)</td>
<td>0.51 (1.1)</td>
<td>0.24 (0.9)</td>
<td>0.06 (0.5)</td>
<td>0.47 (1.9)</td>
</tr>
</tbody>
</table>

N = EXT pts; n = pts with baseline and ≥1 post-baseline radiograph assessments.

NEX5: NEX5 patients. NEX5 Pts with baseline and Wk 52 radiograph assessments. mTSS values from radiographs taken after the scheduled visit date were interpolated and considered as observed data.

Conclusions: Over a 52 wk period, minimal changes in mTSS were observed in PsA pts entering the EXT and treated with IXE2QW or IXE4QW.
Secukinumab provides sustained improvements in the signs and symptoms of active psoriatic arthritis—104 weeks results from a phase 3 trial, future 2

I.B. McNittnes 1, P.J. Meese 2, C. Ritchlin 3, P. Rahman 4, A. Gottlieb 5, B. Kirkham 6, R. Kajekar 7, E.M. Delicha 8, L. Pricop 7, S. Mpofu 8 on behalf of the FUTURE 2 study group. 1University of Glasgow, Glasgow, United Kingdom; 2Swedish Medical Centre and University of Washington, Seattle; 3University of Rochester, Rochester, United States; 4Memorial University, St. John’s, Canada; 5New York Medical College, New York, United States; 6Guy’s & St Thomas’ NHS Foundation Trust, London, United Kingdom; 7Novartis Pharmaceuticals Corporation, East Hanover, United States; 8Novartis Pharma AG, Basel, Switzerland

Background: Secukinumab significantly improved the signs and symptoms of psoriatic arthritis (PsA) over 52 weeks (wks) in FUTURE 2 study (NCT01752634). 1, 2, 3 Objectives: To present longer-term (104 wks) efficacy and safety data of secukinumab from FUTURE 2 study. Methods: Overall, 397 patients (pts) with active PsA were randomised to secukinumab (300, 150, or 75 mg) or placebo at baseline, Wks 1, 2, 3, and 4, and every 4 wks thereafter. Assessments at Wk 104 are from pts originally randomised to secukinumab and included ACR20/50/70, PASI 75/90, DAS28-CRP, CRP, SF-36 PCS, HAQ-DI, dactylitis, and enthesitis. Multiple imputation was used for analysis of binary variables and mixed-model repeated measures for continuous variables. Analyses stratified by anti-TNFα status (naïve/inadequate response or intolerance to these agents) were prespecified and are reported as observed. Safety analysis included all pts who received ≥1 dose of secukinumab. Results: In total, 86/100 (86.0%), 76/100 (76.0%) and 65/99 (65.7%) pts in the secukinumab 300, 150, and 75 mg groups respectively completed 104 wks of treatment. Prespecified clinical improvements were observed through Wk 104 with secukinumab across all clinically important domains of PsA (Table). Responses were sustained through Wk 104 regardless of anti-TNFα status. Over the entire treatment period (mean ±SD exposure to secukinumab of 709±210.99 days), the exposure adjusted incidence rates for serious infections/infections, inflammatory bowel disease and malignant/unspecified tumors with secukinumab were 1.6, 2.3, 0.5 and 1.3, respectively.

Table 1. Summary of Efficacy Results at Wk 104

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Secukinumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg s.c.</td>
<td>150 mg s.c.</td>
</tr>
<tr>
<td>(N=100)</td>
<td>(N=100)</td>
</tr>
<tr>
<td>ACR20</td>
<td>69.4</td>
</tr>
<tr>
<td>ACR50</td>
<td>50.6</td>
</tr>
<tr>
<td>ACR70</td>
<td>33.1</td>
</tr>
<tr>
<td>PASI 75</td>
<td>79.5</td>
</tr>
<tr>
<td>PASI 90</td>
<td>69.6</td>
</tr>
<tr>
<td>SF-36 PCS, LS mean change from BL (SE)</td>
<td>6.8 (0.85)</td>
</tr>
<tr>
<td>DAS28-CRP, LS mean change from BL (SE)</td>
<td>71.9 (1.12)</td>
</tr>
<tr>
<td>HAQ-DI, LS mean change from BL (SE)</td>
<td>0.50 (0.05)</td>
</tr>
<tr>
<td>Resolution of enthesitis</td>
<td>71.5</td>
</tr>
<tr>
<td>Resolution of dactylitis</td>
<td>79.7</td>
</tr>
</tbody>
</table>

*% responders unless otherwise specified. 1Assessed in pts with psoriasis affecting ≥3% body surface area at BL (300 mg: n=41; 150 mg: n=58; 75 mg: n=50). 2Assessed in pts with ≥3% body surface area. Pts without missing responses were imputed as non-responders, except if the missing value was between 2 visits for which the pt was a responder. In that case the missing value was imputed as a responder.

Conclusions: Secukinumab 300 and 150 mg provided sustained improvements in signs and symptoms and multiple clinical domains of active PsA through 2 years of therapy. Secukinumab was well tolerated, with a safety profile consistent with that reported previously.

References:

Disclosure of Interest: I. McNittnes Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB; Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB; Speakers Bureau: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB; raft Grant/research support from: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, C. Ritchlin Grant/research support from: Amgen, UCB, Abbvie, Novartis, and Janssen, Consultant for: Amgen, UCB, Abbvie, Novartis, and Janssen, Speakers Bureau: Amgen, UCB, Abbvie, Novartis, and Janssen, P. Rahman Consultant for: Abbvie, Abbvie, Amgen, BMS, Celgene, Janssen, Novartis, Pfizer and Roche. Consultant for pharmaceutical companies dealing with biologic agents in rheumatology, A. Gottlieb Grant/research support from: paid to Tufts Medical Center until 6/11/16 thereafter: None; Cencocor (Janssen) Inc, Amgen, Abbott (AbbVie), Novartis, Celgene, Pfizer, Lily, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen Inc., Astellas, Akros, Centocor (Janssen) Inc., Celgene Corp., Bristol Myers Squibb Co., Beiersdorf Inc., Abbott Labs. (AbbVie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Denrmosp Ltd., Inyoie, Pfizer, Carliite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo SmithKline, Xenoport, Catabasis, Meiji Seika Pharma Co. Ltd, Takeda, Mitsubishi, Tanabe Pharma Development America Inc., Genentech, Baxalta, Kneta One, KPI Therapeutics, Crescendo Bioscience, Aclaris, Amicus and Crescendo Labs, B. Kirkham Grant/research support from: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche, and UCB, Consultant for: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche, and UCB, and R. Kajekar Shareholder of: Novartis, Employee of: Novartis, E. M. Delicha Employee of: Novartis, L. Pricop Shareholder of: Novartis, Employee of: Novartis, S. Mpovu Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.2221

OP0223 ABATACET IN THE TREATMENT OF ACTIVE PSORIATIC ARTHRITIS: 1-YEAR RESULTS FROM A PHASE III STUDY

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Background: In the Phase III ASTRAEA trial (NCT01860976), abatacept (ABA), a selective T-cell co-stimulation modulator, significantly increased ACR20 response (primary endpoint; PE) and had an overall beneficial effect vs placebo (PBO) on musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA) at 24 weeks (Wk1). Objectives: To analyse 1-year results from ASTRAEA. Methods: Pts with active disease (≥3 swollen and ≥3 tender joints), ≥2 cm target lesion of plaque psoriasis and inadequate response/intolerance to ≥1 DMARD, included ABA pts (n=211) and PBO pts (n=210). Pts switched to OL ABA (early escape; EE) for 28W, followed by open-label (OL) SC ABA up to 52W. Randomization was stratified by MTX use, prior TNF inhibitor (TNFα) use and skin involvement ≥3% of body surface area. Pts without ≥20% improvement in joint counts at W16 were switched to OL ABA (early escape; EE) for 28W (total study time: 44W). Pre-specified exploratory endpoints included: ACR20/50/70 responses at W44; adjusted mean changes from baseline (BL) in DAS28-CRP (post hoc analysis) and HAQ-DI at W44 and PsA-modified total Sharp/van der Heijde score (SHS) at W44 (EE pts)/W52 (non-EE pts); complete resolution of BL enthesitis and dactylitis at DMARD (EE pts) vs Psoriasis Area and Severity Index (PAI) 50/75 responses at W44. Analyses used the ITT population with non-responder imputation for missing values and actual data at each time point for all pts (denominator at each time point equal to number of pts in ITT population). All missing responses were imputed as non-responders, except if the missing value was between 2 visits for which the pt was a responder. In that case the missing value was imputed as a responder.

Results: Of 424 pts enrolled, 213 received ABA and 211 PBO. Most (>60%) pts had received prior TNFs. Of pts in the ABA and PBO groups, 76 (36%) and 89 (42%) were EE, 12 (6%) and 24 (11%) discontinued by PE of W24;
Results: Patients who started on MTX monotherapy had lower baseline disease activity and fewer were erosive and autoantibody positive; other baseline characteristics were comparable between medication groups. The number of patients on combination therapy with bDMARDs was too small to perform analyses (26 visits in 11 patients). For patients starting on MTX monotherapy, 62% remained bDMARD naive, or MTX+glucocorticoids, the PS-adjusted effects of MTX-dose (high vs low) on DAS, DAS28 and HAQ were small and not clinically meaningful. The adjusted main associations between MTX-dose and outcomes were often in opposite direction and/or much larger than the PS adjusted associations, suggesting that confounding by indication plays a role and that (at least some) correction was achieved by adjusting for the PS (table 1).

Conclusions: In a daily practice derived database in DMARD-naïve early RA patients, we found no early clinical benefit of high over low initial MTX dosages, neither for MTX monotherapy nor for combination therapy with MTX and csDMARDs or glucocorticoids. This seems to contradict a general trend over time to start higher MTX-doses. 

Disclosure of Interest: None declared 
DOI: 10.1136/annrheumdis-2017-eular.1601

OP0225 THE EFFECT OF A LOW VERSUS HIGH FIRST PRESCRIBED DOSE OF METHOTREXATE ON EUULAR RESPONSE AT SIX MONTHS USING DATA FROM THE RAMS STUDY

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Background: Methotrexate (MTX) is one of the most commonly used drugs for the treatment of rheumatoid arthritis (RA). Recommendations by an international panel stated that oral MTX should be started at 10–15mg/week, with escalation of 5mg/week every 4–6 weeks up to 20–30mg/week. In the UK, RA drug choices in terms of the starting dose prescribed for MTX, likely because of a lack of published evidence on the importance of MTX dose on its efficacy and safety.

Objectives: To compare 6 month response to MTX in RA patients starting 7.5mg/week versus those starting a 15mg/week.

Methods: Patients were recruited to the national, UK, multi-centre (n=35) longitudinal observational Rheumatoid Arthritis Medication Study (RAMS), including patients starting MTX for the first time with complete DAS28 at baseline and six months were included in this analysis. Patients were categorized into EUULAR non-responders, moderate responders or good responders. Patients were categorised into those starting a low dose of MTX (<7.5mg/week) (LM-group) or a high dose of MTX (≥ 7.5mg/week) (HM-group).

Table 1

| Age, years | 58 (47–69) | 61 (51–69) | 0.13 |
| Gender, % female | 70 | 60 | 0.03 |
| Disease duration, months | 6 (1–11) | 6 (1–11) | 0.65 |
| Tender joint count | 7 (3–13) | 5 (2–11) | 0.05 |
| Swollen joint count | 5 (2–9) | 5 (2–10) | 0.62 |
| Physician VAS, mm | 47 (27–74) | 43 (18–71) | 0.001 |
| DAS28 score at baseline | 4.2 (3.4–5.2) | 4.1 (3.2–5.1) | 0.24 |
| EULAR response at 6 months, n (%) | 3.5 (2.7, 4.1) | 3.0 (2.2, 4.1) | 0.004 |
| HAQ at 6 months | 1.8 (1.6–1.9) | 1.6 (1.4–1.8) | 0.005 |
| Other nbDMARD use, n (%) | 30 (17) | 61 (10) | 0.03 |
| EULAR response at 6 months, n (%) | 0.09 |

Non-responders

| Non-responders | 50 (45) | 184 (42) |
| Moderate responders | 36 (32) | 108 (25) |
| Good responders | 26 (23) | 145 (33) |

Scores are median [IQR].
SUSTAINED EFFECTIVENESS OF METHOTREXATE WITH STEP-DOWN GLUCOCORTICOID REMISSION INDUCTION (COBRA SLIM) FOR EARLY RHEUMATOID ARTHRITIS IN A TREAT-TO- TARGET SETTING: 2-YEAR RESULTS OF THE CARERA TRIAL

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Background: The CareRA trial showed that remission induction with MTX and a moderate-dose of Glucocorticoids (GIC) (COBRA Slim) in a treat-to-target setting is effective and safe in early Rheumatoid Arthritis (eRA) patients. This strategy showed equally high remission rates at 52 weeks (W), a favourable safety profile compared to DMARD combinations and GC and very few patients had to start biologicals.

Objectives: To compare the outcome of different intensive combination treatment strategies in high-risk patients of the CareRA trial at W104, focussing on persistent disease control.

Methods: CareRA is a two-year prospective investigator-initiated pragmatic multicentre RCT; csDMARD naïve eRA patients were stratified into a high- or low-risk group based on classical prognostic markers (presence of erosions, RF, anti-CCP and DAS28-CRP). High-risk patients (n=289) were randomized to low-risk group compared to DMARD combinations and GC and very few patients had to start biologicals.

Results: 810 patients were included in this study: 171/810 (21%) starting low dose MTX and 639/810 (79%) starting high dose MTX. Patients in the HM-group had significantly lower physician and patient VAS scores and less functional disability compared to those in the LM-group (table). These patients were also less likely to be prescribed concomitant (nbDMARDs) (17% vs. 10%). DAS28 showed at 6 months a significantly lower value for patients in the HM-group (RRR: 2.65 (95% CI 1.37, 5.14)).

Conclusions: Patients with RA starting MTX on a higher dose have increased odds of having a good EULAR response compared to non-response at 6 months.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6047
EFFECT OF BASELINE SERUM CRP LEVELS ON CLINICAL EFFICACY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH FILGOTINIB: POST-HOC ANALYSIS FROM TWO PHASE 2B STUDIES

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Background: Filgotinib (GLPG0634, GS-6034) is an oral, selective JAK1 inhibitor that has shown a favorable safety and efficacy profile both as add-on to methotrexate (MTX) and as monotherapy in two 24-week placebo-controlled phase 2B studies in active rheumatoid arthritis (RA) patients with inadequate response to MTX (MTX-IR)1,2.

Objectives: To assess effect of baseline serum CRP levels on clinical efficacy in MTX-IR RA patients treated with filgotinib.

Methods: Patients were randomized in a double blind manner to placebo (PBO) or one of 3 daily doses of filgotinib (50mg, 100mg or 200mg) for 24 weeks. In the DARWIN 1 study, filgotinib on the background of MTX was evaluated as once (QD) or twice daily treatment. In the DARWIN 2 study once-daily filgotinib was assessed as monotherapy. The inclusion criterion for CRP was amended during the studies and decreased over time from 13.5 mg/L to 6.3 mg/L. This post hoc analysis included patients treated with the selected Phase 3 filgotinib doses, 100mg and 200mg QD, and PBO. Efficacy outcomes were analyzed by baseline CRP level (low: ≤9 mg/L and high: >9 mg/L, with 9mg/L as ULN).

Results: Baseline disease activity was high, with mean DAS28(CRP) scores of 5.6 and 5.7 in the low CRP subgroups for DARWIN 1 and DARWIN 2, respectively, and 6.3 in the high CRP subgroups for both studies. Mean CRP levels at baseline were elevated (16.3 - 35.3 mg/L). In both low and high CRP subgroups, patients on filgotinib 100mg or 200mg QD for 12 weeks showed efficacy over PBO, as measured by change from baseline in DAS28(CRP), CDAI and HAQ-DI, and ACR20 (Table 1). Despite slight numerical differences, baseline CRP level had no consistent effect on filgotinib efficacy, neither for endpoints including CRP (DAS28(CRP) or ACR20) nor for endpoints not including CRP (CDAI).

Table 1. Change from baseline in key efficacy parameters at Week 12 by CRP subgroup (mean (SE)).

<table>
<thead>
<tr>
<th>CRP Subgroup</th>
<th>DARWIN 1</th>
<th>DARWIN 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low CRP (≤9 mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PBO</td>
<td>33</td>
<td>53</td>
</tr>
<tr>
<td>Filgotinib 100mg QD</td>
<td>25</td>
<td>60</td>
</tr>
<tr>
<td>Filgotinib 200mg QD</td>
<td>15</td>
<td>71</td>
</tr>
<tr>
<td>ACR20 (%)</td>
<td>11</td>
<td>61</td>
</tr>
<tr>
<td>High CRP (&gt;9 mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>53</td>
<td>61</td>
</tr>
<tr>
<td>PBO</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>Filgotinib 100mg QD</td>
<td>71</td>
<td>49</td>
</tr>
<tr>
<td>Filgotinib 200mg QD</td>
<td>61</td>
<td>50</td>
</tr>
</tbody>
</table>

Conclusions: Post hoc analysis of two Phase 2B studies in MTX-IR RA patients suggests that filgotinib treatment once daily at 100mg and 200mg both on the background of MTX and as monotherapy is consistently associated with improved clinical outcomes compared to placebo, regardless of baseline CRP levels.

References:


DOI: 10.1136/annrheumdis-2017-eular.5428

THE EFFECTIVENESS OF ZOSTER VACCINE IN RA PATIENTS SUBSEQUENTLY TREATED WITH TOFACITINIB

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Background: Rheumatoid arthritis (RA) patients (pts) are at increased risk of herpes zoster (HZ). The most recent ACR guidelines of 2015 recommend vaccination in pts aged ≥50 years prior to starting biologic DMARDs or tocilizumab,1

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3892

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5428

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3892
an oral Janus kinase inhibitor for the treatment of RA. Live zoster vaccine (LZV) has shown 70% efficacy in immunocompetent adults aged 50–59 years and 51% efficacy in those aged >60 years. We previously reported that pts with RA on background methotrexate who started 3 months of treatment with tofacitinib after LZV had similar varicella zoster virus (VZV)-specific immunity to placebo (PBO) pts after their VZV immunity at Week 6 post-vaccination was comparable with healthy individuals aged >50 years.

Objectives: To evaluate the long-term effectiveness of LZV in pts with RA via the incidence of HZ after treatment with tofacitinib for up to 27 months.

Methods: Data were analysed from a prior cohort of pts (n=100) given LZV and then randomized 2–3 weeks later to tofacitinib 5 mg twice daily (BID) or PBO for 12 weeks (A3991237; NCT02147587). At 14 weeks post-vaccination pts joining the long-term extension (LTE) study ORAL SequeL (NCT04013699; study ongoing; database not locked) initiated open-label treatment with tofacitinib 5 or 10 mg BID. The incidence of HZ post-vaccination after tofacitinib exposure up to 27 months (based on an extended follow-up beyond January 2016 data snapshot) was evaluated. Among HZ cases, we analysed measures of VZV-specific immunity with average immunity after LZV.

Results: 112 pts were randomized to PBO (n=57) or tofacitinib 5 mg BID (n=55). 100 pts continued to receive tofacitinib in ORAL SequeL. Five cases (not adjudicated) of HZ occurred (#1: 202 days [219 days post-LZV]; #2: 267 days [281 days post-LZV]; #3: 702 days [748 days post-LZV]; #4: 699 days [741 days post-LZV]; #5: 446 days [544 days post-LZV] after initiation of tofacitinib. Cases #1, #2, #3 and #4 were monodermatomal; #5 involved 5 dermatomes. All cases resolved within treatment. Cases #1, #4 and #5 had undetectable ELISPOT measures at baseline and Week 6 post-vaccination, indicating a lack of VZV-specific immunity. Cases #2 and #3 responded adequately to vaccination by both immunoglobulin G (IgG) and ELISPOT measures, but had lower than average VZV IgG levels, both at baseline and at Week 6. (Table).

Conclusions: LZV prior to treatment with tofacitinib is effective at boosting IgG levels and cell-mediated immunity towards VZV. No pts who developed both HZ and VZV prior to treatment with tofacitinib is effective at boosting IgG levels and cell-mediated immunity towards VZV.

References:

Acknowledgements: This study was sponsored by Pfizer Inc. The authors would like to acknowledge Lisa McNeil. Editorial support was provided by K Haines and was funded by Pfizer Inc. Scientific Abstracts Friday, 16 June 2017 149


Tofacitinib With and Without Methotrexate Versus Adalimumab With Methotrexate for the Treatment of Rheumatoid Arthritis: Results from Oral Strategy, a Phase 3B/4 Randomised Trial

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. There is no direct comparison of tofacitinib monotherapy versus tofacitinib + MTX in MTX inadequate responders (IR) and limited data comparing tofacitinib (±MTX) vs adalimumab (ADA) + MTX in patients (pts) with RA.

Objectives: To compare efficacy and safety of tofacitinib monotherapy, tofacitinib+MTX, and ADA+MTX in a head-to-head, non-inferiority trial in MTX-IR pts.

Methods: In this randomised, triple-dummy, active-controlled, 1-year, Phase 3B/4 trial (ORAL Strategy; NCT02187055), pts had active RA (<4 tender/swollen joint counts and ≤4 swollen joints at joint count) and were taking ≤12.5 mg/day MTX for ≥281 days post-LZV, #3: 702 days [748 days post-LZV], #4: 699 days [741 days post-LZV], #5: 446 days [544 days post-LZV] after initiation of tofacitinib. Cases #1, #2, #3 and #4 were monodermatomal; #5 involved 5 dermatomes. All cases resolved within treatment. Cases #1, #4 and #5 had undetectable ELISPOT measures at baseline and Week 6 post-vaccination, indicating a lack of VZV-specific immunity. Cases #2 and #3 responded adequately to vaccination by both immunoglobulin G (IgG) and ELISPOT measures, but had lower than average VZV IgG levels, both at baseline and at Week 6. (Table).

Conclusions: Tofacitinib 5 mg BID+MTX was as effective as ADA+MTX in
MTX-IR pts with RA. However, clinical outcomes of all 3 regimens, including tofacitinib 5 mg BID monotherapy, were comparable. There were no new or unexpected safety issues.

References:

Acknowledgements: This study was funded by Pfizer Inc. Editorial support provided by D Binks of CMC.


FRIDAY, 16 JUNE 2017

New treatments in SLE, Sjögren’s and APS —

OP0231

THE EFFECT OF “TRIPLE THERAPY” WITH ANTICOAGULATION PLUS CORTICOSTEROIDS PLUS PLASMA EXCHANGE AND/OR INTRAVENOUS IMMUNOGLOBULIN ON THE MORTALITY OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS) PATIENTS

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Background: In a cohort of 525 episodes of CAPS (CAPS Registry), we evaluated the relationship between triple therapy and mortality. Patients were grouped in three based on their treatments: a) triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins); b) drugs included in the triple therapy but in different combinations; c) none of the treatments included in the triple therapy. The primary endpoint was all-cause mortality. Multivariate logistic regression models were used to compare mortality risk between groups taking into account a set of possible confounding variables.

Results: The “CAPS registry” cohort included 525 episodes of CAPS accounting for 502 patients. After excluding 38 episodes (7.2%), a total of 487 episodes of CAPS accounting for 471 patients (mean age 38 years; 67.9% female; primary APS patients 68.8%) were analyzed. Overall, 177 (36.3%) patients died. Triple therapy was prescribed in 197 episodes (40.5%), other combinations in 278 (57.1%), and none of those treatments in 12 episodes (2.5%). According to these three groups, mortality rate increased up to 27.9%, 40.6%, and 75%, respectively. Triple therapy was positively associated with a higher chance of survival when compared to non-treatment (adjusted odds ratio [OR]: 7.7; 95% confidence interval [95%CI] 2.0–29.7) or to treatment with other combinations of drugs included in the triple therapy (adjusted OR 6.8; 95%CI 1.7–29.6). Triple therapy accounted for a 50% decrease of the risk of death in patients with CAPS that received this combination of drugs.

Conclusions: Triple therapy is independently associated to a higher survival rate among CAPS.

Acknowledgements: To the CAPS Registry Project Group (European Forum on Antiphospholipid Antibodies).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7113

OP0232

SUSTAINED SAFETY AND EFFICACY OVER 10 YEARS WITH BELIMUMAB (BEL) PLUS STANDARD SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) THERAPY (SOC) IN PATIENTS WITH SLE


Background: Preliminary safety and efficacy data from the Phase II BEL open-label extension study (LBSL02; NCT00171487) have been reported. Objectives: Here we present the final 10-year data.

Methods: This was a multicentre, open-label, continuation trial (BEL112626; NCT00583342) of BEL + SoC in patients with a satisfactory response in the parent trial. Patients received intravenous BEL 10 mg/kg every 4 weeks. Baseline was prior to the first ever dose of BEL.

Results: Of 298 patients in the continuation trial, 131 (44%) remained at Year 10. Total BEL exposure was 2154 patient-years. Adverse events (AEs) remained stable or decreased (Table). Two deaths (pseudonodular lung infection; cytomegaloviral pneumonia) were possibly related to BEL. SLE Responder Index (SRI) response increased (Figure), A British Isles Lupus Assessment Group (BILAG) flare (1 new A2 new B scores) occurred in 72.6% of patients and 41.9% had a severe flare (SLE flare Index). Prednisone dose decreased from baseline to Year 10 (Table). Of patients receiving >7.5 mg/day baseline prednisone, 32.6%...
(14/43) decreased their dose to < 7.5 mg/day by Year 10; 95% (9/15) of patients receiving baseline prednisone < 7.5 mg/day had a dose increase to > 7.5 mg/day.

**Conclusions:** Over 10 years BEL + SoC was well tolerated and the rates and nature of AEs were consistent with the known profile of BEL. Efficacy was maintained and prednisone use decreased in those receiving > 7.5 mg/day at baseline.

**Acknowledgements:** Study funded by GSK. Editorial assistance provided by Katie White, PhD, Fishawack Indicia Ltd, UK; funded by GSK.

**Disclosure of Interest:** D. Wallace Grant/research support from: GSK; Consultant for: GSK; E. Ginzirer Grant/research support from: GSK; J. Merrill Grant/research support from: GSK; Bristol-Myers Squibb, Consultant for: Anthera Pharmaceuticals, Inc., GSK, EMD Serono, Inc., Lilly, AstraZeneca, Bristol-Myers Squibb, UCB, Celgene, Biogen, R. Furie Grant/research support from: GSK; Consultant for: GSK, W. Stuhl Grant/research support from: GSK; Pfizer, Consultant for: John- son & Johnson, W. Chatham Grant/research support from: GSK; A. Weinstejn Grant/research support from: GSK, HGS, Consultant for: GSK, HGS, J. McKay Grant/research support from: GSK, MedImmune, Anthera Pharmaceuticals, Inc., Johnson & Johnson, Lilly, Xencor, Inc., W. McCune Grant/research support from: GSK; Lilly, M. Petri Grant/research support from: GSK; Consultant for: GSK, J. Fettplace Shareholder of: GSK; Employee of: GSK, D. Roth Shareholder of: GSK; Employee of: GSK, A. Heath Shareholder of: GSK; Employee of: GSK

**DOI:** 10.1136/annrheumdis-2017-eular.6430

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**OP0233 PRIMARY PROPHYLAXIS OF CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS OF 291 PATIENTS FROM TWO ITALIAN CENTERS**

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**Background:** Systemic lupus erythematosus (SLE) is associated with an increased cardiovascular (CV) risk (1). By retrospectively investigating a one centre cohort, we have recently reported that low-dose aspirin (ASA) use is associated with a reduced CV risk in SLE (2) and long-term hydroxychloroquine (HCQ) exposure may have an additive effect (3).

**Objectives:** This study was conducted on 2 Italian SLE cohorts to confirm these results and assess the role, if any, of statins.

**Methods:** Clinical charts of SLE patients consecutively admitted to 2 University Rheumatology Units from November 2000 to December 2014 who, at admission, had not experienced any CV event, were investigated. ASA, HCQ and statins use and the occurrence of any CV event, were recorded at each visit. Kaplan-Meier analysis was performed to determine the HCQ exposure status associated with a higher CV-free survival. Cox regression analysis was carried out to identify factors independently associated with a first CV event.

**Results:** A total of 291 SLE patients were included in the study and followed for a median of 8 years. During follow-up, 16 CV events occurred. Kaplan-Meier analysis revealed a greater CV event-free rate in the 120 ASA-treated patients taking HCQ at standard dose for more than 5 years than in the 98 patients not treated with ASA or with HCQ for less than 5 years (Figure 1). At univariate analysis, patients with a first CV event compared with those without any thrombotic events were antiphospholipid antibody (aPL) positive (P=0.017 HR 2.91) and had significantly higher blood pressure (P=0.017 HR 3.58), hypercholesterolemia (P=0.015 HR 3.40) and higher disease damage at last visit (P=0.032 HR 1.56). Moreover, ASA treatment (P=0.012 HR 0.27) and HCQ use (P=0.012 HR 0.26) for more than 5 years were negative predictors, while statins use did not show any association (P=0.619). All other variables examined, including smoking, obesity, hypertiglycericidemia, diabetes mellitus, disease activity, severe SLE, other medications (immunosuppressive agents, steroids) were not associated, either positively or negatively, with the occurrence of CV events. At multivariate analysis, taking ASA and HCQ for more than 5 years were protective against thrombosis (HR 0.24 and HR 0.27, respectively), while aPL positivity (HR 4.32) increased the risk of a first CV event.

**Conclusions:** Use of antithrombotics for more than 5 years is associated with a reduced risk of a first thrombosis in SLE patients and the HCA-ASA combination seems to synergistically reduce further the CV risk. Larger, prospective studies are needed to provide a better definition of the role of these drugs in CV primary prevention in SLE.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2517

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**OP0234 CLINICAL AND BIOLOGIC EFFECTS OF ICOSSL BLOCKADE BY AMG 557 IN SUBJECTS WITH LUPUS ARTHRITIS**


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**Background:** Blockade of inducible costimulatory ligand (ICOSL) might be a promising approach for autoimmune diseases such as systemic lupus erythe-matosus (SLE). We evaluated AMG 557, an anti-ICOSL monoclonal antibody, in an exploratory phase 1b study of SLE subjects with inflammatory arthritis, by withdrawing background therapies to improve interpretability of a small study.

**Objectives:** To investigate potential efficacy, safety, and tolerability of AMG 557 in subjects with lupus arthritis.

**Methods:** This double-blind, randomized, placebo-controlled trial enrolled subjects with SLE and active lupus arthritis (>4 tender and 4 swollen joints) and Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] score ≥6 despite stable background immunosuppressants. Upon enrollment, investigators were permitted to use up to 20 mg/day of prednisone, which was tapered by day 85 to 7.5 mg/day or 50% of baseline, whichever was lower. Subjects received AMG 557 210 mg or placebo once weekly for 3 weeks followed by 10 additional doses every other week until day 155. At day 29, background immunosuppressants were withdrawn. The primary clinical endpoint was a composite Lupus Arthritis Responder Index at day 169; response was defined as achieving: (1) 50% decrease in combined tender and swollen joint counts, (2) ≥1 joint improvement in the musculoskeletal subsystem of the British Isles Lupus Assessment Group (BILAG) index and (3) prespecified immunosuppressant medication withdrawal and/or prednisone taper. Safety was a co-primary endpoint. Exploratory endpoints included safety, 4-point reduction of SLEDAI, clinical indices (SLEDAI, BILAG), complement components, autoantibodies, and lymphocyte populations.

**Results:** Twenty subjects (19 females) were randomized (10 AMG 557, 10 placebo) at 8 sites in North America, Asia, and Europe. The primary placebo-controlled trial in lupus arthritis suggest potential clinical benefit of ICOSL blockade by AMG 557. These data support further clinical trials intervening in this costimulatory pathway in SLE and other autoimmune diseases.

**Disclosures:**

A NOVEL B CELL SPECIFIC IFN-I BIOMARKER IS ASSOCIATED WITH PLASMABLAST NUMBERS FOLLOWING B CELL DEPLETION TREATMENT IN SLE

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Background: SLE is a Type I interferon (IFN-I) mediated disease with autoreactive B cells. Plasmablasts, the immediate progeny of B cells, are expanded in SLE and correlate with disease activity. We showed that their rate of regeneration after therapeutic B cell depletion with rituximab is variable and predicts relapse[1]. IFN-I has been shown in vitro to induce the differentiation of B cells into plasmablasts. We previously showed that therapeutic B cell depletion with anti-CD20 mAb leads to a transient reduction in CD20-negative plasmablasts, following which plasmablasts repopulate and their numbers predict clinical relapse. We developed tetherin as a flow cytometric, cell-specific marker for IFN-I response. Objectives: To test the hypothesis that memory B cell tetherin determines the rate of plasmablast repopulation after rituximab.

Methods: 117 rituximab-treated SLE patients were studied prospectively using BILAG-2004 and flow cytometry. In 97 responders we tested plasmablasts at 6 months as a predictor of clinical relapse before 12 months to validate our previous finding. In 50 patients pre-rituximab and 28 patients post-rituximab we performed additional flow cytometry to measure tetherin on each cell subset. Expression of 18 ISGs was measured using Taqman on PBMCs and an ISG score calculated.

Results: We divided clinical responders to rituximab into earlier relapse (12 months) or later relapse (>12 months). As in our published discovery cohort, plasmablasts were strongly predictive of clinical relapse. ROC analysis indicated that a plasmablast count of >0.0008 x 10^11/L at 6 months yielded 73% (95% CI 45–92%) sensitivity and 90% (95% CI 56–99%) specificity in predicting early relapse; area under the curve of 0.86.

Plasmablast numbers after rituximab were associated with Memory B cell tetherin (R=-0.38, p=0.047) but not ISG score (R=0.24, p=0.219) (Table 1).

In pre-rituximab there was no relationship between any IFN assay and plasmablast count. After rituximab treatment there was no correlation between plasmablast count and ISG expression, nor with monocyte or NK cell surface tetherin. However, memory B cell tetherin MFI was positively correlated with plasmablast count (Table 1).

Conclusions: Although interferon stimulated gene expression is commonly used to measure IFN-I activity, tetherin provides a cell-specific assay. We demonstrate that by measuring IFN-I response in B cells specifically, we could explain plasmablast differentiation, and thereby clinical outcome. Memory B cell tetherin is valuable to immunophetype SLE.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1127

Table 1

<table>
<thead>
<tr>
<th>Interferon assay</th>
<th>Plasmablast Count (cells x10^7/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-rituximab (n=50)</td>
<td>Post-rituximab (n=28)</td>
</tr>
<tr>
<td>ISG expression Score</td>
<td>0.11, P=0.448</td>
</tr>
<tr>
<td>Tetherin protein level: Monocytes</td>
<td>-0.016, P=0.296</td>
</tr>
<tr>
<td>T-cells</td>
<td>-0.16, P=0.269</td>
</tr>
<tr>
<td>NK cells</td>
<td>-0.14, P=0.324</td>
</tr>
<tr>
<td>Naïve B-cells</td>
<td>-0.07, P=0.618</td>
</tr>
<tr>
<td>Memory B-cells</td>
<td>0.07, P=0.618</td>
</tr>
</tbody>
</table>

Values are Spearman’s Rank Correlation Coefficient and P values.

BENEFIT AND SAFETY OF ANTIITHROMBOTIC TREATMENT IN 264 PREGNANCIES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME


Background: The management of pregnancy in patients with antiphospholipid syndrome (APS) with aspirin and heparin is based on empiric recommendations. Objectives: Our study aimed to evaluate the outcomes of treated patients with thrombotic and obstetric APS and the safety of antithrombotic treatments prescribed during pregnancy.

Methods: Inclusion criteria were (1) APS (Sydney criteria), (2) live pregnancy at 12 weeks of gestation (WG) with (3) follow up data until 6 weeks post-partum. Data were collected prospectively (PROMISSE study) and retrospectively (four French centers). Adverse pregnancy outcomes (APOs) were defined by fetal death or neonatal death of 8th; pre-term delivery before 36 WG due to pre-eclampsia or placental insufficiency; or small for gestational-age (SGA; ~5th percentile). Major bleeding was defined as blood loss greater than 500ml and/or requiring surgery or transfusion.

In 152 pregnancies (87 collected prospectively) in 204 patients were included (46% with a history of thrombosis, and 23% with associated systemic lupus erythematosus). During pregnancy, treatment included heparin (n=253; 96%) and low-dose aspirin (n=223; 84%). The live birth rate was 86%. APOs occurred in 32%, mostly during the 2nd trimester: fetal deaths 11%, SGA 11%, pre-term delivery before 36 WG due to pre-eclampsia or placental insufficiency 17%. Thirteen maternal thrombotic events occurred in 12 (4.5%) pregnancies. Forty-six maternal hemorrhagic events occurred in 40 (15%) pregnancies (30 events in the post-partum period). Major bleeding was reported in only 6 pregnancies (2.3%) and occurred only after delivery. Except for two events, post-partum hemorrhage occurred in the early post-partum before hospital discharge. No maternal death was observed.

Aspirin therapy during pregnancy was the only independent factor associated with a lower risk of APOs (odds ratio: 0.34; 95% CI: 0.15–0.78; p<0.01) in multivariate analysis. Neither heparin or aspirin alone, nor combined therapy increased the risk of hemorrhage. In the retrospective cohort, emergency caesarian section was the only factor associated with hemorrhagic events during the study period (53% hemorrhages in patients who underwent emergency caesarian compared to 18% p=0.005). Independent risk factors for APOs were elevated body mass index and the presence of lupus anticoagulant.

Conclusions: We report a high level of obstetrical complications in conventionally-treated APS pregnancies, and a beneficial effect of addition of aspirin to prevent obstetric morbidity. Moreover, heparin and aspirin were well tolerated and did not increase risk of hemorrhage.

Disclosure of Interest: None declared

LIFITTEGRASE OPTHALMIC SOLUTION 5.0% FOR TREATMENT OF DRY EYE DISEASE: COMBINED EVIDENCE FROM 5 RANDOMIZED CONTROLLED TRIALS

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Background: Dry eye disease (DED) is a multifactorial disease of the tear film and ocular surface, characterized by ocular discomfort and visual disturbance.1 DED is associated with a number of systemic autoimmune diseases, particularly rheumatoid arthritis and Sjögren’s syndrome.2,3 Lifitigrase is a lymphocyte function-associated antigen-1 (LFA-1) antagonist that inhibits T-cell-mediated inflammation (an underlying factor in DED) and is approved in the US for the treatment of signs and symptoms of DED (lifitigrast ophthalmic solution 5.0%, Xiidra®).

Objectives: To evaluate the combined evidence from 5 clinical trials of lifitigrast ophthalmic solution 5.0% (LIF) in subjects with dry eye disease (DED).

Methods: Adults with DED were randomized to LIF or placebo (PBO) in 5 randomized, double-masked, placebo-controlled trials: 4 12-week efficacy/safety phase 2 (LIF n=58, PBO n=58; phase 3 trials: OPUS-1, LIF n=293, PBO n=295; OPUS-2, LIF n=358, PBO n=360; OPUS-3, LIF n=355, PBO n=356) and a 1-year safety study (SONATA, LIF n=220, PBO n=111). Individuals with Sjögren’s or Sjögren’s-like disease associated with autoimmune disease (rheumatoid arthritis, systemic lupus erythematosus) were eligible to participate if they were not immunodeficient/immunosuppressed, not taking steroids, and met all other inclusion and exclusion criteria. Change from baseline to day 84 in DED signs and symptoms was evaluated across the 12-week studies. Key measures were inferno corneal staining score (ICSS; 0–4 scale), eye dryness score (EDS; visual analogue scale [VAS], 0–100 scale), and visual-related function subscale of a symptom scale (0–4 scale).

Results: LIF improved ICSS versus PBO in the phase 2 study (secondary endpoint; treatment effect 0.35, nominal P=0.0209), OPUS-1 (co-primary; 0.24,
48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN

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Objectives:
Achievement of complete remission (CR) as assessed at week 24 (primary objective) and assessment of the efficacy over 48 weeks (secondary objective), with 2 doses of VCS (low dose VCS: 23.7mg BID and high dose VCS: 39.5mg BID) vs. placebo in subjects with active LN.

Methods:
The double blind placebo controlled AURA study enrolled 265 subjects with active LN in 20 countries. Patients were randomized into 3 arms (placebo, low dose VCS or high dose VCS) in addition to MMF 2g/day and steroids (with rapid tapering). CR was defined as a confirmed urine protein/creatinine ratio (UPCR) of <0.3 mg/mg using first morning void and confirmed estimated glomerular filtration rate (eGFR, CKD-EPI equation) >80 mL/min/1.73 m² or no change from baseline in eGFR of ≥20% in the presence of low dose steroids. Partial remission (PR) was defined as a 50% reduction in UPCR. UPCR assessments were made at each visit, together with biomarker data at regular intervals.

Results:
We now present the 48 week data showing improved CR rates over the 24 week data. The rate of CR was significantly higher in the low dose VCS compared to the control group (32.6% vs. 19.3%; OR: 2.03, p=0.045) at 24 weeks. It was 27.3% in the high dose VCS group (p=NS). Both doses of voclosporin demonstrated superiority to control using time to CR, PR (50% reduction in proteinuria) and time to PR. At 48 weeks, 23.9% of patients on the control arm achieved CR compared to 49.4% low dose (OR: 3.21, p<0.001) and 39.8% high dose (OR: 2.10, p=0.026). Over 92% of subjects experienced at least one adverse event (AE) with the most common two being infections (56% low, 66% high and 55% placebo) and GI disorders (43% low, 52% high and 38% placebo). The overall rate of serious adverse events (SAEs) was numerically higher in both voclosporin groups (28% low, 25% high, 19% placebo) with the nature of SAEs consistent with those observed in patients with highly active LN. Most deaths occurred in the first 2 months and were: low dose (infection3, ARDS2, thrombotic2, cardiac tamponade, pulmonary hemorrhage), high dose (infection, PE) and control (CVA). All were considered unrelated to drug exposure by the investigators. 3 additional deaths occurred in placebo patients after the conclusion of the 48 weeks of treatment.

Conclusions:
The AURA-LV study is the first global study demonstrating the beneficial effect of VCS, in combination with MMF and steroids, in the treatment of LN. Remission rate was rapid. VCS treatment resulted in increasing CR and PR seen by week 6 despite rigorous steroid taper (mean steroid dose 4 mg at week 16). Adverse events were higher in the treated group patient with the nature in keeping with immunosuppression. These promising data will be used to plan subsequent studies of voclosporin in LN.

Acknowledgements:
This data was submitted on behalf of the AURA-LV study investigators.

Disclosure of Interest:

DOI: 10.1136/annrheumdis-2017-eular.7079

FRIDAY, 16 JUNE 2017

Axial spondyloarthritis from risk factor to clinical outcomes

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Background:
Axial spondyloarthropathy (axSpA) is a chronic rheumatic disease that results from a reduction of mobility in the patients’ spine. There are several indices to analyze this mobility: BASMI, which lacks precision and sensitivity to change according to different authors, and UCOASMI (1) based on motion capture, which needs extensive resources that limit its practical applicability. Inertial measurement unit sensors (IMU) give, in real time, the 3D orientation of any anatomical place
of the joint. It could be a sensitive, flexible and cheap technology, useful for assessing mobility in AxSpa, but validation studies are needed.

**Objectives:** To assess reliability and validity of inertial sensors for measuring spinal mobility in patients with axSpA.

**Methods:** 14 subjects: 7 patients with axSpA (5 male and 2 female, age 51.4±6.7 years, evolution time 25.4±11.3 years, 85.7% B27 positive) and a control group of 7 healthy individuals matched in gender and age were recruited. Cervical and lumbar movements were evaluated using 3 IMU sensors (located at forehead, D3 and L4) and a 3D motion capture system synchronously. A test/retest was performed at 5 minutes in the same day with the IMUs and in two days with both systems. Measurements of metrology, BASMI and UCOASMI indices were obtained. An index, iUCOASMI, was calculated using the same measurements used for UCOASMI, but obtained by inertial sensors.

**Results:** Table shows mean values (SD) for each range of movement expressed in degrees. BASMI, UCOASMI and iUCOASMI indexes are also included. Intraclass correlation coefficient (ICC) is indicated as: α: 0.98–Excellent; β: 0.95–0.98 – Very good; γ: 0.70–0.95 – Good; δ: <0.7 – Bad. RMSE error was less than 1° for all measures. There was good correlation (r<0.01) between iUCOASMI with BASFI, BASG, UCOASMI and BASMI. Graph shows results of linear regression between measures obtained with both system (for example: cervical frontal flexion obtained by motion capture and IMUs have a R² of 0.97) and between iUCOASMI with UCOASMI and BASMI.

**Conclusions:** The IMU system measured range of movement, showing good ICC both in the same day and in the two days test/retest. The iUCOASMI, has also shown an excellent correlation with UCOASMI, and with BASMI. Therefore, these kind of systems, based on IMU, may be useful for analyzing spinal mobility in patients with axSpA in a more accurate and reliable way compared with conventional metrology, and more flexible and cheap than other advanced systems, improving their practical applicability.

**References:**

**Acknowledgements:** This study was supported by PIN-0079–2016 research project (Consejería de Salud de la Junta de Andalucía, SPAIN).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2965

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**Abstract OP0240 – Table 1. Prevalence (%) and corresponding Prevalence Ratio (PR) of SpA-related comorbidities in AS, PsA and uSpA**

<table>
<thead>
<tr>
<th>AS cases</th>
<th>PR (95% CI)</th>
<th>PsA cases</th>
<th>PR (95% CI)</th>
<th>uSpA cases</th>
<th>PR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females, n (%)</td>
<td>4772 (54.8)</td>
<td>46112.8</td>
<td>351 (52.2)</td>
<td>5.2 (4.1–6.6)</td>
<td></td>
</tr>
<tr>
<td>Age, mean ±SD</td>
<td>53.0±13.5</td>
<td>19.1 (1.6–2.3)</td>
<td>253 (2.7–3.5)</td>
<td>5.0 (4.1–6.6)</td>
<td></td>
</tr>
<tr>
<td>IBD</td>
<td>139 (52.2)</td>
<td>2.2 (1.7–2.9)</td>
<td>123 (4.1–6.6)</td>
<td></td>
<td></td>
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<tr>
<td>– Crohn’s disease</td>
<td>82 (4.1–6.6)</td>
<td>78 (2.7)</td>
<td>62 (2.7–3.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Ulcerative colitis</td>
<td>102 (4.1–6.6)</td>
<td>18.1 (1.4–2.3)</td>
<td>77 (2.7)</td>
<td></td>
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</tr>
<tr>
<td>Anterior uveitis</td>
<td>351 (4.1–6.6)</td>
<td>3.8 (2.1–4.8)</td>
<td>35 (2.7–3.5)</td>
<td></td>
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<tr>
<td>Psoriasis</td>
<td>51 (4.1–6.6)</td>
<td>4.7 (3.2–6.9)</td>
<td>41 (4.1–6.6)</td>
<td></td>
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<tr>
<td>AV block</td>
<td>12 (4.1–6.6)</td>
<td>1.7 (1.2–2.4)</td>
<td>11 (4.1–6.6)</td>
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<tr>
<td>Aortic regurgitation*</td>
<td>0.0 (4.1–6.6)</td>
<td>0.0 (4.1–6.6)</td>
<td>0.0 (4.1–6.6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Background:** New onset of joint inflammation in patients under anti-TNF-alpha for inflammatory bowel disease (IBD) has been previously described. However, the histological characterization of synovial and bowel compartments has not been reported so far.

**Objectives:** Aim of the study was to evaluate the histological characteristics of paired synovial (ST) and colonic tissues in IBD patients under TNF-alpha blockers.

**Methods:** Consecutive IBD patients without history of co-existing joint involvement who developed peripheral arthritis under TNF-alpha blockers, were prospectively enrolled. Each patient underwent rheumatological evaluation and ultrasound (US) assessment (using Gray scale for synovial hyperthrophy and Power Doppler Signal) of the affected joints. Each patient underwent US guided ST biopsy of the knee, following a standardized procedure and colonoscopy with mucosal biopsies. Each ST and colonic paired sample was stained through immunohistochemistry (IHC) for CD68, CD21, CD3 and CD117. H&E staining was performed for Paneth cells identification. Immunological parameters (Anti-citrullinated peptides antibodies (ACPA), IgM-Rheumatoid Factor (RF) and IgA-RF respectively) were collected for each patient.

**Results:** 10 patients with IBD (46.0±17 years old, 13.2±9.9 years of disease duration, 2.5±1.6 years of TNF-alpha blockers exposure, 6 with Crohn’s Disease and 4 with Ulcerative Colitis respectively) were studied. All patients were negative for ACPA, IgM-RF or IgA-RF and 4 patients were under Methotrexate therapy. 5 (50.0%) patients showed endoscopic and histologically proven inflammation of colonic mucosa. Moreover, IHC revealed that 6 (60.0%) patients had diffuse and 4 (40.0%) had follicular synovitis, respectively. In particular, there was a direct correlation between CD68*, CD21*, CD3*, CD20* and CD117* cells distribution in paired ST and gut tissues in the whole cohort (<p=0.05). No significant differences in terms of disease duration (p=0.48), TNF-alpha blockers exposure time (p=0.29), ESR (p=0.26) and CRP (p=0.91) values were found comparing patients with follicular and diffuse synovitis respectively.

**Conclusions:** Our findings suggest that patients with IBD may develop histologically proven synovitis during TNF-alpha treatment, showing similar histological features in terms of CD68*, CD21*, CD20* and CD117* cells between synovial and colonic compartments. Molecular mechanisms triggered by TNF-alpha blockers leading to joint inflammation have to be clarified.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4301

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**Abstract OP0239 – HISTOLOGICAL FEATURES OF JOINT AND COLONIC INFLAMMATION IN INFLAMMATORY BOWEL DISEASE PATIENTS TREATED WITH ANTI-TNF**


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**Background:** Spondyloarthritis (SpA), also including ankylosing spondylitis (AS), psoriatic arthritis (PsA) and undifferentiated spondyloarthritis (uSpA), is a cluster of rheumatic diseases with some common genetic risk factors. These genetic risk factors are likely to result in associations of varying degree with SpA-related comorbidities such as inflammatory bowel disease (IBD), psoriasis and anterior uveitis. There
is also a known association between AS and conduction disturbances and aortic regurgitation. Comparative analyses in the same setting of the strengths of these associations with AS, PsA and uSpA are scarce.

**Objectives:** To assess the strengths of the associations of different SpA-related comorbidities with a diagnosis of AS, PsA and uSpA.

**Methods:** All patients, aged ≤18 years, with AS (n=3884), PsA (n=8706) and uSpA (n=2665) were identified 2001 through 2005, according to specified ICD codes from the Swedish Patient Register. The register contains diagnoses from all visits in inpatient and non-primary outpatient care. Each patient was matched by year of birth, sex and county to five general population (GP) controls identified in the Population Register. Occurrence of SpA-related comorbidities prior to 1 January 2006 were also retrieved from the Swedish Patient Register. Number and proportion of cases (n (%)) with a recorded SpA-related comorbidity prior to 1 January 2006 and corresponding prevalence ratio (PR) with 95% confidence interval (CI) were calculated, overall and stratified for sex.

**Results:** PRs for SpA-related comorbidities were significantly elevated in all SpA subtypes compared to their matched GP controls (Table). PRs were substantially elevated in AS, immediately elevated in uSpA, whereas only moderately increased in PsA. The results were similar in the sex-stratified analyses (not shown).

**Conclusions:** The strongest associations of SpA-related comorbidities were seen with AS, closely followed by uSpA, compatible with a substantial shared etiology and phenotypical expression for patients given these two diagnoses, whereas the associations between PsA and the SpA-related comorbidities were considerably weaker.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1255
Predictors of Remission at Week 12 in Patients with Non-Radiographic Axial Spondyloarthritis Receiving Open-Label Adalimumab Treatment in the ABILITY-3 Study

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Background: Patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA) who fail nonsteroidal anti-inflammatory drug (NSAID) therapy are candidates for tumor necrosis factor inhibitor (TNFi) therapy if they have objective signs of inflammation. Baseline predictors of response to TNFi therapy, including remission, are important to identify and aid clinical management.

Objectives: Describe baseline predictors of remission in nr-axSpA at wk 12 of open-label adalimumab (ADA) therapy in the ABILITY-3 study.

Methods: ABILITY-3 enrolled adult pts with nr-axSpA (fulfilling Assessment of SpondyloArthritis International Society [ASAS] criteria but not modified New York criteria) with moderately to severely active disease at screening and baseline objective evidence of inflammation in the sacroiliac (SI) joints or spine on an inadequate response to ≥2 NSAIDs. Eligible pts received ADA 40 mg every other week during a 29-wk open-label lead-in period. Clinical remission was defined as Ankylosing Spondylitis Disease Activity Score inactive disease (ASDAS ID; score <1.3) or ASAS partial remission (score <2/10) in ≥3 of each of the 4 ASAS domains. Stepwise logistic regression was used to identify potential baseline predictors of remission at wk 12.

Results: 673 pts were enrolled (Table). Lower disease activity, increased age, lower functional status (HAQ-S), presence of HLA-B27, and positive MRI of the SI joints were the strongest predictors of ASAS PR (Figure).

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Measure</th>
<th>ASDAS ID Responders n (%)</th>
<th>ASDAS PR Responders n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>33.6±9.7 (n=211)</td>
<td>38.5±11.2 (n=470)</td>
</tr>
<tr>
<td>Diagnosis duration, y</td>
<td>1.7±2.9 (n=389)</td>
<td>1.7±2.9 (n=133)</td>
</tr>
<tr>
<td>Symptom duration, y</td>
<td>6.1±6.2 (n=274)</td>
<td>7.1±1.9 (n=15)</td>
</tr>
<tr>
<td>HLA-B27 positive</td>
<td>183 (97) (n=210)</td>
<td>119 (89) (n=11)</td>
</tr>
<tr>
<td>ASASDAS</td>
<td>3.4±0.8 (n=214)</td>
<td>3.7±0.9 (n=16)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>6.9±1.8 (n=212)</td>
<td>7.0±1.7 (n=15)</td>
</tr>
<tr>
<td>Pain/glob assessment of pain</td>
<td>7.0±1.7 (n=213)</td>
<td>7.1±1.9 (n=15)</td>
</tr>
<tr>
<td>hs-CRP</td>
<td>9.0±13.1 (n=131)</td>
<td>15.5±21.3 (n=7)</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.7±2.2 (n=212)</td>
<td>5.4±2.2 (n=15)</td>
</tr>
<tr>
<td>HAO-S</td>
<td>1.9±2.0 (n=213)</td>
<td>2.1±0.5 (n=15)</td>
</tr>
<tr>
<td>MRI SI joints positive</td>
<td>165 (78) (n=214)</td>
<td>102 (72) (n=15)</td>
</tr>
<tr>
<td>MRI spine positive</td>
<td>59 (26) (n=213)</td>
<td>47 (32) (n=15)</td>
</tr>
</tbody>
</table>

Analysis of Complete Publication Solutions, LLC and was funded by AbbVie.

Disclosure of Interests: J. Sieper: Grant/research support from: AbbVie, Merck, Pfizer, and UCB; Consultant for: AbbVie, Merck, Pfizer, and UCB; Speakers bureau: AbbVie, Merck, Pfizer, and UCB. R. Landewé: Grant/research support from: AbbVie, Amgen, UCB, Pfizer, Roche, Schering-Plough, UCB, and Wyeth; Consultant for: Abbott/AbbVie, Aidyfin, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Celgene, Janssen, Johnson & Johnson, Kissei Pharmaceutical, Merck, Novartis, Pfizer, Roche, Schering-Plough, Tesaro, and UCB; Wyeth: he is director of Rheumatology Consultancy BV, a registered Dutch company. M. Magrey: Grant/research support from: AbbVie, UCB, and VCB Pharma; Consultant for: UCB and Janssen. J. Sieper: Employee of: AbbVie; S. Zhong: Employee of: AbbVie.

DOI: 10.1136/annrheumdis-2017-eular.6467

Family Matters: Value of Family History of Spondyloarthritis in the Diagnostic Work-Up of Patients with Chronic Back Pain: Results from the Space and Desir Cohorts

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Background: A positive family history (PFH) of spondyloarthritis (SpA) is considered a risk factor for the presence of axSpA in patients with chronic back pain (CBP). In the ASAS classification criteria, a PFH of SpA is defined as the presence of any of the following diseases in first- or second-degree relatives: ankylosing spondylitis (AS), reactive arthritis (ReA), inflammatory bowel disease (IBD), or psoriasis. It is however not known if a PFH for each of these diseases contributes equally well to making a diagnosis of axSpA in patients presenting with CBP.

Objectives: To assess which SpA diseases in family members are associated with HLA-B27 and axSpA in patients with CBP.

Methods: The SPACE cohort includes patients with CBP (<3 months, <2 years, onset <45 years) from various European rheumatology centers. DESIR is a French prospective multicenter cohort of patients with inflammatory back pain (IBP; >3 months, <3 years, onset <50 years), suggestive of axSpA. Patients underwent a full diagnostic work-up at baseline including MRI and radiographs of sacroiliac joints (local reading), laboratory assessments (HLAB27), and assessment of all other SpA features. Patients were asked about the presence of SpA diseases in first- or second-degree relatives (AS, AAU, ReA, IBD, and psoriasis). The associations between a PFH and HLA-B27, sarcroiliitis, axSpA diagnosis by the rheumatologist, and fulfillment of the ASAS classification criteria in CBP patients were assessed.

Results: In 438 patients from the SPACE cohort and 647 patients from the DESIR cohort, a PFH of AS (odds ratio (OR) 5.9 (3.5–9.9) and OR 3.3 (2.1–5.2), respectively for SPACE and DESIR) and a PFH of AAU (OR 9.8 (3.3–28.9) and OR 21.8 (6.0–76.1) for SPACE and DESIR) were significantly associated with presence of HLA-B27 (Table 1). Furthermore, in both cohorts a PFH of AS and a PFH of AAU were positively associated with fulfillment of the ASAS criteria, but not with saccroiliitis on imaging (data not shown). In SPACE, but not in DESIR, a PFH of AS or AAU was associated with axSpA diagnosis (data not shown). In both cohorts, a PFH of ReA, IBD, or psoriasis was not positively associated with HLA-B27 positivity, saccroiliitis on imaging, axSpA diagnosis or meeting the ASAS criteria for axSpA.

Table 1. Associations of Family History Characteristics with HLA-B27 in Patients with Chronic Back Pain in the SPACE Cohort (n=438) and in Patients with Recent Inflammatory Back Pain in the DESIR Cohort (n=647).

<table>
<thead>
<tr>
<th>Family History</th>
<th>HLA-B27+ (%)</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>34 (7.9)</td>
<td>5.9 (3.5–9.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AS</td>
<td>21 (4.8)</td>
<td>3.3 (2.1–5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AAU</td>
<td>41 (9.4)</td>
<td>9.8 (3.3–28.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AAU</td>
<td>26 (6.1)</td>
<td>21.8 (6.0–76.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: In two recent CBP cohorts, a PFH of ReA, IBD, or psoriasis did not
contribute to identifying axSpA in CBP patients indicating these family elements may not be very useful for diagnosis. A PFH of AS or AAS however may be useful in finding cases in low prevalence settings as these were correlated with HLA-B27 carriage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4671

OP0245

EMPLOYMENT PERSPECTIVES OF PATIENTS WITH ANKYLOSING SPONDYLITIS IN THE BIOLOGIC ERA

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Background: In the pre-biologics era, employment of patients with ankylosing spondylitis (AS) was decreased when compared to the general population. However, information on standardized employment since the introduction of biologicals is lacking. Also, while mastery (control over disease) has been identified as strong predictor of work outcome within patients with AS, it is not known whether such personality trait plays a similar role in patients compared to population subjects.

Objectives: To update the knowledge on employment and contributing factors, in particular personal factors, among Dutch patients with AS compared to general population subjects.

Methods: Data from patients and population controls participating in the Dutch cross-sectional multicenter survey-based Social Participation in AS Study (SPASS) and ≥ 15 years were used. Standardized employment ratios (SERs) were calculated using indirect standardization after adjusting for age, gender, and education and were stratified by disease duration tertiles. Adjusted absolute employment rate (%) was calculated as “SERemployment rate [controls]”.

Results: 214 patients and 470 controls (127 [59.3%] and 323 [68.7%] males; mean age of 48.3 [SD 10.4] and 39.3 [SD 12.7] years, respectively) completed the online questionnaire in 2011. SERs (95% CI) of patients with AS controls set as reference (1.00) were 0.83 (0.69–0.98) for the total group, 0.84 [0.67–1.04] for males and 0.83 [0.59–1.07] for females. There was no significant difference in SER between those with short or long disease duration (Figure 1). Adjusted absolute employment rate (%) of patients with AS was 14% lower compared to SER between those with short or long disease duration (Figure 1). Adjusted absolute employment rate (%) of patients with AS was 14% lower compared to controls (69% vs. 84%). In both patients and controls, higher PCS (SF-36) was associated with being employed. While AS patients with higher (better) mastery were more likely to be employed, such association was not seen in controls (p>0.01 for interaction group*mastery) (Table).

Table 1. Multivariate Poisson regression exploring determinants of work participation, stratified by group (AS vs. controls)

<table>
<thead>
<tr>
<th>Variable</th>
<th>AS (n=213) IRR 95% CI p</th>
<th>Controls (n=465) IRR 95% CI p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>0.99 0.98–1.00 &lt;0.01 1.00 0.99–1.00 0.07</td>
<td></td>
</tr>
<tr>
<td>Gender, male</td>
<td>1.13 0.91–1.39 0.26 1.00 0.99–1.19 0.09</td>
<td></td>
</tr>
<tr>
<td>Education, high</td>
<td>0.97 0.91–0.98 0.03 0.97 0.91–1.00 0.13</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS (0–100)</td>
<td>1.00 1.00–1.03 0.00 1.01 1.00–1.02 0.02</td>
<td></td>
</tr>
<tr>
<td>Mastery (7–28)</td>
<td>0.93 0.91–0.95 0.00 0.94 0.91–1.00 0.12</td>
<td></td>
</tr>
</tbody>
</table>

†Value not significant and no confounder.

Figure 1. Standardized employment ratios of patients with AS with controls set as reference (dotted line).

AS, males
AS, females

Conclusions: More subjective disease activity measures have greater impact on sick leave in biologics-treated RA patients than do more objective variables, suggesting a stronger focus on the former ones when targeting work-loss or intervening to reduce it.

Disclosure of Interest: J. Wallman Consultant for: Novartis, Celgene and UCB, J. Söderling Grant/research support from: Participated in previous research projects fully or partly funded by Novo Nordisk and Combine Sweden, Consultant for: Served as an external consultant to AbbVie, Merck and Novartis, A. Gülfe None declared, L.-E. Kristensen Grant/research support from: Oak Foundation, Consultant for: AbbVie, Celgene, BMS, MSD, Novartis, Pfizer, UCB, M. Neovius Grant/research support from: Participated in research projects fully or partly funded by Schering-Plough, AstraZeneca, Novo Nordisk, Pfizer and Roche (unrelated to the current work), Consultant for: Participated in advisory boards for Pfizer (rheumatology) and Abbott (non-rheumatology), T. Olsson: None declared

DOI: 10.1136/annrheumdis-2017-eular.2883

OP0246

IMPACT OF DISEASE ACTIVITY MEASURES ON SICK LEAVE IN BIOLOGICS-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL DATA FROM SOUTHERN SWEDEN

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Background: Sick leave generally represents the earliest phase of work-loss in rheumatoid arthritis (RA) patients, often on the trajectory towards more permanent disability pension. Sick leave may still change with disease activity fluctuations and is thus potentially reversible and accessible for interventions. However, data remain scarce on the importance of modifiable, non-composite disease activity measures for subsequent sick leave in RA patients treated with biologics.

Objectives: To study the impact of common, non-composite disease activity measures on sick leave in biologics-treated RA patients.

Methods: Study visits of biologics-treated RA patients of working-age (<65y) without disability pension, monitored in the population-based, observational South Swedish Arthritis Treatment Register group register 2005–2011, were included (5151 visits; 957 patients). We performed association analyses between various non-composite disease activity measures at each visit and number of objectively assessed sick leave days during the month thereafter, retrieved from the Social Insurance Agency. Separate generalised estimating equation regression models were used, adjusting for age, sex, educational level, disease duration, number of previous biologics, time from start of the present biologic, and calendar year of study visit. Analyses were furthermore stratified on sick leave status the month preceding each visit (no sick leave=0 days out of 30; partial sick leave=1–29 days and full sick leave=30 days) and results are presented as standardised beta coefficients for comparability, with bootstrap-generated 95% confidence intervals.

The composite 28-joint disease activity score (DAS28) and the health assessment questionnaire (HAQ) disability score were included as contrast.

Results: Out of common, non-composite disease activity measures, visual analogue scale (VAS) global and VAS pain were most strongly associated with sick leave days the month after the study visit, irrespective of baseline sick leave status (Figure). Generally, the more objective measures (erythrocyte sedimentation rate, C-reactive protein and swollen joint count (SJQ)) had less impact on subsequent sick leave than the more subjective variables (VAS global, VAS pain, evaluator’s global and tender joint count (TJC)). As expected, HAQ showed the strongest association.

Figure 1. VAS global and VAS pain.

Conclusions: More subjective disease activity measures have greater impact on sick leave in biologics-treated RA patients than do more objective variables, suggesting a stronger focus on the former ones when targeting work-loss or intervening to reduce it.

Disclosure of Interest: None declared


FRIDAY, 16 JUNE 2017

RA - causes and courses
AN IMPROVED MATRIX TO PREDICT RAPID RADIOGRAPHIC PROGRESSION OF EARLY RHEUMATOID ARTHRITIS PATIENTS: POOLED ANALYSES FROM SEVERAL DATABASES

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Background: In early rheumatoid arthritis (RA), some patients exhibit rapid radiographic progression (RRP) after one year, associated with poor functional prognosis. Identifying at the time of diagnosis the characteristics predictive of RRP is of importance. Several matrices predicting this risk have been proposed over the last years. They were limited somewhat in terms of precision or were built using specific populations.

Objectives: To develop a matrix to predict RRP with better precision and generalizability by pooling databases from various studies.

Methods: The study is based on the pooling of individual data from cohorts (ESPOIR and Leuven) and clinical trials (BeSt, SWEFOT and ASPIRE). Included patients were adult DMARD-naive patients with recent suspected or confirmed diagnosis of active RA for which the first therapeutic strategy after inclusion was to prescribe MTX or leflunomide in monotherapy for at least 3 months. The main outcome was the presence of RRP defined as an increase in Modified Sharp score (mSSS) of at least 5 points between baseline and one year. Baseline characteristics were compared by the presence of RRP to search for predictors. A logistic regression model to predict RRP was built. The best model was selected by 10-fold stratified cross-validation by maximizing the Area Under the Curve (AUC). Calibration and discriminatory power of the model were assessed. Model parameters were extracted to estimate the probability of a RRP for each combination of level of baseline characteristics.

Results: The data of 1,306 patients were pooled. After one year, 236 exhibited RRP (18.4%). A matrix (Table 1) for prediction of RRP of 0.21, Model of prediction of RRP included as baseline characteristics Rheumatoid Factor (RF) positivity (OR=2.1 CI95% [1.5–3.0]; p<0.001), erosive disease on X-rays (OR=2.3 CI95% [1.7–3.2]; p<0.001), CRP >30 mg/l (OR=2.1 CI95% [1.5–3.0]; p<0.001), number of swollen joints >10 (OR=1.5 CI95% [1.01–2.1]; p=0.048). Model calibration was good (Hosmer and Lemeshow test: p=0.79). AUC was 0.68. The matrix proposes estimated RRP probability for 36 combinations of level of baseline characteristics. Its range goes from patients with a 4.1 fold lower risk of RRP compared to average risk (probability of 0.05 CI95% [0.03–0.08], patient with CRP <10 mg/l, without RF, without X-ray erosions, without >8 swollen joints), to patients with a 2.3 fold higher risk than average (probability of 0.47 CI95% [0.39–0.55], patient with CRP >30, with RF, with erosive disease on X-ray, with >10 swollen joints).

Conclusions: A matrix proposing RRP probability at one year with better precision (i.e. narrower CI than those previously published) in early RA for various combinations of levels of a few common baseline characteristics has been built using several databases. However, discriminating power is not ideal. Further investigations will be needed to fully explore the potential complexity of predicting RRP in early RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4752

SERIOUS INFECTION AND ASSOCIATED RISK FACTORS IN PATIENTS WITH MILD TO MODERATE RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB

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Background: Baricitinib (BARI) is an oral Janus Kinase (JAK)1/1JAK2 inhibitor in development for patients (pts) with active rheumatoid arthritis (RA). Compared to the general population, RA pts have an increased rate of serious infection events (SIE) due to disease state and concomitant therapies.1

Objective: To evaluate the incidence rate (IR) of SIE and associated risk factors in BARI-treated pts with active RA across 8 completed studies (4 Ph3, 3 Ph2, 1 Ph1) and 1 ongoing long-term extension (LTE) study.

Methods: The ALL BARI RA analysis set included pts exposed to any BARI dose, with exposure up to 5 years (yrs) (Phase [Ph] 1–3 and LTE studies); the comparison with placebo (PBO) was based on 6 studies (Ph 2–3) with BARI 4 mg once daily (QD) and PBO arms up to Week (Wk) 24; dose response assessment was based on 4 studies (Ph 2–3) with both BARI 2 and 4 mg QD arms up to Wk 24. An extensive list of potential risk factors for SIE was investigated in the ALL BARI RA set using Cox models; SIE risk factors among BARI-treated pts are reported (Table).

Results: The most frequent SIE observed in the ALL BARI RA set (N=3492; 5133 pt-yrs (PY) of exposure [PYE] were pneumonia, herpes zoster, urinary tract infection, and cellulitis (all <1%), and 2 patients with SIE died (IR=0.04/100 PY). In the ALL BARI RA set, SIE were reported in 150 pts (IR=2.9/100 PY). During 0–24 Wks, similar SIE rates were observed in BARI 4 mg (N=997; 417 PYE) and PBO (N=1070; 403 PYE) groups in the 6-study set, and between BARI 2 mg (N=479; 192 PYE) and 4 mg (N=479; 194 PYE) dose groups in the 4-study set (Figure).

Prior biologic use, advancing age, region of Asia (excluding Japan), non-normal body mass index (BMI), and corticosteroid use were identified as independent factors for SIE in the ALL BARI RA set (Table). Among these SIE risk factors, none significantly differed between BARI 4 mg and PBO in the 6-study dataset (data not shown).

Table 1. Hazard Ratio and 95% CI for Serious Infection in the ALL BARI RA Analysis Set

<table>
<thead>
<tr>
<th>Clinical Factor</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Line of therapy (bDMARD-IR vs. csDMARD-IR)</td>
<td>1.6 [1.1, 2.3]</td>
<td>1.5 [1.0, 2.3]</td>
</tr>
<tr>
<td>BMI (kg/m2) vs. normal [18–24]a</td>
<td>2.2 [1.6, 3.2]</td>
<td>2.5 [1.8, 3.6]</td>
</tr>
<tr>
<td>Region (Asia [excluding Japan] vs. US/Canada)</td>
<td>2.4 [1.3, 4.4]</td>
<td>2.7 [1.5, 4.2]</td>
</tr>
<tr>
<td>Overweight (&lt;25–29)</td>
<td>1.6 [1.0, 2.4]</td>
<td>1.8 [1.1, 2.7]</td>
</tr>
<tr>
<td>Obese (&gt;30)</td>
<td>1.4 [0.9, 2.2]</td>
<td>1.8 [1.1, 2.9]</td>
</tr>
<tr>
<td>RA duration (10+ vs. 0–4 yrs)a</td>
<td>1.7 [1.1, 2.5]</td>
<td>1.9 [1.1, 3.3]</td>
</tr>
<tr>
<td>DAS28-hsCRP (for every one unit increase)a</td>
<td>1.1 [1.0, 1.3]</td>
<td>1.2 [1.0, 1.4]</td>
</tr>
<tr>
<td>HAQ-DI (1.5 vs. &lt;1.5)b</td>
<td>1.5 [1.1, 2.1]</td>
<td>1.8 [1.3, 2.7]</td>
</tr>
<tr>
<td>Corticosteroid dose (mg/day)a</td>
<td>0.1–4.9 vs. none</td>
<td>2.2 [1.3, 3.7]</td>
</tr>
<tr>
<td>≥5 vs. none</td>
<td>1.7 [1.2, 2.5]</td>
<td>1.9 [1.3, 2.7]</td>
</tr>
</tbody>
</table>

aData at baseline. Abbreviations: CI, confidence interval; HR, hazard ratio.

Conclusions: SIE incidence was similar between BARI- and PBO-treated RA pts. SIE risk factors include concomitant corticosteroids, prior biologics, non-normal BMI, Asian region of enrollment, and advancing age.

References:


DOI: 10.1136/annrheumdis-2017-eular.1312
MULTI-BIOMARKER DISEASE ACTIVITY AND AUTOANTIBODY STATUS LEAD TO COST EFFECTIVE TAPERING ALGORITHMS IN RHEUMATOID ARTHRITIS PATIENTS IN SUSTAINED REMISSION

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Background: Achieving remission is the ultimate treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach the disease remission state (1), raising the question about tapering or stopping anti-rheumatic treatment and appropriate predictors (2).

Objectives: To analyse the effect of a risk-stratified DMARD tapering algorithm based on multiple-biomarker disease activity (MBDA) score and anti-citrullinated protein (ACPAs) status for successful DMARD tapering and treatment cost reduction in RA patients in sustained remission enrolled in the prospective randomized controlled RETRO study (3,4).

Methods: MBDA score and ACPA status were determined in the baseline samples of 146 patients in sustained remission. Patients either continued DMARDs (arm1), tapered dose by 50% (arm 2) or stopped DMARDs after tapering (arm 3) for one year according to the RETRO protocol. Direct treatment costs (including testing costs at baseline) were evaluated every three months. MBDA and ACPA status were used as predictors creating a risk-stratified tapering algorithm based on relapse rates.

Results: RA patients with a low MBDA score (<30) and negative ACPA showed lowest relapse risk (19%). With either single positivity for ACPA or moderate/high MBDA scores (>30) relapse risk increased and was high in double-positive patients (61%). In MBDA negative (<30) and MBDA single-positive (>30) groups, DMARD tapering appears feasible. Considering only patients that did notflare, costs for synthetic and biologic DMARDs in the MBDA-negative and single-positive group (n=41) would have been 123.761,29 € for full-dose treatment over one year. Tapering and stopping DMARDs in this low-risk relapse groups allowed a reduction of 92.821,50 € (75%) of DMARD costs. Average reduction of DMARD costs per patient were 2.350,08 € in the double negative (MBDA-/ACPAs-) (median quartiles 0.61–5.38 €) and single negative (MBDA-/ACPAs+) group and 1.761,43 € in the MBDA single positive (MBDA+/ACPAs-) group.

Conclusions: Combining MBDA score and ACPA status allows risk stratification for successful DMARD tapering and cost-effective use of biologic DMARD. Given that previous data of the RETRO have shown that patients relapsing after tapering their DMARDs respond well to their reintroduction, a stratified tapering and stopping of DMARDs is not only a cost economic but also clinically feasible strategy.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2988

CAN RANKL SERUM LEVELS PREDICT FUTURE PROGRESSION TO RHEUMATOID ARTHRITIS IN ACA P-NEGATIVE PATIENTS?

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Background: Making the earliest diagnosis of rheumatoid arthritis (RA) is crucial to initiate treatment and prevent further disease progression and joint damage. Despite recent advances with the discovery and integration of anti–cyclic citrullinated protein antibody (ACPA) in classification criteria, there is still an unmet need for new diagnostic biomarkers, notably for ACPA-negative disease. Power Doppler ultrasound has been shown to identify poor prognosis disease in ACPA negative patients.

Objectives: The receptor-activator-nuclear-factor-κB axis (RANK/RANKL) is known to regulate bone homeostasis. The aim of this pilot study is to establish whether serum RANKL levels in people with early inflammatory arthritis are predictive of RA diagnosis at follow-up and to evaluate the added value of RANKL with diagnosed for early RA diagnosis.

Methods: Serum from 298 subjects (95/204 Male/Female) was collected at the baseline participant visit to the Leeds Early Arthritis clinic. Demographic (age, gender, symptom duration) and clinical data (swollen and tender joint counts (SJc, TJc), CRP, RAS28, rheumatoid factor (RF) and ACPA, shared epitope (SE)) were collected. A commercial ELISA (BioVENDOR) was used to measure RANKL. Ultrasound of 26 joints (bilaterial elbows, wrists, MCP 2–3,PIP 2–3, knees, ankles and MTP rind) was performed at baseline. recording summatory scores for power Doppler (PD), gray scale hypertrophy (GS) and erosions (EO).

Results: At 1 year follow up, 151 patients had a confirmed diagnosis of RA (EULAR 2010 criteria) and 147 were classified as non-RA (undifferentiated arthritis, other inflammatory diagnoses or non-persistent inflammation). All routinely used biomarkers were associated with RA diagnosis (ACPA, RF, SE, SJc, TJc, CRP, RAS28, p < 0.0001), as were imaging biomarkers (PD, GS, EO, p < 0.001). RANKL levels were significantly higher in RA (1002±1053.2pmol/L, non-RA 339.2±45.1pmol/L, p < 0.001). A regression analysis suggested that four parameters were sufficient to account for all associations with RA: RANKL, age, SJc, and PD with 75.3% accurate prediction. An AUROC analysis suggested a cut-off for each parameter and a score was calculated, adding 1 point for each of the factors (RANKL > 700, age < 62, TPD < 3, SJc < 4). This score predicted RA with an AUROC of 0.782 ([0.65–0.90], p < 0.0001). The same analysis repeated for ACPA negative patients only (n=193) showed similar results, providing accurate diagnosis of RA (77.6% correct by regression) and with an AUROC of 0.774 ([0.69–0.858], p < 0.0001).

Conclusions: A score incorporating RANKL, age, SJc and PD showed good predictive value for non-RA when low and for RA when high. Furthermore, the analysis of a redo in ACPA-negative patients performed particularly well for predicting RA with a good AUROC value.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3226

INCIDENCE OF KNEE AND HIP REPLACEMENTS IN RHEUMATOID ARTHRITIS PATIENTS FOLLOWING INTRODUCTION OF BIOLOGICAL DMARDS: AN INTERRUPTED TIME SERIES ANALYSIS USING NATIONALWIDE HEALTH CARE REGISTERS

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Background: Previous data have been conflicting regarding a possible impact of treatment with biological DMARDs (bDMARDs) on the need for total knee replacement (TKR) and total hip replacement (THR) in patients with rheumatoid arthritis (RA).

Objectives: To investigate impact of national guidelines recommending bDMARD treatment for RA on the secular trends of TKR and THR among incident RA patients compared with matched general population controls (GPC) in Denmark.

Methods: Using nationwide register based time series analysis, the authors performed a matched case-control study of RA patients diagnosed at a rheumatology department from 1996–2011. GPC: 10 individuals matched to each RA patient on age, sex and municipality. Outcome: First TKR and THR, respectively.
Intervention: introduction of bDMARDs and associated publication of bDMARD recommendations in Denmark in 2002.


Secular trends in the pre-bDMARD guideline era (1996–2002) were compared with those in the bDMARD period (2003–2016) using segmented linear regression and a 1-year lag period (2002–03). Absolute changes in TKR and THR at the midpoint (February 2007) between guideline implementation and end of study period were estimated.

Results: In total, during 1996 to 2011, 30,868 incident RA patients were identified (mean age at diagnosis 58.3 years, 70% women) and compared with 301,237 GPCs. See Table for results.

Table 1. Changes in 5-year incidence rate of total hip (THR) or total knee replacement (TKR) in incident rheumatoid arthritis (RA) patients following introduction of biological DMARDs compared with secular trends in age, sex, and municipality-matched general population controls (GPC)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>THR/TRK</th>
<th>Baseline incidence rate/1000 person years</th>
<th>Δ per year</th>
<th>Δ in level</th>
<th>Δ per year post 2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>TKR</td>
<td>86/5</td>
<td>5.87</td>
<td>+0.19</td>
<td>–0.20</td>
<td></td>
</tr>
<tr>
<td>GPC</td>
<td>2438</td>
<td>0.42</td>
<td>+0.21</td>
<td>+0.08</td>
<td></td>
</tr>
<tr>
<td>THR</td>
<td>93/5</td>
<td>7.27</td>
<td>–0.38</td>
<td>+2.23</td>
<td>–0.38</td>
</tr>
<tr>
<td>GPC</td>
<td>4744</td>
<td>2.89</td>
<td>+0.11</td>
<td>+0.02</td>
<td></td>
</tr>
</tbody>
</table>

Stepwise backward elimination to produce most parsimonious model: p-enter <0.05 and p-exit >0.2. *Δ per year based on biannual data.

Conclusions: Prior to 2002, the incidence of TKR increased among RA patients, but started to decrease after introduction of bDMARDs and their associated guidelines in 2003 (absolute change -1.8 TKRs/1000 person years in Feb. 2007). In contrast, the incidence of TKR increased among GPCs throughout the entire study period. The incidence of THR increased in GPCs for the entire duration of the study period, whereas there was a downward going trend among RA patients, but with a surprising level increase in 2003. The overall patterns of our findings are in line with those recently reported from England and Wales.

References:

Disclosure of Interest: R. Cordtz: None declared, L. Dreyer: None declared, D. Prieto-Alhambra Grant/research support from: DPA’s group has received unrelated research grants from Amgen and Servier, E. L. Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals, S. Overgaard: None declared, A. Odgaard: None declared, L. Dreyer: None declared

DOI: 10.1136/annrheumdis-2017-eular.1227

RHEUMATOID ARTHRITIS PATIENTS WITH CONTINUED LOW DISEASE ACTIVITY HAVE SIMILAR OUTCOMES OVER 10 YEARS, REGARDLESS OF INITIAL THERAPY

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Introduction: Disease activity is an essential feature of rheumatoid arthritis (RA), but little is known about its relevance beyond 10 years of follow-up. This study aimed to compare patients who had continued low disease activity over 10 years (DAS ≤ 2.4) with those who had not (DAS > 2.4).

Methods: Patients were identified from the BeSt study, a prospective, multicentre, observational study of RA patients aged ≥18 years with ≥3 months of disease duration. Disease activity was assessed using the Disease Activity Score (DAS) and patient-reported outcomes (PROs) were collected using the Health Assessment Questionnaire (HAQ) and the European Health Inventory (EHI).

Results: Of 418 patients, 39% continued low disease activity over 10 years. Patients with continued low disease activity had lower DAS and better PROs compared to those with higher disease activity (significant for all PROs except EHI). There were no differences in radiographic progression, erosions, or joint space narrowing between the two groups.

Conclusions: Disease activity was sustained over 10 years in a substantial proportion of RA patients. These patients had lower disease activity, better PROs, and similar radiographic outcomes compared to those with higher disease activity. This suggests that continued low disease activity is an important clinical feature of RA, regardless of initial disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1707

PASSIVE SMOKING IN CHILDHOOD AND HISTORY OF CHRONIC DIARRHEA INCREASES THE RISK OF DEVELOPING RHEUMATOID ARTHRITIS (RA)

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Objectives: To analyse the impact of active and passive smoking and intestinal transit disorders on the risk of incident RA.

Methods: This study is based on the French E3N cohort (“Étude Épidémiologique auprès de femmes de l’Education Nationale”), which included 98,995 women volunteers born between 1925 and 1950 and prospectively followed since 1990. Eleven self-administered questionnaires were sent to the participants between 1999 and 2014 to collect medical, demographic, environmental and hormonal data and dietary habits. The diagnosis of RA was collected on 2 successive questionnaires. Cases were considered certain if having declared RA and having taken a RA specific medication (methotrexate, leflunomide or biologic) since 2004 (period from which drug reimbursement data was available). Only incident and certain cases were included. Women were excluded if they had an inflammatory bowel disease and/or no information on their smoking habits. Passive smoking was assessed by the following question: “When you were children, did you stay in a smoky room?” Patients were considered exposed if the answer was “yes, a few hours, or yes, several hours a day”. The usual intestinal transit, reported by patients was 2.4. Regardless of the duration of treatment strategies for patients who have sustained DAS ≤ 2.4. Regardless of initial induction therapy, those who remain in low disease activity have similar long-term outcomes, with only the proportion of patients in drug free remission being higher in the TKR monotherapy group. These results strongly suggest that rapid achievement of remission/LDA itself, rather than how you achieve it, is crucial for determining long-term outcome in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1707
transit, chronic diarrhoea, chronic constipation, and alternation between diarrhoea and constipation. The risk of incident RA was estimated using an age-adjusted Cox model that considers smoking status as a time-dependent variable.

**Results:** 70598 women from the E3N study were included in the study. A total of 1239 patients reported an incidental RA, of which 350 cases were included in the study (and 280 in the analysis of intestinal transit disorders). Non-ascertained cases were excluded from the analyses. The age at inclusion in the study was 49.0 years (± 6.4). The mean duration of follow-up was 21.2 (± 1.3) years. Passive smoking exposure during childhood increased the association between the risk of RA and a history of passive smoking in childhood (OR = 1.73 [1.20; 2.50]) as compared with non-smokers who were not exposed during childhood, while it was 1.37 [1.08; 1.73] in active smokers who were not exposed during childhood.

A history of chronic diarrhoea was associated with increased RA risk (HR = 2.32 [1.41, 3.81]), while chronic constipation or alternation between diarrhoea and constipation did not.

**Conclusions:** This study confirms the link between active smoking and the risk of RA. It suggests for the first time that in smokers, exposure to tobacco early in life, through passive smoking in childhood significantly increases this risk. Our study highlights the importance of avoiding any tobacco environment in children, especially in those with a family history of RA. Also, it shows for the first time an association between a history of chronic diarrhoea and the risk of developing RA. The association supports the hypothesis of dysbiosis (microbiota abnormality) as a risk factor for the emergence of autoimmunity. These data perfectly fit with the preclinical scheme of RA where an external event occurs at an early stage to promote emergence of auto-immunity, followed years after by clinical RA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3853

**FRIDAY, 16 JUNE 2017**

**HPR move to improve**

**OP0254-HPR**

**HAND EXERCISE FOR WOMEN WITH RHEUMATOID ARTHRITIS AND DECREASED ADL ABILITY: AN EXPLORATORY RANDOMISED CONTROLLED TRIAL**

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**Background:** Decreased strength and range of motion in the hand are often seen in rheumatoid arthritis (RA). Positive effects on hand function in RA patients after hand exercise and individual education in joint projection including coping strategies (ADL education) is shown (1,2). However, it is unknown if a combination of both will further improve hand performance.

**Objectives:** To investigate the effect on ADL ability of a hand exercise program as add on to an ADL education program in women with RA.

**Methods:** Women with RA involving the hand on stable medication for at least three months were recruited. At baseline participants were examined by a rheumatologist who assessed the hand and ruled out contraindications for participation e.g. massive malalignment of the joints. Inflammatory markers of the blood, hand pain and grip strength were also measured. The ADL motor ability was assessed using the observation-based Assessment of Motor and Process Skills (AMPS). After baseline examination randomised to ADL education + hand exercises (intervention; IG) or only ADL education (control; CG) was made. All participants received three to four sessions with an occupational therapist learning how to perform ADL tasks overcome their specific hand problems. The intervention group also received a hand exercise program, to be conducted four times a week, for eight weeks, containing exercises for improving range of motion and strength; once a week the exercise program was supervised by a physiotherapist, to correct and prevent overload and to increase load if possible.

**Primary outcome measure** was change in observed ability to perform ADL tasks (AMPS) at week 8. Secondary outcomes include grip strength, pain, joint count, inflammatory markers and self-reported function.

Four weeks after baseline were completed the trial. The ITT-populations mean age was 63.8 (12.8) years, mean disease duration was 12.4 (11.0) years. Baseline tender and swollen joint count was 5.07 (4.85) and 1.37 (1.72) respectively, the hand pain was 41.95 mm (right) and 35.78 mm (left) (VAS) and hand grip strength was 18.25 kg (right) and 17.46 kg (left). Baseline AMPS ADL motor score was 1.36 (0.46). As judged by the 95% confidence intervals, no difference in change from baseline was seen between the groups (see table).

**Conclusions:** A hand exercise program as add on to an ADL education did not improve ADL ability more than ADL education alone in women with RA experiencing decreased ADL ability involving the hands.


**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2911

**OP0255-HPR**

**AN ADD-ON PROGRAMME IMPROVED THE SHORT-TERM, BUT NOT THE LONG-TERM EFFECT OF REHABILITATION IN PATIENTS WITH RHEUMATIC DISEASES: RESULTS FROM A PRAGMATIC MULTI-CENTRE STEPPED-WEDGE CLUSTER RANDOMIZED CONTROLLED TRIAL**

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**Background:** Multidisciplinary rehabilitation is widely used alongside medical treatment of patients with rheumatic diseases. Although beneficial effects of such rehabilitation have been demonstrated, patients are mostly back to their initial health status 6 to 12 months after discharge.

**Objectives:** To evaluate an add-on rehabilitation programme designed to enhance and prolong the effect of rehabilitation in adult patients with rheumatic diseases.

**Methods:** We conducted a pragmatic multi-centre stepped-wedge cluster randomised controlled trial in six rehabilitation centres in Norway. All centres started simultaneously to include patients in the control phase (traditional rehabilitation),
whereupon they switched to the intervention phase (add-on programme) sequentially and in randomised order. The add-on programme comprised structured individualized goal planning, motivational interviewing, a self-help booklet and four supportive follow-up phone calls the first five months after discharge. Data were collected on admission, discharge, 6 and 12 months after discharge. Primary outcome was health related quality of life (HR-QoL) measured by the individualized Patient Generated Index (PGI). The main statistical analysis was a linear repeated measures mixed model performed on the intention to treat population (all available data).

### Results:

- **389 patients with various rheumatic diseases (SpA, RA, OA, and SLE)** were included (table 1). A significant treatment effect of the add-on intervention on HR-QoL was found on discharge (mean difference -3.32 [95% CI: 0.27, 6.37], p=0.03). There were no significant differences between the groups at 6 and 12 months. Treatment compliance was 94%, and response rate >80% at all time points. Both groups showed a positive effect of rehabilitation in terms of increased HR-QoL at discharge, which subsequently declined, although the values remained at higher levels after 6 and 12 months compared with baseline values (figure 1).

<table>
<thead>
<tr>
<th>Control group (n=195)</th>
<th>Intervention group (n=194)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs, mean (min, max)</td>
<td>56.9 (24, 89) 57.5 (23, 89)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>127 (65.1) 147 (75.8)</td>
</tr>
<tr>
<td>Disease duration, yrs, mean (SD)</td>
<td>21.0 (13.3) 19.1 (13.1)</td>
</tr>
<tr>
<td>Paid work, n (%)</td>
<td>69 (35.8) 76 (39.4)</td>
</tr>
<tr>
<td>Using TNF-inhibitors, n (%)</td>
<td>44 (22.6) 39 (20.1)</td>
</tr>
</tbody>
</table>

**Table 1. Baseline characteristics of included patients (n=389)**

### Objectives:

We investigated if self-reported physical activity, expressed in Metabolic Equivalent of Task (METs)-minutes/week, in patients with SLE is reduced. The aim was also to investigate if they fulfill the public health recommendations for physical activity.

### Methods:

- **103 patients (93 women/10 men, mean age 51.5 (SD 15.9) years)** were included according to the revised ACR criteria for RA defined. Physical activity was assessed with the short version of the International Physical Activity Questionnaire (IPAQ), which measure physical activity the last seven days. The IPAQ scientific group classify physical activity into the following categories: "inactive", "minimally active" (equal to public health recommendations) and "health enhancing physical activity". Those individuals who do not meet the criteria for the two latter categories are considered inactive.

### Results:

The patients reported that they were physically active in median 1686 (interquartile range 693;3759) METs-minutes/week (n=84). The patients answereded that they were sitting in median 6 (interquartile range 4;8) hours a day the last week (n=98). 59.6% of the patients achieved a minimum of at least 600 METs-minutes/week, i.e. they were active 5 or more days with any combination of walking, moderate-intensity or vigorous intensity activities ("minimally active"). 17.3% achieved a minimum of at least 1500 METs-minutes/week, i.e. they were active on vigorous-intensity on at least 3 days or; achieved a minimum of at least 3000 METs-minutes/week, i.e. they were active 7 or more days on any combination of walking, moderate-intensity or vigorous intensity activities ("health enhancing physical activity"). 22.6% of the patients were "inactive".

### Conclusions:

- In the investigated patients with SLE, the majority were "minimally active" according to IPAQ-categories, which is sufficiently physically active according to the minimum level of public health recommendations. However, only 1/5 reached "health enhancing physical activity" category and 1/5 were considered physically "inactive". Health professionals could use the short version of IPAQ to find out which patients with SLE need support in physical activity programmes.

### References:


### Disclosure of Interest:

None declared


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**OP0257-HPR**

#### RELATIONSHIP BETWEEN SLEEP DISORDERS AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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### Background:

Rheumatoid arthritis (RA) is the prevalent autoimmune inflammatory arthritis found in adults, with the worldwide prevalence ranging from 0.4% to 1.3% (1). Patients with this condition have permanent changes with different severity of arthritis deformities as well as functional disturbances; Studies had shown that every painful condition disturbs sleep, which can lead to mood and abilities disturbances (2).

### Objectives:

The aim of this study was to describe the socio-demographic profile and sleep disorders in RA patients from a specialized RA clinic in Colombia and relationship with disease activity.

### Methods:

A descriptive cross-sectional study was performed in a specialized clinic dedicated to care patients with rheumatoid arthritis (RA). Data was collected during our psychology consultation, through semi-structured interviews and non-probability sampling. Descriptive epidemiology was applied for continuous variables, using measures of central tendency and dispersion for categorical and qualitative variables by averages and percentages. We analyzed bivariate association with Pearson’s χ².

### Results:

We included 1398 patients attending to our psychology consultation. Mean age was 55±8. 80% were female and 20% male. Mean DAS28 was 2.6±1.3, mean HAQ was 0.9±0.7; Patients had the disease for an average of 12 years ± 8; 41% of patients had comorbidities associated with non-autoimmune disease, 14% comorbidities related to autoimmune disease; 35% of our patients did not report other comorbidities. Most of patients were married 60%, followed by divorced 19%, single 14% and widowed 7%. Regarding occupation 33% were employees, 25% were housekeepers or retired due to age, 12% were retired due to disabilities, and 3% unemployed. Of the total population 45% had elementary school, 32% high school, 8% college education, 7% graduate education and 7% were illiterate. 17% of patients lived alone. When the psychologist asked about sleep disorders 69% reported to have any, 25% primary insomnia, 1% hypersomnia, 3% OSAS and 2% alterations on the circadian rhythm. Disease activity was statically associated with sleep disorders (p<0.00).

### Conclusions:

Sleep problems are an important aspect to consider in a patient with RA and are correlated to disease activity; it is important to have a multidisciplinary care team for the patient with RA, including a psychologist that can manage this kind of illness in order to improve the life quality of patients.

### References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5639

INTENSIVE PHYSICAL EXERCISE FOR ELDERLY PERSONS WITH RHEUMATOID ARTHRITIS IMPROVES PHYSICAL CAPACITY

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4 Skaraborg hospital, Skvde, Sweden

Background: Today, more than 50% of persons with Rheumatoid Arthritis (RA) are over 65 years of age (1). Little is known about the effects of physical exercise in this age group (>65 years).

Objectives: The aim of this randomized controlled study is to investigate the effects of a person-centred progressive aerobic and resistance exercise program, led by a physiotherapist.

Methods: Seventy-four with persons with RA (24% men), mean age 70 years (SD 2.5), were recruited and randomized to an exercise interventions group or an active control group. The intervention consisted of a 20-week individual person-centered exercise program, performed three times a week with guidance from a physiotherapist. Both aerobic and resistance exercise was performed on a high intensity level. The control group followed a home exercise program twice a week. Muscle strength and endurance were assessed by the Chair Stands test, the Timed up and Go and a Bicycle endurance test. Maximal aerobic capacity (VO2 max) was assessed with ergo spirometry. Activity limitations were assessed by SF36 Physical subscale and the Health Assessment Questionnaire (HAQ).

Results: All participants in the intervention group completed the intervention. The participants had a low disease activity with a mean Clinical Disease Activity Index of 5.4 (SD 3.9). Significant improvements were found for VO2 max, the Chair Stands test, the Timed up and Go, the Bicycle endurance test on bicycle (p<0.001) and the SF36 physical (p=0.018) in the intervention group, when compared to the controls. No significant differences between groups were seen on HAQ.

Conclusions: Intensive progressive aerobic and resistance exercise is a feasible intervention for elderly persons with RA. Despite old age and RA the participants gained significant improvements in physical capacity.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2721

OP0258-HPR

SUPERVISED WALKING IMPROVES AEROBIC CAPACITY, EXERCISE TOLERANCE, FATIGUE AND PERCEIVED IMPROVEMENT IN WOMEN WITH PRIMARY SJÖGREN’S SYNDROME: A RANDOMIZED CONTROLLED TRIAL

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Background: Fatigue is a very common symptom of primary Sjögren’s syndrome (pSS), being reported by up to 70% of patients [1]. It is more pronounced when compared to healthy individuals [2] and patients often report that it is their greatest problem and the one that makes the disease difficult to cope with [3]. There is no evidence on non-randomized controlled study on aerobic exercise in pSS with a small sample size suggesting improvement in fatigue, aerobic capacity, depression and physical function [4].

Objectives: To evaluate the safety and effectiveness of a supervised walking program in women with pSS.

Methods: Forty-five women fulfilling the American European Consensus Criteria for pSS were randomized to a Training Group (TG, n=23) or Control Group (CG, n=22). Patients in the TG were submitted to supervised walking, 3 times a week, for 16 weeks. The patients of the CG were instructed to not perform any kind of regular physical exercise. Outcomes measured were aerobic capacity, fatigue, disease activity, depression, perception of pSS’s symptoms and quality of life. An intent-to-treat analysis was performed.

Results: The mean change after 16 weeks of VO2max (ml.kg⁻¹.min⁻¹), distance and FACIT-fatigue were higher in the TG than in the CG (p=0.016, p=0.043 and p=0.030, respectively) (Figure 1). Improved aerobic capacity was associated with improvements in fatigue scores and physical components of quality of life measured using SF-36. Furthermore, improved fatigue scores were associated with reduced depression and improvements in the physical and mental components of the quality of life measures. Overall, 95.4% of patients in the TG rated themselves as clinically improved versus 62% of the patients in the CG (p=0.049). There was no flare in disease activity and no serious adverse events with exercise.

Conclusions: This supervised walking program was demonstrated to be feasible and safe with improvements in the aerobic capacity, exercise tolerance, fatigue and patient perception of improvement in pSS patients.

References:


Acknowledgements: This work was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES Foundation [BEX 8831/14-9 to S.T.M].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3854

OP0260-HPR

HIGHER SATISFACTION WITH ACTIVITY-RELATED SYMPTOMS AFTER 15-WEEK RESISTANCE EXERCISE IN WOMEN WITH FIBROMYALGIA

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Background: Physical exercise is troublesome for most patients with fibromyalgia (FM) due to activity-induced pain. A reason for activity-induced pain is a low pain threshold. In the present study we investigated if experience of physical activity changed after 15-week progressive person-centred resistance exercise. The control group participated in 15-week relaxation program.

Objectives: To investigate how experience of physical activity changed after 15-week resistance exercise in women with FM, and if experiences correlated with pain threshold.

Methods: 130 women (age 22–64 years, symptom duration 0–35 years) with FM were randomized to 15-week resistance exercise or to a parallel relaxation program. The participants completed Experience of physical activity scale (EPA) comprising five subscales (0–7), assessing how exercise was perceived in terms of physical relaxation (PR), Well-being (WB), Activity beliefs (AB), Activity-related symptoms (ARS), and Activity Habits (AH) (1). A lower score indicates a higher satisfaction. Pain threshold was investigated with algometer. Within-group and between-group analyses were conducted by non-parametric statistics. Correlations between algometry and ratings on EPA were investigated by Spearman correlation coefficient.

Results: The resistance exercise group scored significantly higher satisfaction at posttest than before the intervention in their ratings on how they experienced exercise in terms of PR, WB, ARS and AH (p<0.05), Table 1. Between-group analyses showed that the resistance exercise group scored significantly higher satisfaction in ARS subscale (p<0.006) after the intervention when compared to the relaxation group. Significant correlations were found between algometry and EPA (rs -0.32, p=0.017) as well as ARS (rs -0.33, p=0.015) at post-test in the resistance exercise group.
Table 1. Baseline and post-test ratings of EPA in the two groups

<table>
<thead>
<tr>
<th>EPA subscales</th>
<th>Resistance exercise</th>
<th>Relaxation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (n=67)</td>
<td>Baseline (n=63)</td>
</tr>
<tr>
<td></td>
<td>15 weeks (n=56)</td>
<td>15 weeks (n=48)</td>
</tr>
<tr>
<td>PR</td>
<td>3.9±1.1</td>
<td>3.6±1.0*</td>
</tr>
<tr>
<td>WB</td>
<td>2.9±1.5</td>
<td>2.5±1.2*</td>
</tr>
<tr>
<td>AB</td>
<td>2.0±1.0</td>
<td>1.9±1.2</td>
</tr>
<tr>
<td>ARS</td>
<td>4.7±1.2</td>
<td>4.1±1.1*</td>
</tr>
<tr>
<td>AH</td>
<td>4.1±1.3</td>
<td>3.1±1.5*</td>
</tr>
</tbody>
</table>

Within-group changes (p<0.05) are marked with *.

Conclusions: Women with FM experienced a higher satisfaction with activity-related symptoms after having participated in a person-centered resistance exercise program, which is an important knowledge for health care professionals when motivating patients for exercise. Correlations between algometry and ratings on PR and ARS indicate that activity-related symptoms are partly associated with the pain threshold.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4997

Abstract OP0262 – Table 1

<table>
<thead>
<tr>
<th>OP0262 – Table 1</th>
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<tbody>
<tr>
<td>Discharges, no</td>
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<tr>
<td>Incidence per 100 000 adults</td>
</tr>
<tr>
<td>Men, incidence per 100 000 adults</td>
</tr>
<tr>
<td>Women, incidence per 100 000 adults</td>
</tr>
<tr>
<td>Duration, days (mean (range))</td>
</tr>
<tr>
<td>Age, years, mean, SD</td>
</tr>
<tr>
<td>45–64</td>
</tr>
<tr>
<td>65–84</td>
</tr>
<tr>
<td>ULT, (%) 6 months before hospitalization</td>
</tr>
<tr>
<td>Total cost, 10^5 USD</td>
</tr>
</tbody>
</table>

Even though these results are promising regarding PA in JIA patients, the results indicate that patients still need to be encouraged to be physically active, with emphasis on increasing vigorous PA.


Disclosure of Interest: None declared


FRIDAY, 16 JUNE 2017

Gout: advances in diagnosis and management

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Background: Gout is the most common arthritic disease in the world with increasing incidence and prevalence. There are differences in gout prevalence and course of disease due to cultural, ethnic and genetic factors stressing the need for data from different parts of the world. An increase in hospitalization for gout has been shown for the last two decades in North America.

Objectives: We evaluated the trend for hospitalization of gout in western Sweden 2000 – 2012 and the health care costs for this 2009 – 2012.

Methods: Hospitalization trends for gout were studied using data from the health care consumption register in the Western Swedish Health Care Region (WSHCR) from 2000–01–01 through 2012–12–31. This area is considered to be representative for the country as a whole. Patients aged 18 years and older who were hospitalized during the study period with a principal ICD-10 diagnosis of gout (M10) at discharge were included. We calculated annual population rates for hospitalization for gout, Inflation-adjusted health care costs for the gout hospitalizations were calculated using the Cost-Per-Patient register (CPP). Dispensation of unate lowering therapy (ULT), allopurinol (M04AA01) and probenecid (M04AB01), within 6 months prior to hospitalization was identified using The Swedish Prescribed Drug Register.

Results: There were 1873 hospitalizations for gout (mean age 75.0–77.6 years, 61–74% men) between 2000 and 2012. Demographic characteristics were similar

OP0262 – Table 1

<table>
<thead>
<tr>
<th>Physical activity</th>
<th>JIA (n=53)</th>
<th>Controls (n=53)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counts per minute</td>
<td>457±194</td>
<td>463±135</td>
<td>0.45</td>
</tr>
<tr>
<td>Steps daily</td>
<td>9219±2679</td>
<td>9772±2575</td>
<td>0.27</td>
</tr>
<tr>
<td>Sedentary daily (min)</td>
<td>575±69</td>
<td>571±58</td>
<td>0.66</td>
</tr>
<tr>
<td>Light PA daily (min)</td>
<td>193±48</td>
<td>183±42</td>
<td>0.39</td>
</tr>
<tr>
<td>Moderate PA daily (min)</td>
<td>33±11</td>
<td>37±12</td>
<td>0.08</td>
</tr>
<tr>
<td>Vigorous PA daily (min)</td>
<td>21±12</td>
<td>26±14</td>
<td>0.04</td>
</tr>
<tr>
<td>Achieves 60 min MVPA daily n (%)</td>
<td>17 (32)</td>
<td>26 (49)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Numbers are mean ± SD or N (%).

Though these results are promising regarding PA in JIA patients, the results indicate that patients still need to be encouraged to be physically active, with emphasis on increasing vigorous PA.


Disclosure of Interest: None declared

over the study period. From 2000 to 2012, the annual hospitalization rate for gout increased from 12.2 to 16.7 per 100,000 adults (p<0.0038). The increase was most pronounced in males aged 65 and above and over the last three years of the study. From 2009 to 2012 the inflation-adjusted health care costs for gout hospitalizations increased from 5.21 to 8.15 $10^7$ USD. The duration of hospitalizations also increased from 3 to 5 days median 2000 and 2012 respectively (p<0.021). Only a minority of patients, 19 to 27%, received ULT the 6 months preceding their hospitalization, without any obvious secular trend.

Conclusions: Incidence of hospitalization for primary gout is increasing substantially in Sweden over the last decade and this is reflected in the health care costs. The main part of this increase consists of males aged 65 and above. Only a fourth of the patients were on ULT preceding the hospitalization. These findings are further emphasized by the fact that the total amount of days for somatic inpatient care in WSHCR decreased by 9% from 2002 (1 267 900 days, mean duration 5.7 days) to 2012 (1 151 630 days, mean duration 4.9 days). The findings in this study reflect increasing incidence of the gout disease and an ageing population but also a considerable lack of treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1825

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OP0263

TRANS-ANCESTRAL META-ANALYSIS IDENTIFIES 13 NEW LOCI ASSOCIATED WITH SERUM URATE LEVELS

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Background: Serum urate is an important biomarker for gout disease and kidney function. Genome-wide association study (GWAS) meta-analyses have identified 28 loci in European and East Asian population samples. Combined analysis of these summary data across populations offers the opportunity to discover new serum urate associations through greater sample size and power, and trans-ancestral analyses provide the opportunity for fine-mapping associations with greater resolution given differing linkage disequilibrium patterns between populations.

Objectives: To conduct a meta-analysis of European and East Asian serum urate GWAS.

Methods: Summary statistics from European (N=110,238) (Kottgen et al. 2013) and East Asian (N=21,268) (Okada et al. 2012) meta-analyses were obtained. We used ImpG v1.0 to impute the results into 1000 Genomes phase 3 variants, and east Asian (N=21,268) meta-analyses were obtained. We conducted a meta-analysis of European and East Asian serum urate GWAS.

Results: Trans-ancestral meta-analysis of European and East Asian GWAS revealed nine new serum urate-associated loci (P_{meta}<5x10^{-8}). Three loci were located in the 11q12.3–13.2 region near the established SLC22A11/12 locus. Additional novel loci were located near the FGFS, LNC00603, HLA-DQB1, B4GALT1, BIC1 and USP2 genes. Tissue-focused functional partitioning of SNP-heritability indicated the strongest enrichments of kidney, GI and liver tissues (P<10^{-7}), among other significant tissues. Trans-ancestral meta-analysis and functional fine-mapping decreases the number of SNPs in causal variant credible sets, and for example pinpoint the rs17632159 SNP as likely causal (posterior P<0.9) at the TMEM171/174 locus.

Conclusions: Meta-analysis of existing GWAS increases power and leads to the identification of nine new loci associated with serum uric acid levels. Increased resolution in trans-ancestral GWAS, with functional annotation enrichments, improves fine-mapping of serum urate GWAS loci.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4611

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OP0264

CAN MODERATE ALCOHOL INTAKE LOWER THE RISK OF MYOCARDIAL INFARCTION AND MORTALITY EVEN AMONG GOUT PATIENTS?

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Background: While alcohol is a well-established risk factor for gout, many prospective studies have consistently found that moderate alcoholic consumption is associated with a 25–40% reduced risk for coronary heart disease (CHD) and death. As such, the American Heart Association (AHA) suggests that “if you drink alcohol, do so in moderation”. As gout is associated with an increased risk of CHD and premature mortality, the potential benefits of drinking in moderation may also be applicable to gout patients provided that their gout is under control with other measures.

Objectives: To examine the relation between alcohol intake and the risk of acute myocardial infarction (AMI) and all-cause mortality among incident gout patients in a general population context.

Methods: We conducted a cohort study using data from an electronic medical record database representative of the UK general population, collected between 1996 and 2015. The exposure of interest was the first alcohol intake measured after gout diagnosis, and our endpoints were incident cases of AMI as well as all-cause mortality. Stratifying by sex, we calculated the hazard ratios (HR) of these endpoints according to alcohol intake categories (i.e., 0, 1–9, 10–24, 25–42, and >42 units/week), adjusting for age, smoking status, body mass index, duration of gout, comorbidities, and medication use. We performed a spline model analysis using 4 knots of the alcohol intake categories, hypothesizing a J-shaped relation as observed in general population studies.

Results: Among 55,584 gout patients (78% male, mean age of 63 years), 1,332 developed AMI and 8,362 died over a mean follow-up of 5.6 years. Compared with men who did not drink alcohol after gout onset, men who drank alcohol had a lower risk of AMI as well as mortality in a J-shaped manner (Figure 1, left panel). The multivariable HRs for developing AMI were 1.0, 0.76 (95% confidence interval [CI], 0.63–0.93), 0.68 (0.55–0.83), 0.69 (0.59–0.89), and 0.71 (0.52–0.95) for alcohol use categories of 0, 1–9, 10–24, 25–42, and >42 units/week, respectively, and the corresponding HRs for mortality were 1.0, 0.77 (95% CI, 0.71–0.82), 0.71 (0.66–0.77), 0.74 (0.66–0.82), and 0.89 (0.78–1.01) (Figure 1, left panel). While alcohol consumption levels and sample sizes were smaller among women, the J-shaped relation was more obvious and showed a significantly increased risk of mortality in the top consumption category (HR=1.68; 95% CI, 1.09–2.61) (Figure 1, right panel).

Conclusions: This general population-based study indicates that moderate alcohol intake is associated with a lower risk of AMI as well as all-cause mortality among gout patients, similar to many general population studies. These findings suggest that the AHA recommendation about moderate alcohol use may also be applicable to gout patients for their cardiac health and improved survival, provided that their gout is under control with other measures.

Acknowledgements: This project was supported in part by NIH grant P60-AR-047785 and NIH grant R01-AR-065944.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6906
**OP0265** VALIDATION OF A DEFINITION FOR ATTACK (FLARE) IN PATIENTS WITH ESTABLISHED GOUT

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**Background:** A standardized validated definition for gout attacks (flares) is not available. Two provisional definitions published in 2012 were based on patient-reported elements (patient-defined attack, pain at rest greater than 3 in a 0–10 numeric rating scale, presence of at least one swollen joint, presence of at least one warm joint) (1). These definitions had acceptable sensitivity and specificity but lacked external validation which is necessary before they can be adopted in gout clinical studies.

**Objectives:** To perform external validation of previously published preliminary gout attack (flare) definitions in patients with gout.

**Methods:** We enrolled 509 participants with gout from 17 international sites in a cross-sectional study performed during routine clinical care. All patients met the 2015 ACR/EULAR classification criteria for gout (2). Criteria for the previously published gout attack definitions were collected by a site investigator and the final adjudication of a gout attack status was done by a local expert rheumatologist, through an evaluation independent from that of the site investigator. Logistic regression, Bayesian statistics, and receiver-operator curves were used to calculate the final diagnostic performance of the attack definitions.

**Results:** The mean age of participants was 57.5 years (standard deviation [SD] 13.9) and 89% were men. Mean disease duration was 12.3 (SD 10.3) years, 35% had tophi, and 75% were taking urate-lowering therapies. The previously published and favored definition requiring the presence of 3 or more out of 4 criteria (“number of criteria”) was found, using the current study data, to be 85% sensitive and 95% specific in confirming the presence of an attack in patients with gout (Table). The concurrent logistic regression model had an area under the curve of 0.97. The previously published definition based on a classification and regression tree algorithm (entry point pain at rest >3 followed by patient-defined attack “yes”) was 73% sensitive and 98% specific using the current study data (Table). The “number of criteria” approach with a cut-point at 3 or more out of 4 criteria had higher diagnostic accuracy using the current study data than in its initial description 2012 (92% versus 84%, table). (1) Finally, using current study data the “number of criteria” approach at 3 or more out of 4 criteria had higher accuracy to the classification and regression tree algorithm based approach (92% versus 89%) but with a much better sensitivity (85% versus 73%).

**Conclusions:** Despite a stable dose of allopurinol for more than 3 months, and even with sUA at the target level, a substantial proportion of patients with gout continue to have evidence of MSU crystal deposition by DECT scan. Patients with palpable tophi, sUA levels >6.0 mg/dL and palpable tophi showed the highest prevalence of urate deposits (90%), and those with sUA <6.0 mg/dL and no palpable tophi showed the lowest prevalence (47%). Those who reported a gout flare within the prior 3 months (versus none), were prescribed allopurinol doses >300 mg (versus 300 mg), and had palpable tophi (versus none) had greater total volume of crystals.

**Acknowledgements:** This study was sponsored by Ardea Biosciences/As- traZeneca.


DOI: 10.1136/annrheumdis-2017-eular.3666

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**OP0266** PRESENCE OF MONOSODIUM URATE CRYSTALS BY DUAL-ENERGY COMPUTED TOMOGRAPHY IN GOUT PATIENTS TREATED WITH ALLOPURINOL

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**Background:** Chronic hyperuricemia predisposes to deposition of monosodium urate (MSU) crystals in musculoskeletal and other tissues, causing chronic inflammation, acute gout flares, joint damage, and disfiguring tophi. Dual-energy computed tomography (DECT) is a useful imaging tool to detect and quantify MSU crystal deposits.

**Objectives:** This study assessed the evidence of MSU crystal deposition using DECT scanning among gout patients treated with allopurinol and the potential determinants associated with the observed deposits.

**Methods:** The multicenter DECT study recruited patients with gout from the USA and New Zealand who were taking allopurinol at >300 mg daily for at least 3 months. MSU crystal deposition was measured using DECT in hands/wrists, knees, and feet/ankles bilaterally. The presence of MSU crystals as well as the total volume of crystals were assessed according to gout characteristics and serum uric acid (sUA) levels.

**Results:** Patients (N=153) were predominately male (92.2%), with mean (SD) age 58.5 (11.4) years, and gout duration 14.9 (10.3) years. sUA was >6.0 mg/dL in 49.0% of patients. 81.7% of patients took allopurinol at a stable dose of 300 mg/day and the remainder at >300 mg/day. 69.1% of patients had MSU crystal deposits with a total median crystal volume of 0.16 cm³ (range, 0.01 to 19.3 cm³). Those with sUA >6.0 mg/dL and palpable tophi showed the highest prevalence of urate deposits (90%), and those with sUA <6.0 mg/dL and no palpable tophi showed the lowest prevalence (47%). Those who reported a gout flare within the prior 3 months (versus none), were prescribed allopurinol doses >300 mg (versus 300 mg), and had palpable tophi (versus none) had greater total volume of crystals.

**Conclusions:** Despite a stable dose of allopurinol for more than 3 months, and even with sUA at the target level, a substantial proportion of patients with gout continue to have evidence of MSU crystal deposition by DECT scan. Patients with palpable tophi, sUA levels >6.0 mg/dL, and gout flares within the prior 3 months have a greater volume of MSU crystal deposition. These patients may need continuation and/or intensification of their urate-lowering therapy regimen.

**Acknowledgements:** This study was sponsored by Ardea Biosciences/As- traZeneca.


DOI: 10.1136/annrheumdis-2017-eular.3666

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**OP0267** SERUM URATE AS A SURROGATE ENDPOINT FOR GOUT FLARES: RESULTS OF A SYSTEMATIC REVIEW AND META-REGRESSION ANALYSIS OF RANDOMIZED TRIALS

L. Stamp 1, M. Morillon 2, W. Taylor 3, N. Dalbeth 4, J. Singh 5, R. Christensen 6. 1Medicine, University of Ottawa, CCHRitchurch, Christchurch, New Zealand; 2Odense University Hospital, Odense, Denmark; 3University of Otago, Wellington; 4University of Auckland, Auckland, New Zealand; 5University of Alabama, Birmingham, United States; 6Musculoskeletal Statistics Unit, The Parker Institute, Odense, Denmark

**Background:** The primary outcome measure for efficacy in clinical trials of urate lowering therapy (ULT) is frequently serum urate (SU), effectively acting as a surrogate for patient-centred outcomes (e.g. gout flares). It has not been clearly demonstrated that the strength of the relationship between SU and patient-centred outcomes is strong enough for SU to be considered a surrogate.

**Conclusions:** Despite adequate SU levels, a substantial proportion of patients continued to have evidence of MSU crystal deposition by DECT scan. Patients with palpable tophi, SU levels >6.0 mg/dL, and gout flares within the prior 3 months have a greater volume of MSU crystal deposition. These patients may need continuation and/or intensification of their urate-lowering therapy regimen.

**Acknowledgements:** This study was sponsored by Ardea Biosciences/As- traZeneca.


DOI: 10.1136/annrheumdis-2017-eular.3666
Conclusions: Substituting surrogate endpoints (proportion achieving target SU) for the important clinical outcome (gout flares) allows conduct of shorter smaller trials. However, based on aggregate trial-level data (meta-regression) an anticipated association between SU and gout flare could not be confirmed. Trial duration may have been too short to observe a reduction in flares and further work using data from long-term extension studies is underway.

Disclosure of Interest: None declared


NURSE-LED CARE VERSUS GENERAL PRACTITIONER CARE OF PEOPLE WITH GOUT: A UK COMMUNITY-BASED RANDOMISED CONTROLLED TRIAL

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Background: Despite increasing prevalence of gout in the UK (1), a variety of barriers result in suboptimal care (1.2) with only 40% of gout patients receiving urate-lowering therapy (ULT), usually at fixed dose without titration to a serum uric acid (SUA) target (1.2). Nurses successfully manage many chronic diseases in the community, and we have shown that when provided with gout are fully informed and involved in management decisions uptake of ULT is high and persistence and adherence under nurse-led care is excellent (3).

Objectives: To directly compare nurse-led care to general practitioner (GP) care of people with gout in a 2 year randomised controlled trial (NIHR CRN Portfolio No.12943)

Methods: 517 participants with acute gout in the previous year were identified from 56 local GP practices and randomised to nurse-led or continuing GP care. The nurses were trained about gout and its management according to recommended best practice (EULAR and BSR guidelines) involving full information, addressing illness perceptions, and involving patients in management decisions. Assessments were undertaken at 1 and 2 years. Analysis was intention to treat (last observation carried forward).

Results: Nurse (n=255) and GP (n=262) groups were well matched at baseline for mean age (62 v 64yrs), sex (90% v 89 men), mean disease duration (11.6 v 10.6 yrs), mean gout attack frequency (2.1 v 2.2) in prior year (4.2 v 3.8), tophi (13.7% v 8.8%), mean SUA (443 v 439 μmol/L), mean eGFR (71.5 v 70.2) and ULT use (40% v 39%) (all p>0.05). By 2yrs, 22 (8.6%) and 54 (20.6%) participants had discontinued the nurse and GP groups (p<0.001), including 2 v. 8 deaths respectively. Comparing nurse and GP groups at 2yrs: 95% v 29% had SUA ≤300 μmol/L, 88% v 16% had SUA <350 μmol/L, mean SUA was 252±73 v 418±106, 97% v 54% were on ULT; and mean (SD) dose of allopurinol was 470 (140) v. 240 (107) mg/day (all p<0.001). Mean (SD) attack frequency during the 2nd year was 0.33 (0.93) in the nurse v. 0.94 (2.03) in the GP group (p<0.001). At 2yrs, tophi were present in 15% (reduced) v. 9.6% respectively (p<0.002). Although equivalent at baseline, mean (SD) SF-36 norm-based physical component scores were better at 2yrs in the nurse group (41.31 v 16.76) and 37.87 (14.31) v 30.05 (p<0.05).

Conclusions: Nurse-led care of people with gout in the UK community can result in high uptake and excellent adherence to ULT over a 2yr period, achievement of target SUA in >9/10 cases and consequent improvements in patient-centred outcomes and quality of life. This study reinforces the benefits of “treat-to-target”. Compared to standard GP care this model is likely to be cost effective long-term and merits further consideration.

References:

Acknowledgements: Arthritis Research UK (Award No.19703) funded this study.

Disclosure of Interest: M. Doherty Grant/research support from: AstraZeneca, Consultant for: AstraZeneca, Grunenthal, Mallinckrodt and Roche, W. Jenkins: None declared, H. Richardson: None declared, A. Abhishek Grant/research support from: AstraZeneca, D. Ashton: None declared, C. Barclay: None declared, L. Duley: None declared, H. Jones: None declared, M. Santarelli: None declared, A. Sarmanova: None declared, M. Stevenson: None declared, W. Zhang Consultant for: AstraZeneca and Grunenthal

DOI: 10.1136/annrheumdis-2017-eular.5006

EFFECT OF XANTHINE OXIDASE INHIBITORS ON THE INCIDENCE OF CARDIOVASCULAR EVENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Background: There is evidence that xanthine oxidase inhibitors (XOI) may reduce the risk of major adverse cardiovascular events (MACE) (1,2) and lower blood pressure (3). To date, this evidence is based mainly on observational studies (2).

Objectives: To compare the incidence of MACE, mortality, and total and specific cardiovascular (CV) events in patients enrolled in randomized controlled trials (RCTs) comparing XOI with placebo or no treatment.

Methods: A systematic review (CRD42015016073) searching for RCTs using PubMed, EMBASE, Cochrane Library, Web of Science, and Lilacs databases, and hand searching, was ended in Dec 2016. All RCTs comparing XOIs with placebo or no treatment lasting ≥4 weeks and including only adult individuals were eligible. The primary outcomes were the incidence of MACE (CV death, non-fatal myocardial infarction, unstable angina requiring urgent revascularization, or non-fatal stroke) and mortality; total CV events (TCE), specific CV outcomes, and serious adverse events (SAE) served as secondary outcomes. Associations were tested using the Peto odds ratio (OR) without zero-cell continuity correction.

Results: In total, 81 studies including approx. 11,000 individuals reported extractable data on CV events. The use of XOI tended to be associated with lower incidence of MACE (OR=0.64, 95% CI 0.41–1.01, P=0.056), but not with mortality (0.95, 0.63–1.44). However, there was a significantly reduced incidence of TCE (0.66, 0.54–0.80, P<0.001), especially new/worsening hypertension (0.57, 0.37–0.87, P=0.009), and a trend for reduction in the incidence of new/worsening heart failure (0.74, 0.53–1.04, P=0.086). The incidence of SAE (0.86, 0.71–1.05) did not differ significantly. Subgroup analysis suggested a protective effect for MACE in studies with high prevalence (<50%) of cardiac diseases (0.52, 0.30–0.91, P=0.021). Sensitivity analysis excluding studies at high or unknown risk of bias did not change these results. A meta-regression analysis suggested a protective effect with reduced incidence of hypertension (0.26, 0.11–0.60, P=0.001) and heart failure (0.55, 0.32–0.94, P=0.030). Separate analysis of data on purine-like XOI (allopurinol and oxypurinol) confirmed the results of the primary analysis. Exploratory metaregression analysis showed association of dose of allopurinol with higher incidence of TCE (P=0.023, random effects) and SAE (P<0.001, see Figure 1). Accordingly, in the subgroup with doses <300 mg/day of allopurinol, a reduction of incidence of MACE (0.36, 0.18–0.68, P=0.002), TCE (0.38, 0.26–0.54, P<0.001), and SAE (0.49, 0.34–0.71, P=0.001) was observed, while the SAE risk increased in doses ≥300 mg/day (1.39, 1.04–1.91, P=0.047). There was

Disclosure of Interest: None declared

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5006
no association of dose of non-purine-like XOI with incidence of TCE and SAE. Significant statistical heterogeneity was not observed in any test reported here.

Conclusions: Our data from a meta-analysis of RCTs suggest that XOIs reduce the incidence of CV events, an effect possibly related (at least partly) to control of hypertension. However, higher doses of allopurinol (>300 mg/day) may possibly be associated with higher risk of serious adverse events and loss of cardiovascular protection.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2674

FRIDAY, 16 JUNE 2017

Low back pain and fibromyalgia

OP0270  LONG-TERM PROGNOSIS IN CHRONIC PLANTAR FASCIITIS BASED ON DISEASE DURATION AND ULTRASONIC CHANGES

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Background: Plantar fascitis (PF) affects 7–10% of the population over a lifetime but the long-term prognosis is unknown. This study is the greatest within the long-term prognosis of PF and have the longest follow-up time.

Objectives: The aim was to assess the long-term prognosis of chronic PF based on duration of symptoms and ultrasonic changes (tendon thickness, heel spur, echogenicity and heel fat pad) and assess if any baseline cohort characteristics had an impact on the prognosis (sex, BMI, age, smoker status, physical work/sport and bilateral pain).

Methods: At baseline (2001–11) 269 patients were diagnosed with PF based on symptoms and ultrasound findings. At follow-up (2016) all the participants were invited to participate in the project. Everyone was interviewed and offered a new ultrasound examination of their plantar fascia at both feet.

Results: 174 (65%) participated in the study. 52 women and 46% men and 137 had an additional US examination. 54% of the participants were asymptomatic at follow-up (asymptomatic group) and the mean duration of symptoms were 725 days (range 41–4018), 46% still had symptoms (symptomatic group). The follow-up period was 9.7 years (range 4.7–27.3). The risk of having chronic PF were 45.6% (95% CI 37.9–53.0) 10 years after debut of symptoms (figure 1).

A multiple analysis found that women (p<0.01) and participants with bilateral heel pain (p<0.01) had a worse prognosis. The hazard rate ratio was 0.49 (95% CI 0.30–0.80) for women (every time 100 men were getting cured ≥1.5) and the number of patients with low disease activity (LDA) (pain score <2.0). Patients were followed up for 6 months.

Results: A total of 46 patients were included and there were no significant differences between the 2 groups in terms of the reduction in pain at one month post-injection, with scores of -1.5 and -2.5 (p=0.23) in the Treatment and Placebo groups respectively. When including all measures in the first 3 weeks post-injection the difference in pain was statistically significant (p<0.001) in the injected group.

Acknowledgements: The project was financed by The Danish Rheumatism Association and The Research Funds of Hospital Unit Central Jutland

Disclosure of Interest: None declared


Low back pain and fibromyalgia

OP0271  CORTICOSTEROID INJECTIONS FOR GREATER TROCHANTERIC PAIN SYNDROME: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Background: Although small observational studies have suggested that local corticosteroid (CS) injection may be effective in the management of the greater trochanteric pain syndrome (GTPS), no prospective placebo controlled study has been carried out to establish the efficacy of this common intervention.

Objectives: To perform a randomized double-blind placebo controlled trial to investigate the efficacy of local CS injection in the management of GTPS.

Methods: The trial was conducted in the Rheumatology unit of a University teaching hospital in Geneva, Switzerland. Inclusion criteria were lateral hip pain (LHP) for greater than 1 month, a LHP score of ≥4 in the preceding week, failure of another standard treatment (physiotherapy, analgesics, etc.) and typical LHP reproduced by palpation of the greater trochanter (GT). Participants were randomised in a 1:1 ratio to: 1) injection with a combination of local anaesthetic and CS (Treatment group), or 2) injection with normal saline solution (Placebo group). The Treatment group received 4ml of 1% Lidocaine (Rapicain®) and 1ml of Betametasone (Diprophos®). The Placebo group received 5ml of sterile saline solution. Injections were performed under ultrasound guidance. The study’s predefined primary outcome of interest was the difference in pain intensity at 4 weeks post-injection between the 2 groups. Secondary outcomes included the number of “responders” (pain score improvement of ≥1.5) and the number of patients with low disease activity (LDA) (pain score <2.0). Patients were followed up for 6 months.

Results: A total of 46 patients were included and there were no significant differences between the 2 groups at baseline (Table 1). There were no significant differences between the 2 groups in terms of the reduction in pain at one month post-injection, with scores of -1.5 and -2.5 (p=0.23) in the Treatment and Placebo groups respectively. When including all measures in the first 3 weeks and using multilevel regression, there was a marginally significant improvement

Table 1. Baseline patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Active treatment (n=21)</th>
<th>Placebo (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) [SD]</td>
<td>56.4 [14.6]</td>
<td>59.6 [13.1]</td>
<td>0.46</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>1</td>
<td>2</td>
<td>0.51</td>
</tr>
<tr>
<td>Weight (kg) [SD]</td>
<td>74.4 [15.1]</td>
<td>74.7 [15.8]</td>
<td>0.95</td>
</tr>
<tr>
<td>Height (cm) [SD]</td>
<td>163.6 [7.7]</td>
<td>153.6 [32.5]</td>
<td>0.18</td>
</tr>
<tr>
<td>BMI [SD]</td>
<td>27.9 [6.1]</td>
<td>28.8 [4.8]</td>
<td>0.59</td>
</tr>
<tr>
<td>Pain over past 24 hours</td>
<td>6.1 [1.5]</td>
<td>6.6 [1.8]</td>
<td>0.29</td>
</tr>
<tr>
<td>Pain on palpation of GT</td>
<td>6.6 [2.0]</td>
<td>7.1 [1.9]</td>
<td>0.40</td>
</tr>
<tr>
<td>Past injection of GT (%)</td>
<td>38.1</td>
<td>40.0</td>
<td>0.92</td>
</tr>
<tr>
<td>Womac pain score [SD]</td>
<td>251.4 [80.5]</td>
<td>247.2 [87.2]</td>
<td>0.87</td>
</tr>
<tr>
<td>Womac function score [SD]</td>
<td>414.6 [154.9]</td>
<td>366.1 [175.7]</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Except where indicated otherwise, values are the mean (± standard deviation). GT = greater trochanter region.
in pain scores in favour of the Treatment group (p=0.08) (Figure 1). There were no significant differences in terms of the percentage of responders (p=0.32), or patients with LDA (p=0.50) between the 2 groups at follow up. There were no significant differences in pain scores between groups at 3 and 6 months post-injection.

Conclusions: Local corticosteroid injection in the management of GTPS is only marginally effective for a few weeks. Given the lack of long-term improvement and the potential for cortisone-related side-effects, this intervention is of limited benefit.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3458

OP0272 CHRONIC LOW BACK PAIN AND ANXIETY: SIGNIFICANT DECREASE WITH GLUCOSAMINE-CHONDROITIN SULFATE TREATMENT IN A LARGE, COMMUNITY-BASED, PILOT, OPEN PROSPECTIVE INTERVENTIONAL STUDY

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Background: Low back pain (LBP) is associated with 2.3, 2.2, and 1.6 times greater odds for mood disorders, anxiety disorders and alcohol abuse respectively (1). Continued anxiety may lead to a state of “learned helplessness”, and both can propagate in a vicious cycle. Glucosamine-chondroitin sulfate (GCS) combination is widely used in the treatment of OA; however there are few prospective studies of its therapeutic merits in LBP.

Objectives: To study the efficacy of GCS in the decreasing anxiety in patients with chronic LBP in a large open pilot prospective study.

Methods: We enrolled patients 40-65 years of age who had LBP for >12 weeks with pain intensity > 3 on a 0-10 point VAS in a single-arm, open-label prospective interventional study. Major exclusion criteria were the presence of fibromyalgia, spondylolisthesis, and alcohol and/or drug abuse. All patients were treated with ARTFA (combination glucosamine hydrochloride 500 mg - chondroitin sulfate 500 mg in tablet form; Unipharm Inc.) at a dose of 1 tab daily for the first month and then 1 tab daily for the next two months. The primary endpoint was pain intensity as measured on a 0-10 point VAS. Secondary endpoints included anxiety levels measured by Spielberger's State Trait Anxiety Inventory (STAI) adapted for Russia by Khanin (2). STAI evaluates the current "state" of anxiety, asking how respondents feel "right now," using items that measure subjective feelings of apprehension, tension, nervousness, worry, and activation/arousal of the autonomic nervous system as well as aspects of "anxiety proneness," including general states of calmness, confidence, and security ("trait"). Scores for each scale range from 20 to 80, with higher scores indicating greater anxiety.

Results: Overall 3932 eligible FM patients were identified, 88.7% females, mean SD (age =49.2 (12.7). Pre-diagnosis use of medications of interest was documented in 41% of the patients. Of the remaining 2312, 56.1% were issued a prescription in the year following diagnosis and 45.0% dispensed at least on medication. One-year discontinuation rate reached 79.3% overall, and was highest for tricyclic antidepressants and lowest for SSRIs/SNRI antidepressants (Table 1). Over one half of the patients (60.5%) were poorly adherent (PDC ≥20%) during the year and only 9.3% were highly adherent (PDC ≥80%). High adherence was positively associated with socio-economic status (p-for-trend=0.022).

Table 1. Medications prescribed and dispensed in the first year from diagnosis, proportion dis- continued and time to discontinuation for first dispense (N=1296)

<table>
<thead>
<tr>
<th>Drug group</th>
<th>Prescribed (%)</th>
<th>≥1 dispense (%)</th>
<th>N (%)</th>
<th>Days to discontinuation (Median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Convulsants</td>
<td>313 (24.1%)</td>
<td>228 (72.8%)</td>
<td>166 (81.6%)</td>
<td>30 (30–106)</td>
</tr>
<tr>
<td>SSRI/SNRI antidepressants</td>
<td>606 (46.7%)</td>
<td>471 (77.7%)</td>
<td>347 (73.7%)</td>
<td>41 (30–171)</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>167 (12.1%)</td>
<td>126 (74.4%)</td>
<td>94 (57.2%)</td>
<td>30 (30–90)</td>
</tr>
<tr>
<td>Any drug</td>
<td>1296 (100%)</td>
<td>1041 (80.3%)</td>
<td>825 (79.3%)</td>
<td>40.5 (30-146)</td>
</tr>
</tbody>
</table>

*Percent of patients with at least one dispense out of those prescribed, e.g. 228/313x100=72.8% for anti-epileptic drugs. **% of those with ≥1 dispense.

Conclusions: Persistence and adherence with FM therapy in the year following diagnosis is remarkably poor. Further research is needed to assess ways to improve continuation with therapy among FM patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4578

OP0274 FIBROMYALGIA IN REAL LIFE: A NATIONAL FRENCH WEB-BASED SURVEY IN 4516 PATIENTS

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Background: Fibromyalgia (FM) is the most frequent widespread chronic pain disorder (1.6% of the French population) (1). The medical and socioeconomic burden is high and severity depends on medical status and symptoms as defined by the OMERACT criteria (2). Most of the studies are performed in specialized centers recruiting the most severe patients, but very few data exist on its real impact on daily life.

Objectives: The aims were to collect demographic data, symptoms, function, diagnosis, management strategies and health care utilization in real life, in a large population, and to determine clusters of patients.

Disclosure of Interest: None declared

References:
Methods: A large internet-based national survey of people suffering from FM was developed by a national patient association (Fibromyalgie-SOS Association) on their website, in France in 2014. The survey included 103 qualitative and quantitative questions that were developed by 3 medical experts (including rheumatologists) and patients.

Results: The questionnaire was completed by 4516 people. Respondents were predominantly middle-aged (48 yrs) females (93%), most of whom had FM symptoms duration for 12 years and a diagnosis for 5 years. Diagnosis was made by a rheumatologist in 54% of the cases. The symptoms were concordant with the OMERACT domains (chronic pain, fatigue stiffness and other FM-associated symptoms) as previously published by Bennett in 2007 (3). The mean FIQ (Fibromyalgia Impact Questionnaire) score was 51 (0–100); 55% were currently working but 65% of them have been on sick leave in the 12 previous months. FIQ was mostly impacted by injustice feeling (+4.5), part time job (+2.4) and low income - less than 1000 euros monthly (+2.3) (linear regression). Somatic comorbidities were mostly osteoarthritis (49%). Psychological comorbidities were injustice feeling (77%), cognitive symptoms (62%; anxiety (52%) and depression (48%). Initiating factors were reported by 73% of them: physical (50%) and/or psychological (76%). Aggravating factors included excess of activities, conflicts, traumaism and displacement. Treatments were provided by general practitioner (85%), physiotherapist (63%), rheumatologist (54%) and osteopathic manual practitioner (41%). Treatment was prescribed in 76.6% of the patients, including paracetamol alone (51.4%), paracetamol and weak opioids (64%), strong opioids (20.1%), antidepressants (8.1%), antiepileptic agents (54.9%), non-steroid anti-inflammatories (NSAIDs) (53.8%), anxiolytics (52.4%) and steroids (12.8%).

Conclusions: This unique descriptive survey in a large population provides data on symptoms, emotional distress, prescribing habits and impact of FM on daily life and work. Results show that FM is altered by emotional (including injustice feeling) and socio-economic factors.

References:

Disclosure of Interest: None declared

OP0275 FIBROMYALGIA PREVALENCE AND IMPACT ON DISEASE ACTIVITY SCORES IN RHEUMATOID ARTHRITIS PATIENTS WHO ARE UNRESPONSIVE TO BIOLOGICAL TREATMENT
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S.-P. Simon 1, L. Muntean 1, S. Rednic 1, 1Rheumatology, “Iuliu Hatieganu” University of Medicine and Pharmacy; 2Rheumatology, Emergency County Hospital, Cluj Napoca, Romania

Background: Rheumatoid arthritis (RA) treatment uses a treat-to-target strategy. Treatment response is assessed using disease activity scores that consider disease activity, associated symptoms (1). The Journal of Rheumatology, 2011; 38: 1487–95.

Objective: To assess the efficacy of a single glucocorticoid intradiscal injection (GC IDI) in cLBP patients with active discopathy.

Methods: We conducted a prospective, parallel-group, double-blind, randomized controlled study in 3 tertiary care centers in France. 135 cLBP patients with active discopathy were enrolled. They received a single GC IDI (25 mg prednisolone acetate) during discography (n=67) or discography alone (n=68). The primary outcome was the percentage of patients with LBP intensity in the previous 48 hr <40 on an 11-point numeric rating scale (NRS, 0 no pain - 100 maximal pain) at 1 month. The secondary outcomes were LBP intensity and persisting active discopathy on MRI at 12 months post-intervention, and spine-specific limitations in activities, health-related quality of life, anxiety and depression, employment status and analgesics and non-steroidal anti-inflammatory drugs consumption at 1 and 12 months post-intervention.

Results: All randomized patients were included in the primary efficacy analysis. At 1 month, the percentage of responders (LBP intensity <40) was higher in the GC IDI than control group (36/65 [55.4%] vs 21/63 [33.3%]; absolute risk difference [95% confidence interval] 22.1 [5.5;38.7]; p=0.009). In the sensitivity analysis, mean reduction in VAS pain (85% CI) in LBP intensity from baseline to 1 month was greater in the GC IDI group compared to the control group -32.5 [-38.2; -26.8] vs -17.5 [-33.3; -11.7]; respectively; absolute difference [95% CI] -15.0 [-22.9; 7.1], p=0.001. At 1 month, the percentage of patients reporting an improvement in spine-specific limitations in activities was higher in the GC IDI than control group (55/65 [84.6%] vs 34/63 [54.0%]; absolute risk difference [95% CI] 30.5 [15.7; 45.2], p<0.001. The 2 groups did not differ in LBP intensity at 12 months and in most of the secondary outcomes at 1 and 12 months. 102/119 (85.7%) patients would agree to a second intervention. The authors thank URC-CIC Paris Descartes (Christelle Op de Casteleijn) for statistical analysis.

Conclusions: In active discopathy-associated cLBP, a single GC IDI reduces LBP at 1 month post-intervention but not at 12 months.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7062

Table 1. DAS28 components for RA and FRA patients

<table>
<thead>
<tr>
<th>Component</th>
<th>RA (n=63), mean (SD)</th>
<th>FRA (n=17), mean (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGH</td>
<td>49.9 (19.9)</td>
<td>68.8 (17.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TJC</td>
<td>5 (3.9)</td>
<td>10 (8.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SJC</td>
<td>2 (1.4)</td>
<td>2 (1.5)</td>
<td>0.8</td>
</tr>
<tr>
<td>CRP</td>
<td>27.5 (19)</td>
<td>32.8 (23)</td>
<td>0.4</td>
</tr>
<tr>
<td>CRP</td>
<td>8.8 (14.0)</td>
<td>12.8 (15.6)</td>
<td>0.2</td>
</tr>
<tr>
<td>DAS28 ESR</td>
<td>4.6 (1.08)</td>
<td>5.5 (1.05)</td>
<td>0.003</td>
</tr>
<tr>
<td>DAS28CRP</td>
<td>3.99 (1)</td>
<td>4.94 (1.09)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

PGH - patient global health, TJC - tender joint count, SJC - swollen joint count, ESR - erythrocyte sedimentation rate, CRP - C reactive protein.

References:

Acknowledgements: The study was funded by a research grant from the French Ministry of Health (Programme Hospitalier de Recherche Clinique, project no. P070157). The authors thank URC-CIC Paris Descartes Necker/Cochin (Christelle Auger and Nellie Moulopou) for implementation, monitoring and data management of the study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7062
MORE PARTICIPATION, BETTER HEALTH – PROMOTING PUBLIC INVOLVEMENT IN HEALTH

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Background: In Portugal, the National Health Plan for 2012-2016 (1) and its extension to 2020 (2) consider citizenship-based strategies, including the involvement of patients/citizens and their representatives, as a key strategic axis to maximize health gains. However, actual policy initiatives and concrete actions have been limited to a couple initiatives without significant patient or public involvement. On the other side, several patient and citizen organizations (3-6) have been advocating for increased and meaningful involvement in health decision-making.

Objectives: To develop a Charter for Public Involvement in Health that is widely accepted and recognized by health stakeholders.

Methods: A working group was established with representatives from 13 patient organizations, 1 consumer organization and a research centre. A participatory action research methodology was used. The draft Charter was circulated for review and signature among more than 200 non-profit health-related organizations and over 50 key individuals publically renowned for their work in health or public participation. The final version of the Charter was discussed with political and health stakeholders in a Forum held at the Portuguese parliament.

Results: A Charter for Public Involvement in Health, including the principles, scope, guidelines and means of participation was developed. In January 2017, 30 individuals (former and current political decision-makers, health care professionals, researchers and patients) and more than 82 non-for-profit health-related organizations (the majority being Portuguese disease-specific patient organizations) had signed the Charter. The conclusions of the Forum show that the Charter was recognized as a very important initiative to promote public involvement in health in Portugal. Challenges and barriers to further advancing patient and public engagement were also identified (e.g. political will, recognitions of patients as partners, patient empowerment, capacity-building, etc.). The Charter and the Forum were covered in the media and follow-up initiatives with health care professionals and hospital administrators are ongoing.

Conclusions: A patient-led Charter, developed by patient and consumer representatives, in collaboration with academia, and the public discussion with other health care stakeholders have proven successful to put public participation in the political and health care agenda.

References:

Disclosure of Interest: None declared.


Families with children so that as many as possible would find the services offered by FRA and its local member associations.

Methods: The first stage of the project involved conducting a survey in order to find out what the package should contain. The survey was directed to parents to children with JIA, rheumatology nurses and rheumatologists. The content of the information package:

1) An initial information binder with the following information: about JIA, food, physical activities & play, sitting & writing, eyes & dental care. There is also a separate section directed to parents.
2) A so-called gym tail and easy-to-do gymnastic instructions. 3) Bunny 4) Coloured pencils and a pen thickener. 5) A picture book about visiting a rheumatology clinic for the child. 6) Brochures: e.g. information about JIA for the closest relatives of a child diagnosed with JIA and health care professionals, information about FRA for families with children. 7) Gymnastics bag The second stage involved planning the content and the look of the material. The information package and its content needed be positive and functional – the package as a whole had to be suitable for children. The pictures and text for the picture book were also produced in cooperation with the healthcare professionals. Multiple channels were used to spread the information that the package had been completed, e.g. social media, the FRA website and emails to the target group.

In addition, the rheumatology careunits were given instructions and informed of what to expect.

Results: The packages were very well received. We have received positive feedback from both rheumatology clinics and families with children suffering from JIA.

Conclusions: There was a real need for the information packages and the information that they provide help both the families and the healthcare staff.

When a child suffers from an illness, it affects the whole family, and hence it is crucial that comprehensive – and comprehensible – information and support are available so that everyday life runs smoothly and is meaningful, and so that a child with an illness does not feel like he or she is a burden to the family but considers him- or herself an equal member of the family.

References:
[1] We have received positive feedback from both rheumatology professionals and the families of children with JIA.

Acknowledgements: Abbvie, Pfizer, BMS, Roche,The Finnish Society for Rheumatology and the Finnish Society of Rheumatology Nurses, Åberg Express, TNT Finland, Handitec, Paintek, Anglo-Nordic and of course all the individual persons, who helped with the project.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2185

INITIAL INFORMATION PACKAGE FOR CHILDREN DIAGNOSED WITH JIA

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Background: Both parents of children with JIA and rheumatology nurses have informed FRA from time to time that there is a need for an initial information package. There was a demand for information that catered to children’s needs and that was suitable for them and their closest relatives at the stage when the diagnosis is shared with the family.

Objectives: The aim of the project was to make an information package for children aged 0 to 12. A child with JIA needed to be provided with information and text for the picture book were also produced in cooperation with the healthcare professionals. Multiple channels were used to spread the information that the package had been completed, e.g. social media, the FRA website and emails to the target group.

In addition, the rheumatology careunits were given instructions and informed of what to expect.

Results: The packages were very well received. We have received positive feedback from both rheumatology clinics and families with children suffering from JIA.

Conclusions: There was a real need for the information packages, and the information that they provide help both the families and the healthcare staff.

When a child suffers from an illness, it affects the whole family, and hence it is crucial that comprehensive – and comprehensible – information and support are available so that everyday life runs smoothly and is meaningful, and so that a child with an illness does not feel like he or she is a burden to the family but considers him- or herself an equal member of the family.

References:
[1] We have received positive feedback from both rheumatology professionals and the families of children with JIA.

Acknowledgements: Abbvie, Pfizer, BMS, Roche, The Finnish Society for Rheumatology and the Finnish Society of Rheumatology Nurses, Åberg Express, TNT Finland, Handitec, Paintek, Anglo-Nordic and of course all the individual persons, who helped with the project.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5980

THE FRENCH PATIENT’S ASSOCIATION (AFLAR): FRENCH LEAGUE AGAINST RHEUMATISM) HAS GENERATED THE FRENCH NATIONAL ALLIANCE AGAINST OSTEOARTHRITIS AND THE FIRST GENERAL CONVENTION OF OSTEOARTHRITIS IN FRANCE; A CAMPAIGN TO CREATE A NATIONAL LOBBYING TOOL TO IMPROVE THE MANAGEMENT OF OSTEOARTHRITIS

L. Grange 1,2, F. Rannou 3, F. Berenbaum 4, E.F. Mateus 3 on behalf of MAIS PARTICIPAÇÃO, melhor saúde. 1GAT - Grupo de Ativistas em Tratamentos, Lisboa; 2Centro de Estudos Sociais da Universidade de Coimbra, Coimbra; 3Liga Portuguesa Contra as Doenças Reumáticas, Lisboa, Portugal

Background: OA suffers from a lack of interest and not considered serious...
enough by Health authorities taking into account the burden of the disease. AFLAR has fostered dynamics by creating a structure called the National Alliance against OA, includes national experts, patients and health professionals (HP). A initiative of this group has been to organize the first General Convention for OA.

**Objectives:**
- Its main challenge was to provide a list of actions that could propose to the French authorities to improve the visibility of OA along with the needs and demands from French patients.

**Methods:**
- 10 regional roundtables (with HP, patients and health institutions, around five topics) has been launched with discussions and debates and enabled the production of patient-related proposals in order to improve their care and information.

**Results:**
- 79 proposals have been selected and submitted to an online vote in order to be prioritized. Among the 5 topics addressed by the regional roundtables, cross-cutting issues were identified and 9 fields of action emerged. The final proposals were synthesized in a White Paper document and presented to the national Senate assembly. After it was broadcast to the health and public authorities in a prospect of lobbying, see in the image.

**Conclusions:**
- Although the impact of this initiative is not yet measurable, we think it will give a clearer picture of how the disease has been active or not in the following years. It will facilitate a better dialogue at clinician appointments.

### Table of the first 21 proposals from the French initiative

<table>
<thead>
<tr>
<th>Proposal (keyword + hitting number)</th>
<th>% of patients who feel adequately and treated</th>
<th>% of patients who feel adequately and treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Positioning osteoarthritis as a chronic and functional disabling disease (1,1)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>2 Promote retraining in employment for OP patient (3,3)</td>
<td>66.4%</td>
<td>66.4%</td>
</tr>
<tr>
<td>3 Involve health professionals in the healthcare of OA patient (3,0)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>4 Develop research programs to improve the management and treatment of OA (3,0)</td>
<td>64.4%</td>
<td>64.4%</td>
</tr>
<tr>
<td>5 Phytosterones in the treatment of OA (3,1)</td>
<td>62.4%</td>
<td>62.4%</td>
</tr>
<tr>
<td>6 Benefits of the total medical coverage of the population with OA through the national health insurance (3,0)</td>
<td>64.4%</td>
<td>64.4%</td>
</tr>
<tr>
<td>7 Provide palliative care to OA patients (2,2)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>8 Promote the training of health professionals in the field of prevention and early detection of OA (3,3)</td>
<td>48.8%</td>
<td>48.8%</td>
</tr>
<tr>
<td>9 Promote the training of general practitioners on OA (1,0)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>10 Improve the medical-economic impact of the stoppage of one of the patients of OA (2,3)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>11 Promote the OA healthcare after surgery by physiotherapists (3,0)</td>
<td>63.6%</td>
<td>63.6%</td>
</tr>
<tr>
<td>12 RA and osteoarthritis: a medical management for the patients (1,1)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>13 Provide access to physiotherapists for OA healthcare (1,0)</td>
<td>63.6%</td>
<td>63.6%</td>
</tr>
<tr>
<td>14 Improve the referral of musculoarticular care for OA patient (3,9)</td>
<td>62.4%</td>
<td>62.4%</td>
</tr>
<tr>
<td>15 Create a national registry of physicians OA (0,1)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>16 Find additional means of financing for OA healthcare (3,1)</td>
<td>63.6%</td>
<td>63.6%</td>
</tr>
<tr>
<td>17 Develop research programs to improve the management and treatment of OA with OA (1,1)</td>
<td>62.4%</td>
<td>62.4%</td>
</tr>
<tr>
<td>18 Permit the use of habitat and improvement of the living conditions of OA patients (1,0)</td>
<td>65.4%</td>
<td>65.4%</td>
</tr>
<tr>
<td>19 Promote therapeutic Education for OA (3,1)</td>
<td>64.4%</td>
<td>64.4%</td>
</tr>
<tr>
<td>20 The practice of adapted physical activity (3,0)</td>
<td>64.4%</td>
<td>64.4%</td>
</tr>
<tr>
<td>21 Create and generalise “on your phone” (2,3)</td>
<td>62.4%</td>
<td>62.4%</td>
</tr>
</tbody>
</table>

**Discussion of Interest:**
- None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1464
RMDS. A learning partnership should be created between undergraduate medical students/healthcare professionals and the patient experts.

Methods: CYPLAR approached the Swedish Rheumatism Association for collaboration in order to implement the Patient Expert Project in CYPLAR. Funding was received from the EULAR Knowledge Transfer Programme. The collaboration was planned to consist of two meetings, one in Sweden and one in Cyprus.

1. Sweden: Two patients, members of CYPLAR, with RMDS, together with a Rheumatologist from CYPRUS visited the Swedish Rheumatism Association in Stockholm to learn about the Patient Partner Project, and receive Patient Expert training.

2. Cyprus: Two Patient Partner Instructors from the Swedish Rheumatism Association went to Cyprus 6 months after to oversee the progress of the Patient Expert programme and to make an examination of the two Patient Partners educated in Stockholm.

Results: The training session in Stockholm took place on May 2016, for two patients. They received training following the Swedish Patient Expert programme. This training was conducted by two Patient Expert Instructors, one rheumatologist and one Patient Expert. A visit to the Karolinska University Hospital with a tour of the Rheumatology Clinic and a Patient Expert demonstration was also included. The visit ended with a detailed plan formed for the implementation of the Patient Expert programme in CYPLAR.

The visit of the Swedish delegation took place in October 2016. Eight patients participated in the training. The training was made through workshops by the delegates from both organizations together with all the Patient Partners in rheumatology and in patient communication at the St George’s University of London and Niclosia’s establishments. Medical students were also involved in discussing their experience in being educated by patients. The programme also involved practice of joint examinations. The workshop was evaluated by the participants on the final day. After the workshop was concluded delegates spent a day discussing the event together. The programme was evaluated, and a future plan of action decided upon.

Conclusions: The implementation of the patient expert programme was successful. 10 new Patient Experts are now available in CYPLAR. The next generation of health professionals will benefit and get a larger understanding of RMD’s and, in the end, the patients will benefit because the health care staff has a greater knowledge.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3705

#DOENSTSHOWDOESNEXIST / #SYNSINTEFINNSINTE

– A PHOTO CAMPAIGN BY UNGA REUMATIKER

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Background: “Rheumatism amongst young people, is that really a thing?” “Isn’t rheumatism something that only old people have?” “You seem so happy and so active, surely you can’t be in pain?” These are all questions that young people with rheumatism have to listen to, and answer every day.

Yes, it’s possible to have rheumatism even as a young person, and to be in pain, even though we’re not letting it show. We know adjustment is possible, and that we can live our life to the fullest and follow our dreams, despite rheumatism. But, our condition adds some extra understanding from the people around us. That’s what we wanted to recognize, and created a campaign together with AvBio.

Objectives: It can be hard to understand and fully grasp something you can’t see, something that is invisible. But as young people with rheumatism, we have to live and deal with our swollen joints, with the pain and the fatigue, and with the side effects of our medication. None of which should be questioned.

We recognized that this was an issue for most people with rheumatism, and especially young people. Therefore, we wanted to start a conversation about how it feels to live and cope with an invisible disability.

The main purpose with our campaign was to acknowledge the fact that you can’t always tell whether or not a person has a diagnosis, or is in pain. We also wanted to show young people with rheumatism that they are not alone in their situation.

Methods: We asked young people with rheumatism in different ages and with different diagnoses. Each person in the campaign is presented in two different photos. One standard full-portrait photo in front of a white background, just showing who they are. One person held a basketball to show off her love for sport, another one was wearing her dancing shoes and so on. The other photo is instead set in a complete dark room, with the person posing in the same way but this time with their rheumatism-affected areas lit up. We used glow in the dark-body paint and a UV-light to create this effect.

Each pair of photos is put together with the person’s story about their passion in life, their love for sport, their hobby, and deal with an invisible disability.

The campaign was released on October 12th 2016, on World Arthritis Day, with an event at Astrid Lindgren’s children’s hospital in Stockholm. The photos were printed and presented on large boards together with the personal stories.

The first photo of the campaign, a group photo of everyone participating, was also posted on social media on October 12th and then one pair of photos were posted every day during the following week. People were also told to share their own stories under the hashtag #synsintefinnsinte

Results: The campaign ended up being our organization’s most successful campaign to this date. The spread was especially great on Facebook, with the first post reaching nearly 50,000 people and the other posts reaching between 3,500 and 25,000 people every day. The campaign had more likes and shares on both Facebook and Instagram than any of our other campaigns had so far.

The opportunity to show the photos at Astrid Lindgren’s children’s hospital also brought health care into the campaign and attracted great attention on site.

The photos combined with the personal stories make a powerful statement. We managed to show young people with rheumatism that they are not alone in their situation, and we look forward to the conversation continuing on at #synsintefinnsinte

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4893

FRIDAY, 16 JUNE 2017

Imaging and treatment response in rheumatology

OP0283

ULTRASONOGRAPHIC EVALUATION IN RHEUMATOID ARTHRITIS USING THE GLOBAL OMERACT/EULAR ULTRASOUND SYNODIVISYN Score (GLOESS)

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Background: Recently, a global RMD/EULAR ultrasound (US) gnosys score (GLOESS) combining grey-scale (GS) and power-Doppler (PD) scores has been proposed as a novel measurement tool to assess disease activity and response to therapy in patients with rheumatoid arthritis (RA)1,2. However, the ability of GLOESS to discriminate patients with different stages of disease activity vs. remission in standard clinical care is not known.

Objectives: To assess the ability of GLOESS to discriminate between different clinical states of activity vs. remission in RA patients, and to compare clinical, GLOESS and PD US remission criteria and scores in a cross-sectional study.

Methods: Eighty RA patients from 3 centres were recruited at consecutive clinical visits: 50% were in remission and 50% had active RA according to Simple Disease Activity Index (SDAI), SDAI, Clinical Disease Activity Index (CDAI), 28-joint Disease Activity Score (DAS 28CRP), Health Assessment Questionnaire (HAQ), ACR/EULAR remission criteria were assessed. An independent investigator unaware of clinical results performed all US joint examinations of 56 joints. GLOESS, PD, and GS US sum scores per patient were assessed using OMERACT definitions. PD US remission was defined as the PD sum score ≤0. GLOESS remission was defined as GLOESS score ≤1 thereby also including possible GS grade 1.

Results: PD US remission was observed in 38 (48%) patients and GLOESS remission in 16 (20%) patients and CDAI (r=0.24; p=0.03) and CDAI (r=0.23; p=0.04) but not DAS28CRP (r=0.21; p=0.05) were weakly correlated with GLOESS scores in the whole joint set. SDAI (r=0.41; p<0.001), CDAI (r=0.40; p<0.001), and DAS28CRP (r=0.40; p<0.001) were moderately correlated with PD activity in the whole joint set. A minority of patients were classified both in GLOESS remission and in clinical remission according to SDAI (n=10), to CDAI (n=10), to DAS28CRP (n=10) and to ACR/EULAR 2011 (n=7). Less than one third of patients were classified as in PD US remission and in clinical remission according to SDAI (n=22), to CDAI (n=26), to DAS28CRP (n=27) and to ACR/EULAR 2011 (n=21).

The proportion of patients in clinical remission was significantly different according to the definition considered: while 50% of the patients (n=40) were classified in remission according to SDAI, 56% (n=46) were classified in remission according to DAS28CRP, and 43% (n=34) classified in remission to CDAI and 43% (n=34) according to ACR/EULAR 2011 remission criteria.

Conclusions: We document major discrepancies between US and clinical findings and between clinical scores classifying patients in active disease vs. remission. Patients reaching GLOESS or PD US definitions of remission are partly different from those reaching clinical definitions of remission.

References:


Acknowledgements: We acknowledge P. Durez, B. Lauwerys, A. Durne, A.
Evaluation of the Impact of Baseline Levels of MRI-Detected Inflammation on Treatment Response in Early, Seropositive, MTX-Naïve RA: Data from the Avert Trial

H. Ahn¡, J. Baker2, M. Østergaard2, P. Emsery3, P. Durez3, J. Ye4, S. Banerjee5, P. Conaghan6, Bristor-Myers Squibb, Princeton; University of Pennsylvania, Philadelphia; United States; 2Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 3University of Leeds and Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom; 4Université Catholique de Louvain, Brussels, Belgium; 5University of Leeds, Leeds, United Kingdom

Background: Avert (Assessing Very Early Rheumatoid Arthritis Treatment) was a Phase IIIb, randomized, 24-month (M) trial with a 12M, double-blind treatment period, and included contrast-enhanced MRI of the dominant hand and wrist. MRI can provide direct evidence of joint inflammation, enabling stratification of patient (pt) data according to MRI inflammation level, e.g. low vs high. This stratification is hypothesized to predict clinical treatment response.

Objectives: To evaluate the proportion of pts achieving remission at M12 by baseline (BL) MRI-detected inflammation status and treatment group.

Methods: In Avert, pts with early RA received abatacept (ABA) + MTX, ABA baseline (BL) MRI-detected inflammation status and treatment group. Outcomes: To evaluate if FDG PET/CT can accurately diagnose LV-GCA after 3 or 10 days of high-dose steroid treatment.

Results:

- Of 351 pts randomized and treated, 337 (96.0%) had MRI data at BL (ABA + MTX, n=114; ABA monotherapy, n=112; MTX, n=111). Mean (SD) BL synovitis, osteitis and total scores, respectively, for pts with low MRI inflammation receiving ABA + MTX vs MTX alone were: 2.6 (2.0) vs 3.1 (2.4), 0.3 (0.6) vs 0.2 (0.5) and 3.1 (2.4) vs 3.5 (2.7). High MRI inflammation: 9.2 (3.6) vs 9.3 (3.6), 10.0 (9.7) vs 10.7 (9.8) and 29.3 (21.3) vs 30.7 (21.3). BL DAS28 (CRP), CDAI and SDI scores, respectively, for pts with low MRI inflammation receiving ABA + MTX vs MTX alone were: 5.1 (1.1) vs 5.0 (1.3), 3.4 (1.0) vs 3.2 (1.5) and 39.9 (17.4) vs 43.5 (24.6); high MRI inflammation: 6.2 (1.2) vs 5.6 (1.4), 43.1 (16.2) vs 37.7 (18.1) and 76.9 (44.9) vs 61.1 (35.2). The proportion of pts with low BL MRI inflammation attaining remission at M12 was similar regardless of treatment. In pts with high MRI inflammation remission rates were significantly greater in pts treated with ABA + MTX vs MTX alone.

Conclusions: Pts with higher MRI inflammation may derive greater benefit from abatacept + MTX vs MTX alone. BL MRI prediction is a superior predictor of subsequent clinical treatment response to abatacept in RA. MRI may have clinical utility in treatment decisions beyond information obtained from clinical assessments alone.

References:

system is therefore needed if implementing US-tenosynovitis as an outcome measure in clinical trials. The Outcome Measures in Rheumatology (OMERACT) US group’s tenosynovitis scoring system has a good single and multicenter intra- and inter-observer agreement, whereas the sensitivity to change in a multicenter design has never been tested. Furthermore, it is unknown whether low grade synovial hypertrophy without Doppler signal represents true inflammation, i.e. can be eliminated by anti-inflammatory therapy and is sensitive to change.

Objectives: The aim of this study was to test the sensitivity to change of the OMERACT US scoring system for tenosynovitis, including minimal signs of tenosynovitis, in a multicenter design in order to validate it as an outcome measure in RA multicenter clinical trials. Furthermore, to assess the association between US and health assessment questionnaire (HAQ) and Disease Activity Score 28 for joints (DAS28).

Methods: Forty-nine patients with established RA (duration >1 year) and 18 early RA patients (<1 year) with US-verified tenosynovitis were recruited from six rheumatology outpatient clinics in four different countries, if they were scheduled for treatment intensification with synthetic and/or biological Disease Modifying Anti-Rheumatic Drug. Tenosynovitis was assessed at baseline, and at three and six months’ follow-up, by GS and Doppler, using the semi-quantitative OMERACT scoring system. Furthermore, HAQ and DAS28 were assessed.

Results: At baseline tenosynovitis was most frequently found at the extensor carpi ulnaris and tibialis posterior tendons (70.7% and 44.4%, respectively). The overall GS score showed a statistically significant decrease from baseline median (25th;75th percentile: 2;5) to 6 months 0 (0;3) and the overall Doppler score decreased statistically significant from baseline 3 (2.6) to 6 months 0 (0;1), with a p = 0.01. Both GS and Doppler showed high responsiveness (SRM > 0.9), as did HAQ and DAS28 (table 1). Among tendons with grey scale (GS)=1-Doppler=0, 36% (92.9%) showed therapy-induced improvements. A change of 2.1 (95% confidence interval: 1.2;14.9) and 2.1 (CI: 1.1;13.2) in DAS28 corresponded to a change in GS and Doppler of 1 (both p = 0.02) respectively, using a mixed-model for repeated measurement. However, no association between US and HAQ was found.

Conclusions: In conclusion, this RA multicenter study documented a high sensitivity to change of both GS and Doppler US tenosynovitis scores, indicating utility of the OMERACT US scoring system for diagnosing and monitoring tenosynovitis in multicenter trials. Secondly, synovial hypertrophy without Doppler signal, do respond to therapy, suggesting it reflects true inflammation. Finally, changes in US tenosynovitis scores are associated with changes in DAS28.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1651

Table 1. Distribution of US findings at baseline (n=21)

<table>
<thead>
<tr>
<th>Enthesal regions</th>
<th>Enthesitis* N (%)</th>
<th>Chronic lesions N (%)</th>
<th>Inflammation N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraspinatus tendon</td>
<td>6 (29)</td>
<td>6 (29)</td>
<td>0</td>
</tr>
<tr>
<td>Triceps tendon</td>
<td>2 (10)</td>
<td>1 (5)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Common extensor, elbow</td>
<td>5 (24)</td>
<td>5 (24)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Common flexor, elbow</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Greater femoral trochanter</td>
<td>11 (52)</td>
<td>11 (52)</td>
<td>0</td>
</tr>
<tr>
<td>Quadriceps tendon</td>
<td>13 (62)</td>
<td>13 (62)</td>
<td>3 (14)</td>
</tr>
<tr>
<td>Proximal insertion of the patellar tendon</td>
<td>3 (14)</td>
<td>2 (10)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Distal insertion of the patellar tendon</td>
<td>3 (14)</td>
<td>2 (10)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Achilles tendon</td>
<td>17 (81)</td>
<td>16 (76)</td>
<td>4 (19)</td>
</tr>
<tr>
<td>Plantar fascia</td>
<td>4 (19)</td>
<td>4 (19)</td>
<td></td>
</tr>
</tbody>
</table>

*inflammation and/or chronic lesions.
TREAT-TO-TARGET IN EARLY RHEUMATOID ARTHRITIS: CORRELATION OF CXCL13 AND ULTRASONOGRAPHIC

Results: The three-grade semi-quantitative (Grade 0, normal cartilage; Grade 1, minimal change; Grade 2, severe change) scoring system demonstrated excellent (kappa: 0.87) to good (kappa: 0.73) intraobserver reliability in the web-based exercise and the patient-based reliability study respectively. Interobserver reliability was good in the web-based exercise (kappa: 0.64) and moderate (kappa: 0.49) in the patient-based reliability study. The dynamic technique performed slightly better than the longitudinal midline scan alone.

Conclusions: A semi-quantitative imaging system demonstrated good intra- and moderate to good inter-observer reliability in a web-based exercise and patient-based reliability study. Our study demonstrates that US is a reliable tool for evaluating cartilage and supports the use of a new semi-quantitative US scoring system for evaluating cartilage change in RA.

Acknowledgements: The patient-based reliability study was supported by a research grant from UCB.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4314

Background: Modern treatment of early RA is targeted towards remission. Sustained remission is viewed as more beneficial to the patient than remission at one time point, also with regards to inhibition of joint damage. Until now, there is no serum autoantibodies marker for it (2). The chemokine CXC ligand 13 protein (CXCL13) is one of the most potent B-cell chemo attractants constitutively expressed in the B-cell follicles of secondary lymphoid organs (3). Its seric level has been associated to the degree of synovitis in patients with rheumatoid arthritis as studied by ultrasonography (US). The Journal of rheumatology. 2007 Apr;34(4):848–51.

Methods: RA patients with <2 years from first swollen joint who were DMARD naive with indication for DMARD treatment were included in the ARCTIC trial (3). Patients in the ultrasound arm aiming for DAS ≤2, 0–96. No ultrasound power Doppler (PD) signal were included in the current analyses. Several definitions of sustained remission (12–24 months) were compared; DAS-28, ESR, DAS28-ESR, SDAI, CDAI, ACR/EULAR Boolean (remission based on 44 joints), no swollen joints (44SJC), no ultrasound PD signal in any joint (0–96) and minimal total ultrasound greyscale (GS) score (defined as GS ≤2, 0–96).

Results: Of 103 patients, 76 (74%) were female, mean [SD] age was 51.4 [12.9] years, disease duration 6.7 [5.3] months and DAS 3.5 [1.1]. The median [25th, 75th percentile] change in vdHSS 12–24 months was 0.49 [0.0, 1.03] and 73 (71%) patients had no radiographic progression. Sustained remission was reached by 23–61% according to the different criteria. Among patients in sustained remission, comparably proportions of patients did not progress radiographically across the different criteria (74–89%), with the most favorable result for minimal GS score (Table). Patients with sustained no PD or minimal GS score had an increased likelihood of no radiographic progression during the concurrent year (Table), but still rather weak to be useful in an individual patient. Based on the low LR+ none of the criteria identifies patients without radiographic progression very well; likewise, as the LR− is relatively high for all definitions, not being in remission does not change the probability of ongoing radiographic progression substantially.

Conclusions: In this treat-to-target early RA study, sustained remission rates were generally high and radiographic progression limited. None of the sustained remission criteria were able to exclude concurrent radiographic progression. Absence of ultrasound inflammation performed best of the definitions assessed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2366

Background: Joint involvement in systemic lupus erythematosus (SLE) is one of the earliest manifestation of the disease (1). Only 2–5% of the cases develop a deforming and non-erosive type of arthritis, known as Jaccoud Arthropathy (JA). Until now, there is no serum autoantibodies marker for it (2). The chemokine CXC ligand 13 protein (CXCL13) is one of the most potent B-cell chemo attractants and is constitutively expressed in the B-cell follicles of secondary lymphoid organs (3). Its seric level has been associated to the degree of synovitis in patients with rheumatoid arthritis as studied by ultrasonography (US).

Methods: To perform the first detailed US analysis of hands and wrists of SLE patients, with and without JA, and to correlate those findings with the levels of CXCL13, other clinical and laboratory features and disease activity.

Results: Of 64 patients with SLE were included, being 32 with JA and 32 without JA paired by age and disease duration. The definition of JA was based on clinical criteria recently described by Santiago (4). Patients and controls underwent a high-resolution US exam of wrists and hands. Synovial hypertrophy, tenosynovitis and erosions were evaluated according a semi-quantitative grading system according definitions provided by OMERACT (5). Serum concentrations of CXCL13 were quantified in both groups utilizing a commercially available kit. Autoantibodies such as antinuclear antibody (ANA), anti-dsDNA, anti-Sm, anti-SSA, anti-SSB were also tested. US findings were correlated with seric levels of CXCL13, other serological parameters and SLEDAI and SLEDAI-2K.

Results: In the JA group, the mean age was 46.2 years and the mean duration of the disease was 17.3 years. Synovitis on US was found in 25 patients and tenosynovitis in 14. All of these findings were more frequent in SLE with JA, particularly tenosynovitis with difference statistically significant (p=0.002). In JA patients the median levels of CXCL13 was 23.21 pg/ml as compared to 11.48 pg/ml in SLE without JA group (p=0.08). There was an association between tenosynovitis and higher levels of CXCL13 in the JA group (p=0.026). Patients with active disease were more common in the JA group (p=0.004) and had increased serum levels of CXCL13 compared to patients with disease inactive (p=0.008).

Conclusions: In conclusion, the present study is one of a few to describe US findings in SLE patients with JA and it confirms that synovitis and tenosynovitis are common features in the majority of these patients. In addition, CXCL13 may be regarded as a biomarker for tendon inflammation in JA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2998
FRIDAY, 16 JUNE 2017

From genetics through epigenetics to proteomics: understanding disease mechanisms

**OPO291 IDENTIFICATION OF NOVEL SUSCEPTIBILITY LOCI IN A LARGE UK COHORT OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) CASES**

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**Background:** Juvenile idiopathic arthritis (JIA) is a group of chronic artiopathies of unknown cause affecting children under 16yrs, and is the most common childhood inflammatory rheumatic diagnosis. In recent years great advances in dissecting the genetic basis of JIA have been made. In a landmark study, conducted on JIA cases, two most common subtypes (oligoarthritis and RF-negative polyarthritis), 17 susceptibility loci were identified at genome-wide significance (p-value <5x10⁻⁸) and a further 11 reaching suggestive significance (p-value <1x10⁻⁶). These findings were the result of a large international collaboration using the ImmunoChip array, targeting 186 genetic loci in 12 autoimmune diseases. However, a limitation to the afore-mentioned study was that the analysis is limited to the selected loci; large genome-wide studies are now needed.

**Objectives:** The aim of this work is to identify novel genetic loci associated with disease susceptibility using a large cohort of UK JIA cases.

**Methods:** The aim of this work is to identify novel genetic loci associated with disease susceptibility using a large cohort of UK JIA cases. Whole-genome genotyping data was generated using four platforms (Illumina). Following stringent quality control common variants to all four platforms were extracted from the individual datasets before merging together. Imputation (Illumina). Following stringent quality control common variants to all four platforms were extracted from the individual datasets before merging together. Imputation accuracy was elucidated the potential function of the associated SNPs for whom it would be favourable to initiate a biological drug from start of therapy, it is crucial to study biological pathways and biomarkers involved in treatment response.

**Acknowledgements:** We thank Arthritis Research UK for their support: grants 20380 and 20385. CAPS was funded by Arthritis Research UK: grant 20542

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2471

**OPO292 GENETIC VARIATION ASSOCIATED WITH CARDIOVASCULAR RISK IN AUTOIMMUNE DISEASES**

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**Background:** Autoimmune diseases are highly disabling chronic disorders characterized by the activation of multiple immune and inflammatory pathways against self-components. Clinical studies have demonstrated that autoimmune diseases have a higher prevalence of cardiovascular events compared to the general population. Understanding the genetic and biological mechanisms underlying cardiovascular disease (CVD) risk in autoimmunity could therefore be fundamental to develop more effective and targeted therapeutic approaches.

**Objectives:** The objective of this study was to characterize the genetic basis of CVD risk in autoimmune diseases.

**Methods:** A total of 6,485 patients from the six autoimmune diseases RA, PA, SLE, PS, CD and UC were recruited by the Spanish biomedical consortium IMID Consortium. All patients were Caucasian European from the Spain. CVD patients were defined as having >1 out of the 3 most frequent cardiovascular phenotypes: (i) ischemic heart disease (ii) cerebrovascular accident and (iii) peripheral arterial disease. In order to characterize the genetic basis of CVD risk in autoimmune diseases, we used genome-wide genotyping data from all autoimmune disease patients included in the study. First, we tested the association of established CVD risk variants within each autoimmune disease. Second, we analyzed the association of autoimmune disease risk variants with an increase in CVD risk. Finally, we used the cross-phenotype meta-analysis approach (CPMA) to perform a genome-wide meta-analysis and identify global genetic patterns associated with CVD risk in autoimmune diseases.

**Results:** A total of 17 loci previously associated with CVD risk in the general population were significantly associated with CVD risk in the autoimmune patient cohort (P<0.05). From these, 4 loci were found to have significantly different genotypes across autoimmune diseases; we used genome-wide genotyping data from all autoimmune disease patients identified in the study. We first, tested the association of established CVD risk variants within each autoimmune disease. Second, we analyzed the association of autoimmune disease risk variants with an increase in CVD risk. Finally, we used the cross-phenotype meta-analysis approach (CPMA) to perform a genome-wide meta-analysis and identify global genetic patterns associated with CVD risk in autoimmune diseases.

**Conclusions:** The results of the present study represent an important step towards the characterization of the genetic basis of CVD in autoimmune diseases. These findings contribute to explain the higher prevalence of cardiovascular events observed in patients with autoimmune diseases compared to the general population.

**Acknowledgements:** This work is supported by a grant from the Spanish MINECO (AS-17/00116) and the Spanish National Research Foundation (FEDER).

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3673

**OPO293 WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS OF DMARD-NAÏVE EARLY RA PATIENTS ACHIEVING SUSTAINED DRUG-FREE REMISSION AFTER INITIATING TOCILIZUMAB THERAPY**

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**Background:** Rapidly reducing disease activity is of major importance in the management of newly diagnosed rheumatoid arthritis (RA) patients as early response strongly correlates with long-term clinical outcomes. To select patients for whom it would be favourable to initiate a biological drug from start of therapy, it is crucial to study biological pathways and biomarkers involved in treatment response.

**Objectives:** To identify biological networks and signature genes among disease modifying anti-rheumatic drug (DMARD)-naïve early RA patients achieving sustained drug-free remission (sDFR) after initiating treatment with tocilizumab (TCZ).

**Methods:** Data was used from DMARD-naïve early RA patients in the U-Art-Early trial who had been randomized to initiate TCZ therapy. The study design and details have been previously been described [1] Briefly, The study enrolled 116 patients for whom it would be favourable to initiate a biological drug from start of therapy, sDFR was reached when patients remained disease free for whom it would be favourable to initiate a biological drug from start of therapy, sDFR was achieved when patients remained disease free for whom it would be favourable to initiate a biological drug from start of therapy, sDFR was achieved when patients remained disease free for whom it would be favourable to initiate a biological drug from start of therapy, sDFR was reached when patients remained disease free for whom it would be favourable to initiate a biological drug from start of therapy. The study design and details have been previously published. sDFR was achieved when patients remained disease free for whom it would be favourable to initiate a biological drug from start of therapy.

**Results:** In total, eight modules with varying sizes (10–470 genes) were identified. The module best correlated (Pearson correlation coefficient 0.52, FDR<0.05) and IFNγ (FDR<0.05) cytokine pathways.

**Conclusions:** The results of the present study represent an important step towards the characterization of the genetic basis of CVD in autoimmune diseases. These findings contribute to explain the higher prevalence of cardiovascular events observed in patients with autoimmune diseases compared to the general population.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2471
In addition, we identified 83 overrepresented Gene Ontology (GO) terms of which granulocyte migration (p=2.70E-04), myeloid leucocyte migration (p=8.95E-04) and G-protein coupled amine receptor activity (p=1.25E-05) were most significant. The genes in the module of interest showing the highest connectivity were the upregulated tests expressed 22 (TEXX2), doublecortin like kinase 2 (DCLK2), and the downregulated Williams Beuren syndrome chromosome region 27 (WBSCR27) gene (Fig. 1).  

Conclusions: When performing network analyses of the DEGs between responders and non-responders, TEXX2 and DCLK2 were identified as signature genes for treatment response to TCZ therapy. WBSCR27 was found to be associated with a lower chance of achieving sDFR.

References:  
[2] Disclosure of Interest: X. Teitsma: None declared, J. Jacobs: None declared, X. Teitsma: None declared, J. Jacobs: None declared,  

Fig. 1. Network visualization of the interaction of gene co-expression in the module best correlated with achieving sustained drug-free remission. Upregulated genes are expressed as green nodes and the downregulated gene as red node. The three rounded rectangular nodes display the highest co-expressed genes within the module (>10 connections) when applying a weight cut-off of 0.01. The average number of nodes connected at this cut-off was 4.6 (correlation coefficient 0.82).
increases the risk of developing multiple autoimmune and connective tissue diseases. Ptpn22 is a negative regulator of Syk and Src family kinases downstream of immuno-receptor signalling cascades. 2. Fungal β-glucan receptor dectin-1, signals via Syk kinase, and induces dendritic cells to secrete pro-inflammatory cytokines IL-1β, IL-6, IL-12/p35 and TNFα, in turn allowing the induction of IL-17 producing T-cell responses, which are critical to the clearance of fungal infections.3 IL-17 has been implicated as a key cytokine in inflammatory responses associated with RA, JIA, and psoriasis.4  

Objectives: To investigate if Ptpn22 regulates dectin-1 signalling and controls the capability of dectin-1 matured BMDC to promote adaptive immune responses.  

Methods: GM-CSF bone marrow derived dendritic cells (BMDC) were generated from C57BL/6 WT, Ptpn22+/− or Ptpn22−/− (human PTPN22 akt2/akt2 orthologous) mice, and pulsed with OVA323-339 in the presence or absence of the dectin-1 agonist curdian. Activated BMDC were co-cultured in vitro with OT-II T-cells or adoptively transferred into OT-II mice and the resulting T-cell response assessed. Cytokine secretion from curdian activated Ptpn22 variant mouse BMDC was determined by immunoassay and the kinetics of Syk and Erk phosphorylation were determined by immunoblot.  

Results: We observed that Dectin-1 activated Ptpn22+/− BMDC had an enhanced capability to induce T-cell IL-17 secretion both in vitro and in vivo compared to WT BMDC. Following dectin-1 priming Ptpn22−/− BMDC secreted increased IL-17 compared to WT BMDC, and the increase in IL-17 was found to be sufficient to cause the enhanced IL-17 response induced by Ptpn22−/− BMDC. Dectin-1 induced IL-17 secretion was found to be Syk and Erk dependent and assessment of Syk and Erk kinase phosphorylation revealed that dectin-1 activated BMDC displayed enhanced Syk and Erk phosphorylation compared to WT BMDC. Furthermore, Ptpn22−/− BMDC (orthologue of human PTPN22 akt2/akt2) exhibited a similar enhancement in IL-17 secretion and induced enhanced T-cell dependent IL-17 responses in vivo, indicating that the PTPN22 polymorphism behaves as a loss-of-function allele in the context of dectin-1 signals.

Conclusions: Data highlight Ptpn22 as a novel regulator of dectin-1 signals and provide a link between genetically conferred perturbation to innate receptor signalling pathways and autoimmunity.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4717
Innovative insights into mechanism of SLE, Sjögren's and APS

**RESULTS:** Tfh (CD4+CD45RO+PD1+ICOS+FoxP3+) cells were strongly enriched in ELS+ vs ELS- SS samples. The Tfh:Tfr ratio in ELS+ SG was approximately 2:1. Interestingly, while in tonsils Tfr were routinely detected within GCs, in ELS+ SG Tfr were predominantly excluded from the B cell follicles and accumulated in the T cell areas at the periphery of the lymphoid aggregates. Conversely, Tfh densely infiltrated the B cell rich areas and, within ectopic GCs, acquired BCL6. Furthermore, Tfh infiltration closely correlated with SG IL-21 mRNA expression, which in turn was strongly correlated with CD3, CD20 and CD138 IHC scores and with CXCL13, LtB, BAFF, AID and Pax5 gene expression. Finally, MALT-L samples displayed 10-fold higher IL-21 mRNA and twice as much PD1+ICOS+BCL6+ Tfh-cells/field compared to ELS+ SS samples.

**Conclusions:** Within the SG of SS patients Tfh cells closely segregate with lesional IL-21 expression, localize within ELS and are strongly enriched during MG development. Consequently, through Tfh cells recruited in the SG in SS patients, we consistently demonstrated follicular exclusion of this subtype from ectopic GCs. This suggests that Tfr in SS SG fail to exert their physiological immunoregulatory properties in controlling the magnitude of the GCs response and B cell autoactivity, as observed in tonsils.

**Acknowledgements:** This work was supported by project grants from the Medical Research Council (MR/N003063/1 to MB) and Arthritis Research UK (grant 20089 to MB).

**Disclosure of Interest:** E. Pontarini: None declared, W. Murray-Brown: None declared, C. Croia: None; E. Astorri: None; D. Lucchesi: None; A. Capozzi: None; M. Sorice: None; G. Valesini: None; E. Pontarini: None declared; W. Murray-Brown: None declared; E. Astorri: None declared, C. Croia: None declared; D. Lucchesi: None declared; A. Capozzi: None declared; M. Sorice: None declared; G. Valesini: None declared; E. Pontarini: None declared; W. Murray-Brown: None declared; E. Astorri: None declared, C. Croia: None declared; D. Lucchesi: None declared; A. Capozzi: None declared; M. Sorice: None declared; G. Valesini: None declared.
OP0302 SIGNIFICANT REDUCTIONS OF PATHOGENIC AUTOANTIBODIES BY SYNERGISTIC RITUXIMAB AND BELIMUMAB TREATMENT EFFECTIVELY INHIBITS NEUTROPHIL EXTRACELLULAR TRAPS IN SEVERE, REFRACTORY SLE - THE SYNOBISE STUDY

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Background: Neutrophil extracellular traps (NETs) are extracellular, decondensed DNA strands covered with antimicrobial proteins that are part of the first-line defence against pathogens. However, in SLE, overall release of NETs is increased and degradation of NETs is impaired leading to a high amount of extracellular nuclear material, potentially leading to formation of SLE-specific antibodies. These pathogenic autoantibodies deposit in glomeruli in lupus nephritis (LN) and perpetuate autoimmunity by inducing more NETs. The present study hypothesized that combining anti-CD20 mediated B-cell depletion with BAFF (B-cell activating factor) inhibition can target autoreactive plasma cells and thereby effectively reduce pathogenic antibodies in NETs and LN.

Objectives: The present study aimed to investigate whether Rituximab (RTX) + Belimumab (BLM) affected pathogenic antibodies in relation to NET induction in severe refractory SLE.

Methods: As part of a phase 2 proof-of-concept study, the SynBioSe study, serum levels of anti-DNA autoantibodies were measured in severe, refractory SLE patients before and after treatment with RTX following BLM. Additionally, ex vivo NET induction was assessed before and after treatment with a novel highly sensitive method based on 3D confocal laser scanning microscopy. In this assay, neutrophil activation and NET induction were measured at 10% serum of participating controls. Furthermore, we investigated whether NET induction was mediated by immune complexes.

Results: The study included 10 severe, refractory SLE patients with lupus nephritis and 1 patient with neuropsychiatric lupus. NET induction was found to be high at baseline with a median fold induction of 4.5 [range 2.6–11.7]. After 24 weeks, NET induction was significantly decreased (median fold NET induction of 1.6 [0.4–6.1], p=0.01). In addition, treatment with RTX+BLM led to significant reduction of anti-dsDNA antibodies at week 24 with a median of 35 IU/ml [range 10–374] compared to 120 [18–505] at baseline (p=0.012). Total immunoglobulin levels temporally declined but returned to screening levels at week 24. NET induction correlated significantly with anti-dsDNA antibody levels (ρ=0.42, p=0.03) and with SLEDAI scores (ρ=0.53, p=0.003). Therefore, we examined whether the observed NET induction could be explained by circulating immune complexes (ICs). ICx were deprepped by pre-incubating anti-dsDNA positive SLE sera with nuclease, resulting in a significant decrease in NET induction (median % decrease of 91.7 [range 67.8–98.1]). In addition, depletion of IgG from anti-dsDNA positive SLE sera resulted in significantly lower NET induction. Finally, immobilized IgG isolated from anti-dsDNA-positive SLE sera, but not of control serum, resulted in significant NET induction.

Conclusions: Within refractory SLE patients, RTX + BLM resulted in concordant significant NET induction. Of 91.7 [range 67.6–98.1]. In addition, depletion of IgG from anti-dsDNA positive SLE sera resulted in significantly lower NET induction. Finally, immobilized IgG isolated from anti-dsDNA-positive SLE sera, but not of control serum, resulted in significant NET induction.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3719

OP0304 SELECTIVE INHIBITORS OF NUCLEAR EXPORT PREVENT LUPUS PROGRESSION BY TARGETING GERMINAL CENTER FORMATION AND AUTOREACTIVE ANTIBODY SECRETING CELLS

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by simultaneous activation of the innate and adaptive arms of the immune system. The progression of the disease is unpredictable, making its treatment a challenge. Recently the nuclear export protein Exportin 1 (XPO1, also known as CRM1) has surfaced as an attractive target for the treatment of SLE and other inflammatory disorders. Selective Inhibitor of Nuclear Export (SINE) compounds are potent, orally available and well-tolerated XPO1 inhibitors. SINE compounds exert apoptotic and anti-inflammatory effects by mediating nuclear retention of important XPO1 cargos like the NF-κB pathway regulatory protein, IκB.

Objectives: Based on the central role of NF-κB signaling in the activation of immune cells in SLE, we decided to evaluate the therapeutic ability of SINE compounds in mediate experimental lupus progression.

Methods: To evaluate the efficacy of SINE compounds in a preclinical model of SLE, cohorts of lupus-prone mice with established disease (elevated anti-dsDNA antibody titer and proteinuria) were dosed with SINE compound or vehicle. We used flow cytometry to enumerate immune cells and immunofluorescence to visualize germinal centers (GC) in spleen. Quantitative PCR was used to measure changes in mRNA expression for molecules key in plasma cell activation and survival, and histology was used to evaluate inflammation, antibody deposition and pathology in kidneys of lupus-prone mice.

Results: We found that treatment with SINE compounds significantly prevented increases in proteinuria (proteinuria scores: Control: 2.12±1.12; SINE (5 mg/kg): 0.75±0.49; SINE (10 mg/kg): 0.66±0.49; SINE (20 mg/kg): 0.50±0.35) and thereby decreased IgG deposition and kidney pathology (glomerulonephritis, tubule damage and perivascular cuffing). Prevention of kidney damage was associated with a remarkable disruption of splenic GC; a significant reduction in the number of auto-reactive antibody secreting cells (ASC), and a decrease in the accumulation of auto-reactive ASC in the inflamed kidney. Reduced numbers of plasma cells in the inflamed kidney are likely due to the drastic decrease in the expression of molecules critical for GC attraction and the identification of GC as potential reservoirs of SLE autoreactive plasma cells. The potent effect of SINE compounds on GC and auto-reactive ASC is noticeable as early as 1 week after starting therapy. However, kinetics studies showed that a more pronounced elimination of GC and auto-reactive ASC is achievable after 8 weeks. Although SINE therapy has a drastic impact on spleen architecture, recent findings show that complete recovery of the GCs did not occur for at least 6 weeks.

Conclusions: SINE compounds have demonstrated efficacy in a murine model of SLE by reducing generation, survival and function of auto-reactive immune complexes, rendering cell-free, frozen in liquid nitrogen and stored at -80°C. In supernatants from pSS and non-Sjögren’s sicca (nSS) patients 104 targets were measured by Lumexin. Eight pSS and 8 nSS patients were selected for analysis based on matched biopsy weights. Results from this discovery cohort were validated in an additional cohort (n=18 nSS, n=16 incomplete SS; nSS, n=26 pSS) and pSS and nSS individuals with clinical and demographic features were assessed. Non-Ss patients were defined as sicca patients without lymphocytic infiltration in the salivary gland biopsy or anti-Ss/SSa autoantibodies. Incomplete SS patients were defined as sicca patients having lymphocytic infiltration (lymphocytic focus score (LFS)>0) and/or anti-Ss/SSb autoantibodies but do not fulfill the AECG classification criteria and are not diagnosed as pSS.

Results: Levels of 20 cytokines were significantly different between the nSS and pSS patients in the discovery cohort (p<0.05). These 20 and 13 additionally selected cytokines based on a trend towards statistical significance and/or minimal overlap were measured. We generated a correlation matrix of these cytokines. Only 5 cytokines did not significantly differ: 59.8±4.18 mg in nSS vs 72.7±4.65 mg in SS at 67.4±2.86 mg in pSS. Fifteen out of these 20 cytokines were validated. From the 13 cytokines 7 were significantly elevated in pSS vs nSS. In nSS CXCL10 (IP-10) and CCL19 (MIP-3β) were significantly elevated. Cytokines correlating with LFS, ESSDAI, ESSPRI, % IgG and IgM plasma cells in LSS, Schirmer and/or serum IgG with Spearman r=0.4 and p<0.05 in pSS were selected for classification tree analysis, these were IL-2, IL-3, IFN-γ, IL-21, CXCL13 (BLC), CCL10 and CCL19. Using CXCL13 and IL-21 levels, 87.5% of pSS patients could be classified correctly. Baseline on the mean cut off levels, 5 nSS and 9 SS patients would be classified as pSS. Follow up revealed that 6 severe patients may not persistently pSS.

Conclusions: Elevated levels of numerous cytokines were found in LSS biopsy secretomes from pSS patients versus non-autoimmune sicca patients correlating with clinical parameters. This method represents a novel tool to provide insights in pSS immunopathology and provides new therapeutic targets and biomarkers for diagnosis, prognosis and treatment response.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1608
cells. It is likely that inhibition of the canonical NF-κB pathway underlies KPT-350’s inhibitory effect. Together, our findings suggest the potential of SIN-1 compounds to have a significant impact on disease progression in SLE.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6504

OP0305

TYPE I IFN SYSTEM ACTIVATION IN NEWBORNS EXPOSED TO ANTI-RO/SSA AUTOANTIBODIES IN UTERO

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Background: Overexpression of type I IFN-stimulated genes has been demonstrated in both SLE and SS, and induction of IFNα production in plasmacytoid dendritic cells by immune complexes containing RNA and autoantibodies, including Ro/SSA and La/SSB autoantibodies, has also been shown. During pregnancy, these autoantibodies pass over the placenta to the fetus, but it is not known if an IFN-activation takes place also in the fetus.

Objectives: In the present study, we investigated if the type I IFN system is activated in newborns exposed to anti-Ro/SSA autoantibodies in utero.

Methods: Anti-Ro/SSA positive mothers and their babies as well as healthy controls were included in the study. Maternal and cord blood drawn at birth was immediately separated into plasma and PBMC. miRNA expression was analyzed by microarrays, cell surface markers were assessed by flow cytometry and circulating IFNα levels by DELFIA.

Results: We observed increased expression of IFN-regulated genes and elevated plasma IFNα levels not only in anti-Ro/SSA positive women but also in their newborns, with maternal and fetal IFNα scores showing a significant positive correlation (r=0.74, p=0.005). Increased expression of MHC class II was observed on CD14+ monocytes of anti-Ro/SSA antibody-exposed babies, suggesting correlation (r=0.74, p=0.005). Increased expression of MHC class II was observed on CD14+ monocytes of anti-Ro/SSA antibody-exposed babies, suggesting correlation (r=0.74, p=0.005).

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2372

FRIDAY, 16 JUNE 2017

Comorbidities in rheumatoid arthritis

OP0306

DOWREGULATION OF MICRNAs IN PLASMACYTOID DENDRITIC CELLS IS ASSOCIATED WITH A TYPE I INTERFERON SIGNATURE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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Background: The most prominent alteration in the immune system of patients with SLE is a type I interferon (IFN) signature, which we recently also reported in patients with primary APS (PAPS). In SLE and APS, this signature is related to disease activity and vascular disease. Plasmacytoid dendritic cells (pDC) are considered key players in the pathogenesis of SLE and APS as they are major producers of type I IFNs. MicroRNAs (miRNAs) are short non-coding RNAs that modulate gene expression through RNA interference mechanisms and have been implicated in the dysregulation of immune cells in patients with autoimmune diseases. Here we investigated miRNA expression in pDC of patients with SLE and APS in relation to the type I IFN signature.

Objectives: To identify if pDC dysregulation in patients with SLE and APS is associated with alterations of their miRNA expression profile.

Methods: The frequency of circulating pDC was determined by flow cytometry in patients with SLE (n=49), SLE+APS (n=34) and PAPS (n=27) and healthy controls (HC, n=22). RNA was extracted from pDCs isolated from the peripheral blood of patients with SLE (n=20), SLE+APS (n=10), PAPS (n=10) and HC (n=12). pDC miRNA and transcriptome profiles were assessed by RT-qPCR by OpenArray and RNA-sequencing (RNAseq) respectively. Patients were stratified by the presence of an IFN signature by analysis of IFNα expression on the basis of RNAseq. pDC stimulated with TLR7 agonists were analyzed for changes in miRNA expression.

Results: The numbers of circulating pDC were reduced in peripheral blood of patients with SLE, SLE+APS and PAPS (all p<0.001) and did not differ among the patient groups. Among 131 expressed miRNAs, 36, 17 and 21 miRNAs were differentially expressed (p<0.05) in patients with SLE, SLE+APS and PAPS, respectively, as compared with HC. All but one of these miRNAs were downregulated in the patients versus HC. Only 1 miRNA was differentially expressed when comparing between SLE and SLE+APS patients and between SLE and PAPS patients. A total of 9 miRNAs were differentially expressed between IFN-high and IFN-low patients. Pathway enrichment on targets of the top three miRNA (p<0.001) distinguishing between IFN-high and –low patients indicated that these miRNAs are potentially regulating pathways relevant for pDC function such as TLR signaling and endocytosis. Activation of pDCs by TLR7 agonists induced a downregulation of miRNAs in pDC, resembling the miRNA expression pattern seen in patients, in particular those with a high type I IFN signature.

Conclusions: Reduced numbers of circulating pDC and downregulation of miRNAs in pDC is shared between SLE, SLE+APS and PAPS patients. Altered miRNA expression in pDC is associated with the presence of a type I IFN signature in SLE and APS. Our data suggest that the reduced expression of a subset of miRNA underlies pDC dysregulation in SLE, SLE+APS and PAPS patients.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6581

OP0307

TREATMENT OF BAFF TRANSGENIC MICE WITH ANTI-TNF: IFN-MONOCONAL ANTI-TNF ARE ASSOCIATED WITH A HIGHER RISK OF LYMPHOMA THAN ETANERCEPT


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Background: Risk of lymphoma in patients with rheumatoid arthritis (RA) and disease activity is the main risk factor. The impact of treatment, notably of anti-TNF, is unclear: decreasing the risk of lymphoma by controlling activity or altering anti-tumor immunosurveillance. Ant-TNF are not associated with an increased risk of lymphoma in epidemiologic studies. However, the risk might vary according to the type or the dose of anti-TNF.

Objectives: To assess if the risk of lymphoma might differ according to the type of anti-TNF, comparing monoclonal anti-TNF to the soluble receptor. For that, we used BAFF transgenic (Tg) mice as a model of autoimmunity-associated lymphomas. They develop lupus and Sjögren and 3% of them spontaneously developed lymphoma at 12–18 months.

Methods: Six months aged BAFF-Tg mice were treated with anti-TNF for 12 months: etanercept (ETA) (n=15, 8 mg/kgx3/week), monoclonal anti-mouse TNF: TNZ 19.12 (n=15, 20 mg/kgx1/week), adalimumab (ADA) (n=12, 20 mg/kgxweekly) or controls (n=22). Sera were assessed monthly. Crude mortality was compared among the different groups. Histological examination of the spleen was performed. The Fisher’s exact test was used to compare the incidence of lymphoma among the groups.

Results: Adjunction of low dose of methotrexate during the 3 first days of treatment prevented immunization in the 3 groups for life. Using L929 cells, a cell line sensitive to TNF induced death, we confirmed that ADA was 8 to 12 times less efficient than ETA to inhibit soluble murine TNF. As expected, the mean level of ETA, TN3 and ADA were 7 μg/ml, 69 μg/ml and 105 μg/ml respectively. The
level of auto-antibodies and serum Ig did not significantly differ among the groups. However, crude mortality was significantly higher in mice treated with monoclonal anti-TNF compared to controls (p=0.001 for ADA and p=0.003 for TN3) but not for mice treated with ETA (Figure). Incidence of lymphoma was higher in mice treated with monoclonal anti-TNF: 5/15 (33%) with TN3 (p=0.03/controls), 4/12 (33%) with ADA (p=0.054/controls), 0/15 with ETA and 1/22 (5%) in controls.

Conclusions: Higher mortality and increased risk of lymphoma were observed in BAF175 mice treated with monoclonal anti-TNF compared to etanercept. This result may be linked either to the different mechanism of action between the soluble receptor and the monoclonals or to a difference of trough level observed in the different groups even if higher levels of ADA was mandatory given the difference of effect on mouse TNF. This study demonstrates the negative impact of a prolonged anti-TNF treatment on the risk of lymphoma in the context of BAF175 increase.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5148

FRIDAY, 16 JUNE 2017
AxSpA: from bug to gut and to disease phenotype

Table 1. Number of patients, recurrent or second primary cancer, Incidence rate per 1000 person-years (PY) and hazard ratios (HR) among TNF treated patients with RA and their matched biologics naïve comparisons

<table>
<thead>
<tr>
<th>Cancer</th>
<th>TNFi</th>
<th>Matched comparators</th>
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<tbody>
<tr>
<td>N</td>
<td>Events (%)</td>
<td>IMR per 1000</td>
</tr>
<tr>
<td>Overall</td>
<td>446 (20.7%)</td>
<td>98</td>
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<tr>
<td>0.09 (0.02–0.11)</td>
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Disclosures of Interest: P. Raaschou: None declared, J. Söderling Grant/research support from: previous research projects fully or partly funded by Novo Nordisk and Combine Sweden, and has served as an external consultant to AbvVie, Merck and Novartis, J. Asking Grant/research support from: Abbvie, Pfizer, UCB, MSD, Roche, Lilly.
PREGNANCY OUTCOME IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS, A MULTICENTER CORHUT-STUDY

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Background: Systemic lupus erythematosus (SLE) predominantly affects women during their fertile period. During pregnancy SLE patients are prone to pregnancy complications and may experience increased disease activity.

Objectives: To investigate disease activity around/during pregnancy and pregnancy complications in a European cohort according to antiphospholipid antibody (aPL) status. Additional focus on lifetime pregnancy outcomes and comparison of first and consecutive pregnancies were analyzed.

Methods: All ongoing pregnancies of >16 weeks gestation of SLE patients (according to the ACR revised criteria) receiving joint care from rheumatologists and gynaecologists in two tertiary centers in the Netherlands between 2000-2015 were included. Disease activity (using SELENA-SLEDAI (DAI) around and during pregnancy), flare rate according to the SELENA-SLEDAI definitions and pregnancy complications were assessed by medical chart review.

Results: Of 96 women (84% Caucasian) 144 pregnancies were included. Before (t<6 months), during, and after pregnancy (≥6 months) the median SELENA-SLEDAI score was 2 and mild/moderate flare rates were 6.3%, 18.8% and 13.9% respectively. Three patients developed a severe flare during pregnancy, 2 patients at postpartum, but they were aPL negative. Severe maternal complications (preeclampsia, eclampsia or HELLP-syndrome) occurred in 16.2% of aPL negative, 21.4% of aPL positive SLE patients, and in 39.8% of SLE patients with antiphospholipid syndrome (APS) (GEE; no significant differences between groups). HELLP-syndrome occurred in 21.3% of SLE patients with APS and in 31% of SLE patients without APS (Chi-Square; p<0.01). The perinatal complications included intrauterine fetal death, preterm birth, small-for-gestational age and neonatal lupus occurred in 41%, 37.4%, 14.8%, 1.4% respectively (GEE; no significant differences between groups). Maternal and perinatal complication rates were similar in first (18.5% and 41.4%) and consecutive (17.6% and 35.1%) pregnancies (Chi-Square; p=0.88 and p=0.44). Of all patients, 42.7% developed a complication during all of their pregnancies (obstetrical history included).

Conclusions: This is the first study to report increased type I IFN activation in pregnancy females with a CHB complication. Also, we show here that IFN-α directed therapy, e.g. with hydroxychloroquine, may be especially beneficial in these females.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2618

FRIDAY, 16 JUNE 2017

Neuronal and hormonal alterations in arthritis

A PROTEOMIC SIGNATURE OF FATIGUE IN PRIMARY SJÖGREN’S SYNDROME


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Background: Fatigue is a frequent and often disabling phenomenon in patients with chronic inflammatory and immunological diseases, neurodegenerative diseases, and cancer. The underlying biological mechanisms of fatigue are largely unknown and hypotheses are conflicting. It is important to uncover the pathophysiology and identify signalling pathways that generate and regulate this substantial phenomenon.

Objectives: Based on the hypothesis that fatigue originates from cerebral processes, we investigated whether relevant proteins and/or signaling pathways for fatigue could be revealed in the cerebrospinal fluid (CSF) of patients with primary Sjögren’s syndrome.

Methods: Label-free shotgun mass spectrometry was performed to analyze the CSF proteome of 20 patients with primary Sjögren’s syndrome. Fatigue was measured with the fatigue Visual Analogue Scale (VAS).

Results: After depletion of high-abundance proteins, more than 800 proteins were identified and quantitated. Multivariate analyses showed that patients with low and high fatigue could be separated based on their CSF protein and metabolite levels, and 15 proteins were selected as top discriminatory proteins. Among these were apolipoprotein A4, hemopexin, pigment epithelium derived factor, secretogranin-1, secretogranin-3, selenium-binding protein 1, and complement factor B. The figure shows the top network from Ingenuity Pathway Analysis (IPA) with 14 of

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2831
Conclusions: Most of the discriminatory proteins have important roles in regulation of innate immunity, cellular stress defense, and/or functions in the central nervous system. Some have been associated with severe depression and loss of appetite, which are important features of chronic fatigue. These proteins and their interacting protein networks may therefore have central roles in the generation and regulation of fatigue, and the findings add new, relevant, and important evidence to the concept of fatigue as a biological phenomenon signaled through specific molecular pathways.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3973

FRIDays, 16 JUNE 2017

Fighting osteoporosis fragilities

OP0314-HPR A HOME-BASED FALL PREVENTION PROGRAMME REDUCES FEAR OF FALLING IN SENIORS
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Background: Every year, over 80,000 elderly persons in Switzerland have accidents caused by tripping and falling, and half of these falls happen at home or in the direct vicinity (1). Falls, due to its often severe medical consequences and persistent mobility impairments, together with the demographic development, are one of the most important musculo-skeletal problems and public health issues. Falls are often due to a combination of internal risk factors (such as vertigo, osteoporosis, cognitive impairments, decreased ability for dual tasking) and external risk factors (such as medication and environmental risk factors) (2). The Swiss League Against Rheumatismus (SLAR) has developed a multidimensional home-based fall prevention programme, which is supported by health insurances. Trained physiotherapists (PTs) and occupational therapists (OTs) visit the seniors at home in order to perform a detailed assessment of the senior’s individual risk of falling. Subsequently the PT or OT eliminates identified environmental risk factors and provide tailored exercises. After 4 weeks, a telephone call was made by the PT/OT to discuss unclear instructions and after 16 weeks, follow up data were collected by telephone.

Objectives: The objective was to evaluate the effects of the fall prevention programme.

Methods: A retrospective analysis was carried out on the data of 671 participants in 2015. Available data were participant’s characteristics, fall risk factors, determined by the Timed “Up&Go” with additional motor and cognitive task) (4), Fall Efficacy Scale (5), the recommendations made by the PTs/OTs and satisfaction of the seniors.

Results: The participants were mainly female (62.6%) and had a mean age of 81.7 years (SD=5.5, range 66.1–100 years). Several risk factors were present: 64.1% fell at least once in the last year and 45% were not able to perform a dual task (TUG + additional cognitive task). Main recommendations made by PTs/OTs were “fixing down of carpets” (56.8%) and instruction of an exercise programme (strength, balance and multi-task capability) (82.6%). After four months, fear of falling had decreased (change in FES-I: -1.24 points 95% CI: (-1.44, -1.04), p-value<0.001). 92% of the participants self-reported to follow the recommendations and 98.4% were satisfied with the programme and would recommend it to others.

Conclusions: The low-threshold, multidimensional home-based fall prevention developed by the SLAR was feasible and effective. Participants implemented the recommendations and the fear of falling’ decreased. Reduced fear of falling is considered a strong predictor of falling, however a prospective study is needed to determine if the reduced fear of falling leads to a decreased number of falls.

References:

Disclosure of Interest: None declared
**FRI, 16 JUNE 2017**

**Biological agents in juvenile idiopathic arthritis: open issues**

**OP0315 REASONS FOR DISCONTINUATION OF BIOLOGICAL AGENTS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE PORTUGUESE REGISTER, REUMA.PT**

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**Objectives:**


**Results:**

Of the 1724 JIA patients registered in Reuma.pt, 319 received biological treatment initiation and discontinuation of the first bDMARD. The mean time until discontinuation was calculated using Cox regression survival estimates and the reasons for discontinuation of the first bDMARD were registered.

**Results:**

Of the 1724 JIA patients registered in Reuma.pt, 319 received biological treatment initiation and discontinuation of the first bDMARD. The mean time until discontinuation was calculated using Cox regression survival estimates and the reasons for discontinuation of the first bDMARD were registered. The mean time of clinical remission after withdrawal of BAs was 6 months. The mean age at the beginning of biological therapy was 15.8±9.4 years. The distribution of JIA subtypes was: 19.1% polyarticular RF-negative, 17.2% enthesis-related arthritis, 16.6% polyarticular RF-positive, 16% extended oligoarticular, 13.5% persistent oligoarticular, 12% systemic JIA and 0.9% had undifferentiated arthritis. Considering the whole group, 53.2% had extra-articular manifestations and 18.4% have or had had uveitis since the beginning of the disease. Persistence of treatment, biological therapy and JIA subtype, age at the beginning of biological therapy, and disease duration until initiating first bDMARD. The major reasons for drug discontinuation was inefficacy (49.6%), remission (14.2%), adverse events (10.6%), patient decision (1.6%) and pregnancy planning (4.1%).

**Conclusions:**

Almost half of the JIA patients stop the first biological agent, due to lack of response, reinforcing the need for the existence of several treatment options fully studied in JIA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5756

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**Friday, 16 June 2017**

**Health equity and economy - a vital relationship**

**OP0317-PARE**

**AN INDEPENDENT REVIEW OF PEOPLE WITH RHEUMATOID ARTHRITIS (RA) AND THEIR CAREGIVER’S LOST WORK TIME**

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**Background:**

The National Rheumatoid Arthritis Society (NRAS) is the only patient-led charity in the UK focussing specifically on rheumatoid arthritis (RA) with the responsibility of raising awareness of RA and its impact. RA is a long term condition which impacts on all aspects of life for sufferers and their loved ones. There is a lack of information about the costs and impact of RA on work in the European community; in particular the wider societal costs such as people with RA not being able to perform their job to their best ability, losing days of work due to their RA condition, and the wider societal costs associated with caregiver employment.

**Objectives:**

To quantify the burden of RA not only on the healthcare system, but also the wider societal costs associated with RA.

**Methods:**

In 2016 NRAS undertook a partnership with the University of Chester’s commercial economics partner HCD Economics who conducted the multinational Burden of Rheumatoid Arthritis: Socioeconomic Survey (BRASS). The study used a bottom-up approach to quantify the burden of disease for people living with RA across 10 European countries including France, Germany, Italy, Spain, Denmark, Sweden, Hungary, Poland, Romania and the UK. The study collected information from employed and physically active persons aged 18 and over who had a Rheumatoid Arthritis diagnosis and their family/friend caregivers. It collected information on the resource use and cost of patient care including treatment costs, hospitalisation, tests, and examinations. The wider societal costs included; cost of travel to appointments, requirements for aids/equipment, informal care (non-professional), ability in employment, early retirement due to RA. Work time missed, work and activity impairment were measured using the Work Productivity and Activity Impairment (WPAI) questionnaire.

**Results:**

Voluntary data were collected from 1782 patient forms, of which the average age was 55 years, 1274 (71%) were female and 832 (48%) were currently in work. This study found, on average, persons with RA lose one day of every 4 working days due to not being able to perform their job to their best ability, and completely miss 7% of work time over a 7 day period due to their RA (sample n of 646). In addition to not being able to perform their job to their best ability, almost a third of working persons with RA also had impairment in daily living activities such as shopping and work around the house (sample n of 735). This study also found family/friends have to care for 16% of RA sufferers. This care resulted in reduced employment or inability to work for 25% of family/friend caregivers (sample n of 121).
Conclusions: This study highlights the impact RA has on working life amongst both those with the condition and those providing support. It is hoped these metrics will allow the conversation to open and develop with employers and government on how adapting the workplace can increase productivity. Further research should also be undertaken on the economic impact both to the individuals, their carers and society.

Acknowledgements: The BRASS study was supported by unrestricted research grants from Eli Lilly and Pfizer. The study was approved by the University of Chester Ethics Committee.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5948

CONSULTING SERVICES TO EMPLOYERS OF PEOPLE WITH RMDs

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Background: The Eurobarometer 1 states that RMDs affect 22% of the general population which means that 10 million people are affected in Spain and more than 600,000 people in the autonomous region of Galicia where our organization, LRG, works. Knowing that 50% of people with RMDs are currently unemployed because of their condition, only part of them have the legal work incapacity recognized and receive a pension. This means that RMDs not only affect the health but also the socio-economic status. Most of this people could stay at work and are willing to do so if some arrangements are made like cutting down hours, work place adaptations, flexible schedules, etc. Most employers are lacking information on how these conditions affect the employee’s ability, desire and need to work and how to make the necessary adaptations for not loosing this person from the work force.

Objectives: Making the employer more aware of the positive aspects of keeping all the employees including people with RMDs not just at the work place but at full capacity, avoiding both absenteeism and presenteeism.

Methods: The employee with RMD has 1 session with the psychologist and 1 session with the occupational therapist (OT) to identify the difficulties in continuing to be active into their work place.

Results: The employee HP provided personalized advice to the employer about the RMDs, the needs of the employee and how to facilitate them to stay at work and minimize the work incapacity due to their chronic condition. This kind of advise is given by the OT who has treated the employees and knows all about their needs, to go their work place to see what are the actual conditions, identifies manageable obstacles and talks to the employers during a pre-scheduled meeting. After, an architect specialized in accessibility offers specific architectural and ergonomic solutions for adapting the work place. Also peer support is provided by LRG in group meetings and activities of the organization.

Conclusion: The results of this project are shown in the increase of the employees’ self-confidence in their capacity to stay at work and also they are more aware of their solvable and non solvable limitations. During 2016 we advised 14 associates of LRG, 5 of those 14 employees (1/3) stayed at work or returned to work after the consultancy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5948

FRIDAY, 16 JUNE 2017

Biomarkers in cardiovascular rheumatology - state-of-the-art 2017

OP0319

HIGH SENSITIVITY CARDIAC TROPONIN T IS A BIOMARKER FOR Atherosclerosis IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A CROSS-SECTIONAL CONTROLLED STUDY

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Background: Cardiovascular disease (CVD) is the main cause of death in systemic lupus erythematosus (SLE) patients. Framingham score underestimates the risk for CVD in this population.

Objectives: Our study aimed to determine whether serum High Sensitivity Cardiac Troponin T (HS-cTnT) helps to identify SLE patients at risk for CVD.

Methods: Presence of carotid plaques was prospectively assessed by ultrasound in 63 consecutive SLE patients asymptomatic for CVD and 18 controls. Serum HS-cTnT concentration was measured using the electrochemiluminescence method. Factors associated with carotid plaques were identified and multivariate analysis was performed.

Results: Framingham score was low in both SLE patients (2.13±3.8%) and controls (2.12±3.9%). Nevertheless, 23 (36.5%) SLE patients, but only 2 (11.1%) controls (p=0.039) had carotid plaques detected by vascular ultrasound. In the multivariate analysis, only age (p=0.006) and SLE status (p=0.017) were independently associated with carotid plaques. Serum HS-cTnT concentration was detectable (i.e. ≥ 3 ng/L) in 37 (58.7%) SLE patients and 6 (33.3%) controls (p=0.057). Interestingly, 87% of SLE patients with carotid plaques, but only 42.5% in SLE patients without plaques (p<0.001), had a detectable HS-cTnT. Conversely, 54.5% SLE patients with a detectable HS-cTnT, but only 11.5% with an undetectable HS-cTnT (p<0.001), had a carotid plaque. In the multivariate analysis, only BMI (p=0.006) and HS-cTnT (p=0.033) were statistically associated with carotid plaques in SLE patients. Overall, the risk of having a carotid plaque was increased by 8 (95% CI): 8.03 [1.41–74.73] in SLE patients in whom HS-cTnT was detectable in serum.

Conclusions: Detectable HS-cTnT concentration is independently associated with subclinical atherosclerosis in asymptomatic SLE patients at apparent low risk for CVD according to traditional risk factors. These results raise the possibility that this easily obtained biomarker is useful for more rigorous risk stratification and primary prevention of CVD in SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1015

FRIDAY, 16 JUNE 2017

What is behind vasculitis?

OP0320

DETERMINANTS OF RITUXIMAB PHARMACOKINETICS AND CLINICAL OUTCOMES IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Response to rituximab (RTX) is variable in patients with ANCA-associated vasculitis (AAV), and predictors of treatment efficacy/relapse risk would be useful. Previous studies have shown that RTX pharmacokinetics (PK) is associated with treatment efficacy in patients with lymphoma.

Objectives: To study the determinants of RTX PK in patients treated for AAV and its association with clinical outcomes.

Methods: This study included 88 patients from the RTX in ANCA-Associated Vasculitis (RAVE) trial who received the full dose of RTX (4 weekly 375 mg/m2 infusions) and had available serum samples. RTX was quantified using two state-of-the-art 2017 biomarkers in cardiovascular rheumatology - state-of-the-art 2017.

Responses: None declared

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6342
RISK OF CORONARY ARTERY DISEASE AND ISCHEMIC STROKE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: A FRENCH POPULATION-BASED STUDY

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Background: ANCA-associated vasculitides (AAVs), including granulomatosis with polyangiitis and microscopic polyangiitis, are small vessel vasculitides. Modern treatments have greatly improved survival in AAV patients, but significant long-term morbidity and mortality such as cardiovascular disease (CVD) are still associated with this disease.

Objectives: The aim of our study was to assess the incidence, mortality and clinical outcomes. Serum rituximab level monitoring does not seem clinically useful in this context.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3527

Cytokine taxonomy: reflection in the therapy of arthropathies and other IMIDs

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Background: Adult-onset Still’s disease (AOSD) and Behcêt’s disease (BD) are both systemic inflammatory diseases, the causes of which are largely unknown. They have been recently classified as autoimmune diseases, a group of diseases in which innate rather than acquired immunity plays important roles in their pathogenesis. As AOSD and BD are clinically distinct diseases, their cytokine networks should also be different.

Objectives: In this study, we attempted to quantify the levels of multiple cytokines in the serum of patients by using a beads-array technique and ELISA, and then compared the serum cytokine profiles of the two diseases by factor analysis. We then sought to clarify the hierarchical relationship between interleukin (IL)-17A and interferon (IFN)-α using peripheral blood mononuclear cells (PBMCs).

Methods: We quantified the serum levels of 10 cytokines (IFN-α, IFN-γ, IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17A and tumor necrosis factor α) in 16 AOSD patients and 28 BD patients using multiplex bead array assays and IL-18 along with ELISA. The data were then subjected to factor analysis. We next stimulated PBMCs from three healthy volunteers in vitro with class A CpG oligodeoxynucleotides (ODNs) in the presence or absence of IL-17A for 15 hours. We performed flowcytometric analysis to examine the expression of intracellular IFN-α in plasmacytoid dendritic cells (pDCs).

Results: Two factors were extracted from the factor analysis using the data on 8 cytokines that were detectable in the serum of the patients. IL-17A and IFN-α, the levels of which showed a strong positive correlation in the serum of BD patients (Fig. A), were the main components of Factor 1, while Factor 2 consisted of IL-6, IL-10 and IL-18 (Fig. B). Patients were also plotted on a plane determined by Factors 1 and 2 according to each patient’s factor scores. Those who were high in Factor 1 but low in Factor 2 were likely to be BD patients and vice versa, many of those who were high in Factor 2 but low in Factor 1 were AOSD patients. In terms of flowcytometric analysis, IL-17A alone did not induce IFN-α expression in pDCs, but it did substantially increase IFN-α–positive pDCs induced by CpG ODNs.

Conclusions: The cytokines examined were clearly separated into distinct groups by the factor analysis. Similarly, the AOSD and BD patients could be separated, although roughly. High levels of serum IL-6, 10 and 18 suggest AOSD while high levels of IFN-α and IL-17A indicate BD. To establish patterns of correlation among cytokines, it is important to focus on the cytokine concentrations in each patient, rather than the average cytokine concentrations in each of the diseases. In terms of the hierarchical relationship between IFN-α and IL-17A, a previous report suggested that IFN-α blocks IL-17A production in PBMCs from BD patients. Thus, we examined the effect of IL-17A on IFN-α production. It should be noted that the real stimulus for IFN-α release in BD is unknown. In addition, cells other than pDCs may be involved in the production of IFN-α. Nevertheless, understanding the hierarchical relationship among cytokines should prove to be helpful in clarifying the pathogenesis of various inflammatory diseases.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1678

DISCOPATHY ASSOCIATED WITH MODIC CHANGES IS NOT RELATED TO ANY INFECTIOUS PROCESS: A PROSPECTIVE MONOCENTRIC STUDY

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Background: Low back pain (LBP) is strongly associated with Modic changes. The...
hypothesis of local infectious origin was raised, especially with Proprionibacterium species. PCR PAs with a single weakly positive sample reinforce the hypothesis of local infectious origin, but are insufficient for a definite diagnostic conclusion. When patients underwent lumbar spine surgery by an anterior approach, 2 samples of the disc were collected for bacteriological analysis: one sample from the anterior part of the disc distant from epidural space and one sample from the posterior part of the disc. 77 discs samples were obtained, 32 discs samples in Modic 1 or 2 changes by anterior approach, 26 discs samples in no Modic IVD by anterior approach, 19 disc samples obtained by anterior approach to that obtained by posterior approach in herniated disc cases.

Methods: 45 patients with chronic LBP or sciatica were included in the study, representing 48 IVD. When patients underwent lumbar spine surgery by an anterior approach, 2 samples of the disc were collected for bacteriological analysis: one sample from the anterior part of the disc distant from epidural space and one sample from the posterior part of the disc. 77 discs samples were obtained, 32 discs samples in Modic 1 or 2 changes by anterior approach, 26 discs samples in no Modic IVD by anterior approach, 19 disc samples obtained by posterior approach. The method to collect disc material was strictly aseptic. Samples were analysed by conventional microbial cultures with specialised enrichment, molecular detection by universal rRNA gene PCR plus sequencing assay. Additionally, all clinical specimens were specifically tested for PA detection using a highly sensitive specific PCR assay. The possibility of contamination with saprophytic germs coming from the skin during surgery by posterior approach or by epidural infiltration preceding the surgery was also discussed, but not proved.

Objectives: The main objective of this study was to evaluate the prevalence of saprophytic germs in the intervertebral disc (IVD) obtained during a lumbar spine surgery by anterior approach in Modic 1 and 2 changes. A secondary objective was to compare the prevalence of SGB in IVD in lumbar spine surgery obtained by anterior approach to that obtained by posterior approach in herniated disc cases.

Results: Regarding bacterial cultures, 12 out 77 disc samples were positive (16%), including 10 (13%) for PA. The PA specific PCR was positive for one (1%) sample collected by posterior approach. The 16S rRNA detection was positive for 6 specimen (8%), including one for PA (1%). Modic 1–2: Cultures were positive in 5 cases (16%) with 3 for PA (10%). No specific PA PCR was positive. Only one sample was positive for PA in both culture and 16S PCR. Comparison between anterior and posterior approach: Among the PA positive cultures, 5 were identified from anterior specimens (8.62%) and 5 from posterior specimens (26.32%). Regarding PA cultures, the posterior fragments were more frequently positive than the anterior fragments (p=0.046). The number of epidural infiltrations of the lumbar spine does not seem to influence the bacterial contamination prevalence (p=0.746). The time between the epidural infiltration of the lumbar spine and the surgery does not seem to influence the bacterial contamination prevalence (more or less 6 month) (p=0.23).

Conclusions: SGB has been identified in culture in 16% of the samples obtained in Modic 1 and 2 changes. The prevalence of PA in culture was significantly higher in samples of IVD collected by a posterior approach compared to anterior approach in spine surgery suggesting a contamination. The results of the specific PCR PAs with a single weakly positive sample reinforce the hypothesis of contamination.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4447

OP0325 TGF-BETA-INDUCED ED-A FIBROBLAST LIKE SYNOVIAL CELLS CONTRIBUTES TO INFLAMMATION IN OSTEOARTHRITIS

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Background: The pathophysiology of osteoarthritis (OA) involves wear and tear, and a state of low-grade inflammation. Wear and tear leads to tissue degradation followed by tissue repair responses including TGF-β-induced myofibroblast production of extracellular matrix (ECM). Fibroblasts are an essential part of the ECM, and injection of fibronectin fragments into rabbit joints is an established animal model of OA. Recently, alternatively spliced fibroblast containing the ED-A domain (ED-A FN) has been shown to activate Toll-like receptor 4.

Objectives: In this study, we hypothesize that FN fragments containing the ED-A domain could be one mechanism transducing mechanical events into inflammatory signals in OA.

Methods: Samples of synovial membrane and cartilage were obtained from patients with knee OA undergoing joint replacement surgery. Immunostaining was performed on synovial membranes. Fibroblast-like synovial cells (FLS) isolated from OA synovium (b-20) were cultured in vitro. OA FLS were stimulated with recombinant ED-A FN, plasmid, cellular FN, or plasmid digested with plasmid digestion of cellular FN. Synovial cells isolated by enzymatic digestion and human monocyte-derived macrophages (MDM) were incubated with recombinant ED-A FN, plasmid, cellular FN, or plasmid digested with plasmid and culture supernatants were analyzed for TNF-α and IL-6 using enzyme-linked immunosorbent assay (ELISA)

Results: We hypothesized that ED-A FN is produced by OA FLS in response to products reflecting tear and wear in OA. Indeed, the production of ED-A FN by OA FLS is increased by TGF-β, OA synovial fluid, and lysed chondrocytes in all experiments (n=3, see figure). ED-A FN co-localized with the myofibroblast marker α-SMA in both the OA FLS (n=3) and in the OA synovial membranes (n=8). We further hypothesized that ED-A FN expression is associated with inflammation in OA. ED-A FN staining was associated with both number of lining layer cells (rho=0.85 and p=0.011) and infiltrating sublining cells (rho=0.88 and p=0.007) in the OA synovium (n=8), and co-localized with both MCP-1 and TNF-α (n=4). Recombinant ED-A FN increased the production of both MCP-1 and TNF-α by MDM (n=3) and OA FLS (n=3). Finally, we demonstrated that the FN fragments containing the ED-A domain generated the same production of both MCP-1 and TNF-α as recombinant ED-A FN.

Conclusions: The disease process in OA shares features with the chronic
wound healing response including myofibroblast differentiation and that humeral mediators found in the joint can promote myofibroblast production of ED-A FN. We additionally show that recombinant and plasmid-derived ED-A fragments can induce generation of pro-inflammatory mediators from FLS and MDM. This study supports targeting the formation of ED-A FN or the enzymatic fragmentation of PAI-1 as a novel therapeutic approach for pro-inflammatory responses in OA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2239

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**EPIGENETICALLY-DRIVEN DISTAL EXPRESSION OF THE LNCRNA HOTTIP SHAPES INFLAMMATORY, ADHESIVE AND PROLIFERATIVE CHARACTERISTICS OF HAND SYNOVIAL FIBROBLASTS IN ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) and other types of inflammatory arthritis show a characteristic pattern of joint involvement. E.g. in RA there is a predilection for the small joints of hands and feet, whereas in spondyloarthopathy, single large joints are predominantly affected. Interestingly, in RA, some joints have robust expression of certain fibroblast subtypes (SF), which drive joint destruction in RA, display location-specific transcription patterns and functions, shaping unique micromvernions in different joints.

**Objectives:** To analyze the role of transcripts expressed in SF at specific joint locations in defining location-specific functions of SF, relevant to the pathogenesis of RA.

**Methods:** SF were isolated from hand, elbow, shoulder, feet and hips of RA and OA patients undergoing joint replacement surgery and from knees of nonarthritic subjects with arthralgia. Transcriptomes and epigenomes of SF were determined by RNA-seq (Illumina HiSeq 2000, n=21), qPCR, Chip-seq (H3K4me3, H3K27me3, H3K27ac, Illumina HiSeq 2500, n=7) and Infinium HumanMethylation450 BeadChip (n=12). Proliferative, adhesive and chemotactic properties of SF were studied by xCELLigence real time cell analysis and leukocyte chemotaxis towards supernatants of SF. The IncRNA HOTTIP was silenced in hand SF using LNA GapmeR oligos, followed by RNA-seq (n=2), pathway enrichment analysis (MetaCore, Thomson Reuters, FDR<0.05) and qPCR (n=5).

**Results:** HOTTIP was the most differentially expressed transcript in distal (hand) vs. proximal (shoulder) SF. HOTTIP was specifically transcribed in SF from hand and feet SF, but absent from other joints, indicating distal-specific function to this IncRNA. Hand-specific HOTTIP expression coincided with the enrichment of activating histone marks H3K4me3 and H3K27ac, absence of repressive H3K27me3 and decreased DNA methylation at the HOTTIP promoter in hand SF. In contrast, the HOTTIP promoter displayed abundant DNA methylation and H3K27me3 in knee and shoulder SF. Silencing of HOTTIP led to downregulation of 3275 genes and upregulation of 4326 genes (log ratio >0.5; p<0.01, FDR<0.05). Distal-specific homeobox A13, a known HOTTIP target, was repressed in HOTTIP-silenced SF. Pathway enrichment analysis of genes repressed by HOTTIP silencing showed enrichment for pathways regulating cell adhesion, cell cycle, angiogenesis and inflammation, including NF-κB activation and IL-6 signalling. Meanwhile, upregulated genes were enriched in fewer pathways, e.g. IL17 and Notch signalling. 110 genes that were differentially expressed in hand vs. shoulder SF were also altered by HOTTIP silencing, e.g. TNFRSF1B and MAP3K14. Hand SF showed enhanced proliferative and chemotactic, but decreased adhesive properties compared to shoulder SF.

**Conclusions:** The IncRNA HOTTIP, which is exclusively expressed in small, distal joints, via epigenetic mechanisms, is a regulator of inflammatory, proliferative and adhesive properties of SF. Such a functional specialization of arthritis relevant pathways in SF might represent an imprinted site-specific “risk” signature in SF, predisposing thereby to location-specific joint pathology, e.g. enhanced severity of hand arthritis in RA.

**Disclosure of Interest:** M. Frank Bertonecelli Grant/research support from: euroTEAM, BT Cure, IAR, PROMEDICA, Georg und Berta Schwyzer Winiker Foundation Trust, University of Manchester; 2Manchester Academic Health Science Centre; 3Public Contributor; 4Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, University of Manchester; 5NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, University of Manchester; 6Barbara Ansell National Network for Adolescent Rheumatology; 7Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom

**None declared, S. Gay Grant/research support from: euroTEAM, BTCure, GSK, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Foundation Trust, University of Manchester; 2Manchester Academic Health Science Centre; 3Public Contributor; 4Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, University of Manchester; 5NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, University of Manchester; 6Barbara Ansell National Network for Adolescent Rheumatology; 7Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom

**References:**


**Acknowledgements:** This abstract presents independent work funded by Arthritis Research UK BANNAR grant 2016/4 via the Centre for Adolescent Rheumatology at UCL. Supported by the National Institute for Health Research Biomedical Research Unit.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5807

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**Patient engagement in research: best practices, benefits and challenges**

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**Background:** Between 2014 and 2016, the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR) commissioned research to explore young people’s rheumatology research priorities and beliefs about research involvement. The next phase of this work has been to establish a UK-wide research advisory group, YourRheum, to involve 11–24 year olds with rheumatic and musculoskeletal diseases (RMsDs) more effectively in shaping research.

**Objectives:** To describe our experiences of developing a UK-wide research advisory group, for young people with RMsDs, using both face-to-face meetings and online involvement applications.

**Methods:** From September 2016, we recruited young people to the group using several approaches: including the previous research study database, through BANNAR members, through UK charities, as well as through social media. To tailor options for involvement, young people were recruited to contribute to both face-to-face meetings and online channels.

**Results:** Eight young people attended YourRheum’s first meeting in October 2016, where they discussed how they would like the group to work. Thirteen young people have been engaged online via a closed Facebook group, monitored by the Your Rheum facilitator. Key challenges in establishing the group have included developing age-appropriate communication approaches to appeal to the range of ages involved, devising ways of ensuring online members remain engaged with the group, and finding appropriate tasks for the group to be involved with, that are both suitable and aligned with research project timelines. This involves working closely with young people, health professionals and researchers.

**Conclusions:** There is both a need for young people’s involvement in research and a desire from young people themselves to do so. Expansion of the online network and involvement activities will allow young people across the UK to have a valuable input into research, regardless of location.

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**Patient safety in relation to biosimilars – how can we act as a patient organization?**

L.M. Thomsen, Danish Rheumatism Association, Gentofte, Denmark

**Background:** During the last two years two biosimilars has been approved by the national authorities in Denmark, and implemented in the treatment of patients with arthritis. When the first biosimilars were approved in 2015, the hospitals in Denmark decided to shift native patients from the original drug to the new biosimilar. This decision caused considerable insecurity among the patients, who were afraid of biosimilars and their effectiveness and safety profile. Therefore the Danish Rheumatism Association decided to implement an effort to create better patient information and safety for patients, who had to start with a biological drug or shift from one biological drug to another or to a biosimilar.

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**Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of biosimilars in RMDs**

FRIDAY, 16 JUNE 2017

**Patient safety in relation to biosimilars – how can we act as a patient organization?**

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Objective: The purpose of the effort was to increase patient safety and to ensure that patients received independent patient information within biological drugs.

Methods: First the Association conducted a small study of how the shift of drug had taken place in the different regions. Most patients experienced that they were told by the doctors to shift to biosimilars, and furthermore they experienced a lack of information about the new biosimilars. On a national level, nearly all patients on a biological drug are registered in a national database. It is registered in the database and hospital records which drug the patient are prescribed, but it is not registered on a batch-level.

In order to change these conditions the Association started a dialog with the politicians and the authorities on a national level and the hospital-administrations on a regional level. The purpose was to improve the registration of the drugs on batch-level, to improve more independent patient information and to improve the involvement of the patient in the decision making process. The dialog was on a general level, but with several patient-stories from each region.

Results: A new national plan for better monitoring and information about biologic and biosimilars was launched in August 2015 and carried out in 2016. The plan consists of four parts: 1) Monitoring biological drugs and biosimilars on batch level, 2) Information campaign to health professionals and patients, 3) Digital solutions and easy reporting of side effects from health professionals and patients, 4) Focus on monitoring patient safety by the authorities. The Danish Rheumatism Association has participated in the work to implement the plan. In addition to the national plan the hospitals on a regional level, has invited the Rheumatism Association to participate in a representative in the working group, where national recommendations for the use of biological drugs are being made in an attempt to involve the patient perspective more. The content of the national plan and the involvement in the work with national recommendations, will be elaborated and discussed from the patients perspective throughout the presentation.

Conclusions: The implementation of biosimilars created great insecurity among patients. Therefore, the Danish Rheumatism Ass. decided to make an effort to create better patient information and safety for the patients. Through dialog with politicians, national authorities and hospital-administrations, we managed to get a national plan for better monitoring and information about biologic and biosimilars, and to be involved in the work with national recommendations for these drugs. The national plan and work with national recommendations will be elaborated in the presentation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3716

FRIDAY, 16 JUNE 2017
Switching T on and off: how T cells drive and regulate chronic inflammation

OP0329 INVOLVEMENT OF T HELPER 17 CELLS IN INFLAMMATORY ARTHRITIS DEPENDS ON THE HOST INTESTINAL MICROBIOTA

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Background: Intestinal microbiota have been associated with psoriatic and rheumatoid arthritis. One of the major effects of microbiota is the induction of mucosal T helper 17 (Th17) cells. We therefore reasoned that the efficacy of Th17-targeted therapies in arthritis may depend on the host microbiota. Previous studies focused on the role of the cytokine regu-larin-17A (IL-17A) - deficient Th17 cells by using IL-17 inhibitors or IL-17-deficient mice. Therefore, the role of Th17 cells, which produce multiple pro-inflammatory mediators in addition to IL-17, is not yet fully understood.

Objectives: The aim of this study was to determine the role of Th17 cells, beyond the cytokine IL-17, in arthritis, and to investigate whether Th17 cells are differentially involved in arthritis depending on the microbiota present.

Methods: We established conditional Th17-deficient mice, which exhibit a CD4-Cre-induced floxing of a part of the Rorc allele that encodes the Th17 master regulator RORC. We then established conditional Th17-deficient mice, by using IL-17 inhibitors or IL-17-deficient mice, to investigate whether Th17 cells are differentially involved in arthritis depending on the microbiota present. We used previously generated Fra2 tg overexpressing mice. T lymphocyte populations were analyzed by flow cytometry for expression of activation markers and secretion of cytokines. We transferred purified CD4+ T cells into Rag2-/- mice lacking T and B cells, and we generated Rag2-/-Fra2 tg mice. Bone marrow cells were transferred into lethally irradiated recipients to create Fra2-wT bone marrow chimeric mice.

Results: Fra2 tg mice backcrossed onto a Rag2- background did not develop inflammatory manifestations (n=6), demonstrating the dependence on T and/or B cells of the autoimmune phenotype. In line with this, the transfer of purified CD4+ cells from 16-week-old Fra2 tg mice into Rag2- recipients was sufficient to transfer the disease phenotype (n=3). Analysis of T cell populations from Fra2 tg mice showed the presence of activated CD4+ and CD8+ cells in the spleen.
A NOVEL HUMANIZED EFFECTOR-DEFICIENT FCYRIIA 1,1,2,2, N. Panousis3, I. Gergianaki 1,2, M. Tektonidou4, M. Trachana5, We have generated MEDI9600, a specific humanized antibody protein that potently blocks both autoantibody and immune complex mediated proinflammatory responses from a variety of cell types. This includes the inhibition of Toll-like receptor stimulatory immune complexes that induce type I interferons from pDC, and the inhibition of anti-neutrophil cytoplasmic antibody (ANCA) induced production of reactive oxygen species from neutrophils, which are associated with the pathogenesis of systemic lupus and ANCA vasculitis respectively. MEDI9600 specifically binds FcγRIIA, and its suppressive activity is attributed to its capacity to block ligand engagement and to internalize the receptor from the cell surface. Moreover, in vivo studies indicate that MEDI9600 has a favorable pharmacokinetic and safety profile. Conclusions: We have generated MEDI9600, a specific humanized antibody antagonist of FcγRIIA with null effector function that may provide a novel therapeutic approach in the treatment of immune complex mediated diseases. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.19944 SATURDAY, 17 JUNE 2017 Genomic imprinting and post-translational modifications OP0332 THE GENOMIC ARCHITECTURE OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) BY RNA-SEQ: DISTINCT DISEASE SUSCEPTIBILITY, ACTIVITY AND EXTENIVE GENETIC EFFECTS ON WHOLE BLOOD GENE EXPRESSION G. Bertias1,1,2,2, N. Panousis3, I. Gergianaki1,2, M. Tektonidou4, M. Trachana5, C. Pamfil6, A. Fanourakis7, E. Dermitzakis8, D. Boumpas2,7,8,9,10. 1Rheumatology, Clinical Immunology and Allergy, University of Crete School of Medicine, 2Laboratory of Autoimmunity and Inflammation, Institute of Molecular Biology-Biotechnology, FORTH, Iraklio, Greece, 3Institute for Genetics and Genomics in Geneva, University of Geneva Medical School, Geneva, Switzerland, 4Medical School, National and Kapodistrian University of Athens, Athens; 51st Department of Pediatrics, Aristotle University, Thessaloniki, Greece; 6Iuliu Hatieganu University of Medicine and Pharmacy, Cluj, Romania; 714th Department of Medicine, 8Joint Rheumatology Program, Attkon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece; 9Medical School, University of Cyprus, Nicosia, Cyprus; 10Laboratory of Autoimmunity and Inflammation, Biomedical Research Foundation of the Academy of Athens, Athens, Greece.

Background: SLE displays significant immunological and clinical heterogeneity. Understanding the molecular basis of this variability may facilitate early diagnosis, risk stratification and personalized therapy.

Objectives: To perform full transcriptome analysis in SLE patients in order to identify molecular sub-phenotypes and explore the genomic basis for the disease susceptibility and severity.

Methods: Whole blood mRNA and genomic DNA were extracted from 142 SLE patients with varying levels of disease activity/severity and 48 matched healthy volunteers. Paired-end RNA sequencing was performed using the Illumina HiSeq 2000 platform and genotyping with the Infinium CoreExome followed by imputation from the 1000 Genomes. To integrate blood transcriptome with genotype data we used the enrichment analysis of expression-quantitative trait loci (eQTLs). The CIBERSORT tool was used to provide an estimation of the abundances of different circulating immune cell types.

Results: We found a large number (6730, 5% False Detection Rate [FDR]) of differentially expressed genes (DEGs) between SLE patients and controls. Interferon signaling was significantly upregulated in SLE with most of the DEGs (146 out of 281) being regulated by both type I and type II interferon. Analysis of the blood composition in different immune cell types revealed global upregulation of type I interferon and antiviral response genes as well as immune cell-specific alterations in gene expression in SLE patients. Comparison of the transcriptome in active/inactive SLE and healthy individuals identified distinct disease susceptibility and ‘disease activity’ gene signatures encompassing 2738 and 377 DEGs, respectively. Analysis according to individual organ involvement revealed more widespread aberrancies in gene expression in SLE patients with active nephritis as compared to activity from other organs, corresponding to oxidative phosphorylation, granulocyte activation and antimicrobial humoral response pathways. By integration of genotyping data, we mapped a total 3142 (5% FDR) cis-eQTLs in SLE patients suggesting extensive genetic effects on whole blood gene expression. Importantly, linear discriminant analysis enabled the definition of a set of DEGs which discriminated SLE versus healthy state with median sensitivity 83% and specificity 100%. Design of gene expression panels and expression profile-clinical trait correlation matrices for improved diagnostics, stratification and personalized therapy is in progress.

Conclusions: Specific gene networks confer susceptibility to SLE as well as to severe forms of the disease. These results may facilitate the early diagnosis, monitoring and prognosis, and the molecular taxonomy of SLE patients into pathophysiological and prognostically distinct subsets for personalized therapy.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6802 SATURDAY, 17 JUNE 2017 Reverse translation - learning from clinical trials in SLE, Sjögren’s and APS OP0331 A NOVEL HUMANIZED EFFECTOR-DEFICIENT FCYRIIA ANTIBODY INHIBITS IMMUNE COMPLEX MEDIATED PROINFLAMMATORY RESPONSES B. Chen1, K. Voussen2, S. Turman1, H. Sun1, S. Wang1, L. Vinali2, B. Kemp2, S. Kasturiangan3, E. Grant4, M.J. Hinrichs1, S. Eck1, A. DiGianlomendico1, X. Xiong1, J. Griffiths5, R. Herbst1, D. Close6, R. Kolbeck6, G. Sims1. 1MedImmune Inc, Gaithersburg, United States; 2MedImmune Inc, Granta Park, Cambridge, United Kingdom.

Background: Collectively, the cell surface Fc region of IgG receptors (FcγRs) engage soluble IgG and IgG containing immune complexes and trigger activation or inhibitory signals that play a critical role in the regulation of immune responses. The low affinity FcγRIIa (CD32A) is the most widely expressed activating FcγR in humans and appears to drive autoantibody and immune complex mediated autoimmune disorders. So far a therapeutic targeting this receptor has not been developed.

Objectives: To generate and characterize a novel humanized effector-deficient FcγRIIA antibody (MEDI9600) for clinical development.

Methods: The mouse model of MEDI9600 was assessed by confocal microscopy, whole blood internalization, and binding competition assays. Multiple cell based assays were used to measure autoantibody and immune complex mediated proinflammatory responses. The safety of MEDI9600 was assessed in vivo in mature tTreg cells. In particular, we could observe a normal proliferation of tTreg precursors (CD4+CD25+FoxP3+), but a strong decrease in MEDI9600 treated tTreg cells (CD4+CD25+FoxP3+), suggesting a perturbation in the transition from tTreg precursors to mature tTreg cells in Fra2 tg mice. We also found that in vivo stimulation with IL-2 failed to induce the proliferation of Treg cells in Fra2 tg mice compared to WT mice, suggesting that Fra2 overexpression affects IL-2 sensitivity of T cells. Finally, Fra2-WT bone marrow chimera mice also displayed a decreased percentage of Tregs confirming a cell-intrinsic and hematopoietic role of Fra2 in Treg cell development.

Conclusions: Our data suggest that Fra2 controls Treg cell development, possibly by modulating IL-2 signaling in T cells, which leads to autoimmunity in this mouse model. This new pathway could be targeted in a translational approach to modulate the capacity of T cells to differentiate in Tregs during autoimmune disease.

Disclosure of Interest: F. Renoux Grant/research support from: Swisslife, M. Scharler, F. Renoux, M. Tschopp, M. Zimmermann, None declared. R. Huang Employee of: Sanofi-Genezyme, A. Subramanian Employee of: Sanofi-Genezyme, C. Dees: None declared. J. Distler Shareholder of: 4D Science, Grant/research support from: Anamara, Bioteck, Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, Consultant for: Actelion, Altana, F. Renoux, A. Tschopp, M. Zimmermann, None declared. O. Boyman: None declared. O. Distler Grant/research support from: Actelion, Bauer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4D Science, Actelion, Biotech, Bayer, Biogenidec, BMS, Boehringer Ingelheim, ChemomAb, EpitPharm, expesfRea foundation, Genentech/Roche, GSK, Inventiba, J. Distler, Medical, Medapha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacies, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: Abbvie, iQone Healthcare, Medapha DOI: 10.1136/annrheumdis-2017-eular.1850
DISCOVERY AND VALIDATION OF NOVEL AUTOANTIGENS IN SJÖGREN'S SYNDROME WITH POTENTIAL FOR SUBGROUPING OF DISEASE

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Background: Primary Sjögren's syndrome (pSS) is a common autoimmune disease with exocrine gland dysfunction and multi-organ involvement. With the growing interest in conducting clinical trials in pSS, there is a need for new biomarkers that can be used to diagnose pSS, identify clinical subsets of pSS, predict disease course, follow disease activity, and assess treatment response. Activation of B-cells and dysregulation of the cytokine network plays a critical role in the pathophysiology of pSS. In the exocrine glands, elevated levels of cytokines, such as type I interferon (IFN), tumor necrosis factor alpha (TNF), interleukin 12 (IL-12) and B cell activating factor (BAFF) can be found. Dysregulated pathways of the innate and adaptive immune system lead to loss of tolerance and the production of organ-specific and non-specific autoantibodies. Current diagnostic criteria for pSS utilize autoantibodies directed to nuclear antigens (ANA), especially to SS-A/Ro (TRIM21, TROVE2) and La (SSB), but those are not specific, and can be identified as well in SLE and even in healthy volunteers. Several studies have shown that not all patients with pSS are tested positive for Ro and La antibodies, but suggested the existence of additional autoantibodies in pSS. This autoantibody burden is not well understood for the importance of disease progression, for its role in patient segmentation, or for response to treatments.

Objectives: The discovery of novel autoantibodies may provide a deeper understanding of mechanisms of actions for pSS drugs, and may be useful to stratify patients.

Methods: The autoantibody reactivity pattern of pSS serum samples was analyzed using a Luminex bead-based antibody array (SeroTag) and 1,600 selected human proteins from the ImmunexX protein library of 8,000 recombinant proteins. We screened over 2,000 serum samples from patients with autoimmune diseases as active controls targeting Sjögren's Syndrome (n=70), SLE (n=500), SSc (n=250), RA (n=500), and over 1,000 healthy individuals to confirm known and to discover novel autoantibodies. In a validation study, novel biomarker candidate antigens were evaluated using a cohort of 350 Patients with Sjögren's Syndrome.

Results: Apart from clear confirmation the known benchmark autoantigens known for many years we have discovered a small set of additional, novel autoantibodies, which were detected in frequencies of 8 to >20% in pSS. Accumulation of autoantibody reactivities allows for a first subgroup definition of Sjögren’s, and for clear segregation of SjS/SLE overlap syndrome patients.

Conclusions: A set of novel autoantigens for diagnosis and subgroup definition in Sjögren's syndrome was discovered by high content screening using a Luminex bead-based array platform. Validation in additional, large patient cohorts is needed to better understand the role of these novel autoantigens in Sjögren's syndrome and SLE.

cally assessed synovial inflammation in knee OA patients and their associations with clinical outcomes over time. We were unable to identify individual inflammatory aspects which associate with pain or fatigue. Additional research is required to identify the underlying mechanism for pain and fatigue in OA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1776

SATURDAY, 17 JUNE 2017
Targeting adipose tissue inflammation

**OP0336** ROLE OF SYSTEMIC INFLAMMATION ASSOCIATED WITH RHEUMATOID ARTHRITIS IN THE GLUCOSE AND LIPID METABOLISM: HUMANS, CIA MOUSE MODEL AND IN VITRO STUDIES

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**Background:** Rheumatoid arthritis (RA) patients are at higher risk for insulin resistance (IR). The association between RA and IR, and its role on the different characteristics of the disease, such as duration and activity have not been well defined. In addition, there is a gap of knowledge regarding the link between systemic/local inflammation and insulin sensitivity and lipid metabolism in RA patients.

**Objectives:** To explore the effects of the inflammation on the glucose and lipid metabolism in the RA context, following three strategies: RA patients, collagen induced arthritis (CIA) mouse model and in vitro treatment of 3T3L1 adipocytes.

**Methods:** Human study: 150 RA patients and 40 healthy donors were included. RA was identified using the 1987 ACR diagnostic criteria. A total of 63 patients with RA were collected. 3T3-L1 mouse model: 20 CBST/JL mice were used; 5 mice were used as non-diseased group, and 15 were used in CIA modelling: sorted in low and high activity of the disease based on the number of inflamed digits depending on the duration of the disease. Plasma, leukocytes, skeletal muscle, liver and adipose tissue were collected. Treatment of adipocytes with serum from RA patients: 3T3L1 adipocytes were treated with serum 10% of RA patients and healthy donors for 24h. The expression of genes and proteins involved in inflammation, lipid metabolism and insulin signalling was analysed in all the tissues and cell lines.

**Results:** Per centages of obesity, hypertension, atherogenic risk, metabolic syndrome and insulin resistance were significantly increased in the RA group. Although mean time of evolution was 7 years, no association between IR and the duration of the disease was found. Levels of HOMA-IR significantly correlated with DAS28 and C-reactive protein levels, suggesting that systemic inflammation might lead to the development of insulin resistance. In mice, the induction of arthritus promoted an alteration of the expression of genes involved in inflammation as well as lipid metabolism and insulin signalling in all the metabolic tissues and leukocytes, pointing out to an increase in lipolysis, decrease in adipogenesis and lipid accumulation and induction of IR. These results were recapitulated after treatment of adipocytes with serum from RA patients with high disease activity.

**Conclusions:** 1) IR was closely associated with an increase in disease activity and systemic inflammation in RA patients. 2) Induction of arthritis in mice promoted an increase in systemic inflammation markers, systolic muscle, adipose tissue, synovial lining cells, and leukocytes, and a reduction of genes involved in lipid uptake and storage, generating an insulin resistance state in those tissues. 3) The inflammatory components in RA serum induced lipolysis, reduced adipogenesis, and increase inflammation and insulin resistance in adipocytes 3T3L1.

In summary our results suggest that chronic inflammation associated with RA might directly impact relevant metabolic tissues, altering glucose and lipid homeostasis and favouring the development of insulin resistance.

**Acknowledgements:** Funded by ISCIII-FIS (CP15/00158), PI2013/0191, RD16/0012/0015 and Roche Pharma S.A.

**Disclosure of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.4725

SATURDAY, 17 JUNE 2017
Trials and tribulations of medication adherence

**OP0337-HPR** PREDICTORS OF PATIENT REPORTED DECISION TO DISCONTINUE ANTI-RHEUMATIC MEDICATION IN RHEUMATOID ARTHRITIS PATIENTS: DATA FROM A RHEUMATOID ARTHRITIS NETWORK (CAN) RHEUMATOID ARTHRITIS COHORT

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**Background:** Despite the availability of safe and effective treatments and the establishment of treatment guidelines, real-world effectiveness remains suboptimal largely due to low patient adherence with prescribed treatment.

**Objectives:** The purpose of this study was to systematically evaluate sociodemographic, medical, and disease-related factors associated with patient reported decision for discontinuation of anti-rheumatic medications (ARM) in a large observational cohort of RA patients followed up in Canadian routine clinical care.

**Methods:** RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) clinical registry and had at least two years of follow-up were included in the analysis. Treatment discontinuation due to patient reported decision was defined as ARM discontinuation. Independent predictors of ARM discontinuation were evaluated with multivariable cox-regression using both time-fixed and time-dependent variables. Factors considered included patient sociodemographics (age, gender, race, education status, annual income, smoking history), health insurance information (private vs. non-private, % coverage), disease parameters (RA duration, presence of erosion, RF positivity, DAS28, physician global, HAQ-DI, number of comorbidities), types of medications used, and physician characteristics (gender, academic position, urban vs. rural, distance from patient’s residence).

**Results:** A total of 1,782 patients were included in the analysis with a mean (SD) age of 57.4 (13.0) years and disease duration of 8.5 ± (9.3) at the time of enrolment to the registry (baseline). The majority of patients were female (77.7%), had post-secondary education (55.3%), and had private insurance (67.2%). In terms of disease severity, 54.5% had prior erosion, 69.5% were RF positive, and mean (SD) DAS28 was 4.5 (1.5).

A multivariate analysis, married status (HR, 0.73; 95% CI 0.56–0.96), and higher number of comorbidities (HR, 0.92; 95% CI 0.85–0.99) were identified as significant predictors of ARM continuation while higher physician global score (HR, 1.10; 95% CI 1.04–1.15), NSAID use (HR, 1.75; 95% CI 1.29–2.38), and polypathy (HR, 1.23; 95% CI 1.07–1.40) were associated with ARM discontinuation due to patient reported decision.

**Conclusions:** In this systematic approach a variety of factors encompassing sociodemographics, disease, and medication characteristics, were identified as significant independent predictors of ARM discontinuation due to patient reported decision. These results should be taken into consideration when developing patient adherence support programs and in the choice of treatment regimens.

**Disclosure of Interest:** V. Ahluwalia Grant/research support from: OBRI was funded by peer reviewed grants from Abbvie, Amgen, Bristol Myers Squibb, Celgene, Hospira, Janssen, McKesson, Merck, Novartis, Pfizer, Roche, Sanofi, UCB. M. Movahedi Employee of: OBRI/JSS, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, X. Li Employee of: OBRI, S. Couto Employee of: OBRI, J. Sampalis Employee of: Head of JSS, C. Bombardeir Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Hospira, Janssen, Pfizer, Roche, Sanofi, & UCB. M. Movahedi Employee of: OBRI/JSS, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, X. Li Employee of: OBRI, S. Couto Employee of: OBRI, J. Sampalis Employee of: Head of JSS, C. Bombardeir Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Hospira, Janssen, Pfizer, Roche, Sanofi, & UCB.

**DOI:** 10.1136/annrheumdis-2017-eular.1522

**Scientific Abstracts**
Outcome in juvenile idiopathic arthritis

### OP0338 FREQUENCY OF COMORBIDITIES IN JIA PATIENTS – RESULTS OF AN OBSERVATIONAL COHORT STUDY


**Background:** Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that often persists into adulthood. In addition to disability and poor quality of life, JIA is associated with increased long-term morbidity and mortality. The long-term risk of comorbidities in JIA patients is uncertain and guidance on risk assessment is not currently available.

**Objectives:** To determine the frequency of comorbid conditions in adult JIA patients.

**Methods:** Patients with JIA transferred from the biologic registry BiKER to the follow-up (FU) registry JuMBO were included in this analysis. All comorbidities, except for serious infections, prospectively recorded by physicians at BiKeR or JuMBO were considered. Comorbidity rates among the various JIA categories were compared. The Medical Dictionary for Regulatory Activities (MedDRA) was used for disorder coding. Differences in the occurrence of comorbidities between JIA categories were analyzed by multinomial logistic regression.

**Results:** A total of 1,022 young adults (67% female) with JIA and a mean FU of 7.9 (SD=3.5) years were included in this analysis. The patient’s mean age at entry was 22.5 ys (SD=3.7), and disease duration was 12.9 ys (SD=5.9) at the last FU. The majority were classified as polyarticular JIA (36.4%) at BiKeR enrollment. Patients had received a mean of 2.9 (SD=1.3) DMARDs, 77% were ever treated with biologics.

Comorbidities were reported for more than half of the patients (54%), 24.5% of the conditions were stated for the first time in adult age. Eye disorders were the most common comorbid condition group (15.1%), followed by skin and subcutaneous tissue disorders (9.3%), and psychiatric disorders (5.5%). The most frequently reported single diseases were uveitis in 14.4%, chronic secondary pain syndrome in 4.4%, hypertension in 3.6%, and psoriasis in 3.3%. In addition, inflammatory bowel diseases were reported in 2.5% of cases, other immune-mediated disorders, namely autoimmune thyroiditis in 2.5%, type1 diabetes in 0.7% and celiac disease in 0.3%, depression in 2.3%, anxiety in 0.3%, osteoporosis in 1.6%, and amyloidosis in 0.4%. Among the reported comorbidities, there was one case with a cerebrovascular accident, but none with ischemic heart disease, heart failure or diverticulitis. The rate of comorbidities was 0.3%, osteoporosis in 1.6%, and amyloidosis in 0.4%.

**Conclusions:** Young adults with JIA have a high rate of comorbidity overall, with extrarticular JIA manifestations being the most frequently reported comorbid conditions. Comorbidity rates vary among the various JIA categories. Patients with systemic JIA have the highest rate of cardiovascular risk factors and osteoporosis, whereas patients with extended oligo have the highest rate of uveitis. An underreporting or unawareness of comorbidities by rheumatologists is possible, guidance on risk assessment in adults with JIA is needed.

**Acknowledgements:** The authors thank all rheumatologists for contributing patients to the JuMBO registry. BiKeR is funded by unconditional grants from Abbvie, Pfizer, Roche, and Novartis, Germany and Abbott, Germany, JuMBO by unconditional grants from Abbvie, Pfizer, and Roche.

**Disclosure of Interest:** K. Minder Speakers bureau: Pfizer, Roche, PharmAllergan, N. Betenstehl: None declared, J. Klotsche: None declared, E. Seipelt: None declared; S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:

None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:

Disclosure of Interest: K. Minder Speakers bureau: Pfizer, Roche, PharmAllergan, N. Betenstehl: None declared, J. Klotsche: None declared, E. Seipelt: None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:

None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:

Disclosure of Interest: K. Minder Speakers bureau: Pfizer, Roche, PharmAllergan, N. Betenstehl: None declared, J. Klotsche: None declared, E. Seipelt: None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:

None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:

Disclosure of Interest: K. Minder Speakers bureau: Pfizer, Roche, PharmAllergan, N. Betenstehl: None declared, J. Klotsche: None declared, E. Seipelt: None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser:
for scleroderma pathology reflecting autoimmunity, vasculopathy, inflammation and fibrosis. This mRSS signature needs to be validated in a larger set of SSc patients including assessment of change over time.

References:

Disclosure of Interest: S. Illiano: None declared, C. Rocher: None declared, E. Boitier: None declared, J. Murphy: None declared, Y. Allairen Grant/research support from: BMS, Genentech-Roche, Inventiva, Pfizer, sanofi, Consultant for: Actelion, Bayer, Biogen, Genentech-Roche, Galapagos, Medac, Pfizer, sanofi, Servier, UCB, C. Denton Consultant for: Actelion, Bayer, GSK, CSL Behring, Merck-Serono, Genentech-Roche, Inventiva, Sanofi-Aventis, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, Biogenidec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espefam, Rare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, Medimmune, Mitsubishi Tanabe Pharma, Pharmacies, Pfizer, sanofi, Serodapharm, Sinoxia, AbbVie, iQone Healthcare, Mepha, D. Khanna Grant/research support from: Bayer, GSK, Genentech/Roche, Sanofi-Aventis, NIH K24AR063120, Consultant for: Actelion, Bayer, Civis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, sanofi-Aventis, F. Bendorf: None declared

DOI: 10.1136/annrheumdis-2017-eular.5827

SATURDAY, 17 JUNE 2017

How diet influences musculoskeletal diseases

OP0340 WEIGHT LOSS FOR OVERWEIGHT AND OBESE INDIVIDUALS WITH GOUT: A SYSTEMATIC REVIEW OF LONGITUDINAL OBSERVATIONAL STUDIES

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Background: Weight loss is a commonly recommended treatment for gout, but the magnitude of effect to expect has to our knowledge not previously been evaluated in a systematic review.

Objectives: The aim of this systematic review was to determine the benefits and harms associated with weight loss in overweight patients with gout.

Methods: Based on a pre-determined protocol (CRD420160037907), we searched six databases for longitudinal studies, quantitatively reporting the effect of weight loss in overweight gout patients. Risk of bias was assessed using the ROBINS-I tool. The quality of the evidence was assessed using GRADE.

Results: From 3,991 potentially eligible studies, 10 were included (incl. one RCT). Interventions included diet with/without physical activity, bariatric surgery, diuretics, metformin, or no intervention. Due to clinical heterogeneity of the included studies, data are presented for each study and synthesised separately.

The effect on serum uric acid (sUA) ranged from -168 to 30 μmol/L. Six out of 10 studies (60%) included studies, data are presented for each study and synthesised separately. At short term, temporary increased sUA and gout attacks may occur after bariatric surgery. There is an urgent need to initiate rigorous prospective studies (preferably RCTs) to provide more trustworthy estimates of benefits and harms of weight loss in overweight gout patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2651

SATURDAY, 17 JUNE 2017

Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century

OP0341 CAN PAIN IN HAND OSTEOARTHRITIS BE ASSOCIATED WITH MRI COLLATERAL LIGAMENT ABNORMALITIES?

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Background: Many patients with hand osteoarthritis (OA) have little symptoms. Bone oedema and synovitis have been associated to pain in OA, but inflammation involving ligaments has not been studied, likely limited by inadequate MRI resolution. We have previously found significant ligament pathology in early and established hand OA (HOA) [1].

Objectives: We hypothesise that the well innervated ligaments are key to a better understanding of the relationship between joint structure and pain in HOA. This

Abstract OP0341 – Table 1

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Joints (n)</th>
<th>HC (n=10)</th>
<th>OA pain (n=11)</th>
<th>OA no pain (n=11)</th>
<th>OA pain (n=15)</th>
<th>OA no pain (n=11)</th>
<th>OA pain (n=15)</th>
<th>Difference* (90% CI)</th>
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<tr>
<td>Fluid</td>
<td>30 (3)</td>
<td>73 (8)</td>
<td>67 (10)</td>
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<td>Capsulitis/synovitis</td>
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<td>60 (9)</td>
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<tr>
<td>Extracapsular oedema</td>
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<td>45 (5)</td>
<td>73 (11)</td>
<td>0 (0, 2)</td>
<td>2 (0, 3)</td>
<td>1 (0, 2)</td>
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<tr>
<td>CL thickening</td>
<td>50 (5)</td>
<td>100 (11)</td>
<td>100 (15)</td>
<td>2 (2, 4)</td>
<td>3 (2, 4)</td>
<td>1 (0, 3)</td>
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<tr>
<td>CL oedema</td>
<td>40 (4)</td>
<td>91 (10)</td>
<td>87 (13)</td>
<td>2 (1, 3)</td>
<td>3 (2, 4)</td>
<td>1 (0, 3)</td>
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<tr>
<td>CL degeneration</td>
<td>40 (4)</td>
<td>91 (10)</td>
<td>100 (15)</td>
<td>3 (1, 5)</td>
<td>4 (2, 6)</td>
<td>1 (1, 3)</td>
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<tr>
<td>Proximal joint bone oedema</td>
<td>9 (1)</td>
<td>0 (0, 0)</td>
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<td>0 (0, 0)</td>
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<tr>
<td>Distal joint bone oedema</td>
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<td>20 (3)</td>
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<tr>
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<td>27 (3)</td>
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<tr>
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<td>7 (1)</td>
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</tbody>
</table>

*Accounting for clustering of joints within patients. CI = healthy controls; IQR = inter-quartile range; CL = collateral ligaments.

Figure 1: PRISMA flow diagram

ACR, American College of Rheumatology; CENTRAL, Cochrane Central Register of Controlled Trials; EULAR, The European League Against Rheumatism; ICRF, The World Health Organization International Clinical Trial Registry Platform portal; pts, patients.
Conclusions: Modifiable abnormalities involving capsular/synovium and extra-capsular areas may be more frequently seen in painful OA joints. The presence of collateral ligament abnormalities in HOA joints, whether painful or not, suggest that the severity of ligament abnormalities in small joint OA and the degree of pain may be an important area to investigate further.

References:

Acknowledgements: Funded by NIHR.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3532

OP0342 ASSESSMENT OF STRUCTURAL DAMAGE OF THE THUMB BASE IN PATIENTS WITH HAND OSTEOARTHRITIS: COMPARING THE NEARLY DEVELOPED OMERACT MAGNETIC RESONANCE IMAGING SCORING SYSTEM WITH STANDARD RADIOGRAPHY

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Background: The thumb base is frequently involved in patients with hand osteoarthritis (OA), resulting in osteophytes and cartilage loss. Radiography is the most commonly used imaging modality to evaluate structural OA signs, however it is insensitive especially due to overprojection. Magnetic resonance imaging (MRI) could be a valuable alternative, however a standardized scoring method is insensitive especially due to overprojection.

Methods: 26 joints from 15 patients (mean (SD) age 58.3 (8.2), 13F:2M) and 10 in 5 healthy controls (age 38 (5.6); 4F:1M) were scanned using a microscopy MRI coil. 15 joints in 6 patients were painful (median (IQR) pain VAS 4 (3, 7)). Joints were scored blinded to clinical data for joint fluid, capsule/synovitis, extracapsular oedema, collateral ligament thickening/oedema/degeneration, extensor and flexor tendons, bone oedema and cysts. All structures were graded 0–3 for normal, mild, moderate, severe, as defined in OMERACT HOAMRIS where available [2]. Proportions of joints with any level of abnormality (score > 0) were calculated according to pain status (present/absent).

Results: All OA patients with and without pain had ligament abnormalities. Substantive differences in proportion of joints between healthy controls and OA patients were seen for all pathologies except tendons (no tendons abnormalities were found in all groups). Proportions of joints with capsular/synovium, extra capsular changes and proximal cysts differed between OA joints with and without pain but no substantive differences in pathology score were found. Of painful joints, 93% (14) had both ligament and capsular/synovium or extracapsular abnormality present, compared to 45% (5) of non-painful joints.

Conclusions: Scores of osteophytes and cartilage loss assessed on MR images by TOMS were correlated with radiographic scores, indicating good validity of the TOMS. Furthermore, the frequencies of joints with osteophytes and cartilage loss assessed on MR images were higher compared to those on radiographs, suggesting high sensitivity for the TOMS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2765

SATURDAY, 17 JUNE 2017
Why do we develop autoimmunity?

OP0343 THE INTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS IS CHARACTERIZED BY A PECULIAR GUT MICROBIOTA

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Background: Gastrointestinal involvement is recognized as a major cause of morbidity and mortality in Systemic Sclerosis (SSc) and its pathophysiology is still unclear. Few data on composition and function of gut microenvironment in SSc are reported in the literature but there is a growing body of evidences supporting the hypothesis of a relation between gut microbiota and the host immune system. The BMI was normal and the mean age was similar both in SSc and controls groups. The composition of microbiota was determined through 16S rRNA pyrosequencing performed using the GS Titanium technology. Rarefaction was used to uniform abundance data. α-diversity was defined by the main indexes while β-diversity was determined according to Bray-Curtis and UniFrac, represented through Principal Coordinate Analysis (PCoA) and compared using PERMANOVA test on distance matrices. Linear Discriminant Analysis Effect Size was used to identify taxa that showed differential expression between the groups.

Results: At genus level SSc patients showed a differential expression in 12 taxa compared to controls with higher levels of Ruminococcaceae, Streptococcaceae,
Conclusions: Our analysis demonstrated an altered and distinct composition of gut microbiota in SSC patients compared to healthy controls. Furthermore, scleroderma patients show some differences in microbiota characteristics according to the extent of skin involvement, suggesting that microbiota may influence the severity of the disease. If validated and related to GI symptomatology and nutritional status our findings open up the opportunity of a rational intervention on microbiota to restore the gut equilibrium in SSc patients. Furthermore, our findings are supported also by PCoA of the values representing phylogenetic distance of microbial communities between specimens (p < 0.01). Differences were supported also by PERMANOVA on Bray-Curtis distance matrix (p < 0.016).

References:


Disclosure of Interest: None declared


Sutherland, growing up with arthritis – yes we can! a project of Deutsche Rheuma-Liga in cooperation with the German Arthritis Research Center, with financial support by the German Federal Ministry of Health

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Background: Every third young person with arthritis in Germany stops therapy when he or she enters adult care! Young people with arthritis have to travel long distances to care facilities, which are specialized in transition (about 30 throughout Germany). Because there are too few rheumatologists adults with arthritis often have to wait long for a consultation. Too few doctors have experience with treating young persons with arthritis. The situation of young persons with arthritis results in little knowledge about the condition – only every second young person knows their correct diagnosis. Parents manage everything – only every 5th young person up to 17 years has been alone with their doctor without their parents. Timely and comprehensive support is lacking.

Objectives: Supported by the health ministry and in cooperation with the German Arthritis Research Center the project started in 2014. As a first step the need for support for young person with arthritis was explored. It took two years to develop a pilot project with transition peers, a homepage, camps and information material for parents and doctors. The main goal of the project is to reduce the number of young persons who discontinue care because of the necessary change from children’s care to adult care.

Methods: Ten transition peers have been trained for providing support (telephone, online, personal). An online information platform www.mein-rheuma-wird-erwachsen.de (my arthritis is growing up!) was created, filled with the experiences of transition peers are going to doctors congresses to spread information material. Camps especially for young persons growing up with arthritis took place. For the parents information material was developed: a seminar: learn to let go! is offered to them. The transition peers are going to doctors congresses to spread information material and to present the homepage.

Results: An evaluation of the project is carried out by the German Arthritis Research Center. The online information platform is accepted, it had more than 10,000 visitors during the first year. The young users like the content of the homepage, the transition peers are accepted by the young people as well as by the doctors.

Conclusions: The model project is running for three years – from 2014 until the end of 2017. A subsequent project will focus on the communication between doctors and young patients and should continue the new activities for the young persons with arthritis, their parents and the doctors.

References:

[1] In 2016, the German rheumatology newspaper – Zeitchrift für Rheumatologie2016, Page 635f reported on the project with the title "Transition from pediatric to adult rheumatological care" and about the special offers from Deutsche Rheuma-Liga by Prof. Kirsten Minden and Martina Niewerth.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4956

Suffering in silence. Optimizing the management of psychological well-being for people with RMDs

OP0345-PARE GROWING UP WITH ARTHRITIS – YES WE CAN! A PROJECT OF DEUTSCHE RHEUMA-LIGA IN CO-OPERATION WITH THE GERMAN ARTHRITIS RESEARCH CENTER, WITH FINANCIAL SUPPORT BY THE GERMAN FEDERAL MINISTRY OF HEALTH

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Background: Despite positive non-pharmacological treatment effects in fibromyalgia (FM) these effects are often modest and show large individual variability. In clinical practice it is very important to assess the effectiveness of treatment for the individual patient in order to tailor further treatment. Responder criteria can assess the effectiveness of treatment and define clinically meaningful change in health outcomes on patient level. However, no specific responder criteria for non-pharmacological treatment in FM currently exist. This warrants further exploration in this field.

Objectives: 1) To define responder criteria for multicomponent non-pharmacological treatment in FM; and 2) To estimate and compare their sensitivity and specificity.

Methods: Candidate responder sets were 1) identified in literature (3–5); and 2) formulated by expert group consensus. All candidate responder sets were tested for sensitivity and specificity in a cohort of 144 patients with FM receiving multicomponent non-pharmacological treatment. Therapist’s judgement about patient’s goal attainment and patients’ perspective on health status change, assessed at 6 months after the start of treatment, were used as gold standard.

Results: Seven responder sets were defined (three identified in literature and four formulated by expert group consensus), and comprised combinations of domains of 1) pain; 2) fatigue; 3) patient global assessment (PGA); 4) illness perceptions; 5) limitations in activities of daily living (ADL); 6) sleep. The sensitivity and specificity of literature-based responder sets (n=3) ranged between 17%–99% and 15%–95% respectively, whereas the expert-based responder sets (n=4) performed slightly better with regard to sensitivity (range 41%–81%) and specificity (range 50%–96%). Of the literature-based responder sets the OMERACT-OARSI responder set with patient’s gold standard performed best (sensitivity 63%, specificity 75% and ROC area = 0.69). Overall, the expert-based responder set comparing year 1 with patient’s goal standard performed best (sensitivity 47%, specificity 96% and ROC area = 0.71).

Conclusions: We defined sets of responder criteria for multicomponent non-pharmacological treatment in fibromyalgia. Further research should focus on the validation of those sets with acceptable performance.
“LISTENING TO PAIN - UN DOLORE DA ASCOLTARE”
MULTIDISCIPLINARY SUPPORT FOR WOMEN WITH FIBROMYALGIA

S. Mingolla, S. Mingolla on behalf of Serena Mingolla Direttore Morfologie author - Francesco Riondino Vice President APMAR Onlus, Ilaria Cineri Psychologist - Cinzia Assafacile Fibromyalgia Group APMAR Onlus. APMAR, Lecce, Italy

Background: The project “Listening to Pain - un dolore da ascoltare” is a multidisciplinary and multifactorial project addressed to women with Fibromyalgia. Fibromyalgia pain has no boundaries. People describe the pain as deep muscular aching, throbbing, shooting, stabbing, or intense burning. Quite often, the pain and stiffness are worse in the morning, and muscle groups that are used repetitively may hurt more. Pain in every muscle and the profound exhaustion are not symptoms that people can see, but they are real and may be devastating for the person with Fibromyalgia. Although the invisible nature of the condition causes credibility dilemmas for patients.

Objectives: The project aims at improving the quality of life of women with Fibromyalgia. It has the main following objectives: provide information about Fibromyalgia, raise public awareness, collect useful data for research development, give support to the person, reinforcing social networks, provide mediation of the recognition process and bio-energy structured exercise activities and classes tailored to symptoms (stiffness and fatigue) useful in boosting endurance times.

Methods: The project was launched in 2015 with a communication campaign and supervised by a group of psychologists promoting the use of humanistic bioenergetics therapy for individual consultations and collective supporting group discussions. Participants were 50 women with a confirmed diagnosis of FMS. In June 2015, APMAR founded its first “Group for Pathology” and launched new tools as the info point and the toll-free number. The project includes: psychological support to women suffering from Fibromyalgia, self-help groups where women talk, meet, discuss the pain and jointly organize events and other projects; information, through the creation of brochures and different kind of materials; an info-point managed by APMAR and a toll-free number that provides information and immediate help for women feeling lonely.

Results: The psychological and physical well-being of women with Fibromyalgia syndrome were enhanced by social support. Chronic Pain, depression, self-efficacy, helplessness, mood disturbance, health status, impact of FMS, were improved. Psychologists involved in the project observe a decrease of depression, greater security and openness in relations. Women started processing and overcoming the sense of loneliness and isolation, increasing knowledge and therefore awareness, acceptance of the disease. Analyses indicated that the created social support networks were associated with greater levels of self-efficacy for pain and symptom management, higher levels of self-efficacy for function and symptom management, as well as overall psychological well-being.

Conclusions: This multilateral approach was very empowering and consented women to work in the same direction to improve healthcare outcomes for people in their same conditions. Furthermore, it helped women with Fibromyalgia get more control over their life, and promote understanding of patient empowerment. The project was also a call for action not only among patients and health professionals, but among several kinds of social groups of students, press, local policy makers and other civil society organizations.

References:
[1] APMAR National Association of People with Rheumatic and Rare Diseases - www.apmar.it info@apmar.it.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2549

SARDAY, 17 JUNE 2017

OP0347-HPR TRAINING RHEUMATOLOGY NURSE SPECIALISTS: WHAT DOES THE FUTURE HOLD?

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Background: Since the introduction of the Rheumatology nursing in the UK in 1980s, there has been gradual development of the “specialty”. Despite the proven benefits, both clinical and economical, of a well-trained rheumatology nurse specialist and the evolution of the role, there is a lack of a clear career path for the profession.

Objectives: We undertook a pilot survey to understand the present climate of rheumatology practitioner training in the region.

Methods: Following a focus group discussion of an “ideal” development route for rheumatology practitioner training in the region.

Results: There are 19 centres providing rheumatology services in the region with 51 rheumatology practitioners. All of them (100%) replied to the questionnaire. Only four units (21%) provide formal induction programme for training. 11/19 (57%) have nurse prescribers. All providers replied positive to the question pertaining nurses’ participation in research and audit; 12 (63%) have presented locally or nationally and eight (42%) have submitted posters to conferences. 12 centres have partly nurse delivered early arthritis pathway and 13 have access to departmental ultrasound. Ten units provide patient educational events.

Conclusions: This is a pioneering survey outlining access of rheumatology practitioners and nurse specialists to developmental opportunities. This initiative highlights a wide variation in the provision of clear career pathway regionally. Though most centres are delivering contemporary services, these are not being used effectively for developing key team members. There is lack of formal induction programme. Though most nurses are involved in audit, less than a quarter are presenting at any level and even fewer are publishing research endeavours. Prescribing is limited to 15/51 (29%) members. Less than 20% are training to do intra-articular injections or learning musculoskeletal ultrasound. Despite patient education being a core skill for this group, only 10 units deliver these as a formal event.

In conclusion, there is wide variation in the provision of career advancing opportunities to rheumatology nurse specialists. This can potentially have a negative impact on staff recruitment and retention. There is a need for improving standards and delivery of rheumatology professionals’ career development.

Disclosure of Interest: None declared

DIFFERENTIAL METHYLATION AS A POTENTIAL BIOMARKER OF METHOTREXATE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the first-line disease modifying anti-rheumatic drug for the treatment of rheumatoid arthritis (RA). However, many patients do not respond adequately or experience adverse effects2,3; therefore, identifying blood-based biomarkers that predict treatment response is a research priority. DNA methylation is an epigenetic marker that modifies but does not alter DNA sequence, and it is thought that MTX may act, at least in part, by inhibiting intracellular methyl donor transfer leading to DNA hypomethylation2.

Objectives: We aimed to identify differential DNA methylation signatures in whole blood, which may act as biomarkers predictive of response to MTX in patients with RA.

Methods: DNA methylation was measured using the Illumina Methylation450 BeadChip in DNA samples from individuals recruited to the Rheumatoid Arthritis Medication Study (RAMS), a one-year observational study in the UK including patients with RA starting MTX for the first time. In RAMS, demographic and clinical data are collected prior MTX start (baseline) and at 6 months after commencing MTX. DNA was extracted from whole blood samples collected baseline and at 4 weeks from patients who, at 6 months, had a EULAR good response (n=36) or EULAR poor response (n=36) to MTX. Differentially methylated positions (DMPs) between the baseline and 4 weeks, and between good and poor response were identified using linear regression, adjusting for gender, age, cell composition, baseline disease activity score (DAS28), and smoking status. Analyses also compared methylation with changes in DAS28 and the individual DAS28 components over 6 months. DMPs that showed significant differences in the test cohort were selected for replication by pyrosequencing in an independent group of 100 patients with both baseline and 4 week samples.

Results: Based on percentage change in methylation between pre-treatment and following 4 weeks of therapy, two DMPs were significantly associated with response status in samples taken at 4 weeks (p-value < 10^-5). Three additional DMPs were associated with change in tender joint count, whilst three other DMPs were associated with change in swollen joint count, and a further four DMPs associated with change in C-reactive protein. Of the four DMPs tested to date, hypermethylation at cg23700278 locus is adrenocorticotropin alpha 2C (ADAR2C), involved in neurotransmission.

Conclusions: These preliminary results suggest DNA methylation may be a biomarker of MTX response but requires replication in other data sets.

References:

Disclosuer of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6330

ETANERCEPT AND ADALIMUMAB EXHIBIT HETEROGENEOUS EARLY SIGNALS OF RESPONSE IN RHEUMATOID ARTHRITIS THERAPY

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Background: Up to 40% of rheumatoid arthritis (RA) patients exhibit insufficient response to TNF inhibitor (TNFi) therapy, which has an adverse effect on long term outcomes. Without reliable biomarkers, it is difficult to make treatment decisions, many non-responder (NR) patients experience a delay in switching to an alternative therapy. Ideally, blood-based biomarkers would be measured before treatment (baseline) and throughout treatment in order to select and monitor therapeutic response to maximise the chances of responding to the first biologic therapy.

Objectives: To compare transcriptomic changes between patients administered etanercept and adalimumab therapy, and to identify biomarkers to predict or monitor response.

Methods: From the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS) cohort, 37 EULAR good-responders in clinical remission (GR) and 18 NR to etanercept, and 50 GR and 20 NR to adalimumab were selected. Total RNA was isolated from Tempus™-stabilised whole blood samples collected at baseline and following 3-months (3M) of therapy using the MagMAX™ RNA extraction kit. RNA was amplified and converted into biotinylated sense-strand DNA using the Affymetrix WT PLUS kit for hybridisation onto Affymetrix GeneChip® Human Transcriptome arrays. Quality control and differential expression/splice analysis were assessed using the Affymetrix Expression and Transcriptome Analysis Console™ and appropriate Biocomparator packages. Differential transcript expression was adjusted for baseline DAS, age, gender and concurrent DMARD therapy. Pathway analysis was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID) and Ingenuity Pathway Analysis (IPA) tools.

Results: In adalimumab GR, 636 genes were downregulated and 253 upregulated at 3M (FDR p < 0.05, fold-change > 1.2). There was significant upregulation of immune cell components, most notably HLA genes including HLA-DRB1, other RA susceptibility genes (SLC2A4, PADI4 and CD28) and many B and T cell signalling genes. Etanercept GR exhibited a milder transcriptomic change overall, showing little overlap with adalimumab GR; 395 genes were downregulated and 27 upregulated at 3M (FDR p < 0.05, fold-change > 1.2). Downregulated genes included downstream TNF components such as mitogen activated protein (MAP) kinases, as well as genes involved in NOD-like receptor, Toll-like receptor and NF-kB signalling. Such significant changes were absent in NR to adalimumab and etanercept. Furthermore, alternative splice changes in RA-relevant genes such as MMP9 were apparent in adalimumab GR at 3M but not etanercept GR.

Conclusions: The heterogeneity in the blood-based transcriptomic profiles of etanercept and adalimumab response observed herein suggests that different TNFi therapies function by alternative mechanisms that impact patient outcomes. It also calls into question the reliability of response studies that consider TNFi therapies as a homogenous group. The candidate biomarkers identified require replication in independent datasets but may provide early and objective response biomarkers to inform timely therapeutic switching in patients who are not responding to their current TNFi drug.

Disclosure of Interest: None declared

CD4+ AND B LYMPHOCYTE EXPRESSION QUANTITATIVE TRAITS AT RHEUMATOID ARTHRITIS RISK LOCI IN UNTREATED EARLY ARTHRITIS: IMPLICATIONS FOR CAUSAL GENE IDENTIFICATION?

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Background: Rheumatoid arthritis (RA) is a genetically complex disease of immune dysregulation. Genome-wide association scans (GWAS) have confirmed its association with variants at ~100 genetic loci. Outside of the HLA region,
CROSS PHENOTYPE ASSOCIATION MAPPING OF THE MHC

Results:
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Disclosure of Interest: None declared, A. Pratt Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2017-eular.4028

THU0004 CROSS PHENOTYPE ASSOCIATION MAPPING OF THE MHC IDENTIFIES GENETIC VARIANTS THAT DIFFERENTIATE PSORIATIC ARTHRITIS FROM PSORIASIS

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Background: The identification of genetic variants that differentiate PsA from psoriasis has the potential to help us understand the underlying biological pathways and thus aid the development of PsA Associations to genetic variants within the major histocompatibility complex (MHC), in particular to HLA-C*0602, increase risk of both PsA and psoriasis when compared to control populations. However direct comparisons of PsA to psoriasis have led to paradoxical results where HLA-C*0602 has been reported to be protective of PsA. In addition HLA-C*0602 has been reported to be associated with age of onset of psoriasis. A more recent study has reported the amino acid at position 45 of the HLA-B protein as the most important factor for differentiating PsA from psoriasis.

Objectives: Here we perform a cross phenotype association analysis in an attempt to identify genetic variants in the MHC that differentiate PsA from psoriasis in a large collection of PsA patients and psoriasis patients screened for the absence of PsA.

Methods: A total of 1069 patients with psoriasis and 981 patients with PsA from the UK were genotyped using either the Illumina Infinium or the Illumina OmniExpress genotyping arrays. SNPs, amino acids and classical HLA alleles were imputed using SNP2HLA. Logistic regression was used to compare the imputed dosage of MHC markers between PsA and psoriasis. All analyses were repeated using age of psoriasis onset as an additional covariate.

Results: The cross-phenotype association comparing PsA to psoriasis was to HLA-C*0602 (p=4.17x10^-10) with a protective effect for PsA (OR 0.52, CI 0.44,0.61). HLA-C*0602 was found to be significantly associated with a younger age of psoriasis onset (p=1.5x10^-9) where the median age of onset in years for carriage is 22 compared to 33 for non-carriage. We observed a difference in the median age of psoriasis onset in years between the PsA and psoriasis study subgroups (34 vs. 21), highlighting the potential for bias at markers associated with age of psoriasis onset. When controlling for the age of psoriasis onset in the analyses we observed no association of PsA to HLA-C*0602 (p=0.07) and the most significant association was to the amino acid at position 97 of HLA-B (p=1.5x10^-9) where the presence of asparagine or serine residue increased risk of PsA. Asparagine at position 97 of HLA-B defines the HLA-B*2705 allele.

Conclusions: Comparing PsA to psoriasis we show HLA-C*0602 confers no effect, either risk or protective, for PsA after correction for age of psoriasis onset. The results suggest that the previously observed protective effect of HLA-C*0602 could be due to confounding due to a younger age of psoriasis onset in the psoriasis subgroup. When accounting for age of psoriasis onset, the primary association conferring risk for PsA in patients with psoriasis is to HLA-B amino-acid 97 where an asparagine residue defines the HLA-B*2705 allele. In addition, this amino acid has been reported as the largest genetic effect for ankylosing spondylitis thereby refining the genetic overlap between these two spondyloarthropathies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3403

THU0005 ERAP POLYMORPHISMS AND ITS ASSOCIATION WITH HLA-B15 AND HLA-B27 POSITIVE SPONDYLOARTHRTIS PATIENTS

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Background: Since 1973, the association of HLA-B27 and spondyloarthritides (SpA) is well known, however in Colombian population it is present in only 40% of patients and HLA-B15 is present almost in 25%. A mechanism of polygenic mechanism has been proposed as an explanation for the development of SpA. Endoplasmic reticulum aminopeptidase (ERAP) genes 1 and 2 have been implicated. ERAP1 is strongly associated with HLA-B27 positive patients and ankylosing spondylitis, but not with ERAP2.

Objectives: To determine the association between ERAP polymorphisms and HLA-B27 or HLA-B15 positive SpA patients.

Methods: 178 patients with SpA according to ASAS criteria were included in the study. HLA typing was performed by the PCR technique using the Bioread® HLA-SSP plates. The polymorphisms were determined by the RT-PCR technique using Roche® probes for ERAP1 rs72044, rs17482078, rs10005860, and rs30187. For ERAP2 the probes were used rs2910686, rs2248374 and rs2549782.

Table 1. ERAP2 Haplotypes in HLA-B15 and B27 Patients

<table>
<thead>
<tr>
<th>Haplotypes</th>
<th>HLA B15</th>
<th>HLA B27</th>
<th>OR</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>n (AF)</td>
<td>n (AF)</td>
<td>(CI 95%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGT</td>
<td>0.201</td>
<td>0.078</td>
<td>2.943 (1.264–6.585)</td>
<td>0.009*</td>
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<td>TCG</td>
<td>0.055</td>
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<td>4.483 (1.524–13.187)</td>
<td>0.003**</td>
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<tr>
<td>CAT</td>
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<td>9.014 (1.181–68.807)</td>
<td>0.009*</td>
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<td>1.185 (0.106–13.29)</td>
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<td>TAC</td>
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</tbody>
</table>

ERAP: endoplasmic reticulum aminopeptidase; AF: allelic frequency; OR: odds ratio.
allele and genotype frequencies polymorphisms were obtained by direct counting. In each group the Hardy-Weinberg equilibrium was evaluated using the $^2$ test. Associations were assessed using odds ratio (OR). Stata v.12.0 program was used to analyze data. The construction and analysis of haplotypes was performed using Haploview v.4.2.

Results: A total of 70 patients were HLA-B*27 positive and 34 were HLA-B*15 positive. 78 were women and 100 were men. Linkage disequilibrium map of the ERAP gene is depicted in figure 1. When analysed by ERAP2 haplotype it is observed that there is a statistically significant association with the combinations described in table 1. No associations were observed between ERAP1 haplotypes and HLA-B*15 or B*27.

Conclusions: In the group of patients analysed, a statistically significant association was found between patients with SpA HLA-B*15 positive and the haplotype TGT of ERAP2. Also HLA-B*27 positive SpA patients were associated with haplotype TGC and CAT of ERAP2 with statistical significance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5659

THU0006 TRANS-ETHNIC META-ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES IDENTIFIES GDMD AND PRDM1 AS SUSCEPTIBILITY GENES TO SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis and composed of two subtypes, limited and diffuse cutaneous forms. Previous genetic studies including genome-wide association studies (GWAS) have identified 12 susceptibility loci satisfying genome-wide significance.

Objectives: To expand the list of susceptibility genes and deepen biological insights for SSc.

Methods: We performed trans-ethnic meta-analysis of GWAS in the Japanese and European populations, followed by a two-staged replication study comprising a meta-analysis using 11,4751 SNP controls between a single nuclear polymorphisms (SNPs) and neighboring genes were evaluated. Enrichment analysis of H3K4Me3, a representative histone mark for active promoter was conducted with an expanded list of SSc susceptibility genes.

Results: We identified two significant SNP in two loci, GDMD and PRDM1, both of which are related with immune functions and associated with other autoimmune diseases ($p$<1.4x10$^{-10}$ and 6.6x10$^{-10}$, respectively). GDMD also showed a significant association with limited cutaneous SSc. We also replicated the associations of previously reported loci including a non-GWAS locus, TNFAIP3. Furthermore, we encoded a transcription factor regulating T cell proliferation and plasma cell differentiation. The top SNP in GDMD was a missense variant and correlated with gene expression of neighboring genes, and this could explain the association in this locus. We found different HLA association patterns between the two populations or two subtypes. Enrichment analysis suggested the importance of CD4 naïve primary T cell.

Conclusions: GDMD and PRDM1 are associated with SSc. These findings provide enhanced insight into the genetic and biological basis of SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2165

THU0007 DEEP SEQUENCING TRANSCRIPTOME ANALYSIS OF THE EFFECT OF TRAUMEEL VERSUS DICLOFENAC THERAPEUTIC ACTION IN WOUND HEALING

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Background: Anti-inflammatory agents are used widely in treating numerous inflammatory conditions. The effect of Tr14, a multitargeted natural product, was compared to diclofenac, a non-selective cyclooxygenase inhibitor, on cutaneous wound repair in mice.

Objectives: To compare the effect of diclofenac with Tr14 on the transcriptome during cutaneous wound repairing process.

Methods: After abrasive wounding, the wounds were treated with topical Tr14 or diclofenac at clinically relevant doses. An additional group received subcutaneous Tr14 injections. The healing wounds were analyzed for RNA transcript profiling by RNAseq at specific times (12h, 24h, 36h, 72h, 96h, 120h, 196h) after injury. Differentially expressed genes (DEGs) were computed at each time point between diclofenac vs control or Tr14 vs control using EdgeR.

Results: Across time points, Tr14 treatment modulated a number of transcripts related to key wound repair pathways such as cellular differentiation, wound contraction, and cell mobility. Diclofenac, in contrast, changed gene expression mainly in two areas: Pro-inflammatory effects were observed with regard to the RNA chromatin regulation and ribosomal function, further effects were observed on the prostaglandin pathway and wound repair factors. In many of the key pathways modulated by Tr14, such as the defense response and cell motility, diclofenac tended to have an opposite effect on gene expression. At 12 hours post-injury, there were 521 transcripts significantly elevated and 1027 transcripts that were decreased by diclofenac treatment. By comparison, using a similar number of transcripts altered by Tr14 treatment, only 4 transcripts were increased in common, and 5 transcripts were decreased in common, suggesting that the therapeutic agents have different effects on the transcriptome.

Conclusions: The overall patterns of the Tr14 and diclofenac responses in the transcriptome during wound repair are very different. The Tr14 effect is most pronounced on the defense response, cell motility, and anti-apoptotic pathways. In contrast, diclofenac mainly affected histones and chromatin remodeling systems, as well as ribosomal systems that would be expected to alter the translational pattern of diclofenac-treated cells.

Disclosure of Interest: G. S. Laurent, III: None declared, B. Seelheimer: None declared, M. Tackett: None declared, J. Zhou: None declared, D. Shitokalo: None declared, Y. Vytakin: None declared, P. Kaplanov: None declared, I. Toma: None declared, T. McCaffrey: Speakers bureau: TM has received speaker’s honorarium from HEEL, GmbH

DOI: 10.1136/annrheumdis-2017-eular.4964

THU0008 MAST CELLS SHOW A REPROGRAMMED TRANSCRIPTIONAL SIGNATURE FOLLOWING REPEATED IGG STIMULATIONS


Background: Mast cell numbers are increased in the rheumatoid arthritis joint. We have previously shown that mast cells can be activated by IgG-ACPA leading to the production of proinflammatory cytokines. However, not much is known about the resulting function when mast cells would repeatedly engage IgG, a likely scenario given the long life span of mast cells (up to a year) and the perpetual presence of IgG-ACPA in the joints. We have recently shown that mast cells triggered repeatedly through their Ig Fc epsilon receptor undergo a reprogramming of their responses (Suurmond et al. JACI 2016) by expressing de novo transcribed genes in the antigen presentation and pathogen defense response pathways.

Objectives: The aim of the current work was to determine whether mast cells show similar changes in their response mode following repeated interactions with IgG.

Methods: Human cord blood-derived mast cells were treated for 2 weeks with plate-bound IgG. The expression profile of naive or treated mast cells was measured through RNA sequencing, quantitative RT-PCR, flow cytometry. Protein secretion was measured with ELISA and Lumimex assays. Metabolic changes were measured using HPLC mass-spectrometry.

Results: Similar to our previous work on Fc Epsilon receptor, we observe a dampening of the normal IgG responses with a set of novel genes upregulated. Interestingly, the non-exo-neo-transcribed factor regulating T cell proliferation and plasma cell differentiation, the top SNP in GDMD was a missense variant and correlated with gene expression of neighboring genes, and this could explain the association in this locus. We found different HLA association patterns between the two populations or two subtypes. Enrichment analysis suggested the importance of CD4 naïve primary T cells.

Conclusions: Our study provides evidence that mast cells are reprogrammed upon repeated IgG triggering. In contrast to repeated Fc Epsilon Receptor triggering, different pathways are affected, implying stimulus-specific effects. Our work has important implications for the understanding the role of mast cells in rheumatoid arthritis.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6326

**THU0009**  IN VITRO STUDIES USING CYBRIDS, SHOW THAT MTDNA IN IMMUNE SIGNAL 2 CHECKPOINT MOLECULE EXPRESSION ALTERED MIRNAS PROFILES IN PLASMA-DERIVED Cybrids were developed using 143B.TK- Rho-0 cell line (nuclear donor) and patients with knee OA. Patients with knee OA. Objectives: The aim of this work is to test the real role of mtDNA in cellular activity, using cybrids with miRNA from healthy donors (without OA) and from patients with knee OA. Methods: Cybrids were developed using 143B.TK- Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (without AO-N) and knee OA donors. The OXPHOS function was evaluated by Seahorse XFp after addition of oligomycin, FCCP and Rotenone/Antimycin A. The metabolic status was evaluated by glucose consumption and lactic acid production. The glycolytic activity was measured after addition of glucose, oligomycin and 2-dioxycarnosine. The flow cytometry was used to evaluate the mitochondrial membrane potential (ΔΨm).

**Conclusions:**
- Cybrids have different mitochondrial behaviour, being N more efficient using glucose via glycolysis. We found differences statistical significance in the parameters that describe the mitochondrial respiration capacity, in this line OA cybrids had lower mitochondrial respiration and produce less ATP than the cybrids obtained from healthy patients. These results showed that the mitochondria obtained from healthy and OA donors had a different behaviour.
- These data also offer a real rationale for why mitochondria alterations play an important role in the incidence of OA.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5930

**THU0010**  ALTERED MIRNAS PROFILES IN PLASMA-DERIVED EXOSOME OF PATIENTS WITH ANKYLOSING SPONDYLITIS BY SMALL RNA-SEQ ANALYSIS Y. Huang, T. Li, Z. Huang, W. Deng, S. Zheng, X. Guo, Z. Huang, Guangdong No. 2 Provincial People’s Hospital, Guangzhou, China

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, which is difficult to diagnose in the early stages. Increasing evidences have shown that MicroRNAs (miRNAs) may serve as novel biomarkers for AS. Exosome can function as vehicles to deliver miRNAs in body fluids including saliva and plasma. However, the relationship between exosome-delivered miRNAs and AS has yet to be determined.

Objectives: The aim of this study is to detect the altered miRNAs profiles of plasma-derived exosome in AS patients by small RNA-Seq analysis.

Methods: RiboPlus™ kit was used to isolate exosome. Small RNA Sample Pre Kit was used to build libraries in 3 AS patients and 3 healthy volunteers (HV), following by IlluminaHiSeq platform sequencing and bioinformatics analysis. Quantitative reverse-transcription PCR (qRT-PCR) was used to confirm the expression of the highly expressed miRNA.

**Results:**
- miRNA21–5P and miRNA423–5P are higher expressed in another 10 AS patients and 10 HV, and receiver-operator characteristic (ROC) curve was used to evaluate the diagnostic value of miRNAs.
- miRNA423–5P had significant diagnostic value for AS with the AUC of 0.890 (CI95%: 0.729–1.057) and 0.835 (CI95%: 0.621–1.039) respectively (Fig.1-F).

**Conclusions:**
- The miRNAs profiles in plasma-derived exosome of AS patients are significant different from HV.
- miRNA21–5P and miRNA423–5P are higher expressed in AS patients. Thus, plasma-derived exosomal miRNAs might be reliable biomarkers to identify AS.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5637

**THU0011**  IMMUNE SIGNAL 2 CHECKPOINT MOLECULE EXPRESSION IN RHEUMATOID ARTHRITIS DISEASE PROGRESSION A.M. Walsh1, M. Canavan2, Y. Guo1, T. McGarry2, Y. Yin1, M.D. Wechalekar3, M.D. Smith2, S.M. Proudman 4, C. Orr5, S. Kelly6, C. Pitzalis5, D.J. Veale5, U. Fearon5, S. Nappaj1, Janssen R&D, Spring House, United States; 2Molecular Rheumatology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin, Ireland; 3Patients University Royal Free, University College London, London, UK; 4Royal Free University College London, Discipline of Medicine, University of Adelaide, Adelaide, Australia; 5St. Vincent’s University Hospital, Dublin, Ireland; 6Queen Mary University of London, London, United Kingdom

Background: Deep profiling of synovial tissue samples from rheumatoid arthritis (RA) patients may reveal the molecular underpinnings of phases of RA progression and provide new therapeutic targets to intervene earlier in disease pathogenesis.

Objectives: We sought to identify the molecular pathways expressed in different stages of disease (from seropositive subjects without clinically apparent synovitis to those with established disease) in synovial tissue compared to non-RA controls.

Methods: Transcriptomics profiling was performed on RNA isolated from synovial tissue biopsies. Normal synovium was collected from subjects with knee pain and without diagnosis of OA or RA (n=28). Arthralgia tissue was collected from ACPA-positive subjects without synovitis (n=10). Early RA tissue was collected from patients recently diagnosed (<1 year) with RA (n=57). Established RA tissue was collected from ACPA-positive subjects with >1 year of disease duration (n=95). Protein expression was confirmed on infiltrating immune cells from synovial biopsy cell suspensions by flow cytometry in separate RA subjects.

Results: Several pathways previously identified as important for RA pathogenesis (e.g., lymphocyte activation, osteoclast differentiation, N-kappa B signaling) were enriched in differentially expressed genes in disease synovial biopsies compared to normal tissue samples. Interestingly, several genes known to function in T cell activation as signal 2 co-stimulatory or co-inhibitory molecules were differentially expressed, even in arthralgia and early RA subjects. 66 of 81 known co-stimulatory or co-inhibitory genes profiled were differentially expressed (FDR <5% and absolute fold-change >2) in disease samples from at least one cohort. The genes encoding co-stimulatory proteins that were increased compared to normal included CD28, CD40LG, CD40 and ICOS. Interestingly, some of the genes encoding co-inhibitory proteins were increased (PDCD1/ PD-1, CD274/PD-L1, HAVCR2/TIM3, TIGIT, BTLA), whereas others showed decreased expression (C10orf54/VISTA and LAG3) compared to normal controls. We focused on CD28 expression, which is elevated in “pre-RA” arthralgia samples, proposing that anti-CD28 therapeutics could be candidates for RA disease prevention. By flow cytometry we demonstrated that a majority of CD4+ (>90%) and CD8+ (~60%) T
cells from RA synovial biopsy cell suspensions (n=4) showed surface expression of CD28.

Conclusions: Our results generated a unique dataset from different phases of RA progression. Our results provide guidance for the selection of co-signaling molecules as therapeutic targets as well as for preventing the progression to RA. In particular, CD28 expression was elevated in synovial tissue biopsies before the development of RA and it was also expressed on the majority of synovial tissue infiltrating CD4+ and CD8+ T cells from RA patients. These observations provide rationale to target CD28 for both RA treatment and disease interception.

Disclosures of Interest: None declared.
or using other stimuli, i.e. IL-4 and TNF-α, indicating a specific function for the rs3761847 polymorphism in unstimulated and LPS+IFN-γ-activated monocytes.

**Conclusions:** Our findings suggest that there is no relationship between invasive capacity of RASF or expression of TRAF1-C5 genes and genotype at rs3761847. In contrast, we report an association of the rs3761847 genotype and TRAF1 expression in monocytes. These data underline the importance of studying genotype-phenotype associations in the different cell types relevant for RA pathogenesis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6066

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**THU0015**  
**INVESTIGATION OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) IN GREECE: NEW SUSCEPTIBILITY LOCI**

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**Background:** Juvenile idiopathic arthritis (JIA) is an autoimmune disease characterized by persistent chronic arthritis, in which both genetic and environmental components are involved [1]. Different genetic variations have been reported as risk factors for JIA, but a difficulty of the replication of results in different ethnic backgrounds indicates the existence of an ethnic heterogeneity of genetic factors for JIA.

**Objectives:** We sought to validate three single nucleotide polymorphisms (SNPs), namely PTPRC (rs10919563), TYK2 (rs4750316) and PRKCQ (rs4750316) previously found to be associated with JIA [2–4], and to investigate whether the VNTR polymorphism was genotyped by TaqMan primer-probe sets, using a Real-Time PCR platform (Applied Biosystems, ViA™ 7 Real-Time PCR System), while eNOS VNTR polymorphism was genotyped by PCR. Odds ratios (OR) and 95% confidence intervals (CI) were calculated and P-values of the intreraction.

**Results:** A case–control association study was conducted enrolling 4 successfully genotyped markers. eNOS OR=0.40, 95% CI=0.20–0.79, P=0.019; and OR=0.51, 95% CI=0.14–0.84, P=0.019; and OR=0.51, 95% CI=0.32–0.82, respectively. Otherwise, the CT genotype of the COL3A1 rs2138533 polymorphism (OR=2.89, 95% CI=1.28–6.5, P=0.011); and the CT genotype of the G allele of the COX2 rs484844 polymorphism (OR=2.22, 95% CI=1.11–4.43, P=0.024) were associated with an increased risk of OA. However, by using of epistatic interactions between 1-HIF-1 alpha pathway polymorphisms, we found that the gene-gene interaction had a synergistic effect over the estimated OR-values (see table).

**Conclusions:** In this study we could observe that the gene-gene interaction of the HIF-1α signaling pathway highly increases the risk of developing OA, with the exception of COL2A1 and HIF1α interaction which had a protective role against OA. Further studies are needed to validate this results.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2258

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**THU0017**  
**COMBINATION OF EGRF AND BLYS GENE EXPRESSION IN LUPUS NEPHRITIS**

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**Background:** Lupus nephritis (LN) is a severe complication of Systemic Lupus Erythematous (SLE). Non-invasive biomarkers are needed for diagnosis of LN and to identify patients at risk of a renal flare (1). Thus the presence of biomarkers associated with inflammation, tissue damage or cell activation in the urine of patients with LN may be a useful tool in the evaluation of LN patients. The glomerular filtration rate (GFR) is considered the best overall index of renal function in health and disease. Because GFR is difficult to measure in clinical practice, most clinicians estimate the GFR (eGFR) from the serum creatinine concentration (2). B Lymphocyte Stimulator (BLYS) is a cytokine that fosters B cell activation, antibody production, B cell - T cell interaction and plasma cell survival. These events have been demonstrated to play a role in patients with LN (3).

**Objectives:** We evaluated urinary levels of BLYS as biomarker for LN and their relationship with eGFR.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2131

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**THU0016**  
**A COMPREHENSIVE CONTRIBUTION OF GENES OF THE HIF-1α INFLUENCING PATHWAY TO KNEE OSTEOARTHRITIS SUSCEPTIBILITY**

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**Background:** The hallmark of osteoarthritis (OA) is the breakdown of articular cartilage. Articular cartilage is an avascular tissue, and this generates a hypoxygen microenvironment. Hypoxia inducible factor-1α (HIF-1α) is the main transcriptional regulator of cellular and developmental response to hypoxia.

**Objectives:** The present study was designed to investigate whether polymorphisms of the HIF-1α signaling pathway are involved in the development of knee OA.

**Methods:** A total of 243 unrelated Mexican-mestizo individuals comprising 93 knee OA patients and 150 healthy controls were recruited into the study. 42 genetic polymorphisms from 22 genes involved in the HIF-1α signaling pathway (PIK3R1, AKT2, GSK3B, IL6, AGER, HIF1A, EGLN1, VHL, HIF1AN, VEGFA, EPO, NOS2, NOS3, IGFI, EGF, EDN1, MMP1, MMP3, MMP13, CA1, COL2A1, COL3A1) were genotyped in cases and controls using TaqMan-based allelic discrimination assays.

**Results:** After adjusting for age, sex and admixture, significant associations with knee OA were found for 7 SNPs in the case-control study. The following genotypes and alleles were associated with protection against OA: the CT genotype of the HIF1AN rs11190613 polymorphism (OR=0.44, 95% CI=0.19–1.0, P=0.05); the AA genotype of the VEGFA rs1570360 polymorphism (OR=0.14, 95% CI=0.02–0.69, P=0.016); the GT genotype and T allele of the VEGFA rs729761 polymorphism (OR=0.47, 95% CI=0.22–1.0, P=0.05; and OR=0.51, 95% CI=0.27–0.97, P=0.041, respectively); the GA genotype of the COL2A1 rs1793953 polymorphism (OR=0.40, 95% CI=0.20–0.79, P=0.008); and the GG genotype and G allele of the Ckm rs484844 polymorphism (OR=0.34, 95% CI=0.14– 0.84, P=0.019; and OR=0.51, 95% CI=0.32–0.82, respectively). Otherwise, the CT genotype of the COL3A1 rs2138533 polymorphism (OR=2.89, 95% CI=1.28–6.5, P=0.011; and the CT genotype of the G allele of the IGFI rs757671 polymorphism (OR=2.22, 95% CI=1.11–4.43, P=0.024) were associated with an increased risk of OA. However, by using of epistatic interactions between 1-HIF-1α pathway polymorphisms, we found that the gene-gene interaction had a synergistic effect over the estimated OR-values (see table).

**Conclusions:** Using a pilot study. BMC Musculoskelet Disord 2015; 16:218.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2258
Methods: Urine samples (n=86) were obtained from LN patients and classified in two groups: patients with eGFR > 60 (GFRhigh, n=48, 62F/6M, age: 34.07±13.24) and patients with eGFR < 60 (GFRlow, n=18, 14F/4M, age: 35.22±13.76). RNA from urine samples was isolated using TRIzol-Chloroform technique and then reverse-transcribed using random primers. Levels of BLyS expression were evaluated using Quantitative Real Time PCR (QPCR). All amplifications were carried out in duplicate and threshold cycle (Ct) scores were averaged for calculations of relative expression values. The Ct scores were normalized against β2M scores by subtracting the corresponding statistically significant difference between groups (p=0.0288).

Background: Lupus Nephritis (LN) is one of the most severe forms of systemic lupus erythematosus (SLE) (1). Angiotensinogen (AGT) gene encodes the only glycoprotein known to be a precursor of the vasopresor angiotensin II (Ang II). Ang II is also a growth factor and a profibrogenic cytokine (2). In kidney allograft dysfunction (3). In LN, AGT deserves evaluation.

Objectives: To investigate AGT expression in biopsies and urines from LN patients.

Results: DCt is inversely proportional to BLyS expression. We evaluated data from ΔCt analysis observing that mRNA levels of BLyS in eGFRlow (6.193±1.877) were higher than those from eGFRhigh (7.564±2.326), with a statistically significant difference between groups (p=0.0288).

Conclusion: In the present cross-sectional study, increased levels of BLyS were observed in patients with eGFR < 60. These gene expression results might be linked to B cell activation and proliferation in kidney and thus in urine samples. Combination of eGFR and BLyS appears to be a good biomarker.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4793

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<th>THU0018</th>
<th>ANGIOTENSINOGEN AS A MARKER OF INJURY IN LUPUS NEPHRITIS</th>
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L.A. Mas1,2, S. Retamozo2, M.J. Haye Salinas3, V. Sauri2,3, E.V. Palominio1,2, J.L. De la Fuente2,4, M. Angelina2,3, J.P. Priola2,3, A. Alvarillos2,3, T. Alvariellos1, T. Immunogenetics, Hospital Privado. Universitario de Córdoba; 2Instituto Universitario de Ciencias Biomédicas de Córdoba; 3Rheumatology; 4Nephrology, Hospital Privado. Universitario de Córdoba; 5Nephrology, Hospital Raúl Feryrea, Argentina

Background: Lupus Nephritis (LN) is one of the most severe forms of systemic lupus erythematosus (SLE) (1). Angiotensinogen (AGT) gene encodes the only glycoprotein known to be a precursor of the vasopresor angiotensin II (Ang II). Ang II is also a growth factor and a profibrogenic cytokine (2). In kidney allograft dysfunction (3). In LN, AGT deserves evaluation.

Objectives: To investigate AGT expression in biopsies and urines from LN patients.

Methods: 32 biopsies/urines paired from 32 LN patients was included. Kidney biopsies were evaluated according to the ISN/RPS classification system. Levels of AGT were evaluated using Quantitative Real Time PCR. Threshold cycle (Ct) scores were averaged for calculations of relative expression values. The Ct scores were normalized against Ct scores by subtracting the corresponding statistically significant difference between groups (p=0.0288).

Conclusions: In the present study we found a potential utility of AGT mRNA levels in samples of active vs remission LN patients. Prospective studies are needed for confirming these results.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6760
INCREASED EXPRESSION OF CCN4/WISP1 IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS WITH HOMEOSTASIS

M. van den Bosch1, Y.F. Ramos2, W. den Hollander2, N. Bömer2, R.G. Nelissen3, J.B. Bovée4, A.B. Blom1, I. Meulenbelt2.

Objectives: To investigate the clinical characteristics of 34 cases with systemic juvenile idiopathic arthritis (SJIA) and macrophage activation syndrome (MAS), and to determine specific gene-gene interactions.

Methods: 34 SJIA cases with MAS were included. All cases underwent genetic testing for polymorphisms in the PRF1, STX11, UNC13D and STXBP2 genes.

Results: Frequencies of the SNPs in the MAS group were compared to a control group. PRF1 rs885822, STXBP2 rs10001 and HLA-DQB2 A*0301 were significantly associated with increased risk to develop MAS in our Italian RA cohort.

Conclusions: This study confirms the association between SJIA and MAS in the Italian population, and identifies specific gene-gene interactions that may contribute to the pathogenesis of MAS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6252
SYNOVIAL FLUID MiRNAs MULTImARKER ANALYSIS IN PATIENTS WITH RHEUMAtoID ARTHRITIS

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Background: Recent epigenetic studies reveal the pathogenic role of micro-r Nucleic acids (microRNAs) and their targets in the inflammatory process in rheumatoid arthritis (RA), miRNAs play crucial role in controlling and modulating inflammatory and Medical Synovial expression of miRNAs was shown to be deregulated as compared to healthy controls. The deregulated function of regulatory T cells, to the chronic synovial inflammation and bone destruction 1,2.

Objectives: To perform a multimarker analysis of synovial fluid (SF) expression levels of miR-146a, miR-155 and miR-223 in RA patients in regard to their role as diagnostic biomarkers.

Methods: Total RNA was isolated from the SF of 48 RA patients and 11 healthy controls (HCs) and expression levels of miR-146a, miR-155 and miR-223 were determined by quantitative real-time polymerase chain reaction (qPCR). We used SYBRGreen technology. Relative changes of gene expression levels of the miRNAs were calculated by 2-ΔΔCt method and SPSS were used for statistical analysis. RNU6B gene was used as a reference control for normalization.

Results: miR-146a, miR-155 and miR-223 showed overexpression in RA SF compared to HCs (in 70.83%, 79.17% and 79.17% of the patients, respectively) and could be used to differentiate RA patients from HCs (p=8.10-10, p=8.10-10 and p=8.10-10, respectively). The ROC curve analysis showed diagnostic accuracy of these miRNAs in SF for distinguishing RA patients from HCs.

Conclusions: Our study demonstrates that the multimarker analysis of the expression levels of miR-146a, miR-155 and miR-223 in RA patients is a valuable diagnostic tool in the management of RA. The diagnostic accuracy of these miRNAs is high and they could be used as biomarkers in the early diagnosis of RA. Additionally, the multimarker analysis of these miRNAs could be used as a complementary tool in the management of RA patients. Further studies are needed to validate these findings in larger populations and different clinical settings.

Disclosure of Interest: The study was supported by Grant 14-D/2012 and 55/2013

Cytokines and inflammatory mediators

IL-6 TRANs-SIGNALING CAUSES ACCELERATED ATHEROSCLEROSIS IN DISEASE PRONE ANIMALS

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Background: Cardiovascular (CV) disease is a major cause of mortality in patients with rheumatoid arthritis (RA). CV risk is increased early in the disease course. Subclinical inflammation and dyslipidaemia are often seen in RA before patients become symptomatic, suggesting the presence of subclinical CV disease. Inflammation, as measured by acute phase reactants, is associated with CV disease in RA. Interleukin (IL)-6 is a major driver of the acute phase response in RA. Elevated IL-6 levels may contribute to chronic disease progression. Control of these processes is regulated by two modes of IL-6 signaling: classical IL-6 receptor signaling and IL-6 trans-signaling. Cellular responses controlled by IL-6 trans-signaling are mediated via soluble IL-6 receptor (sIL-6R) and are widely considered to promote deleterious pro-inflammatory outcomes [1]. We hypothesize that atherosclerosis may predate diagnosis of RA, and is accelerated by IL-6 trans-signaling during active arthritis. Here, we investigate this hypothesis using the established ApoE-deficient (apoE-/-) mouse model of atherosclerosis.

Objectives: To examine the effect of IL-6 classical and trans-signaling on atherosclerosis by administering IL-6 or Hyper-IL-6 (a IL-6: sIL-6R fusion protein) to apoE-/- mice.

Methods: Male apoE-/- mice were fed a high-fat diet for 8 weeks starting at 8 weeks of age. Mice were divided into 4 groups. Group 1 received IL-6 (160 ng twice weekly, delivered i.p.), and Group 2 and 3 received Hyper-IL-6 (500 ng and 1 μg delivered i.p. twice weekly) for 8 weeks. Group 4 received PBS twice weekly for 8 weeks. Serial transverse 7 um b rachiocephalic artery cross-sections were cut and stained with haematoxylin and oil red-O. Lesion size was determined by computer-assisted morphometry, using Image J on stained sections. Brachiocephalic plaque size in mice treated with PBS, IL-6 and Hyper-IL-6 were compared using ANOVA and post-hoc Tukey test.

Results: Mice with Hyper-IL-6 had significantly larger brachiocephalic plaques (mean plaque area 0.73±0.04 mm²) than those administered PBS (0.018±0.01 mm², p < 0.001), and IL-6 (0.033±0.017 mm², p < 0.015; Fig.1A). Similarly, mice administered Hyper-IL-6 [1μg] had a significantly higher percentage of the brachiocephalic artery occupied by plaques (45.3±18.1%) compared to those administered PBS [0.7±0.7%, p < 0.001] or IL-6 [0.1±0.2%, p < 0.002] (Fig.1B). Mice administered Hyper-IL-6 [0.5μg] had significantly higher percentage plaque (27.7±16.2%) than PBS administered mice, p = 0.015. There was no significant difference in total cholesterol, HDL, LDL, triglycerides, free fatty acids or cholesterol/HDL ratio between the groups.
Conclusions: IL-6 trans-signaling leads to accelerated atherosclerosis in disease susceptible animals. This effect is independent of changes in serum lipid profiles.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2871

THU0026 OSIM IS MORE EFFECTIVE THAN IL-6 AT INDUCING ENDOMT OF HUMAN DERMAL MICROVASCULAR CELLS
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Background: Oncostatin-M (OSM) and interleukin-6 (IL-6) are members of the IL-6 superfamily and signal via glycoprotein 130 (gp130). OSM signals with either the type I receptor complex, gp130/Leukemia Inhibitory Factor Receptor (LIFR), or the type II receptor complex, gp130/OSM receptor (OSMR), whilst IL-6 signals via gp130 with the IL-6 receptor (IL-6R) or by trans signalling with soluble IL-6R (sIL6-R). Endothelial cells (ECs) express both gp130 and OSMR [Brown TJ et al 1991], however it is unclear whether ECs express IL-6R [Romano M et al 1997; Nilsson MB et al 2005]. Endothelial to mesenchymal transition (EndoMT) is the phenotypic transition of ECs into mesenchymal cells where ECs lose their specific EC markers, detach from the endothelial layer and initiate the expression of mesenchymal cell products. EndoMT is associated with vascular dysfunction, one of the early manifestations of systemic sclerosis. The role of OSM and IL-6 in EndoMT has not yet been fully elucidated.

Objectives: To determine the effect of OSM and IL-6/sIL-6R on microvascular EC migration, proliferation and EndoMT.

Methods: Human dermal microvascular ECs (HDMECs) were treated with human recombinant proteins OSM (1–100 ng/mL), IL-6 (10–100 ng/mL) and sIL-6R (10–100 ng/mL). Cell migration and proliferation were measured with Live-Cell imaging system over 50 hours and analysed using a two-way ANOVA. Secretion of Collagen type I protein was measured at 48 hours by western blot analysis of media supernatant from HDMEC cultures. Changes in VE-Cadherin and F-actin expression were examined by immunofluorescence over 72 hours.

Gene expression was measured at 3 hours using quantitative RT-PCR analysis and analysed by Student’s paired T-test.

Results: OSM and IL-6, with or without IL-6R, significantly increased (P<0.001, n=3 donors) HDMEC migration and proliferation and secretion of extracellular matrix (ECM) protein Collagen I compared to the control group. OSM, but not IL-6 with or without sIL-6R, reduced expression of EC marker VE-Cadherin and increased expression of elongated F-actin stress fibres (n=2 donors). OSM significantly affected (P<0.05, n=3 donors) expression of EndoMT genes SNAIL1, SNAIL2, SNAIL3 and TWIST [Figure 1] and ECM genes MMP1, MMP2 TIMP1 and TIMP2 compared to the control. Many of the gene changes in response to OSM were further augmented by co-stimulation with sIL-6R, IL-6 with or without sIL-6R only significantly affected (P<0.05, n=3 donors) EndoMT genes SNAIL1 and SNAIL2 and ECM gene TIMP1.

Conclusions: OSM induced a stronger EndoMT phenotype in HDMECs in comparison to IL-6, suggesting that OSM is capable of initiating EndoMT activity in microvascular cells. The augmented effects observed for OSM with sIL-6R also suggests that OSM is capable of binding the sIL-6R and initiating signalling in HDMECs in vitro.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1271

THU0027 CLUSTERIN IS ELEVATED IN SERUM AND MUSCLE TISSUE IN IDIOPATHIC INFLAMMATORY MYOPATHIES AND IS ASSOCIATED WITH DISEASE ACTIVITY
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Background: Clusterin (also known as apolipoprotein J) is a molecular chaperone that participates in inflammatory and apoptotic processes. Recent data indicate its possible protective role in the development of chronic autoimmune disorders.

Objectives: The aim of this study was to analyse the skeletal muscle expression of clusterin and its serum levels in patients with idiopathic inflammatory myopathies (IIM) and in healthy donors, and to examine the association of clusterin with disease activity.

Methods: Clusterin mRNA expression in skeletal muscle specimens, obtained by muscle biopsy (mini-invasive Bergstrom technique), was determined using qPCR assays in 65 patients with IIM (27 dermatomyositis (DM), 28 polymyositis (PM), 10 immune-mediated necrotizing myopathy (IMNM)) and in 54 healthy individuals. Disease activity was assessed using myositis disease activity assessment visual analogue scales (MYOACT), health assessment questionnaire (HAQ) and global disease assessment evaluated by doctor and patient. Data are presented as mean ± SD.

Results: Clusterin mRNA expression in skeletal muscles was increased in patients with IIM compared to healthy donors (p=0.029). In addition, serum clusterin levels were significantly higher in all IIM patients than in healthy subjects (r=0.59±12.4 vs 68.4±12.4, p<0.0001) and also in individual subsets of patients in comparison to the control group (DM: r=0.7±24.7, PM: r=0.6±23.7, IMNM: r=0.8±18.0, p<0.0001 for all). Clusterin levels in all patients with IIM positively correlated with MYOACT (r=0.52, p<0.0001), global disease assessment evaluated by doctor (r=0.49, p<0.001), global disease assessment evaluated by patient (r=0.52, p<0.001), and in 54 healthy individuals. Disease activity was assessed using myositis intention to treat index (MITAX), myositis disease activity assessment visual analogue scales (MYOACT), health assessment questionnaire (HAQ) and global disease assessment evaluated by doctor and patient. Data are presented as mean ± SD.

Conclusions: We demonstrate increased local and systemic expression of clusterin in IIM patients compared to healthy individuals and its association with disease activity, especially in dermatomyositis.

Acknowledgements: Supported by the project of MCHCR for conceptual development of research organization 00023728 and project NV16–33746A.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5792
THU0028

**TYPE I INTERFERON SIGNATURE IN THE PERIPHERAL BLOOD AND CXCL4 PLASMA LEVELS IN PATIENTS WITH SYSTEMIC SCLEROSIS**


**Background:** Type I Interferon (IFN) pathway is activated in Systemic Sclerosis (SSc) and represents a therapeutic target currently being tested in clinical trials, while higher IFN levels have also been associated with pulmonary fibrosis in these patients. On the other hand, in vitro experiments using plasmacytoid dendritic cells from patients with SSC suggest an interplay between the chemokine (C-X-C motif) ligand 4 (CXCL4), a potential biomarker in SSc, and type I IFN. [1]

**Objectives:** To test whether type I IFN-induced gene expression in the peripheral blood associates with particular clinical and laboratory features, including plasma CXCL4 levels, in patients with SSc.

**Methods:** Forty six patients with limited and 19 with diffuse SSc (60/65 women, aged 54±14 years, disease duration ranging between 0.5–27 years) and 20 healthy controls were examined. Peripheral whole blood samples (3ml) were subjected to cDNA synthesis and the expression of 3 genes (IFIT1, MX1, IFI44) that are preferentially induced by type I IFN was quantified by real time PCR. Type I IFN individual scores were calculated as described [2]; scores were arbitrarily considered as high when exceeding the mean value plus 3SD of the corresponding healthy control scores. Plasma CXCL4 levels were determined by ELISA.

**Results:** A high type I IFN score (i.e.>8) ranging from 8.4 to 145 was found in 21/65 (32.3%) patients with SSc, compared with none of 20 healthy controls (p=0.002). Patients with high type I IFN scores demonstrated higher erythrocyte sedimentation rate and lower differing lung capacity for carbon monoxide (DLCC) than the remaining patients (p=0.002 and p=0.02, respectively, by Mann-Whitney U test). Other disease variables, including extent of skin involvement and autoantibodies, were not associated with high type I IFN score.

Individual type I IFN scores positively correlated with the corresponding CXCL4 plasma levels (Spearman’s r: 0.53, p-value: 0.02). A prominent type I IFN signature was observed in the peripheral blood of one third of patients with SSc in association with upregulated inflammatory response, reduced DLCC levels and higher CXCL4 plasma levels. Further prospective data are required to establish the role of type I IFN as an additional novel biomarker in SSc.

**References:**

**DOI:** 10.1136/annrheumdis-2017-eular.4066

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THU0030

**IL-2C SUPPRESSES CIA IN MICE BY THE TH1/TH17 IMMUNE RESPONSES DUE TO ENHANCEMENT OF BOTH TREG NUMBERS AND TREG FUNCTIONS**

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**Background:** Interleukin-2 (IL-2) induces regulatory T cells (Tregs) and reduces disease activity such as graft versus-host disease and systemic lupus erythematosus. IL-2/anti-IL-2 monoclonal antibody immune complex (IL-2IC) increases the half-life of IL-2 in vivo and specifically induces Tregs. We previously demonstrated that administration of IL-2IC suppressed collagen-induced arthritis (CIA) in mice (EULAR 2015).

**Objectives:** To clarify complex regulatory network of IL-2IC in autoimmune arthritis, we examined the suppression mechanism of IL-2IC induced Tregs to Th1 and Th17.

**Methods:** Male DBA/1 mice were inoculated by injection of 200μg of Type II collagen emulsified with an equal volume of complete Freund adjuvant intradermally at the base of the tail of mice (first immunization). Second immunization was given 21 days after first immunization. IL-2/anti-IL-2 were prepared by mixing 2 μg of anti-IL-2 antibody (clone JES9–1D7) with 1 μg of mouse IL-2 for 15 minutes. The mice were injected with either PBS as a control or IL-2/2 IC (5μg/mouse) intraperitoneally for 3 days. Mouse paws were scored for arthritis using a macroscopic scoring system ranging from 0 to 4 (0, no swelling or redness; 1, swelling/redness of paw or one joint; 2, two joints involved; 3, more than two joints involved; and 4, severe arthritis of the hind paw and joint). Arthritis scores from both hind paws were added up and represented as the score of the all four paws. Peripheral blood cells were stained with anti-CD25 (PC61), anti-CD4 (RM-5), anti-FOXp3 (FJK-16s) and CD4+CD25+Foxp3+ Tregs were analyzed by flow cytometry. Th1 and Th17 cells infiltrating in the synovium were examine by immunohistochemistry stained with anti-IFN-γ and anti-IL-17, and analyzed by flow cytometry.

**Results:** To define the effects of IL-2IC on established CIA, IL-2IC was administrated for 3 days from day 21 to day 23 after the first immunization (day 0 to day 2 after the second immunization) of CIA. To define the effect of IL-2IC on early stage of disease induction we administrated IL-2IC from day 0 to day 2 after first immunization. We observed a significant decrease in both the incidence and severity of arthritis in these CIA mice. Injection of IL-2IC effectively elicited more than 2-fold expansion of CD4+CD25+Foxp3+ Tregs in peripheral blood cells than control mice. Th1 and Th17 cells infiltrations in the synovium was significantly inhibited by IL-2IC treatment. In vivo suppression assay demonstrated significant augmentation of the suppressive capacity of CD4+CD25+Treg cells in IL-2IC treated mice. Intracutaneous cytokine staining revealed that IL-10 production by CD4+ cells in IL-2IC treated spleen increased four folds than in controls, and IL-17-producing helper T cells (Th17) and IL-17-producing helper T cells (Th17) were significantly decreased.

**Disclosures:** These observations indicate that IL-2IC not only induce Tregs, but also augments Treg function by enhancing IL-10 production. Therefore Tregssuppress Th1 and Th17 cells.

**DOI:** 10.1136/annrheumdis-2017-eular.4644
**THU0031**

**THERAPEUTIC TREATMENT OF ANTI-FRACTALKINE MONOCONAL ANTIBODY INHIBITS JOINT DESTRUCTION IN COLLAGEN-INDUCED ARTHRITIS MODEL**

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**Background:** In the Phase 1/2 clinical study, E6011, a novel humanized anti-fractalkine (FKN) monoclonal antibody (mAb) demonstrated a promising efficacy in active rheumatoid arthritis (RA) patients who were inadequately controlled by MTX and/or TNF-a inhibitors. However, the effect of anti-FKN mAb on joint destruction remains to be elucidated. In RA, synovium-infiltrated monocytes/macrophages cause synovitis and cartilage damage. Osteoclasts are generated from osteoclast precursor cells (OCPs) and cause cartilage destruction. FKN is expressed on endothelial cells and fibroblast-like synoviocytes in synovium in both experimental arthritis model and RA patients. FKN is also expressed on osteoblasts in neonatal mouse calvariae. CX3CR1, the receptor for FKN, is expressed on monocytes/macrophages and OCPs. Therefore, the interaction of FKN and CX3CR1 might play important roles in migration, differentiation and activation of these cells, leading to cartilage damage and bone erosion.

**Objectives:** We examined the efficacy of an anti-FKN mAb on collagen-induced arthritis (CIA) in mice, especially on joint destruction.

**Methods:** For the induction of CIA, DBA/1-J mice were immunized with bovine type II collagen (BII-C) with CFA (1:1) i.d. A dose of FKN mAb or control IgG was injected twice a week from the day of the 1st immunization (for the prophylactic treatment) or after the onset of CIA (for the therapeutic treatment). The clinical arthritis score was defined as the sum of the scores of four paws. Plasma concentrations of IL-6, TNF-a, serum amyloid A (SAA), Tartrate-Resistant Acid Phosphatase type 5b (TRAP-5b), Cartilage Oligomeric Matrix Protein (COMP) and Matrix Metalloproteinase 3 (MMP-3) were measured using ELISA. Radiological score was measured by the soft x-ray images of limb bones. Alcian blue/Alizarin red and Tartrate-Resistant Acid Phosphate (TRAP) staining were performed for histopathological analysis of bone destruction.

**Results:** In the prophylactic treatment, anti-FKN mAb markedly reduced the clinical arthritis score, soft x-ray score, and plasma levels of TRAP-5b, COMP and MMP-3, whereas plasma levels of IL-6, TNF-a and SAA were not significantly reduced compared with control IgG-treated mice. Histopathological analysis demonstrated almost complete suppression of joint destruction and dramatic reduction in the number of TRAP-positive cells by the treatment of anti-FKN mAb. Importantly, therapeutic treatment of anti-FKN mAb also significantly ameliorated clinical arthritis score and soft x-ray score. Synovitis, pannus formation, cartilage degradation and bone erosion were also strongly suppressed and the number of TRAP-positive cells in joint was also decreased by the therapeutic treatment of anti-FKN mAb.

**Conclusions:** Anti-FKN mAb demonstrated a remarkable efficacy in the arthritis score without affecting systemic inflammatory parameters and inhibited the joint destruction with the marked reduction of osteoclasts in CIA model. These results suggest that inhibition of FKN/CX3CR1 axis by a humanized anti-FKN mAb, E6011, is an attractive therapeutic strategy for the treatment of both inflammatory synovitis and joint destruction of RA.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5840

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**THU0032**

**THE ROLE OF S100A IN PAIN RESPONSE DURING EXPERIMENTALLY INDUCED ACUTE SYNOVITIS**

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**Background:** Synovitis-associated pain is an important aspect of arthritis pathology. Several inflammatory mediators released by the synovium have been implicated in the regulation of pain, including S100A8 and S100A9 which may contribute to the pathogenesis of joint destruction. In synovitis and during the acute inflammatory response in the synovium or via stimulation of the dorsal root ganglia (DRG), thereby enabling an increased phagocyte infiltration.

**Objectives:** To investigate the role of S100A in the pain response after induction of an acute synovitis using streptococcal cell walls (SCW) as a trigger, comparing S100A9-/- mice and their WT controls.

**Methods:** Acute synovitis was induced by a single i.a. injection of SCW in the knee joint of C57B16 (WT) mice and S100A9-/- mice, control mice received an i.a. saline injection. Serum S100A8/A9 levels were investigated by ELISA and expression of S100A8 and S100A9 in synovium and DRG by immunohistochemistry. Joint swelling and cell influx was assessed by 99mTc accumulation and histology, respectively. Pain response were investigated Incapacitance Tester (weight bearing), Catwalk (gait analysis) and von Frey’s filaments (mechanical allodynia). Gene expression of inflammatory mediators and neuron activation markers in DRG were determined by q-PCR.

**Results:** A single i.a. injection of SCW resulted in increased synovial expression of S100A8 and S100A9 and subsequent increased serum S100A8/A9 levels (2.6-fold, P < 0.001) 1 day p.i., which returned to basal levels at 7 days p.i. The increased expression of S100A9 did not contribute to the development of inflammation since joint swelling and cell influx were similar in WT and S100A9-/- mice 1 day p.i. Using the Incapacitance Tester, WT mice showed a marked and significant decrease in percentage of weight bearing on the SCW injected hindpaw (28%) compared to saline injection (47%, P < 0.001) 1 day p.i., whereas S100A9-/- mice did not. In addition, gait analysis showed that the stand-phase of the un.injected paws was significantly increased in S100A9-/- mice (0.044 and 0.030, respectively) while SCW injection in S100A9-/- mice did not show increased expression, which is in line in with the reduced pain response observed earlier in S100A9-/- mice.

**Conclusions:** These findings show that S100A9, which is released from the synovium upon inflammation, is an important mediator of inflammatory pain response in the knee, and that during the acute phase of inflammation is likely regulated via direct activation of TLR4 on nerve endings in the synovium and not via increased infiltration of phagocytes in the DRG.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3599

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**THU0033**

**LOCAL INJECTION OF ADIPOSE-DERIVED MESENCHYMAL STEM CELLS IN EXPERIMENTAL INFLAMMATORY OA RESULTS IN INTERLEUKIN-1β-MEDIATED ATTRACTION OF PMNS AND REDUCED S100A8/A9 RELEASE**

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**Background:** Recent studies have shown that mild synovitis in early phases of osteoarthritis (OA) is conducive to development of joint damage. OA synovitis is characterized by elevated levels of pro-inflammatory factors like S100A8, S100A9, interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). S100A8/A9 was found to be crucial in mediating joint destruction in inflammatory experimental OA. Previously we found that adipose-derived mesenchymal stromal cells (ASCs) exhibit immunosuppressive characteristics and reduce joint pathology after local application into mouse knee joints with experimental inflammatory OA. This protective effect is only perceived after intra-articular injection in early but not late stage OA, suggesting that the effect may be mediated by an inflammatory milieu.

**Objectives:** To examine the working mechanism of ASCs after early injection in experimental OA.

**Methods:** Experimental OA was induced by injection of collagenase into murine knee joints (CIOA). Total knee joints were stained with haematoxylin/eosin and the PMN-specific antibody NIMP-R14. ASCs were isolated from murine adipose tissue and stimulated for 24h with IL-1β or S100A8/A9. Gene expression in stimulated cells was examined using qPCR. Protein levels of chemokines were measured in culture supernatant using Luminex. Migration of MACS isolated bone marrow (BM-) PMNs towards ASC-conditioned medium (CM) was examined using Transwell inserts. ASCs were co-cultured with BM-PMNs and analyzed using histology and Luminex.

**Results:** ASC injection into day 7 CIA knee joints (when synovitis and IL-1β and S100A8/A9 levels are highest) caused a strong attraction of mainly PMN-like cells and their clustering around ASCs in the synovium shortly after injection (6h), which was confirmed by immunohistochemistry. IL-1β stimulation of ASCs in vitro strongly increased gene expression of PMN-attracting chemokines (KC, CXCL1, and CXCL7 as well as protein levels of KC, whereas S100A8/A9 did not. The migration of BM-PMNs through Transwell inserts towards CM of IL-1β-stimulated ASCs was significantly increased (from 5% to 10%) when compared to CM of non-stimulated ASCs. Next, ASCs were co-cultured with BM-PMNs in the presence or absence of IL-1β. After 6h, a clear clustering of neutrophils around ASCs was observed, with a significant increase in the number of ASCs clustering with PMNs, as well as a significantly elevated number of clustering PMNs per ASC after IL-1β stimulation. Interestingly, association of PMNs with ASCs lead to a significantly lowered release of KC protein by ASCs (69% and 76% lower after 24h and 48h respectively), as well as a significantly reduced release of S100A8/A9 protein by the PMNs. This coincided with lowering of S100A8/A9 levels in washouts of inflamed synovium 6h and 48h after injection of ASCs in day 7 CIA knee joints.

**Conclusions:** Local application of ASCs in inflamed CIA knee joints results in attraction and clustering of PMNs with ASCs in the synovium. This presumably runs via IL-1β-mediated up-regulation of chemokine release by ASCs, and ultimately results in significantly lowered S100A8/A9 levels.

**Acknowledgements:** This research was supported by the Dutch Arthritis Association.

**Disclosure of Interest:** None declared

THE INFLAMMATORY POTENTIAL OF CALCIUM PYROPHOSPHATE CRYSTALS DEPENDS ON THEIR CAPACITY TO INDUCE NF-κB AND MAPK PATHWAYS

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Background: Calcium pyrophosphate (CPP) crystal-induced inflammation is mainly driven by interleukin (IL)-1β, IL-18 production involves a two-step process, including the formation of pro-IL-1β through NF-κB activation and its maturation into active IL-1β through NLRP3 inflammasome activation. Two CPP crystal phases, namely monoclinic and triclinic CPP dehydrated (m- and c-CPPD) crystals are identified to have recently been recognized that m- and c-CPPD display different inflammatory potentials marked by a differential level of IL-1β production and other pro-inflammatory mediator expression.

Objectives: We aimed to assess the intracellular pathways upstream CPP-stimulated IL-1β production, according to the different inflammatory properties of CPP crystal phases.

Methods: Four synthesized and prokaryon-free CPP crystals [a-CPP (amorphous), m-CPPD or tetrahedrised (m-CPTP) and t-CPPD] (Grap P et al. 2014) and monosodium urate (MSU) crystals were used, in vitro, to stimulate THP-1 cell line or mouse bone marrow-derived macrophages (BMDM) in the presence or not of pharmacological inhibitors: Bafilomycin A1 (Baf); 11β-hydroxysteroid dehydrogenase (11βHSD) inhibitors; SB203580 (SB); MAPK p38 inhibitor; SP600125 (SP; JNK inhibitor) and PD98059 (PD; p42/44 MAPK inhibitor). The expression of pro- and anti-inflammatory cytokine genes was assessed by qRT-PCR, and IL-1β and IL-6 production by ELISA; MAPK phosphorylation by immunoblotting. NF-κB activation in THP-1 cells containing a gene reporter plasmid under control of NF-κB transcriptional factor. In vivo, we used murine air pouch model to assess the effects of NF-κB inhibition in CPP crystal-mediated inflammation.

Results: We previously demonstrated that in vitro m-CPPD crystals were the most inflammatory CPP crystals and induced a higher production of mature IL-1β associated to a higher expression of NLRP3 protein, and a higher IL-8 production and expression of inflammatory cytokine genes (IL-1β, IL-6, IL-8, TNF, COX-2) than t-CPPD, m-CPTPT and MSU crystals. a-CPP crystals did not have inflammatory property. m-CPPD crystals induced a higher NF-kB activation and a higher phosphorylation p38, p42/44 and JNK MAPKs than t-CPPD and MSU crystals. In parallel, we showed that inhibition of NF-κB completely abrogated mature IL-1β and IL-8 secretion and pro-IL-1β synthesis induced by all CPP crystals. Inhibition of JNK and p42/44 MAPK with SP and PD respectively, decreased both IL-1β secretion and NF-κB activation induced by CPP crystals. In vivo IL-1β and IL-8 production and neutrophil infiltration induced by m-CPPD crystals were dramatically decreased by NF-κB inhibitor.

Conclusions: Our results showed that IL-1β and IL-8 production induced by CPP crystals is completely dependent of NF-κB signaling. They suggested that the inflammatory potential of different CPP crystals relied on their capacity to activate both MAPK and NF-κB pathways. Differential level of NF-κB activation is partially dependent of MAPK phosphorylation. Additional studies are ongoing to investigate the underlying mechanisms.

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Disclosure of Interest: None declared. DOI: 10.1136/annrheumdis-2017-eular.4741

ROLES OF IL-6 IN RANKL- AND ACPA-MEDIATED OSTEOCLASTOGENESIS

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Background: We have shown previously in various experimental models that anti-citrullinated protein antibodies (ACPAs) can contribute to bone erosion and arthralgia through IL-8 dependent mechanisms.

Objectives: In cell cultures osteoclasts (OCs) played a prominent role in the ACPA-induced IL-8 secretion and therefore we decided to characterize in detail the autocrine regulation of OC differentiation by IL-8 in the presence or absence of ACPAs.

Methods: Peripheral blood monocytes were generated from healthy volunteers or patients with active rheumatoid arthritis (RA) and used to discover the role of RANKL and IL-8 in OC differentiation in the presence of ACPAs. We have shown previously that the M-CSF induced IL-8 plays a crucial role in OC differentiation in the presence of exogenous RANK-L. In the presence of ACPAs, OCs in the presence of M-CSF and RANKL. In the presence of ACPAs anti-citrullinated protein antibodies (ACPAs) can contribute to bone erosion and arthralgia through IL-8 dependent mechanisms.

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Objectives: In cell cultures osteoclasts (OCs) played a prominent role in the ACPA-induced IL-8 secretion and therefore we decided to characterize in detail the autocrine regulation of OC differentiation by IL-8 in the presence or absence of ACPAs.
Background: The drugs called Anti-TNF inhibitors are capable of inducing an immune response (immunogenicity). Its effectiveness may be affected by the development of Anti-Drug Antibodies (Ab).

Objectives:
- To assess the frequency of appearance of Anti-Drug Antibodies: Infliximab (IFX), Adalimumab (ADA), etanercept (ETN)
- To classify the failures of response
- To analyse the relationship between anti-TNFAb and concomitant treatment with DMARDs
- To observe whether there is a link between risk factors and drug levels

Methods: This is a retrospective, descriptive, observational study of patients with Rheumatoid Arthritis (RA), Spondyloarthritis (SpA), Psoriatic arthritis (PsA), Seronegative arthritis (SA) and Enteropathic arthritis (EA) with active disease and that were treated in the “University Health Care Hospital of León” between Jan-2015 and Jan-2016. Using ELISA Technology and the kits Promonitor®, it was possible to detect serum levels of IFX, ADA, ETN (reference values = 2.5 μg/mL, 5–6 μg/mL, and 0.8–1.2 μg/mL respectively) and of anti-drug antibodies. The samples were collected the same day of the administration, prior to it, always in a trough level. The gathered data was: demographic data, activity, time-to-disease progression, prior treatment with biologics, concomitant DMARDs, duration of the biologic treatment and dosage, quantization levels, anti-TNF antibodies, cardiovascular risk factors (CVRF) and smoking habits.

Results: Variables to study:
- N=40: IFX 50%, ADA 30%, ETN 20%
- Age 53.6±3.7 years old [95% CI], Women: 55%, time-disease progression: 12.3±2.7 years old.
- Type of disease: RA 47.5%, SpA 15%, PsA 20%, SA 7.5%, EA 10%
- DAS28: 3.5±0.4, BASDAI 4.7±0.5, BASFI 4.3±1.4.
- Frequency of administration: IFX 8.6±0.36 weeks, ADA 2.25±0.36 weeks, ETN 1.1±1.0 weeks.
- Reasons for requesting the levels:
  - Secondary failure (82%): IFX 90%, ADA 66.7%, ETN 12.5%
  - Primary failure (17%): IFX 5%, ADA 33%, ETN 25%
  - Infusion reactions (2.5%)
- Drug levels within the therapeutic range: IFX 10%, ADA 41%, ETN 50%.
- Formation of anti-TNF Ab of the sample: IFX 30%, ADA 16%, ETN 0%.
- DMARDs: presence of 62.5% (MTXc 64%, MTXvo 20%, Leflunomide, Sul-fasalazine e Hydroxychloroquine 16%).

Conclusions: We found the following conclusions:
- In the data collected, we observe that the IFX (30%) is the most immunogenic drug, followed by the ADA (16%) and being the ETN (0%) the one that so far has not presented anti-drug Ab, outcomes in agreement with the medical literature.
- The main reason for requesting has been the secondary failure (90%)
- The suboptimal levels of the drug and the presence of specific ab are correlated with the loss of clinical response. In our case, the proper range of drug is only objective in 10% of the patients treated with IFX, 41% with ADA and 50% with ETN.
- The concomitant use of DMARDs in our study has not shown to decrease levels of Ab, being the MTX the most used in our patients (84%). We observed no correlation between the occurrence of Ab, the use of DMARDs or the type of disease.
- The monitoring of the levels of anti-TNF drug may be useful to individualize the treatment, to avoid possible side effects and to make decisions regarding the continuation or change of therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2800
spondylitis (SA) are associated with an increased cardiovascular (CV) mortality. Quantitative abnormalities in lipid profiles are insufficient to explain this excess of CV risk and a qualitative approach of HDL composition is required to identify loss of atheroprotective functions and to correctly identify patients at risk. Atheroprotective functions of HDL are directly linked to the structure of HDL mainly composed of phospholipids (PL).

**Objectives:** The main objective of this study is to analyze the PL composition of HDL in patients with chronic inflammatory rheumatic diseases and to compare to matched healthy controls.

**Methods:** HDL structure was assessed in patients with active RA (ACR criteria), PsA (CASPAR criteria) and SA (ASAS criteria) patients before initiating first biologic and in healthy controls matched for age, sex and body mass index. Dyslipidemia treatment or pathology which could interfere with lipid profile were excluded. Demographics data, disease activity, cardiometabolic profile and plasma samples were collected. HDL particle were isolated from plasma by two-step ultracentrifugation using gradient of density. Lipidomics analysis were performed using liquid chromatography coupled with mass spectrometry. Phospholipid composition between patients and controls was compared using multivariate analyses to take into account possible confounding variables determined according to univariate results and clinical relevance (age, tobacco consumption, steroids use). Multidimensional analyses as factorial mixed data analysis (FMDA) were performed to complete these analyses.

**Results:** 19 RA, 19 PsA and 12 SA were analyzed (table 1). 220 phospholipid species were identified among which 82 major classes were modified in inflammatory diseases. Phosphatidylcholine (PC) decreased in RA and PsA (p < 0.01 and < 0.05 respectively) while lysophosphatidylcholine (LPC) increased significantly (p < 0.01 and < 0.05 respectively). Some phospholipid species as PC 40: 8 (p < 0.001), LPC 16:0 (p < 0.001), LPC 18:3 (p < 0.001) were identified as discriminant marker of HDL composition in rheumatic disease as compared to controls.

**Conclusions:** Phospholipid composition of HDL is altered in RA and PsA. These alterations could explain a loss of atheroprotective functions and the excess of CV risk observed in RA and PsA patients. Chronic inflammation, through the activation of phospholipid A2 type lipases which hydrolyze PC into LPC, could modify the structure of HDL phospholipids and thus could impact HDL functionality such as cholesterol efflux, LDL oxidation modulation, anti-inflammatory and vasculoprotective properties. These preliminary data suggest the major role of inflammation in these alterations.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5491

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**THU0040**

**NOVEL AKT ACTIVATOR SC-79 IS A POTENTIAL TREATMENT FOR ALCOHOL-INDUCED OSTEOGENESIS OF THE FEMORAL HEAD**

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**Background:** Alcohol is known to be one of the leading risk factors for osteonecrosis of the femoral head. However, the underlying etiology and protective strategies of alcohol-induced osteonecrosis of the femoral head have not been clarified.

**Objectives:** The aim of this study was to explore the molecular mechanism of alcohol-induced osteonecrosis of the femoral head, and to investigate the protective effect of SC-79 on the disease.

**Methods:** In vitro, we employed RT-PCR, alizarin red staining, alkaline phosphatase activity testing, western blot, immunofluorescence staining to investigate the effect of ethanol on hBMSCs. In vivo experiments, immunofluorescence staining, TRAP, TUNEL and micro-CT were performed to investigate the development of ONFH.

**Results:** In vitro, we found that ethanol could significantly impair the expression of osteogenic genes of RUNX2 and OCN, downregulate osteogenic differentiation, impair IGF-1 induced membrane recruitment of the Akt, suppress the Akt-Ser473 phosphorylation and the subsequent activation of Akt/GSK3β/β-catenin signaling in bone mesenchymal stem cells. Functional studies further confirmed this signaling was the critical mediator during the ethanol-induced inhibitory effects on osteogenesis of BMSCs. Thus, the dephosphorylation of Akt-Ser473 in Akt/GSK3β/β-catenin signaling pathway might be a potential therapeutic target.

**Conclusions:** Hence, we discovered alcohol-induced osteonecrosis of the femoral head was associated with the suppression of the Akt-Ser473 in Akt/GSK3β/β-catenin pathway in BMSCs. The administration of SC-79, to elevate Akt activation, might be a clinical strategy to prevent the development of alcohol-induced osteonecrosis of the femoral head.

**Acknowledgements:** The current study was supported by National Natural Science Foundation of China (81272003, 81301572) and SMC-Chen Xing Plan for Splendid Young Investigators of Shanghai Jiao Tong University.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1927
LONGITUDINAL IP-10 SERUM LEVELS ASSOCIATE WITH THE COURSE OF DISEASE ACTIVITY AND ACHIEVING DMARD-FREE SUSTAINED REMISSION IN RHEUMATOID ARTHRITIS

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Background: Although rheumatoid arthritis (RA) is a chronic autoimmune disease that is persistent in the majority of patients, 10–15% of the RA patients achieve disease modifying anti-rheumatic drugs (DMARD)-free sustained remission over time. Biological mechanisms underlying the persistence of inflammation in RA are not yet identified. It is well established that increased serum levels of IFN-γ-induced protein 10 (IP-10) are associated with (acute) increased inflammatory responses against mycobacterial pathogens causing leprosy and tuberculosis, thereby providing useful diagnostic tools in these infectious diseases. Based on previous and ongoing studies, we have hypothesised that there is an overlap between inflammatory responses observed in these mycobacterial diseases and those observed in RA. Therefore, we determined the association between serial IP-10 serum levels and achieving DMARD-free sustained remission as well as disease activity scores (DAS)-remission.

Objectives: To 1) assess the association between IP-10 levels over time in patients that have persistent RA versus patients that achieve DMARD-free sustained remission, and 2) determine the association between IP-10 levels and DAS.

Methods: 139 serum samples of 34 RA-patients (1907–criteria), obtained at the time of diagnosis and at yearly intervals thereafter, were studied. 15 patients had persistent RA and 19 patients achieved DMARD-free sustained remission after a median follow up of 2.7 years. IP-10 serum levels were measured using a previously developed, user-friendly lateral flow assay. Baseline and change in IP-10 serum levels were compared between patients with persistent RA and patients achieving DMARD-free sustained remission. The association between the change in IP-10 level and the change in DAS was studied; in addition the course of the absolute IP-10 levels and the DAS over time was plotted for individual patients.

Results: IP-10 serum levels varied from 316 – 53,685 pg/ml between RA-patients. Patients that had persistent arthritis or achieved DMARD-free sustained remission over time did not differ in baseline IP-10 levels (median persistent RA 1991 pg/ml and median DMARD-free sustained remission 3392 pg/ml, p=0.19). However, a significant decrease in IP-10 levels over time was observed in patients achieving DMARD-free sustained remission (p<0.003), whereas IP-10 levels remained stable in patients with persistent RA. Changes in IP-10 levels correlated well with changes in DAS scores (p=0.05). Also at the level of individual patients, a strong correlation between IP-10 levels and DAS over time was observed.

Conclusions: Baseline and longitudinal IP-10 levels are associated with perseverance of RA as well as with disease activity. Rapid diagnostic tests measuring IP-10 levels can therefore be helpful in monitoring of RA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5170
IL-21 AND IL-22 ARE INVOLVED IN BONE DESTRUCTION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Inflammatory process in bone marrow (BM) observed on MRI scans of rheumatoid arthritis (RA) patients (called bone marrow oedema) was shown to proceed joint destruction in RA. Our previous studies supported the concept that BM actively participate in the pathogenesis of RA by TLR triggered B cell activity (1), increased number of activated T cells and increased level of proinflammatory cytokines (2,3). Cytokines play a key role in the bone destruction of rheumatoid arthritis.

Objectives: To investigate the levels of IL-21 and IL-22 in RA BM plasma and their association with bone destruction.

Methods: BM samples were obtained from RA and osteoarthrosis (OA) patients during total hip replacement surgery. Levels of IL-17AF, IL-21, IL-22, RANKL and cathepsin K in BM plasma were determined by specific ELISA tests. We analyzed pelvic radiographs of 22 patients with RA admitted to the NIGRR and subjected to total hip replacement. Radiographs were taken a day or two before surgery. In our study we assessed hip joint changes semi-quantitatively with the use of the proposed scoring system including primary RA (juxta-articular osteoporosis, axial joint space narrowing, inflammatory cyst presence, bony erosion) and late RA changes (axial migration of the femoral head, femoral head deformation, avascular necrosis of femoral head, femoral head subluxation).

Results: We found increased levels of activated T cell associated cytokines IL-21 (924.8 pg/ml vs 688.6 pg/ml, p<0.05) and IL-22 (94.5 pg/ml vs 65.8 pg/ml, p<0.05) in BM plasma of RA patients in comparison to osteoarthrosis (OA) patients. Increased levels of both of these cytokines strongly correlated positively with concentration of osteoclastogenesis/osteoclast activity marker RANKL and cathepsin K. Surprisingly level of IL-17AF did not correlate with RANKL or cathepsin K. Furthermore, concentration of IL-21 was statistically significantly higher in patients with more severe radiologically assessed bone destruction. Median value of concentration of IL-21 in RA patients with small bone destruction was 797.4 pg/ml, with mild bone destruction was 1037.8 pg/ml, with severe bone destruction (1079.0 pg/ml).

Conclusions: Our results show an association between BM plasma levels of IL-21 and IL-22 and bone destruction, supporting the hypothesis that IL-21 and IL-22 are important pathogenic factors of this disease. Therapy targeting IL-21 and IL-22 may be of value in preventing bone erosions in patients with RA.

References:

Acknowledgements: This work was sponsored by grant No UMO-2011/03/B/NZ6/05035 from National Science Centre, Poland.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2140

THU0046 CALCIUM PYROPHOSPHATE AND MONOSODIUM URATE CRYSTAL-INDUCED PROSTAGLANDIN E2 PRODUCTION INVOLVES NF-κB ACTIVATION AND ROS PRODUCTION, INDEPENDENTLY OF INTERLEUKIN-1BETA AXIS

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Background: Monoclinic and triclinic calcium pyrophosphate dihydrate (mCPP and tCPPD) and monosodium urate (MSU) crystals are responsible in human for relapsing acute arthritis. CPP and MSU crystal-triggered inflammation depends on several proinflammatory intercellular pathways like cyclooxygenase (COX) and NLRP3 inflammasome activation. COX-2 and NLRP3 inflammasome activation involves NF-κB activation.

Objectives: To evaluate how CPP crystals induce PG-E2 production and the role of NF-κB in this process.

Methods: Synthetic and pyrogen-free m-CPPD, t-CPPD and MSU crystals were used to stimulate human monocyte cell line (THP-1) and primary bone marrow derived macrophages (BMMDM) or murine type II macrophages (pC6) with different concentrations of CPP crystals. CPP crystal-induced IL-1β production was assayed in THP-1 cells containing a reporter gene under control of NF-κB promoter.

Results: CPP crystal-induced PG-E2 production was evaluated in the air pouch model in the presence or not of NF-κB inhibitor.

Conclusions: CPP crystal-induced PG-E2 production was completely abrogated by NF-κB inhibitor treatment and significantly decreased by the antioxidant NAC; in both case, COX-2 gene expression was dramatically inhibited.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5505

THU0047 RESVERATROL AND ITS NATURAL PRECURSOR POLYDATIN INHIBIT CRYSTAL-INDUCED INFLAMMATION IN VITRO BY DECREASING OXIDATIVE STRESS AND IL-1BETA ACTIVATING PATHWAYS

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Background: Resveratol (RES) and its natural precursor polydatin (PD) are polyphenols with broad variety of beneficial effects including anti-inflammatory properties. This study aimed to investigate the role of RES and PD in the inflammatory process induced by monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals in vitro. Their effect was evaluated though IL-1β, ROS mediation and cellular infiltrate induced by CPP crystals.

Objectives: To assess the role of oxidative stress (N-acetyl-L-cysteine, NAC) and NF-κB and NLRP3 expression was assessed by qRT-PCR. Reactive oxygen species (ROS) and NO were measured by cytometric flow cytometry analysis using fluorogenic probes (CellROX Deep Red Reagent and DAF-FM, respectively).

Results: RES and PD inhibited IL-1β by crystals both at extracellular
and intracellular level. This inhibition was more pronounced after polyphenol pretreatment. In this case cytokine production was completely suppressed in both control and stimulated cells. Cell pretreatment was extremely effective also in reducing mRNA expression of IL-1 after crystal stimulation while NLRP3 expression was to some extent affected by RES. RES and PD had a slight inhibitory effect on crystal-induced phagocytosis when added along with the stimulus, while pretreated cells did not show any difference in the phagocytosis index. ROS production induced by MSU crystals was more pronounced (4 fold increase) with respect to CPP crystals (2 fold increase). RES was more effective than PD in inhibiting ROS production (p<0.05 crystals vs crystals+RES). The pretreatment showed a more marked decrease of ROS than the simultaneous treatment and the effect reached significance for both PD and RES. Similar inhibitory effects have been obtained when NO production was considered. **Conclusions:** Our results demonstrated that RES and PD are effective in inhibiting crystal-induced inflammation affecting IL-1 production and NLRP3 expression and activation. Data obtained after cell pretreatment allow us to hypothesize that these polyphenols act on specific signaling pathway preventing inflammation, and that this action is independent from crystal phagocytosis. **Disclosure of Interest:** None declared **DOI:** 10.1136/annrheumdis-2017-eular.6330

**THU0048** SOLUBLE URIC ACID INCREASED THE EXPRESSION OF PDZK1 AND ABCG2 IN HUMAN INTESTINAL CELL LINES THROUGH THE TLR4/NLRP3/CASPASE-1 AND PI3K/AKT SIGNALING PATHWAYS

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**Background:** Hyperuricemia is the key pathophysiological basis of gout[1]. The most common reason generating hyperuricemia is the failure of urate excretion by current researches[2]. The intestine is known as the most important organ involved the excretion of uric acid besides the kidney [1]. ABCG2 has a key role in mediating urate excretion by the intestine[3]. PDZK1 is a kind of an important structural protein regulated ABCG2 function, with potential molecular interaction with ABCG2[4].

**Objectives:** The present study was undertaken to explore the effect and its related mechanisms of soluble uric acid on the urate excretion PDZK1 and ABCG2 in human intestinal cell lines. It also activated TLR4/NLRP3/caspase-1 inflammasome and PDZK1/AKT signalling pathway through the phosphorylation of pAkt. The increased expression of PDZK1 and ABCG2 was suppressed by a block of TLR4 (TAK-242) and caspase-1 inhibitor (acetyl–YVAD–chromomethylketone) and partly reduced by wortmannin, a specific inhibitor of PI3K. Additionally, lipopolysaccharide (LPS), the potent inducer of inflammatory responses mediated through TLR4, activated TLR4/NLRP3/caspase-1 inflammasome and up regulated the expression of ABCG2 and PDZK1. Besides, the stimulation of soluble uric acid facilitated the translocation of ABCG2 from intracellular compartment to plasma membrane and increased the transport activity. Furthermore, PDZK1 knockdown via siRNA significantly inhibited the expression and transport activity of ABCG2 regardless of the activation by soluble uric acid.

**Conclusions:** These results demonstrated that 29-kDa FN-f has a harmful impact on chondrocytes though suppressing HMGB1-dependent autophagy pathway and releasing HMGB1, DAMP to extracellular space. **References:**


**Acknowledgements:** This study was supported by a grant (HI14C2248 and HI15C2699) from the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea and the Basic Science Research Program through the National Research Foundation (NRF) of Korea funded by the Ministry of Education (2014R1A1A2059822).

**Disclosure of Interest:** None declared **DOI:** 10.1136/annrheumdis-2017-eular.2812

**THU0049** 29-KDA FIBRONECTIN FRAGMENT SUPPRESSED HMGB1-DEPENDENT AUTOPHAGY PATHWAY IN HUMAN ARTICULAR CHONDROCYTES

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**Background:** Fibronectin fragments found in synovial fluid induce the catabolic responses in cartilage. High mobility group protein Box 1 (HMGB1), a damage-associated molecular pattern (DAMP), resides in the nucleus, translocates into the cytosol in response to various stimuli, and is subsequently released into the extracellular space.

**Objectives:** In this study, we investigated the effect of 29-kDa fibronectin fragment (29-kDa FN-f) on HMGB1-mediated autophagy pathway in primary human chondrocytes.

**Methods:** Human articular chondrocytes were enzymatically isolated from articular cartilage. The mRNA and protein levels of HMGB1 were measured by quantitative real-time PCR (qRT PCR) and Western blot analysis. The translocation of nuclear HMGB1 into cytoplasm was determined by western blot and immunofluorescence microscopy. Activation of mammalian target of rapamycin (mTOR), protein kinase B (Akt) and 1A/1B-light chain 3 (LC3) was measured by western blot analysis. Interaction of HMGB1 and Beclin-1 were evaluated by Immunoprecipitation (IP). Release of HMGB1 into extracellular medium was measured by ELISA.

**Results:** HMGB1 was significantly reduced in human osteoarthritis (OA) cartilage compared to normal cartilage. qRT PCR and Immunoblotting assay revealed that 29-kDa FN-f significantly reduced expression of HMGB1 at the mRNA and protein levels and also led to the translocation of the nuclear HMGB1 into the cytoplasm, together with decreased levels of Beclin-1 and phosphorylated Beclin-1. Using IP analysis, we demonstrated that in the presence of 29-kDa FN-f the association of HMGB1 and Beclin-1, which led to HMGB1-dependent autophagy pathway, was decreased, whereas the association of Beclin-1 and Beclin-1 was increased. In addition, prolonged treatment with 29-kDa FN-f significantly increased the release of HMGB1 into the culture medium. A variety of evidence, including down-regulated LC3-II, an autophagy marker, and increased phosphorylated 4EBP1 and p70S6K, substrates of mTOR, revealed that 29-kDa FN-f subsequently suppressed autophagy in primary chondrocytes by activating Akt/mTOR signaling pathway.

**Conclusions:** These results demonstrated that 29-kDa FN-f has a harmful impact on chondrocytes through suppressing HMGB1-dependent autophagy pathway and releasing HMGB1, DAMP to extracellular space.

**References:**

domain protein-1/hypoxia-inducible factor-2α (EPAS-1/HIF-2α) is a catabolic transcription factor that regulates osteoarthritis (OA) cartilage destruction. **Objectives:** In this study, we examined whether microRNA-365 (miR-365) affects interleukin (IL)-1β-induced expression of catabolic factors in chondrocytes via regulation of HIF-2α.

**Methods:** Total RNA was isolated from normal and OA cartilage tissues and human chondrocytes. miR-365 expression was quantified by TaqMan assay. The effects of miR-365 on HIF-2α and HIF-2α-modulated genes were assessed by quantitative real-time reverse polymerase chain reaction (qRT-PCR), Western blot analysis, and enzyme-linked immunosorbent assay (ELISA). Direct interaction of miR-365 with the 3' untranslated region (UTR) of HIF-2α mRNA was examined using a luciferase reporter assay. Nitric concentration was measured in culture medium using a Griess assay.

**Results:** miR-365 levels were significantly decreased in human OA cartilage relative to normal cartilage. Overexpression of miR-365 significantly suppressed IL-1β-induced expression of HIF-2α in human articular chondrocytes. Pharmacological inhibition of various IL-1β-associated signaling pathways revealed mitogen-activated protein kinase and nuclear factor-kB as the primary pathways driving IL-1β-mediated decreases in miR-365 and subsequent increase in HIF-2α expression. Using a luciferase reporter assay encoding the 3'UTR of human HIF-2α mRNA, we showed that overexpression of miR-365 significantly suppressed IL-1β-induced up-regulation of HIF-2α. Furthermore, miR-365 overexpression significantly suppressed IL-1β-induced expression of catabolic factors, including cyclooxygenase-2, inducible nitric oxide synthase, and matrix metalloproteinase-1,-3 and -13, and nitric oxide (NO) production in chondrocytes.

**Conclusions:** MiR-365 regulates IL-1β-stimulated catabolic effects in human chondrocytes by modulating HIF-2α expression.

**References:**


**Acknowledgements:** This study was supported by the Basic Science Research Program through the National Research Foundation (NRF) of Korea funded by the Ministry of Education (2014R1A1A2059823 and 2016R1D1A1B0392259).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2818

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**THU0051**

**ASSOCIATION BETWEEN BIOACTIVE TNF AND EULAR RESPONSE TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS**

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**Background:** ROC study provided data to manage rheumatoid arthritis (RA) treatment after a failure to a first TNF blocker (1). We previously reported that high circulating TNF bioactivity was associated with good clinical response (2). **Objectives:** To explore ability of TNF bioactivity to predict response to second TNF blocker. **Methods:** Here, we assessed TNF bioactivity in 130 RA patients from the group rotation to a second TNF blocker at the time of randomisation and after 6 months. Clinical and biological data were recorded at baseline and 6 month with Eular response assessed at 6 month. TNF bioactivity was assessed with HEK-Dual TNF cells adapted from our previous work (2). Due to non-normalised distribution, non parametrical analysis were performed. **Results:** Baseline circulating TNF bioactivity was similar according to Eular response. However, circulating TNF bioactivity at 6 month was associated with clinical response with low TNF bioactivity in responders. A ROC analysis suggested a cut-off at 0.320 with a sensitivity at 92% and a specificity at 41%.

**Conclusions:** After a failure of a first TNF blocker, circulating TNF bioactivity is not able to predict response to a second TNF blocker despite a lower level in responders compared to non-responders.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4227

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**THU0052**

**LEVELS OF INFLAMMATORY SEROLOGIC BIOMARKERS IN HLA-B27 AND HLA-B15 POSITIVE PATIENTS WITH SPONDYLOARTHRITIS**


**Background:** A main challenge in spondyloarthritis (SpA) management was the availability of reliable biomarkers related with disease activity, or predicting joint damage and the response to treatment. Although erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are currently used as biomarkers for disease activity, they lack sensitivity, specificity and reproducibility. With the understanding of SpA pathogenesis, additional biomarkers like metalloproteinase 3 (MMP-3), interleukin (IL)-1α, IL-6, lipopolysaccharide-binding protein (LBP), tumour necrosis factor α (TNFa), macrophage colony stimulating factor (M-CSF), interferon gamma (INF-g), IL-17 and IL-23, had been proposed.

**Objectives:** We aimed to evaluate the associations of MMP-3, IL-1α, IL-6, M-CSF, LBP, IL-17 and IL-23 levels in SpA patients positive for HLA-B27 or HLA-B15. **Methods:** 176 patients (100 men and 76 women) with SpA according to ASAS criteria were included in the study. HLA typing was performed by PCR using the Biorad® HLA-SSP ABDR plates. The levels of TNFa, IL-1α, IL-6, INF-g and IL-17 were measured by a cyrometric bead-array (CBA Flex Set) using a FACS Canto II Flow Cytometer®. Enzyme-linked immunosorbent assay (ELISA) was used to determine serum levels of IL-23, M-CSF and MMP-3. CRP and LBP levels were measured by chemiluminescence. Statistical analysis was made with SPSS v19. For comparison of quantitative variables with a normal distribution we used the Student’s t-test. Categorical variables were presented in frequency charts and percentages, and the Chi-squared test and Fisher’s exact test were used when necessary, for comparing groups. Two-tailed P-value <0.05 was considered statistically significant.

**Results:** Of the 178 patients, 70 were positive for HLA-B27, 34 for HLA-B15 and 74 had other HLA-B. According to ASAS classification criteria, 152 patients had axial SpA (axSpA) manifestations, 161 had peripheral SpA (pSpA) manifestations, and 148 patients had mixed axial and peripheral manifestations. Figure 1 shows the mean levels of inflammatory serologic biomarkers in these subgroups of patients.

**Conclusions:** High levels of IL-17 and IL-23 were associated with the presence of HLA-B27, which mainly correlates with an axial presentation of the disease as
SELECTIVE ACTIVATION OF AN AMPK-CREB-NF-κB-DEPENDENT PATHWAY BY CELECOXIB INDUCES VASCULOPROTECTIVE GENES AND MITIGATES AGAINST CARDIOVASCULAR RISK


Background: Although concern remains about the athero-thrombotic risk posed by COX-2-selective inhibitors (COXIBs), the recent PRECISION trial demonstrated non-inferiority of moderate dose celecoxib when compared to naproxen and ibuprofen with respect to cardiovascular safety, with fewer actual CV events recorded for celecoxib. Moreover, celecoxib proved significantly safer than either comparator in regard to gastrointestinal events1. Given the markedly different cardiovascular risk associated with celecoxib and rofecoxib, we investigated the hypothesis that, in addition to cyclo-oxygenase inhibition, celecoxib specifically activates COX-2-independent AMPK signalling to exert protective effects in the vascular endothelium. Objectives: To investigate COX-2-independent vasculoprotective signalling pathways activated by celecoxib in human endothelium. Methods: In vitro studies of celecoxib, rofecoxib, ibuprofen and naproxen were performed on human umbilical vein and human aortic endothelial cells (HUVEC and HAEC). Inhibition of signalling pathways was achieved using siRNA. The vascular effects of celecoxib in vivo were studied in C57Bl/6 mice fed celecoxib (1000 ppm) or control chow (48 hrs). Aortic tissue was snap-frozen and sections studied by immunohistochemical techniques. Results: At therapeutically relevant concentrations celecoxib (1–10 μM) protected the vasculoprotective protein heme oxygenase-1 (HO-1) in HUVEC and HAEC (EC) (p < 0.01). In contrast, rofecoxib and the commonly used non-selective NSAIDs ibuprofen and naproxen failed to induce HO-1. Celecoxib derivative 2,5-dimethyl-celecoxib (DMC), which lacks COX-2 inhibition, also upregulated HO-1, NSD1 and SIRT1 (p < 0.05). Similarly, celecoxib prevented the IL-1-mediated silencing of HO-1 induced by IL-1α-induced NF-κB (p < 0.05). These responses were not seen with ibuprofen or naproxen, while siRNA depletion of AMPKα2 abrogated celecoxib-mediated CREB and NFκB activation (p < 0.05). Acting via the same pathway, celecoxib induced additional cytoprotective genes including H-ferritin. In vivo, celecoxib similarly increased HO-1 and H-ferritin in murine aortic endothelium when compared to control-fed mice (p < 0.05). Functionally, celecoxib treatment inhibited TNFα-induced NFκB p65/SIRT1 phosphorylation by increasing AMPK activity. This attenuated VCAM-1 upregulation via induction of HO-1, as revealed by HO-1 siRNA (p < 0.05). Similarly, celecoxib prevented the IL-1 mediated increase of IL-6 mRNA (p < 0.01). These responses were not seen with ibuprofen or naproxen. Conclusions: Celecoxib induces anti-inflammatory, anti-oxidant proteins HO-1 and H-ferritin in human vascular endothelium via a novel AMPK-CREB-NFκB-dependent pathway. This mechanism may contribute to the important and marketed cardiovascular risk reduction between celecoxib and rofecoxib. Understanding mechanisms underlying NSAID heterogeneity may ultimately lead to the development of safer anti-inflammatory drugs.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5628

LOW MOLECULAR WEIGHT BAFF SIGNALING INHIBITORS AMELIORATE IL-6, IL-10 AND IGG PRODUCTION IN VITRO AND IN VIVO MODELS OF AUTOIMMUNE DISEASES

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Background: In our previous study, we reported that soluble BAFF (sBAFF) robustly enhanced IL-6 production by peripheral monocytes of patients with primary Sjögren’s syndrome (pSS) and that the expression level of a BAFF receptor (BR3) was significantly elevated in pSS monocytes. We also found that the proportion of BR3-positive monocytes to total monocytes was positively and significantly correlated with the serum IgG level of pSS patients. Investigation of the interaction of monocytes and B cells showed that IgG production by B cells was enhanced by sBAFF-stimulated monocytes. These data collectively suggest that the elevated expression of BR3 on monocytes is involved in IgG overproduction by B cells. We then often observed IgG overproduction by B cells resulting in IgG overproduction. Interestingly, serum levels of an anti-dsDNA antibody, IL-6 and IL-10 were measured in patients with primary Sjögren’s syndrome and the expression level of a BAFF receptor (BR3) was significantly elevated in pSS monocytes. We also found that the proportion of BR3-positive monocytes to total monocytes was positively and significantly correlated with the serum IgG level of pSS patients. Investigation of the interaction of monocytes and B cells showed that IgG production by B cells was enhanced by sBAFF-stimulated monocytes. These data collectively suggest that the elevated expression of BR3 on monocytes is involved in IgG overproduction by B cells. We then often observed IgG overproduction by B cells resulting in IgG overproduction.

Objectives: To elucidate the mechanism of inhibitory activities of these compounds on BAFF signaling pathways, we measured production of IL-6 as well as IL-10 by monocytes in vitro with or without peripheral B cells in the presence of BIK-12 or BIK-13. The amounts of IL-6, IL-10 and IgG were measured by ELISA. BIK-13 was administered intraperitoneally to MRL/lpr mice, an animal model of autoimmune diseases, three times a week for 6 months. Serum levels of an anti-ds DNA antibody, IL-6 and IL-10 were measured by ELISA.

Methods: The study included 98 GCA patients (67% female) with a median (IQR) age 74.1 (67.3–78.8) years and a median (IQR) symptome duration time of 30 (20–90) days. Healthy blood donors (HDs, n=52, 61.5% female, median (IQR) age of 41.95 (20.64–63.1) years) served as controls. GCA complications studied were visual disturbances (including permanent loss of vision), relapses, peripheral artery disease and claudication. Levels of 27 serum analytes were measured using Lumine xMAP Technology. Interleukin-6 (IL-6) and serum amyloid A (SAA) levels were tested using ELISA and nephelometry, respectively.

Results: The highest, significantly elevated analytes in GCA vs. HDs were SAA (85-fold > HDs mean values), IL-23 (63-fold) and IL-6 (11-fold). IL-13, a-efetoprotein and MMP-2 were significantly increased in GCA, while levels of IL-2, IL-17A and TNFα were unchanged. PCA analysis revealed a signature analyte profile positioning towards the HD cluster. SAA, CRP, haptoglobin, ESR, thrombocyte # and matrix metalloproteinase-1 (MMP-1) all negatively associated with visual disturbances, confirming visual examination data. Age showed significant association to permanent visual loss, with older patients being more affected2. SAA, CRP and ESR at presentation were found to be predictive of relapsing disease, while MMP-2 negatively associated with relapse. VCAM-1, a-efetoprotein, MARCO and IL-27 were all negatively associated with peripheral artery involvement. MMP-2 and MARCO showed positive association with claudication, while IL-18 was negatively associated.

Conclusions: In our large study of untreated GCA patients we highlight the importance of using serological acute phase parameters, MMPs and other analytes for predicting complications.

References:

Disclosure of Interest: None declared

by B cells through affecting monocytes. IL-6 and/or IL-10 may mediate the effect. Our findings strongly suggest that BAFF signaling via BR3 is a possible therapeutic target for drug discovery to treat pSS or other intractable autoimmune diseases which accompany hypergamaglobulinemia. Moreover, these compounds may provide novel tools to explore the pathological mechanism of the development of these autoimmune diseases.


THU0056 | FREE FATTY ACIDS PROMOTE INFLAMMATION VIA OSTEOSTRALLS AND OSTEOCLASTS FROM PATIENTS WITH RHEUMATOID ARTHRITIS OR OSTEOARTHRITIS

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Background: Various inflammatory cardiovascular and metabolic diseases such as atherosclerosis, coronary heart diseases and type 2 diabetes are associated with chronically elevated free fatty acid (FFA) levels. With inflammation being a factor in pathological bone loss, FFA may also be contributors to bone loss in context of these autoinflammatory diseases.

Objectives: To investigate whether FFA have an influence on osteoblasts and osteoclasts from patients with RA or OA, in a way that may alter bone degradation in these diseases.

Methods: Primary osteoblasts (OB) were isolated from cancellous bone of OA and RA patients undergoing knee joint surgery. Osteoclasts (OC) were differentiated from peripheral blood mononuclear cells (PBMC). OB and OC were stimulated with the saturated FFA palmitic acid (PA) and the unsaturated FFA linoleic acid (LA) (100 μM each). Immunofluorescence was used to quantify protein secretion, mRNA expression levels were quantified by real-time PCR. Mineralization activity was quantified using Alizarin Red S staining, differentiated OC were quantified by counting TRAP-positive multinuclear cells (>2 nuclei). Toll-like receptor (TLR) 4 and TLR2 were blocked by neutralizing antibodies.

Results: When stimulated with FFA, OB from RA and OA patients secreted higher amounts of the proinflammatory cytokine IL-6 (up to 9-fold) and the chemokines IL-8 (up to 221-fold), GRO-a (from below detection level to detectable levels) and MCP-1 (up to 16-fold). Differences in the degree of response were more dependent on the patient than the disease. RANKL and OPG, OB-secreted modulators of OC differentiation, as well as OB differentiation markers (e.g. osteonectin) were not influenced by FFA on mRNA or protein level. The effect of FFA on mineralization activity of OB varied between patients, yet overall there was a significant difference between FFA-treated and untreated OB. Expression of the two Wnt signaling molecules, axin-2 and b-catenin, was not altered. RA patients showed a 2-3 fold increase in TRAP secretion by a factor of 2–3 at d14. mRNA expression of various osteoclast activity markers (CLCN7, CTSK, TCIRG) was not altered.

Conclusions: Inflammation is promoted by FFA both via OB and OC from patients with RA or OA, thus possibly indirectly contributing to bone loss while no direct effect on OB/OC activity could be observed. In OB, these effects are probably mainly mediated by TLR4, while TLR2 and Wnt pathways do not play a role.


THU0057 | LIPID PROFILING OF PLASMA IN RHEUMATOID ARTHRITIS PATIENTS BY LIQUID CHROMATOGRAPHY–TANDEM MASS SPECTROMETRY

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Background: Previously it has been described that lipid and lipid mediators are present in synovial fluid from patients with rheumatoid arthritis (RA). It is, however, currently unknown to what extent these lipid mediators are involved in disease pathophysiology.

Objectives: The aim of this study is to clarify which lipid mediators in plasma correlate with disease activity of RA.

Methods: We obtained blood from RA patients registered in the KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort. None of the patients was treated with glucocorticoids or NSAIDs, both of which could affect lipid metabolism. Targeted lipids, using a LC–MS/MS (liquid chromatography–tandem mass spectrometry) platform was used for the identification of lipids present in the patients’ plasma. SDAI (simplified disease activity index) was examined in this cohort. Lipidomics profiling and disease status were combined. Data were statistically analyzed by Spearman’s rank correlation coefficient test or multivariate regression analysis.

Results: Twenty-six RA patients were enrolled; female ratio: 84%, mean age: 63.5, disease duration: 18.7 years and mean SDAI 5.28. In this group, patients age was significantly correlated with SDAI (p value <0.005, Spearman’s rho = -0.552). By LC-MS/MS analyses, 23 lipid components were identified and quantified. Multivariate regression analysis (Standard Least Squares) revealed that 19,20-diHDPA (Dihydroxydocosapentaenoic acid) and 14,15-diHETE (Dihydroxyeicosatetraenoic acid) significantly explained SDAI score independently of sex and age.

Among the composite measure for SDAI, the best correlated component with TJC (tender joint count) was LA (Linoleic acid, p=0.002, rho = -0.611), while with patient global analogue scale was 19,20-diHDP (p=0.032, rho = -0.440), and that with CRP was DHA (Docosahexaenoic acid, p=0.021, rho = -0.452). Additionally, principal component analysis was carried out. In the first principal component (PC1), absolute eigenvector values of ADA (Adrenic acid), ALA (Alpha-linolenic acid), DHA, EPA (Docosahexaenoic acid) and LA are more than 0.25, among which they are strongly correlated with PC1 (p = 0.001, rho = -0.902). PC1 positively and significantly explained TJC count independent of sex and age.

Table. Parameter Estimates by Standard Least Squares (Role variant = SDAI)

<p>| Parameter Estimates by Standard Least Squares (Role variant = SDAI) |
|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Lower 85%</th>
<th>Upper 85%</th>
<th>Std. Beta</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-39.2</td>
<td>-6.63</td>
<td>0</td>
</tr>
<tr>
<td>19,20-diHDP</td>
<td>14.5</td>
<td>10.55</td>
<td>0.707</td>
</tr>
<tr>
<td>14,15-diHETE</td>
<td>28.4</td>
<td>23.64</td>
<td>0.303</td>
</tr>
<tr>
<td>Age</td>
<td>0.05</td>
<td>0.45</td>
<td>0.455</td>
</tr>
<tr>
<td>Sex</td>
<td>0.475</td>
<td>0.475</td>
<td>0.475</td>
</tr>
</tbody>
</table>

Conclusions: Since 19, 20-diHDP (metabolized from DHA) and 14,15-diHETE (from EPA, eicosapentaenoic acid) are both generated by cytochrome P450-catalyzed epoxidation followed by conversion to the vicinal diols by epoxide hydrase, such kind of enzymes might be key molecules connecting lipid metabolism and RA. Although a replication study is inevitable, a certain kinds of lipid and lipid mediator profiles may be associated with disease activity, especially analgesic descriptors such as tender joint count.


Acknowledgements: None.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4052

THU0058 | S100A11 PROTEIN IS UP-REGULATED IN PATIENTS WITH IDIOPTIC INFLAMMATORY MYOPATHIES AND IS ASSOCIATED WITH DISEASE ACTIVITY

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Background: S100A11 (calgazzin) is a member of the S100 protein family that participates in regulating number of biologic functions and is associated with oncogenesis and inflammation. Recent data suggest involvement of S100A11 in myocardial damage.

Objectives: The aim of our study was to analyze the expression of S100A11 in patients with idiopathic inflammatory myopathies (IMMs) and its potential association with disease activity parameters and IMMs-related clinical features.

Methods: Immunohistochemistry in patients with polymyositis/dermatomyositis (PM/DM, n=5/6) and control individuals with myasthenia gravis (MG, n=5). S100A11 in plasma was measured by ELISA (Biovendor) in 112 patients with IMMs (PM, n=41; DM, n=41; and cancer associated myositis (CAM), n=30) and in 42 healthy controls (HC). Patients with PM/DM fulfilled Bohan and Peter diagnostic criteria and CAM was defined as cancer occurring within 3 years of the diagnosis of myositis. Clinical disease activity was assessed by myositis disease activity (MDACT), physician and patient’s global activity using visual analogue scales (VAS), manual muscle testing (MMT) and health assessment questionnaire (HAQ); Muscle enzymes CK, LD, ALT and CRP were measured by routine laboratory techniques. Autoantibodies were detected by immunoprecipitation.
Results: S100A11 protein was up-regulated in the muscle from patients with IIMs compared to MG. In PM/DM patients, S100A11 was accumulated in the muscle of most fibers. Only some mononuclear infiltrate cells showed S100A11 positivity. In patients with MG, S100A11 was detected on the sarcolemma only. Moreover, S100A11 staining was observed on the sarcolemma of all muscle fibers in S100A11-positive patients.

Background: S100A11 has been described as a marker for skeletal muscle inflammation, regeneration, and hypertrophy. However, the role of S100A11 in IIMs is not well understood. In this study, we aimed to investigate the expression of S100A11 in various muscle diseases and its potential association with disease activity.

Methods: Muscle biopsies were obtained from patients with IIMs and healthy controls. The muscle tissue was immunostained with anti-S100A11 antibody and counterstained with hematoxylin.

Results: S100A11 was significantly increased in the muscle biopsies of patients with IIMs compared to controls. The intensity of S100A11 staining was positively correlated with muscle strength and fiber regeneration.

Conclusions: S100A11 is a useful marker for muscle inflammation in IIMs. Its expression can be used as a clinical indicator for disease activity and muscle regeneration.

Disclosure of Interest: None declared.

DOI: 10.1016/j.ymgme.2017.09.088

THU0059
ONCOSTATIN M INDUCES INFLAMMATION AND DIFFERENTIALLY REGULATES TNF-ALPHA-INDUCED PRO-INFLAMMATORY MECHANISMS AND NOTCH SIGNALLING IN THE RA JOINT

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Background: Oncostatin M (OSM) is a pleiotropic cytokine, highly expressed in the RA joint that displays both agonistic and antagonistic effects depending on the inflammatory microenvironment. This study examines the effect of OSM on inflammation, the Notch-1 signalling pathway which plays a critical role in vascular development and angiogenesis and finally on TNFα-induced pro-inflammatory mechanisms in Rheumatoid Arthritis.

Objectives: To examine the effect of OSM on cytokine/chemokine production, angiogenesis and the Notch-1 signalling pathway in synovial fibroblasts and endothelial cells and whether OSM potentiates the effects of TNFα-induced pro-inflammatory effects.

Methods: Primary RA synovial fibroblasts (RASF) isolated from RA synovial biopsies obtained at time of knee arthroscopy and human dermal microvascular endothelial cells (HMVEC) were grown to confluence. RASFC and HMVEC were cultured with OSM (10ng/ml) alone or in combination with increasing concentrations of TNFα (0.01–1ng/ml). IL-6, IL-8, RANTES, GROα and MCP-1 cytokines/chemokines were quantified in culture supernatants by ELISA. Notch-1, its ligands Delta-like-ligand 4 (DLL-4) and Jagged-1 (Jag-1) and downstream transcriptional repressors – Hey-1 and Hey-2 were quantified by Real-time PCR. Finally, Notch-1, its ligands Delta-like-ligand 4 (DLL-4) and Jagged-1 (Jag-1) and downstream transcriptional repressors – Hey-1 and Hey-2 were quantified by Real-time PCR.

Results: OSM alone significantly induced IL-6 and MCP-1 while inhibiting IL-8 and GROα in RASF and HMVEC culture supernatants, compared to basal control. OSM alone induced RANTES expression in HMVEC with little effect observed for RASF. OSM potentiated the effect of increasing concentrations of TNFα on IL-6 and MCP-1 secretion from RASF and HMVEC. Conversely OSM significantly inhibited TNFα-induced IL-8 and GROα secretion from both RASF and HMVEC. Interestingly, OSM significantly inhibited TNFα-induced RANTES expression in HMVEC yet conversely potentiated this effect in RASF. At a functional level, OSM alone induced RASFC invasion whereas matrigel tube formation and Transwell invasions assays respectively, and VEGF in cell lysates quantified by Real-time PCR. Finally, Notch-1, its ligands Delta-like-ligand 4 (DLL-4) and Jagged-1 (Jag-1) and downstream transcriptional repressors – Hey-1 and Hey-2 were quantified by Real-time PCR.

Discussion: Our data show that both IL-17A and IL-17F enhance in vitro osteogenic differentiation and bone formation from hPDSCs. The source of these cytokines has not been established but is likely to involve entheseal resident γδ-T cells. We propose that following their release, IL-17A and IL-17F drive pathological bone formation resulting in entheseopathies at the enthesis/periostium interface.

Conclusions: These data show that both IL-17A and IL-17F enhance in vitro osteogenic differentiation and bone formation from hPDSCs. The source of these cytokines has not been established but is likely to involve entheseal resident γδ-T cells. We propose that following their release, IL-17A and IL-17F drive pathological bone formation resulting in entheseopathies at the enthesis/periostium interface.

References:

Disclosure of Interest: None declared.
Second, human osteoarthritic (OA) patients who underwent total knee arthroplasty. First passage human OA OB were treated either with RvD1 (0.1 – 1 μM) alone, or with 20 nM VitD3 with or without RvD1 (0.1 - 1 μM), for 48 hours. Cell viability was evaluated with the MTS test. Alkaline phosphatase (PAP) activity and osteocalcin (OCN) release was determined by colorimetric reaction and ELISA, respectively.

**Results:** In RAW264.7 cells, our results clearly show that RvD1 strongly reduces OC recruitment and activation as indicated by the inhibition of TRAP and cathepsin K expression as well as TNF-α, IL-1β, IL-6, PGE2 and NO release, as well as the concurrent enhancement of IL-10 levels. Besides, RvD1 decreases bone resorption through the inhibition of plots formation in hydroxyapatite matrix. In human OA OB, RvD1 partially decreases VitD3-induced PAP activity, while it maintains OCN expression at control levels.

**Conclusions:** Our in vitro results clearly show that RvD1 may play an important role in the regulation of bone metabolism. Additionally to our previous data, our findings suggest that RvD1 may offer a novel and original perspective to make a real contribution to musculoskeletal and bone diseases therapy.

**Acknowledgements:** This study was supported by Canadian Institute of Health Research (CIHR) grant (#IMH 131570) and by the Center of Excellence for Arthroplasty Research.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2934

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**THU0062**

**NOVEL ANIMAL MODEL OF AROMATASE INHIBITOR-INDUCED ARTHRALGIA SUGGESTS AN ESTROGEN-INDEPENDENT INFLAMMATORY MECHANISM**


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**Background:** Aromatase Inhibitors (Ais) block physiological estrogen production in peripheral tissues and significantly improve overall survival rates of post-menopausal, hormone receptor-positive breast cancer patients by reducing tumor recurrences. However, half of patients taking these drugs develop aromatase inhibitor induced arthralgia (AIA), which is characterized by severe pain and inflammation in various joints. Since AIA leads to suspension of therapy in 20% of patients, reducing incidence may provide sustained AI treatment and enhanced long-term survival.

**Objectives:** In order to establish a better understanding of the inflammatory mechanism and to create a platform that can be used to explore interventional strategies, our objective in this study was to design a novel animal model of AIA.

**Methods:** Female BALB/c-Tg (Nf-β-RE-luc)-Xen mice, which have a firefly luciferase cDNA reporter gene under the regulation of 3 β responsive binding sites, were oophorectomized and treated with AI (letrozole) by daily subcutaneous injections. Control groups included oophorectomized mice receiving vehicle control injections and non-oophorectomized mice treated with AI. Bioluminescent imaging of hind limbs was performed after 3 weeks on the in vivo imaging system (IVIS) to measure NF-κB activation. At 5 weeks, knee joints and surrounding tissue were imaged on the BioSpec 94/30 micro-MRI. Legs were collected for histopathological analysis and serum cytokine levels were measured at experimental endpoint.

**Results:** Bioluminescent imaging showed significantly enhanced NF-κB activation in the hind limbs compared to oophorectomized controls receiving vehicle treatment. Analysis of knee joints and legs by MRI imaging showed enhanced signal detection in the joint space and surrounding tissue following AI treatment. Surprisingly, enhanced MRI detection was also demonstrated in non-oophorectomized mice that were treated with AI. Histopathological analysis further demonstrated mild inflammation in the synovial tissue and joint damage in mice treated receiving AI both with and without oophorectomy. Moreover, tenosynovitis and inflammatory muscle tissue infiltrates were detected in AI-treated mice and serum cytokine levels of IL-2, IL-4, IL-6, and CXCL1 were significantly elevated.

**Conclusions:** Collectively, these data establish a novel mouse model of AIA and suggest that the pathogenesis of AI-induced inflammation is estrogen-independent. Future studies will be directed into the characterization of this inflammatory mechanism to provide insight into potential therapeutic strategies directed at mitigating this adverse inflammatory burden.


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5424

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**THU0063**

**IL-1 FAMILY CYTOKINES AND RECEPTORS IN IGG4-RELATED DISEASE**


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**Background:** IgG4-related disease (IgG4-RD) is a fibroinflammatory condition that can affect almost any organ, characterized by lymphoplasmacytoid infiltrate, obliteratoric phlebitis and storiform fibrosis often associated with eosinophilia and increased levels of IgG4. Cytotoxic CD4 T cells producing IL-1β [D1], TGFB1 and IFN-gare detectable in peripheral blood of patients and high IL-18 expression has been found in affected organs.

**Objectives:** To evaluate the role of IL-1 family cytokines in IgG4-RD, by analyzing cytokines and receptors in sera.

**Methods:** Nine patients fulfilling the proposed criteria (Umehara, 2012) for the diagnosis of IgG4-RD were recruited. Cytokines of the IL-1 family (IL-1α, IL-1β, IL-33, IL-18), soluble receptors (sIL-1R1, sIL-1R2, sIL-1R3, sIL-1R4) and antagonists (IL-1Ra, IL-18BP) were measured in sera by multiaxial ELISA assay. Free IL-1β was calculated using the law of mass action.

**Results:** Most patients had a multiorgan disease; retroperitoneum, salivary glands, pancreas and lymph nodes were most frequently affected. IL-18 (p=0.007) and free IL-1β (p<0.0001), sIL-1R1 (p=0.0005), sIL-1R2 (p=0.0013), and sIL-1R4 (p=0.0006) were significantly increased in IgG4-RD sera compared with healthy controls.

**Conclusions:** In IgG4-RD patients, at variance with other autoimmune or autoinflammatory conditions, the increase in IL-18 levels is not counterbalanced by IL-18BP, leading to high levels of free IL-1β. The free cytokine may affect T cell subset balance and induce IFN-g production. The parallel increase of sIL-1R1 and sIL-1R2 suggests an efficient dampening of inflammatory IL-1βsignaling at the tissue level, while high levels of sIL-1R4 may be associated with vascular remodeling and fibrosis, as observed in animal models of obesity and in human cardiovascular disorders.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5816

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**THU0064**

**ADAM-10 AS A TICLOZUMAB TREATMENT PREDICTIVE FACTOR IN RHEUMATOID ARTHRITIS**


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**Background:** A disintegrin and metalloproteinases (ADAMs) are a family of transmembrane and secreted proteins. ADAM-10 has been reported to be the enzyme responsible for the release of a number of chemokines and cytokine receptors. We have shown that ADAM-10 is overexpressed on rheumatoid arthritis (RA) synovial tissue endothelial cells (ECs) and lining cells compared with osteoarthritides and normal tissues. We also demonstrated that ADAM-10 mediates EC migration and tube formation.

**Objectives:** In order to demonstrate for ADAM-10 in clinical side, we focused on ADAM-10 as predictive factor for treatment with biologics in RA.

**Methods:** The serum was collected from patients before the initial treatment with biological therapies. Fifteen patients were treated with adalimumab (ADA), and 20 patients were treated with tocilizumab (TCZ). ADAM-10 and fractalkine/OCX/CL1 were measured by enzyme-linked immunosorbent assay at 0, 12, 24 and 54 weeks. Clinical disease activity was evaluated by clinical disease activity index (CDAI). Following biological therapies, we defined biologic-responders as patients whose DAS28 scores decreased by more than 1.2 at 24 weeks. ADAM-10 baseline was also compared between responders and nonresponders at 24 weeks.

**Results:** There were no significant differences were observed in the mean age, gender ratio, dosages of prednisolone and methotrexate between ADA and TCZ groups. In ADA group, baseline DAS28 for the 15 patients was 4.8±0.3 (2.5–7.2).
On the other hands, baseline DAS28 for the 20 patients was 4.8±0.3 (2.5–6.8) in TCZ group. There were no differences between ADA and TCZ groups. RA patients with an insufficient response to ADA or TCZ showed highly significant improvement of DAS28 after 12 weeks (2.9±0.3 and 2.2±0.4, respectively), and 24 weeks (2.5±0.4 to 2.2±0.2, respectively). ADAM-10 highly correlates with cDAI, and serum ADAM-10 levels in patients with TCZ were significantly higher after treatment with ADA despite decrease of disease activity of RA. On the other hand, serum ADAM-10 levels in patients who were treated with TCZ were significantly diminished following successful treatment and clinical improvement (baseline 408±88 pg/ml and 54 weeks 138±51 pg/ml, p<0.05). Univariate logistic regression of serum activity of DAS28 (Esr) baseline of cDAI and ADAM-10 were selected as significant variables for improvement of DAS28 (Esr) at 24 weeks. Multiple regression analysis showed that ADAM-10 was only identified as an independent predictive variable for improvement of DAS28 (ESR) at 24 weeks. GMR of ADAM-10 baseline in TCZ responder was significantly higher than TCZ nonresponders at 24 weeks (620±134 pg/ml and 105±25 pg/ml, respectively, p<0.05).

Conclusions: This study indicates that ADAM-10 is correlated with RA disease activity, and is higher in TCZ responders. These results suggest that ADAM-10 may be a predictor of treatment effectiveness for RA with TCZ.

Disclose of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4594

THU0065 CYTOKINES AND LIPOCALIN-2 IN PREGNANT WOMEN WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Rheumatoid arthritis (RA), and especially seronegative RA, is often ameliorated by pregnancy, while systemic lupus erythematosus (SLE) is prone to flare and associated with pregnancy complications. Cytokines and chemokines are of great importance for immune processes during pregnancy. The inflammatory marker Lipocalin-2 (LCN2) has become increasingly relevant as a potential clinical biomarker of rheumatic diseases (1). LCN2 is produced in the maternal-fetal interface during normal pregnancies and correlates with the presence and severity of pre eclampsia (2).

Objectives: To obtain a better understanding of immune regulation and the disparate immune responses in pregnant women with RA and SLE. In this study, we analyzed levels of multiple cytokines, chemokines and LCN2 in women with seropositive RA, seronegative RA, SLE and healthy controls during pregnancy and postpartum.

Methods: The Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases collect serum samples in a biobank from women with inflammatory rheumatic diseases before pregnancy, during pregnancy week 10–12, week 23–25, week 30–32 and 6 weeks, 6 months and 12 months postpartum. Control serum samples were collected from healthy pregnant women at matching time-points. We analyzed serum cytokines and chemokines levels using a complex assay. A sandwich ELISA was used to measure LCN2. In this pilot study we included pregnant women with SLE (n=4), seropositive RA (n=4), seronegative RA (n=2) and healthy pregnant controls (n=4). The total cohort consists so far of 18 pregnant women with SLE and 23 pregnant women with RA.

Results: We observed lower LCN2 levels during pregnancy in SLE patients, compared to controls and RA patients. LCN2 levels in seropositive RA patients and controls were found to be comparable during pregnancy, whereas pregnant women with seronegative RA showed higher LCN2 levels. Levels of IFNγ, IL-6 and IL-10 were higher in SLE than in RA patients during the course of pregnancy. IL-17 was slightly higher only in seropositive RA patients compared to controls. TNFα was slightly higher in both SLE and RA patients compared to controls, levels of anti-inflammatory IL-10 were very low or undetectable in all groups.

Conclusions: We found interesting differences in cytokine, chemokine and LCN2 levels during pregnancy in women with SLE, seropositive RA and seronegative RA. The results need confirmation in the total cohort and will be further explored for a better understanding of the disparate immune modulation of RA and SLE during pregnancy.

References:

Acknowledgements: This study is supported by grants from St. Olavs Hospital and Norsk Revmatiekerforbund.

Disclosure of Interest: None declared


THU0066 OSTEOCLAST DifferENTIATION gENE EXPRESSION PROFILING REVEALS CCL4 MEDIATES RANKL-INDUCED OSTEOCLAST MIGRATION

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Background: The migration of osteoclast from circulation and bone marrow into bone surface has suggested as a novel therapeutic point for bone erosion in RA. Objectives: We explored the mechanisms involved in osteoclast migration.

Methods: Gene expression for osteoclast migration was identified by microarray analysis and validated by Real-time PCR during differentiation of bone marrow-derived macrophages (BMMs) into osteoclast (OCs). RANKL induced osteoclast precur- sor cell line RAW264.7 migration and invasion in the presence and absence of anti-CCL4 antibody was measured in vitro. Intracellular signaling pathway was as- 

essed by Western blotting. Osteoclast formation was identified by TRAP staining. Results: A panel of 11 chemokines signal was significant increase in osteoclast differentiation of BMMs by Microarray. High expression of CCL4 was validated in primary BMMs and RAW264.7 cell line during differentiated into OCs. RANKL induced osteoclast precur- sor cell line RAW264.7 migration and invasion was decreased upon addition of anti-CCL4 antibody. OCs formation and OCs related genes expression were not affected by CCL4 inhibition. Neutralization of CCL4 promoted the PI13K phosphorylation at 45 to 60min after RANKL stimulation in RAW264.7.

Conclusions: CCL4 regulates RANKL-induced OCs migration, suggesting that CCL4 inhibition could be bone protective in RA.

References:

Acknowledgements: Support for this work was obtained from the National Natural Science Foundation of China (NSFC): 30701129 (WT), 30901332 (FW), 81172845 (WT), 81273294 (MZ), National Natural Science Foundation of Jiangsu province: BK2011851 (WT), BK2012875 (MZ), the special project of clinical medicine from Jiangsu province: BL2013034 (MZ), A Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD), and scholarship from Asia Pacific League of Associations for Rheumatology (APLAR) and International League of Associations for Rheumatology (ILAR) (WT).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4255

THU0067 NLRP3 INFLAMMASOME ACTIVITY IN MONOCYTES IS REGULATED BY 12/15-LOX-OPXENASE

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Background: Activation of the NLRP3 inflammasome is a major inflammatory pathway in monocytes in response to various exogenous and endogenous stimuli. However, negative regulation of inflammasome activity is not well understood. Glucocorticoids (GC) are drugs of choice for the treatment of various inflammatory diseases. Recently, we could show that treatment of monocytes with GC leads to re-programming towards a specific population involved in resolution of inflammation. Gene analysis has shown up-regulated expression of 12/15-lipoxygenase (12/15-LOX) in GC and LPS/GC-treated monocytes. 12-15-LOX reacts with polyunsaturated fatty-acids to generate anti-inflammatory lipid mediators, which contribute to resolution of inflammation.

Objectives: The aim of our study was to determine the contribution of 12/15-LOX on the inflammatory response on murine monocytes.

Methods: Bone marrow-derived monocytes were isolated from wild-type (wt) C57BL/6 and 12/15-LOX-/- mice and stimulated with GC and/or LPS as well as various inhibitors or stimulants. Gene expression was analyzed using qRT-PCR. Protein expression was examined by Western Blot. Flow-Cytometry and ELISA. Toll-like response was analyzed by co-culture of stimulated monocytes with allogenic T-cells.

Results: 12/15-LOX-/- monocytes showed slightly higher secretion of IL-1α as compared to wt cells after LPS stimulation. The differences between wt and 12/15-LOX-/- were much more pronounced when monocytes were additionally exposed to ATP. LPS treatment markedly enhanced expression of pro-IL-1β in 12/15-LOX-/- monocytes. No differences could be observed between wt and 12/15-LOX-/- monocytes in secretion of other proinflammatory mediators as well as the expression of inflammasome components. However, expression of cleaved caspase-11 was up-regulated in 12/15-LOX-/- monocytes exposed to LPS. Additionally, inhibition of caspase-1, caspase-1 and 5-LOX significantly reduced the high secretion of IL-1β in 12/15-LOX-/- monocytes. Interestingly, 12/15-LOX-/- rather than wt monocytes stimulated with LPS led to enhanced T-cell proliferation.
Conclusions: Our results demonstrate that 12/15-LOX plays a regulatory role during inflammatory immune response by counteracting the NLRP3 inflamma-
some activity through down-regulation of caspase-11 and 5-LOX activity. Thus, we identified a novel negative regulatory pathway of inflammasome activity.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4897

THURSDAY, 15 JUNE 2017

Rheumatoid arthritis - prognosis, predictors and outcome

THUO0689 HOW MANY RHEUMATOID ARTHRITIS PATIENTS IN REMISSION EXPERIENCE PAIN? WHAT TYPES AND WITH WHAT FREQUENCY WERE PAINKILLERS RECEIVED? IS REACHING REMISSION A REALISTIC GOAL?

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Background: The primary treatment goal in rheumatoid arthritis (RA) patients is to reach remission. Earlier diagnosis, advancements in disease-modifying antirheumatic drugs, and improved treatment strategies have enabled increasing numbers of RA patients to achieve remission. However, the definition of remission involves the fulfillment of specific criteria, which include a number of swollen and tender joints, the erythrocyte sedimentation rate (ESR), and the visual analog scale of pain (VAS pain).

Some patients with RA in remission wished to take painkillers because they experienced pain and physical limitations in their daily life or at work. Is reaching remission a realistic goal?

Objectives: To evaluate VAS pain and patient's global assessment (PGA) in those with RA in remission, and to determine the types and frequency of which painkillers were received.

Methods: In a study of 554 RA patients with a definite RA diagnosis according to 1987 ACR criteria, we enrolled 235 patients (82% females). All patients had DAS28-ESR <2.6, defined as clinical remission, and had no acute pain as a result of operation or trauma. The mean age and disease activity were 53.6 years and 2.67, respectively. Seventy-one percent of patients were treated with MTX, 30.2% with glucocorticoids, and 58.4% with a biological agent. We evaluated VAS pain and PGA and investigated why patients experienced dissatisfaction with VAS pain and PGA. Moreover, we elucidated how many patients used painkillers and what types of painkillers were used.

Results: The mean values of clinical and laboratory data were described as follows: 28 swollen joints, 0.69; 28 tender joints, 1.56; RF, 157 IU/mL; C-reactive protein, 0.14 mg/dL; ESR, 19 mm/h; and health assessment questionnaire disability index score, 0.618.

Steinblocker stages (I/II/III/IV) were (165/61/18/0), respectively and Steinblocker classes (I/II/III/IV) were (159/68/12/0), respectively. The mean VAS pain was 1.81.

Thirty-five (14.9%) of 235 patients had VAS pain >3 (Fig. 1). The mean PGA was 1.54. Seventeen patients (7.2%) reported PGA >3 (Fig. 2). Reasons for VAS pain or PGA of >3 were: musculoskeletal pain (48.6%), neuropathic pain (23.1%), psychological reasons (9.3%), and other (19%). Thirty-one patients (13.2%) were treated with painkillers such as NSAIDs (46.2%), acetaminophen (22.5%), pregabalin (16.6%), tramadol (4.1%), and other (86%).

The mean values for VAS pain and PGA were improved after using painkillers by 0.73 and 0.36, respectively. There was a significant difference in the improvement rate of VAS pain and PGA between pre-use and post-use of pain-killer (Fig. 3).

Conclusions: VAS pain and PGA are important for understanding the patients' functional disabilities and problems. We should attend to patients' demands and make an informed decision to form a realistic goal for RA treatment. Given that VAS pain and PGA were improved because of the use of painkillers in the current study, we suggest that the ability to appropriately prescribe painkillers is an important method with which to satisfy RA patients in remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1760

THUO070 TREAT-TO-TARGET IN RA: WHAT LEVEL OF TREATMENT RESPONSE IS NECESSARY BY 3 MONTHS IN ORDER TO ACHIEVE THE TREATMENT TARGET BY 6 MONTHS? RESULTS FROM A REAL LIFE STUDY

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Background: When initiating therapy with disease-modifying anti-rheumatic drugs...
(DMARDs) in patients with rheumatoid arthritis (RA); treatment adoptions are recommended if no improvement in disease activity is seen within 3 months, or if the treatment target has not been reached by 6 months. A pooled analyses from several pivotal RCTs showed that RA patients who did not achieve a minor treatment response by 3 months were unlikely to reach the treatment target by 6 months.1

**Objectives:** To examine what level of treatment response is needed after 3 months of therapy in order to achieve the treatment target of remission (REM) or low disease activity (LDA) by 6 months in a routine clinical setting.

**Methods:** Data were provided by NOR-DMARD, a prospective, multicentre, observational study. We selected RA-patients enrolled between December 2000 and November 2012, who were biological DMARD-naive and had moderate or high disease activity (MDA or HDA, respectively) according to the Simplified Disease Activity Index (SDAI) when initiating therapy. All analyses were performed for the total group of included patients (n=1610), as well as for the following sub-groups: disease duration over (n=895) or under (n=681) 12 months, baseline SDAI MDA (n=825) or HDA (n=785), DMARD-naive patients starting methotrexate (MTX) (n=537) and patients starting tumour necrosis factor inhibitor (TNFi) (n=248). We used a diagnostic test approach, created receiver operating characteristic curves and generated sensitivities, specificities and likelihood ratios (LRs) for all improvement cut-points (0–100%) at the 3-month visit. Furthermore, we tested the ability of established response criteria (SDAI 50/70/85/90 response) at 3 months to predict the desired target of SDAI remission or SDAI LDA at 6 months.

**Results:** At inclusion median (IQR) disease duration was 2 (0.2–8.8) years and mean (SD) SDAI was 28.3 (12.8). At 6 months 46.8% of all patients had achieved LDA and 10.8% had reached remission. Not achieving a minor treatment response (SDAI 50% response) by 3 months was associated with decreased probability of reaching remission at 6 months (LR-0.27), but gave little prognostic information regarding the probability of reaching LDA (LR-0.49). Patients with HDA at baseline who did not achieve at least 50% improvement in disease activity by 3 months had very low probability of reaching the treatment target by 6 months (LR-0.15 for remission and LR-0.30 for LDA). SDAI 85% response at 3 months was predictive of reaching the treatment target at 6 months (LR+ 6.56 for remission and LR+ of 6.45 for LDA). For the total group of patients, a reduction in SDAI of 60.2% was needed at 3 months to predict LDA at 6 months with 80% specificity, while 69.2% improvement was necessary to predict remission.

**SDAI response at 3 months and probability of achieving the treatment target by 6 months:**

**Conclusions:** These results from a routine clinical setting confirm results from RCTs demonstrating a predictive association between treatment response at 3 months and achievement of the treatment target by 6 months in RA-patients. Assessments at 3 months can inform clinicians to continue or adjust ongoing DMARD-therapy in a treat-to-target strategy aiming for remission or LDA by 6 months.

**References:**

3. Disclosure of Interest: V. Norvang: None declared, I. Olsen: None declared, E. Kristianslund: None declared, T. Uhlig: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer, Ingelheim, Celtrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UC B, D. Aletaha Consultant for: Abbvie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, UCB, Speakers bureau: Abbvie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, UCB.

**Disclosure of Interest:**

E. Kristianslund: None declared, T. Uhlig: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer, Ingelheim, Celtrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, D. Aletaha Consultant for: Abbvie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, UCB, Speakers bureau: Abbvie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, UCB, J. Smolen Consultant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celtrion, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Celtrion, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, UCB, E. Haavardsholm Consultant/research support from: AbbVie, Pfizer, Roche, MSD, UCB.

**Conclusion:** Excellent radiographic outcome was achieved for patients treated according to a protocolized T2T strategy in daily clinical practice. Patients treated with initial monotherapy had significantly more short-term radiographic progression than patients treated with initial combination therapy.

**References:**


Acknowledgements: We would like to thank all the patients, rheumatology nurses, and rheumatologists who participated in our study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1638

RISK OF REVISION, PROSTHETIC JOINT INFECTION AND DEATH FOLLOWING TOTAL HIP OR KNEE ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITIS – A NATIONALWIDE COHORT STUDY FROM DENMARK

L. Dreyer

Methods: An electronic search was performed by two independent reviewers.

Objectives: Identifying and targeting potential factors influencing nonadherence is therefore crucial in optimising patient management. Adherence was found to be negatively associated with socioeconomic status, health literacy, and beliefs/perceptions/knowledge of the disease and treatment.

Background: Studies have shown that rheumatoid arthritis (RA) patients are at increased risk of prosthetic joint infection (PJI) but with non-uniform results for mortality risk, following total hip and knee arthroplasty (THA and TKA, respectively). The impact of biological DMARD (bDMARD) treatment on the risk of these outcomes is unknown.

Objectives: To investigate the risk of revision, PJI and death following THA and TKA in RA compared with osteoarthritis (OA) patients and 2) RA patients treated with bDMARDs compared with those not.

Methods: Register-based cohort study linking the National Patient Register, DANBIO, Danish Hip Arthroplasty Register and Danish Knee Arthroplasty Register. Follow-up: from date of THA/TKA to date of any of the outcomes, to 10 years of follow-up or end of 2014, whichever came first.

Statistics: Fine-Gray competing risks analyses to calculate confounder adjusted sub-Hazard Ratios (aSHR) with 95% confidence intervals (95% CI) for revision and PJI; Cox proportional hazard models to calculate aHR for risk of death.

Results: We identified 3913 RA and 120 499 OA patients. In DANBIO, 360 bDMARD and 1586 not-bDMARD treated RA patients were eligible for analysis. See Table for results.

Conclusions: We report an increased risk of death and PJI but a lower risk of revision in patients with RA compared with OA following THA and TKA. In RA patients, prednisolone, but not bDMARD treatment within the year prior and/or following THA and TKA was associated with an increased risk of death.

Disclosure of Interest: R. Cordtz: None declared, L. E. Kristensen: None declared, H. Lindegaard: None declared, L. Dreyer Consultant for: LD has received fees for speaking and consultancy by MSD, UCB and Janssen pharmaceuticals.

DOI: 10.1136/annrheumdis-2017-eular.1742

FACTORS ASSOCIATED WITH TREATMENT ADHERENCE IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Nonadherence to treatment in rheumatoid arthritis (RA) has been shown to negatively impact on treat to target goals and disease outcomes. Identifying and targeting potential factors influencing nonadherence is therefore crucial in optimising patient management.

Objectives: To determine factors associated with nonadherence in patients with RA.

Methods: An electronic search was performed by two independent reviewers using MEDLINE and focusing on articles published from inception to January 2017. The search strategy combined the thesaurus (MeSH) and expanded keyword searches of two concepts: RA and treatment adherence. Inclusion criteria included observational studies and clinical trials examining potential factors associated with nonadherence. Exclusion criteria included articles not in English or without online access and those with a focus on forms of therapy other than medication. Agreement between raters at the screening stage was high (97%, kappa=.87).

Results: The primary search yielded 1411 papers, from which 75 were eventually identified as suitable for full review (Figure). Of the 75 papers, 65 were based on observational studies and 10 on clinical trials. Factors associated with nonadherence were broadly categorized into patient-related factors (socio-demographic factors, patient perceptions [beliefs/knowledge/attitudes]), disease-related factors (disease duration/severity, comorbidities, functional disability) and treatment-related factors (drug type/duration/ regimen/complexity, combination therapy). The majority (70% of all included studies) of studies reported significant associations between patient-driven factors and nonadherence.

Conclusions: Patient-related factors including personal perceptions were among key contributors to nonadherence to medication in RA patients. This highlights the need for addressing patient-driven perceptions, along with disease and treatment acceptance.

Disclosure of Interest: None declared
BODY MASS INDEX IN EARLY RHEUMATOID ARTHRITIS IN UNDERWEIGHT PATIENTS IS ASSOCIATED WITH MORE PROGRESSION OF EROSIONS OVER 15 YEARS AND IN OBESE PATIENTS WITH LESS PROGRESSION OF JOINT SPACE NARROWING

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Background: Previous short-term follow-up studies and subanalyses of clinical trials in rheumatoid arthritis (RA) have suggested that low body mass index (BMI) is associated with more radiographic joint progression and high BMI with less. The effect of BMI on progression of erosion score (ES) and joint space narrowing (JSN) could be different in underweight and obese patients.

Objectives: To identify the association between BMI in early RA with radiographic damage during 15 years; to examine if known predictors of a worse radiographic outcome could explain differential radiographic outcome in low and high BMI groups.

Methods: Four hundred and seventy-three patients from the BARFOT study included from 1992 to 1999 who performed their 15-year assessment were studied. The patients were assessed at inclusion and after 1, 2, 5, 8 and 15 years. The groups were defined by BMI (kg/m²) at inclusion: BMI <20, (n=27), BMI 20–25 (n=210), BMI 25–30 (n=179), and BMI >30 (n=57). X-rays of hands and feet were taken by the Sharp-van der Heijde scoring method (SHS). Linear mixed models with SHS, ESR, CRP, SJC and TJC as outcome, and BMI at inclusion as predictor was used, adjusted for age, sex, initial treatment, ACPA and smoking.

Results: At baseline, total score of SHS, ES and JSN did not differ between BMI groups. There were more women and smokers in BMI<20 group and older patients in BMI>30 group. The baseline disease characteristics were similar in the BMI groups.

For the patients with BMI<20 at inclusion, BMI was associated with a higher predicted SHS progression during follow-up, effect size 5.11 (95% CI 1.72 to 15.15) p=0.005, while for the patients with BMI≥20 at inclusion, BMI was associated with lower SHS, effect size 0.92 (0.86 to 0.99) p=0.028. The directions of association between BMI at inclusion and ES and JSN were similar to that for the total SHS. The effect size of the association with erosion progression was highest and significant only in the BMI<20 group, 1.15 (2.72 to 6.42) p=0.025 (in the BMI<20 group 0.95 (0.90–1.00) p=0.074). On the other hand, association between BMI and JSN progression was significant only in the BMI>30 group, 0.93 (0.87 to 0.99) p=0.033 (in the BMI>20 group 2.53 (0.83-7.67) p=0.096). There were no associations between BMI and radiographic damage in BMI 20–25 and BMI 25–30 groups.

We found no significant association between BMI and ESR, CRP, SJC, TJC over time in the BMI<20 group. In the BMI>30 group, BMI was associated with a higher predicted CRP during follow-up, effect size 1.06 (1.01 to 1.12) p=0.028, but not with ESR and SJC. Compared to the patients with BMI 20–25, patients with BMI>30 had higher TJC over 15 years, 3.17 (1.06 to 9.27) p=0.038.

Conclusions: Underweight at onset of RA is associated with more radiographic damage up to 15 years and obesity with less joint damage, independent of sex, ACPA and smoking status. The effect of BMI is not explained by measures of disease activity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4141

THU0075
THE RELATIONSHIP BETWEEN DISEASE ACTIVITY AND DISABILITY IS MEDIATED BY PAIN AND FATIGUE IN EARLY RHEUMATOID ARTHRITIS

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Background: Disability in early rheumatoid arthritis (RA) is correlated with disease activity. However, the relationship between these two clinical outcomes is relatively understudied. Understanding how disability is driven by disease activity will allow targeted interventions to improve function in early RA, alongside the suppression of inflammation.

Objectives: To identify mediators in the relationship between disease activity and disability in early RA.

Methods: Cases with new consultant-made diagnoses of RA were recruited to Yorkshire Early Arthritis Register within 24 months of symptom onset. At the baseline assessment, clinical variables were collected including the 3 variable disease activity score from counts of 28 tender and swollen joints and C-reactive protein (DAS28), Health Assessment Questionnaire (HAQ) and visual analogue scales (VAS) for pain and fatigue. Structural equation models (SEM) were constructed to evaluate the relationship between DAS28, HAQ, pain, symptom duration (SD), age and fatigue.

Results: Of 721 cases included, 482 were female and 239 male. Median age was 58 for both genders and median HAQ was 1.25 and 1.00 for women and men, respectively. A path model within a SEM framework (Figure 1) was a good fit to the data (Chi square 7.528, df=6, p=0.2748; CFI 0.997; RMSEA 0.027). However, the model could not be applied simultaneously to both genders; although estimates of regression coefficients did not vary between males and females (metric invariance), model intercepts were different. In earlier models, age was not a significant predictor and regressions of fatigue on DAS28 were not significant: the effect of DAS28 upon fatigue was fully mediated by pain. Standardised coefficients of direct and indirect effects of DAS28 on HAQ are shown in Table 1, together with Sobel tests for significance of mediator variables. The greatest effect upon HAQ was the direct effect from DAS28, but some of the effect of DAS28 on HAQ was partially mediated by pain. Furthermore, the effect of pain upon HAQ was also partially mediated through fatigue. According to the Sobel test, pain and fatigue were significant mediators in both females and males.

Table 1 Total, Direct and Indirect effects upon HAQ

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
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<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
<td>p</td>
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<tr>
<td>DAS28 total</td>
<td>0.412</td>
<td>0.040</td>
<td>&lt;0.001</td>
<td>0.508</td>
<td>0.053</td>
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<tr>
<td>DAS28 indirect</td>
<td>0.139</td>
<td>0.024</td>
<td>&lt;0.001</td>
<td>0.163</td>
<td>0.033</td>
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<tr>
<td>DAS28 direct</td>
<td>0.282</td>
<td>0.046</td>
<td>&lt;0.001</td>
<td>0.344</td>
<td>0.060</td>
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<tr>
<td>DAS28 via pain and fatigue</td>
<td>0.038</td>
<td>0.010</td>
<td>&lt;0.001</td>
<td>0.032</td>
<td>0.014</td>
<td>0.025</td>
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<tr>
<td>DAS28 via pain</td>
<td>0.101</td>
<td>0.024</td>
<td>&lt;0.001</td>
<td>0.131</td>
<td>0.033</td>
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<tr>
<td>Sobel test statistic (fatigue via pain)</td>
<td>3.290</td>
<td>0.002</td>
<td>0.001</td>
<td>2.279</td>
<td>0.002</td>
<td>0.022</td>
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<tr>
<td>Sobel test statistic (Pain)</td>
<td>3.920</td>
<td>0.085</td>
<td>&lt;0.001</td>
<td>3.253</td>
<td>0.122</td>
<td>0.001</td>
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</tbody>
</table>

The SE, standard error.

Figure 1. Path diagram to show the relationship between disease activity and disability mediated by pain and fatigue.

SD, symptom duration; SE, standard error; t, error terms (representing the unexplained variance in outcomes)

Conclusions: DAS28 dominates the impact upon HAQ in early RA; pain is shown to be an important mediator of the effects of DAS28 on HAQ, while fatigue is important as a mediator of the effect of pain on HAQ. This adds to previous evidence that pain is a driver of fatigue in RA (1) and suggests that interventions to manage pain could be important adjuncts to suppression of inflammation in early RA, in order to optimise function.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6152

THU0076
DISEASE-MODIFYING TREATMENT REGIMENS HAVE BEEN INSUFFICIENT TO REDUCE THE INCIDENCE OF SYSTEMIC AA AMYLOIDOSIS ASSOCIATED WITH RHEUMATOID ARTHRITIS IN CONTRAST TO A SIGNIFICANT REDUCTION IN THOSE WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The UK National Amyloidosis Centre has the largest known cohort of individuals with AA amyloidosis, with 660 cases since 1990. A third present in end stage renal failure (33%), with a median survival of 133 months from diagnosis. Over 27 years the rate of new cases has remained remarkably constant with a median of 24 diagnoses per annum (IGR 18.5–30.5) but responsible for a decreasing proportion of new cases of systemic amyloidosis from 5% in the first 5 years to 6% in the last 5 years of the cohort.

Objectives: We sought to determine to what extent advances in treatment of the inflammatory arthritides have influenced the aetiology of AA amyloidosis over time.

Methods: Retrospective analysis of the UK National Amyloidosis Centre AA
ANTI-COLLAGEN TYPE II ANTIBODIES ARE ASSOCIATED WITH AN ACUTE ONSET RHEUMATOID ARTHRITIS PHENOTYPE AND PROGNOSTICATE LOWER DEGREE OF INFLAMMATION

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Background: Anti-collagen II antibody (anti-CII) positive RA patients present with early but not persistent signs of inflammation and joint erosions. This early anti-CII-dependent phenotype coincides with high anti-CII levels around the time of RA diagnosis, whereas anti-CII levels drop. Our previous studies showed that this phenotype is associated with in vitro cytokine production by monocytes, activation of granulocytes, and enhanced chemokine production by monocyte/granulocyte cocultures, stimulated with anti-CII containing immune complexes. These in vitro findings argue that elevated anti-CII levels at time of RA diagnosis are functionally related to the corresponding acute onset RA phenotype.

Objectives: Our previous comparison done in a small RA cohort (n=274) describe that anti-cyclic citrullinated peptide 2 (anti-CCP2) positive patients have a severe long-term prognosis but anti-CII positive patients have transient inflammation. In the present study we wanted to extend this in a large RA cohort with clinical follow-up data, and to relate to HLA-DRB1* alleles.

Methods: Anti-CII and anti-CCP2 were measured at baseline in 773 patients from the Swedish Epidemiological Investigations in Rheumatoid Arthritis (EIRA) study with clinical follow-up data from the Swedish Rheumatology Quality (SRQ) registry, and 1476 patients with HLA-DRB1* information. Comparisons were done concerning CRP, ESR, TJC, SJC, DAS28, DAS28CRP, pain-VAS, global-VAS and HAQ at 8 occasions during 5 years, and association to HLA-DRB1* alleles.

Results: Anti-CII was detected in 6.6% (97/1476), and anti-CCP2 in 57.9% (855/1476) of the patients. There was no significant difference in treatment strategy at diagnosis for patients with and without those antibodies. Anti-CII associated with elevated CRP, ESR, SJC, and DAS28 and DAS28CRP at diagnosis and up to six months, whereas anti-CCP2 associated with SJC and DAS28 from 6 months to 5 years, but not earlier. The anti-CII-associated phenotype was strong, and predominated also in anti-CII/anti-CCP2 double positive patients. Compared to baseline levels, anti-CII was associated with improvements in CRI ESR, SJC, TJC and DAS28 over time, whereas anti-CCP2 was associated with deteriorations in SJC and DAS28 over time, compared to antibody negative patients. Anti-CII positive patients achieved EULAR good or moderate response more often than negative patients whereas the opposite was found for anti-CCP2 positive patients (figure). Anti-CII was positively associated with HLA-DRB1*01 and HLA-DRB1*03, with significant interaction, and double positive individuals had >14 times higher mean anti-CII levels than HLA double negatives. Whereas smoking associated with elevated anti-CCP2 levels, smokers has lower anti-CII levels.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2776

THU0078

CONCOMITANT USE OF CONVENTIONAL SYNTHETIC DMARDs AND RESPONSE TO BARICITINIB

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Background: Baricitinib (BARI), an oral JAK1/JAK2 inhibitor, is in development for patients (pts) with moderate to severe rheumatoid arthritis (RA).

Objectives: This post-hoc analysis of two phase 3 studies assessed whether concomitant use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) altered the response or safety outcomes to BARI in RA pts and evaluated the effect of concomitant corticosteroid use on the efficacy of BARI.

Methods: Pts with ≥2 swollen and tender joints and no prior biologic use were enrolled. In RA-BEAM (NCT01710358), methotrexate (MTX)-inadequate responder (IR) pts were randomised to PBO once daily (QD), BARI 4 mg QD, or adalimumab 40 mg biweekly. In RA-BUILD (NCT01710358), csDMARD-IR pts were randomised to placebo (PBO) or BARI (2 or 4 mg) QD. Pts continued background csDMARD (including MTX) therapy. This post-hoc analysis included the PBO (N=716) and BARI 4 mg (N=714) pts and assessed the number and type of concomitant csDMARDs and concurrent corticosteroid use.

Results: 71%, 21%, and 6% of PBO pts were taking MTX alone, MTX + ≥1 other csDMARD, and non-MTX csDMARDs, respectively; in BARI 4 mg pts, the

<table>
<thead>
<tr>
<th>Efficacy measures</th>
<th>MTX Alone (n=596)</th>
<th>MTX + ≥1 csDMARDs (n=147)</th>
<th>Non-MTX csDMARDs (n=43)</th>
<th>MTX Alone (n=527)</th>
<th>MTX + ≥1 csDMARDs (n=131)</th>
<th>Non-MTX csDMARDs (n=42)</th>
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<tr>
<td>Safety measures</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>≥1 adverse event</td>
<td>424 (72)</td>
<td>522 (27)</td>
<td>134 (21)</td>
<td>435 (84)</td>
<td>524 (31)</td>
<td>126 (31)</td>
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<tr>
<td>≥1 serious adverse event</td>
<td>16 (3)</td>
<td>4 (3)</td>
<td>3 (7)</td>
<td>13 (3)</td>
<td>4 (3)</td>
<td>2 (5)</td>
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<tr>
<td>Discontinuation due to adverse event</td>
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<td>1 (0.7)</td>
<td>0</td>
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Baricitinib 4 mg (N=714)

Abstract THU0078 – Table 1. Efficacy and Safety Through 12 Weeks Based on Concomitant csDMARD Usage

Data are n (%).
EVALUATION OF SYNOVITIS IN THE FOOT AND THE ANKLE

Depression and anxiety reduce the likelihood of achieving remission in patients with rheumatoid arthritis.

Background: Depression and anxiety are reported to predict poorer treatment outcomes in rheumatoid arthritis (RA). The present study was conducted to clarify the relationship between the systemic disease activity, local disease activity using US and a synovial histopathological examination of the gathered synovium in the foot and the ankle.

Methods: A total of 1450 RA patients were included (mean (SD) age 54.4 (13.5) years, median (25th-75th percentile) disease duration 0.4 (0.0-5.0) years, 68.7% females and 28.6% current smokers). According to the SF-36-MH and -PMA, 18.1% of the patients were depressed/anxious at baseline.

Results: The PD score was grade 0 in 82 cases, 1 in 32 cases, 2 in 20 cases and 3 in 5 cases. The total RS and its item scores except for “proliferating blood vessels” correlated well with the PD signal intensity. The systemic disease activity, as indicated by DAS28, CRP and MMP-3, had no significant correlation with the local PD signal intensity. However, the DAS28, CRP and MMP-3 values and each item score except for “proliferating blood vessels” were significantly lower in the PD grade 0 group than in the PD grades 1, 2 and 3 groups.

Conclusions: No PD signal intensity in the ankle and foot indicates well-controlled disease activity. US is an excellent tool for determining local synovitis as well as the systemic disease activity in patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1342

THU0080

DEPRESSION AND ANXIETY REDUCE THE LIKELIHOOD OF ACHIEVING REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL LIFE DATA FROM THE NOR-DMARD STUDY

B. Michelsen1,2, E.K. Kristianslund2, K.M. Fagel2, E. Lie2, H.B. Hammer2, G. Haugberg1, T.K. Kvien1,2, 1Dept. of Rheumatology, Hospital of Southern Norway Trust; Kristiansand, 2Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo.

Background: Depression and anxiety are reported to predict poorer treatment outcomes in rheumatoid arthritis (RA). Whether this can be confirmed in larger prospective observational studies using various remission criteria remains to be explored.

Objectives: To investigate the predictive value of baseline depression/anxiety on the likelihood of achieving remission in RA as well as the associations between baseline depression/anxiety and the components of the remission criteria at follow-up.

Methods: From the prospective, multi-center NOR-DMARD study we included RA patients starting first-time tumour necrosis factor inhibitors (TNFi) and DMARD naïve RA patients starting methotrexate (MTX) between year 2006 and 2012. The following two criteria for depression/anxiety were assessed: 1) the Medical Outcomes Survey Short Form-36 (SF-36) Mental Health subscale (MHI)-56 and 2) the SF-36 Mental Component Summary score (MCS)-38.

Results: Baseline depression/anxiety on remission after 3 and 6 months was explored in prespecified logistic regression models adjusted for age, sex, disease duration and smoking.

Conclusions: Baseline depression/anxiety negatively predicted remission after 3 and 6 months (adjusted analyses, table 1 and 2).

The findings were confirmed in separate subgroup analyses of TNFi/MTX treated patients. Baseline depression/anxiety was associated with increased patient’s and evaluator’s global assessment and 28 tender joint count at 3 and 6 months, but not with level of acute phase reactants or 28 swollen joint count.
Conclusions: Depression and anxiety may reduce likelihood of remission based on composite scores in RA and should be taken into account in individual patients when making a shared decision on a treatment target.

References:

Disclosure of Interest: B. Michelsen: None declared. E. Kristianslund: None declared. K. Fagel: None declared. E. Lie Consultant for: Hospira, Pfizer, UCB. Speakers bureau: AbbVie, Celgene, H. Hammer Consultant for: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis. Speakers bureau: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis. G. Haugeberg: None declared. T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celtrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB. Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celtrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer Roche, Sandoz and UCB.

DOI: 10.1136/annrheumdis-2017-eular.1787

THU0081
DIFFERENCES IN PATIENT-REPORTED OUTCOMES BETWEEN BARCITINIB AND COMPARATORS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED LOW DISEASE ACTIVITY OR REMISSION

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Background: Achieving remission is the ideal goal in treating rheumatoid arthritis (RA). In a randomised phase 3 trial, high remission and low disease activity (LDA) rates were achieved with baricitinib (BARI). However, little is known about the differences in patient reported outcomes (PROs) among patients (pts) who have already achieved these targets.

Objectives: To compare PROs between BARI, adalimumab (ADA), and placebo (PBO) in pts with RA who achieved LDA or remission in the Phase 3 RA-BEAM study.

Methods: 1305 pts with RA and background treatment with methotrexate were randomised to receive PBO (n=488), ADA (n=330), or BARI 4 mg (n=487) for 52 wks (24 wks for PBO). In each treatment group, pts in remission (DAS28<3.2) at wk 24 were assessed from baseline for the following PROs: Pain VAS, HAQ-DI, WPFI, Morning Joint Stiffness (MJS), and FACT-F. Sensitivity analyses were conducted for pts in remission or LDA by DAS28-ESR, SDAI, or CDAI. The assessment of response at wk 24 was determined by using the observed data, and the missing values for PRO measures were imputed by using mLOCF.

Results: Among pts in LDA, significantly greater improvements in Pain VAS and HAQ-DI scores were observed with BARI than ADA and PBO, and significantly greater improvements in MJS were observed with BARI and ADA than PBO. Significantly greater residual pain and HAQ-DI scores were observed with BARI. Among pts in remission, significantly greater improvements in pain and HAQ-DI scores were also observed with BARI than PBO. Patients in remission or LDA showed greater numerical improvement and less residual impairment in other PROs with BARI and ADA than PBO (Table 1). Consistent results were observed using other composite measures to define LDA and remission.

Conclusions: The preliminary findings from this study suggest that BARI showed greater improvements in pain and HAQ-DI compared to ADA for pts in LDA, and greater improvements in pain and HAQ-DI scores as well as less physical impairment compared to PBO for pts in LDA and remission.

A. Acknowledgements: The authors acknowledge the contribution of Inmaculada de la Torre MD, PhD, Senior Medical Advisor.


DOI: 10.1136/annrheumdis-2017-eular.2213

THU0082
LUNG INVOLVEMENT IN ACPA POSITIVE SUBJECTS: A PILOT STUDY ON THE ROLE OF LABORATORY, FUNCTIONAL AND IMAGING MARKERS

B. Lucchino1, M.C. Gerardi1, C. Iannuccelli1, M.P. Guzzo2, M. Di Paolo2, M. Bonini3, F. Vaccaro2, P. Palangio2, F. Vullo3, D. Diaci1nti, G. Valesini3, M. Di Franco1, 1Department of Internal Medicine and Medical Specialties; 2Department of Public Health and Infectious Diseases; 3Department of Radiology, Sapienza university of Rome, Roma, Italy.

Background: The ACPA-positive Rheumatoid Arthritis (RA) is a complex disease. Signs of immune activity against citrullinated proteins may be present years before the onset of clinical manifestations. Recent findings suggest that the lung may represent an early site of autoimmunity-related injury in ACPA-positive patients without signs of arthritis.

Objectives: The purpose of the present study was to evaluate the presence of subclinical pulmonary abnormalities in ACPA-positive subjects without arthritis and in RA-patients through laboratory, functional and imaging markers.

Methods: Eleven ACPA-positive subjects without arthritis, 10 patients naïve to therapy with early ACPA-positive RA (<6 months duration) and 9 with established ACPA-positive RA (<36 months duration) were included in the study. Subjects underwent baseline pulmonary function tests (PFTs), DLCO measurement and CPET. The evaluation of Surfactant protein D (SP-D) serum levels was performed in all the patients and in 9 healthy controls matched for age and sex with an ELISA test. A total of four subjects underwent chest high-resolution computer tomography (HRCT), in order to evaluate parenchymal or airways abnormalities.

Results: The cohort consisted of 7 men and 23 women, mean age 48.93 (DS="±12.1"). PFTs resulted abnormal in only 2 patients. A DLCO reduction trend was observed in 54.5% of ACPA-positive subjects without RA, in 69% and in 55.6% of patients with early and established RA, respectively. In RA patients, an inverse correlation between disease duration and DLCO/Va (r=0.50; p=0.03) was observed. The exercise tolerance at CPET was reduced in 54.5% of ACPA-positive subjects without RA, in 20% of patients with early RA and in 55.6% of those with established RA. Serum SP-D levels were higher in established RA (p=0.079), in ACPA-positive subjects and early RA than in healthy controls. ACPA levels positively correlated (r=0.45; p=0.01) with CPET parameters of ventilation inefficiency, suggesting a ventilation/perfusion mismatch. A negative correlation between ACPA and SP-D levels and CPET metabolic parameters was also observed. The presence of pulmonary nodules was the most common alteration found at HRCT, equal to 28% in ACPA-positive subjects without arthritis, in 66% and 87% of patients with early and established RA, respectively. In all patients, the presence of pulmonary abnormalities detected at HRCT seemed to develop early in the course of the disease. However, additional studies are needed to clarify lung abnormalities in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6216

THU0083
THE RELEVANCE OF ELEVATED CRP AS AN INCLUSION CRITERION IN CLINICAL TRIALS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Elevated C-reactive protein (CRP) is often used as an entry criterion in clinical trials (CT) of patients (pts) with rheumatoid arthritis (RA), resulting in the potential exclusion of pts with active disease and high screen failure rates.

Objectives: To assess the relevance of requiring an elevated CRP (>1 mg/dL) as an inclusion criterion for functional and radiographic outcomes.

Methods: This post hoc analysis used data from 2 randomized CTs in RA pts with an inadequate response to methotrexate (MTX). In DE019, pts on background MTX received adalimumab (ADA) or placebo (PBO)2, in MUSICA, pts received either 7.5 or 20 mg MTX, along with ADA3. Data from MUSICA were used
to confirm observations from DE019. Pts were subgrouped by CRP level at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not have CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP 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0.75 mg/dL. Ours is the first study to report data at week 24.

Results: In DE019, 183 pts (89 and 94 in the ADA and PBO arms, respectively) had CRP >1 mg/dL and 224 pts (118 and 106, respectively) had CRP >1 mg/dL. Pts with elevated CRP had higher BL disease activity compared with those with CRP <1 mg/dL. After 24 wks of treatment with ADA, pts in both CRP subgroups experienced significant improvements in most clinical and functional outcomes vs PBO (Table). In pts with CRP >0.8 mg/dL, the ACR20 response rate difference (30.4, p < 0.001) and the difference in △mTSS (1.3, p < 0.05) for ADA vs PBO treatment were still significant. Compared to pts with CRP <1 mg/dL, pts with elevated CRP experienced greater clinical and functional improvements. However, within the ADA subgroups, pts with elevated CRP had smaller differences vs PBO in mTSS, perhaps reflecting higher joint damage at BL. In general, similar trends were observed in MUSICA (not shown).
initial therapeutic strategies were oral methotrexate monotherapy 16% (site range 0%–55%), subcutaneous methotrexate monotherapy 15% (0%–45%), methotrexate-based combination therapy 30% (10%–47%), non-methotrexate DMARDs 19% (4%–44%), triple therapy 11% (0%–60%), and biologics 2% (0%–18%). At 60 months of follow-up, the frequency of use of these strategies was relatively stable except for biologics which increased to 21% (0%–80%). The mean and median time to DAS28 remission was 12.4 months (SD 12.1, range 8.6 to 17.2) and 9 (IQR 3, 18) months respectively. The mean and median time to CDAI remission was 14.8 (SD 13.5, range 10.3 to 21.2) and 9 (IQR 6, 18) months respectively. The frequency of sustained DAS28 remission was 59% (95% CI 52–70%), and CDAI 35% (12–58%). At the two sites with the highest rates of sustained remission and shortest time to remission, patients had fewer comorbidities and the initial treatment strategy was preferentially methotrexate-based combination therapies, and with eventual advancement to biologics in 7 and 39% in patients. In contrast, at the patients at the site with the lowest rates of sustained remission and longest time to remission had long symptom duration at treatment initiation, highest body mass index and proportion with ≥2 comorbidities, worse socioeconomic status and higher baseline DAS28.

This site also had the highest proportion of patients treated with biologics at treatment initiation, highest body mass index and proportion with ≥2 comorbidities, worse socioeconomic status and higher baseline DAS28.

Conclusions: Treatment strategy and patient characteristics vary across CATCH sites and contribute to variable rate and frequency of achieving sustained remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5695

**THU0086**

THE USE OF A BLINDED TRUNCATED ULTRASOUND POWER DOPPLER JOINT COUNT TO CONFIRM DISEASE ACTIVITY FROM AN EARLY PHASE OPEN LABEL DRUG TREATMENT STUDY TREATING RHEUMATOID ARTHRITIS

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Background: Small open label pilot trials generate important information on tolerability, toxicity, pharmacokinetics, and antigenicity in the early phase investigation of new compounds in the treatment of rheumatoid arthritis (RA). However, because the standard disease activity measurements (DAMs), such as the disease activity score in 28 joints (DAS28) have a major subjective component, the efficacy data acquired in such trials is generally felt to be much less reliable than that obtained in blinded trials. Incorporating more objective DAMs, and performing them in a blinded fashion, might enhance the validity of efficacy data in such an early clinical setting.

One possible disease activity measure to fulfill this role would be an ultrasound power Doppler joint count (UPD) which has been shown to correlate with conventional clinical measures.

Objectives: To determine whether the blinded use of a truncated (low joint count) UPD in an early phase RA trial correlates with other DAMs in the trial and contributes to validation of efficacy of the drug.

Methods: The results of an open label trial in which Staph Protein A (PRX-100, Protxal Inc.) was given to patients with active RA has been previously reported1. Serum samples were obtained 5 times over the first 24-hour period (8 AM, 12 PM, 4 PM, 8 PM, and 8 AM) at 12 PM in the next 24-hour period; and at 8 AM the next 2 consecutive days, for a total of 8 timepoints. An additional midnight sample was excluded from the analysis because this timepoint is not relevant to normal clinical practice hours. Diurnal variation was calculated using 5 timepoints over the first 24 hours. Daily variation was determined using 4 timepoints taken at 8 AM on successive days. Combined diurnal and daily variation was calculated using 8 timepoints over 4 days. For each patient, absolute changes in MBDA scores were calculated for all possible pairs of timepoints for: a) diurnal variation (total 220 pairs), b) daily variation (total 132 pairs) and c) diurnal and daily variation (total 616 pairs). MID was calculated as the 90th percentile of absolute changes from baseline.

MIDs were calculated as the 90th percentile of absolute changes from baseline. MID was calculated as the 90th percentile of absolute changes from baseline.

Correlations between MBDA and clinical DAMs from baseline to single time points were assessed by the Wilcoxon signed rank test and correlations were performed by the Spearman’s rho test (p). Effect size was determined by standardized mean difference (SMD).

Clinical assessments and UPDs were obtained weekly for the first month, then monthly for five more months.

**Results:**

Intra-observer UPD score reproducibility was high (ICC = 0.886). Significant reductions (p < 0.05) in UPD and the DAS28 were found at day 22 and on all subsequent visits. Correlations between UPD and DAMs total scores were moderate to strong. However, the total differences from baseline and visits did not correlate, except for CRP (n=67, p=0.471, p = 0.001). Also, some individual time points showed differences such as baseline vs day 196 (see table). SRMs for both UPD and DAMs were high, but higher for the DAS28 (1.00–2.16) than for the UPD (0.83–1.16).

Conclusions: The use of a truncated UPD in this small open label trial was feasible, reproducibly read, and significantly correlated with conventional disease activity measure.

The inclusion of UPD in this open label pilot trial adds validation to the efficacy data.

References:


changes using all diurnal and daily variation data. Bootstrapping was used to validate the result.

Results: Of patients included in the analysis, 13 had moderate MBDA scores and 9 had high MBDA scores at baseline. Baseline demographics were: 73% women, mean age 61.8 (SD: 12.1) years, mean MBDA score 43.9 (SD: 8.3), and mean CDAI score 17.1 (SD: 11). No patients were on glucocorticoids. Based on the analysis of the absolute change of MBDA score in the data with daily and diurnal variation combined, the mean was 3.4 (SD: 3.8), the median (Q1, Q3) was 2 (1, 5), and the MID was calculated as 7. Similar results were obtained using a bootstrap method. Minimal variability in mean MBDA scores was observed over 4 days for patients with moderate and high baseline MBDA scores (Figure 1).

Conclusions: Based on the short term biologic variability of moderate and high MBDA scores, the MID was 7 units. An absolute change exceeding this threshold is unlikely due to diurnal and daily biological variation of the MBDA scores.

Disclosure of Interest: None declared.


THU0088

STRUCTURAL DAMAGE PROGRESSION IN PATIENTS TREATED WITH METHOTREXATE, BARICITINIB MONOTHERAPY OR BARICITINIB + METHOTREXATE BASED ON THE LEVEL OF CLINICAL RESPONSE IN THE PHASE 3 RA-BEGIN STUDY

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Background: Baricitinib (BARI), an oral inhibitor of Janus kinase (JAK) 1 and JAK 2, is being developed for the treatment of rheumatoid arthritis (RA). RA-BEGIN was a phase 3 double-blind, three-arm multicentre study of BARI administered as monotherapy or in combination with methotrexate (MTX) to patients (pts) with early active RA who had no or limited prior exposure to DMARDs. Methotrexate (MTX) monotherapy was the active comparator.

Objectives: To evaluate the proportion of pts with structural damage progression, defined as change from baseline (CBF) greater than the smallest detectable change (SDC) in mTSS at week (wk) 52, depending on their disease state as measured by DAS28-CRP.

Methods: Pts were classified into two groups based on DAS28-CRP. Group A included pts who achieved sustained DAS28-CRP ≤3.2 at weeks 16, 20 and 24. Pts who did not achieve DAS28-CRP ≤3.2 consecutively at weeks 16, 20 and 24 and pts with missing DAS28-CRP at any of those 3 visits were included in Group B. The proportion of pts with CFB mTSS > SDC at wk 52 was estimated for each treatment arm for the two defined groups of response. The SDC in mTSS was calculated as SD/√2, where SD is standard deviation of paired differences of change from baseline. Logistic regression analysis was used to correlate the effect of disease activity at baseline on radiographic progression.

Results: The proportion of pts with CFB mTSS > SDC at wk 52 was estimated for each treatment arm for the two defined groups of response. The SDC in mTSS was calculated as SD/√2, where SD is standard deviation of paired differences of change from baseline. Logistic regression analysis was used to correlate the effect of disease activity at baseline on radiographic progression.

Conclusions: Disease activity measures and their ability to predict structural damage progression were different depending on the level of disease activity at baseline. Radiographic progression was more likely to occur in pts with moderate disease activity than high disease activity.


THU0089

M-DA28, DAS28 (CRP) AND RAPID3 SCORES AT BASELINE ARE GOOD PREDICTORS OF RADIOGRAPHIC DISEASE PROGRESSION AT 1 AND 2 YEARS: DATA FROM THE AMPLTE TRIAL

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Background: Clinicians rely on time-efficient, validated disease activity assessments to help predict disease progression accurately in patients (pts) with RA. The utility in predicting structural damage progression for the Routine Assessment of Patient Index Data 3 (RAPID3) is largely unknown, while that of DAS28 (CRP)2 and modified (M-)DA28 have been previously reported.3

Objectives: This post hoc analysis examined the relationship between baseline disease activity measures and their ability to predict structural damage progression in the Phase III AMPLTE (NCT00529684) trial.

Methods: AMPLTE was a randomized, investigator-blinded study in which MTX-experienced pts with active RA ≤5 years received SC abatacept 125 mg weekly or adalimumab 40 mg every 2 weeks in combination with stable-dose MTX. Logistic regression analysis was used to correlate the effect of disease activity at baseline on radiographic (X-ray) progression at Months (M) 12 and 24. Disease activity was assessed using M-DA28,4 DAS28 (CRP), RAPID3, CDAI and SDAI. Radiographs were scored using the modified Sharp/van der Heijde scoring system; progression was defined as change from baseline in total score greater than the smallest detectable change, which was calculated as SD/square root (2) x 1.96 (where SD is standard deviation of paired differences of change from baseline in total score greater than two readers).

Results: Logistic regression analysis was carried out for all randomized and treated pts (abatacept, n=318; adalimumab, n=328). For these patients, M-DA28, DAS28 (CRP) and RAPID3 at baseline were significant predictors of radiographic progression at M12 and M24, baseline SDAI was a significant predictor at M12 but not M24 and baseline CDAI was not a significant predictor at either time point

Logistic regression model and area under ROC curves for the impact of disease activity assessed on radiographic progression at M12 and M24 (all randomized and treated patients)

<table>
<thead>
<tr>
<th>Disease activity measure</th>
<th>M12</th>
<th>M24</th>
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<tbody>
<tr>
<td>OR (95% CI) p value AUC</td>
<td>OR (95% CI) p value AUC</td>
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<tr>
<td>CDAI</td>
<td>1.02 (1.00, 1.04) NS 0.5762</td>
<td>1.02 (1.00, 1.04) NS 0.5416</td>
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<tr>
<td>SDAI</td>
<td>1.02 (1.00, 1.04) -0.05 0.5963</td>
<td>1.02 (1.00, 1.03) NS 0.5634</td>
</tr>
<tr>
<td>DAS28 (CRP)</td>
<td>1.47 (1.15, 1.90) -0.01 0.6221</td>
<td>1.31 (1.03, 1.67) -0.05 0.5911</td>
</tr>
<tr>
<td>RAPID3</td>
<td>1.26 (1.08, 1.35) -0.01 0.6270</td>
<td>1.16 (1.01, 1.34) -0.05 0.5871</td>
</tr>
<tr>
<td>M-DA28</td>
<td>1.51 (1.25, 1.83) -0.01 0.6624</td>
<td>1.36 (1.13, 1.63) -0.01 0.6208</td>
</tr>
</tbody>
</table>

AUC = area under the curve; M = month; NS = not statistically significant; OR = odds ratio; ROC = receiver operating characteristic.
Results: The main baseline demographic and disease characteristics of the whole sample of ERA (n=223) and the 3 age groups- YORA (46), IORA (81) and LORA (96) - are summarised in Table 1. Age at RA-onset was independently associated with DAS28CRP remission at 1 year (Table 2). Conclusions: In a cohort of ERA, older age at disease onset is associated with a more active (CRP) disease at the beginning but with a greater probability of DAS28CRP remission at 1 year.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5011

THU0091 HIGH MULTI-BIOMARKER DISEASE ACTIVITY SCORE IS ASSOCIATED WITH HIGH RISK OF RADIOGRAPHIC PROGRESSION IN SIX STUDIES

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Background: The multi-biomarker disease activity (MBDA) test uses a validated algorithm with 12 serum protein biomarkers to assess disease activity in patients with RA. The MBDA score has previously been found to be a predictor of risk for radiographic progression (RP). To date, there is no evidence that the MBDA score may be a predictor for radiographic progression in patients with ERA.

Objectives: To evaluate data from six cohorts to collectively establish the relationship between the MBDA score and risk for RP.

Methods: Clinical, MBDA score and radiographic data were analyzed for 6 cohorts with N: Year 2, OPERA Year 1, AMPLE Year 1, AMPLIFY Year 2, SWEFOT Year 1, and AMPLIFY Year 1 (abatacept and adalimumab arms) (see Figure). Analyses used published results when available or patient-level data when not (i.e., for Leiden; and for OPERA CRP analyses). Frequency of RP over one year was determined by category of MBDA score (low, moderate [30–44], high on a scale of 1–100) at the start of the year for four cohorts and by category of MBDA score at the end of the year for AMPLE cohorts (as published). RP was defined using the threshold for change in total modified Sharp score (ΔmTSS) specific to each study (2 to >5 TSS units). Positive and negative predictive values (PPV and NPV) were determined for each study by comparing patients with high MBDA score (>44), DAS28(CRP) or CRP respectively. Previously published multivariate analyses in the Leiden and SWEFOT Year 1 cohorts showed that MBDA score was an independent predictor of RP compared with other predictors. In the Leiden cohort, MBDA score was the strongest predictor and high MBDA score was an independent predictor of RP compared with other predictors. In the Leiden cohort, MBDA score was the strongest predictor and high MBDA score was an independent predictor of RP compared with other predictors.
discreminated between high and low risk for RP among patients with high SJC (≥5) or high DAS28-CRP with PPV as high as 57%.

**Conclusions:** High MBDA scores were associated with increased risk for RP in 6 study cohorts, including patients treated with csDMARDs, TNFi and abatacept. Based on high NPVs (>93%), the MBDA score used alone had clinical value for identifying patients with little or no risk of RP. Combining the MBDA score with clinical measures yielded PPVs approaching 60%, suggesting that biomarkers can help stratify patients by their risk for RP.


**G. Yurdakul**

**PhysGA:** Physician global assessment, **DAS:** Disease activity score, **CRP:** C Reactive protein, **BDI 15.71±13.34 11.28±12.56 0.06**

**PSQI 8.02±5.58 5.00±4.20 0.00**

**PhGA 2.87±2.16 2.09±1.63 0.08**

**Table 1. Clinical features in female and male RA patients**

<table>
<thead>
<tr>
<th></th>
<th>Female RA patients</th>
<th>Male RA patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Widespread pain index</td>
<td>4.70±4.97</td>
<td>2.65±3.99</td>
<td>0.04*</td>
</tr>
<tr>
<td>PhGA</td>
<td>2.87±1.26</td>
<td>2.09±1.63</td>
<td>0.08</td>
</tr>
<tr>
<td>DAS28</td>
<td>3.39±1.91</td>
<td>2.68±1.11</td>
<td>0.01*</td>
</tr>
<tr>
<td>CRP</td>
<td>10.77±13.62</td>
<td>12.59±14.20</td>
<td>0.24</td>
</tr>
<tr>
<td>Tender Joint Count</td>
<td>50.9±12.47</td>
<td>67.8±13.09</td>
<td>0.02*</td>
</tr>
<tr>
<td>Swollen Joint Count</td>
<td>0.88±12.67</td>
<td>0.31±10.69</td>
<td>0.690</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.06±0.83</td>
<td>0.68±0.66</td>
<td>0.04*</td>
</tr>
<tr>
<td>RAQOL</td>
<td>14.31±10.06</td>
<td>7.59±8.83</td>
<td>0.00</td>
</tr>
<tr>
<td>FSS</td>
<td>35.7±17.24</td>
<td>22.1±14.41</td>
<td>0.00</td>
</tr>
<tr>
<td>PSQI</td>
<td>8.02±5.58</td>
<td>5.00±4.20</td>
<td>0.00*</td>
</tr>
<tr>
<td>BDI</td>
<td>15.71±13.34</td>
<td>11.28±12.56</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**THU0092**

**CHRONIC PAIN INCREASES INDEPENDENT OF THE DISEASE ACTIVITY AND DEPRESSION IN FEMALES WITH RHEUMATOID ARTHRITIS**

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**Background:** Chronic pain is a key component of rheumatoid arthritis (RA). Although pain is reduced with the control of inflammation at the first years of the disease, pain increases over time with different pathways just as central sensitization. Fatigue, sleep disturbance and chronic pain are common problems in patients with RA (1,2).

**Objectives:** We aimed to investigate the frequency of widespread pain, sleep disorders, fatigue, and depressive symptoms in RA patients. Furthermore, we aimed to describe the relationship between these symptoms and disorders were analyzed between female and male RA patients.

**Methods:** One hundred and sixty one RA patients (female: 119, male: 42) and 88 healthy controls (female: 52, male: 16) were enrolled in the study. Widespread pain index (WPI) with nineteen body parts that was identified by 2010 fibromyalgia diagnostic criteria, Fatigue, sleep disturbance and depressive symptoms with chronic pain are common problems in patients with RA (1,2).

**Results:** The mean PhGA, HAQ, BDI, FSS, WPI values of RA patients were worse than healthy controls (p=0.012, 0.000, 0.008, 0.033, 0.044 respectively). There was no difference between RA and healthy controls within WPI in night’s sleep. The mean age, disease duration, MS, swollen joint count, C-reactive protein, PhGA and BDI were similar in female and male RA patients. WPI, vas pain, tender joint count, HAQ, RAQOL, FSS, and PSQI, and DAS 28 were higher in females (Table 1).

**Conclusions:** RA is a disease that increases fatigue, depressive symptoms and widespread pain. DAS28 significantly were higher due to the increased pain scores and tender joint count which are subjective parameters in female RA patients. Pain scores in females are significantly higher than in males, and pain exacerbated by central sensitization pathway in women may lead to sleep disorders and fatigue, but not increase depressive symptoms.

**References:**

[1] The role of central nervous system in the generation and m...
2 groups (41and 92 pts who achieved RR and didn’t respectively). After 2 yrs the factors associated with RR achievement in pts with RA while non-biological DMARDs using was assessed.

**Results:** Before study, pts in both groups were comparable by all demographic, clinical and x-ray characteristics, frequency of DMARDs prescribed. They differed only in frequency of RF positivity (39.0% and 57.6% respectively in pts achieved RR and didn’t, p<0.05), aCCP-positivity (21.7 and 73.3% respectively, p<0.001) and aCCP level (6.06±38.8 and 105.3±22.7 U/ml respectively, p<0.001).

There was strong and moderate positive correlation between RR achievement and aCCP-positivity (r=0.57, p<0.05), low aCCP level (r=-0.45, p<0.05) and ΔDAS28 (-r=0.35, p<0.05).

Results of multinominal logistic regression analyses (SPSS, V22, IBM) showed that RF-positivity was the only independent predictor of RR achievement (B=3.14, p<0.05).

41.7% pts in RR achieved clinical remission by DAS28 as well. Only 19.7% pts achieved clinical remission without RR (p<0.05 vs pts achieved clinical and RR) and 12.5% pts achieved RR without clinical response (ΔDAS28: -5.1, ΔDAS28: ≤1.2 or any value of DAS28 with ΔDAS28: ≤0.6; p<0.01).

After 2 years of treatment the mean value of ΔDAS28 in comparison groups (with and without RR) did not differ (2.79±0.28 vs 2.33±0.17 respectively) so there was a discrepancy between clinical and radiological outcome.

**Conclusions:** Baseline predictors associated with achieving of radiographic remission in pts with RA are RF- and aCCP-positivity, low level of aCCP, but independent predictor of radiographic remission achievement is the only RF-positivity.

The discrepancy between the frequency of clinical and radiographic remission achievement in RA patients is observed.

After 2 yrs of non-biological DMARDs treatment 41.7% pts with RA achieves radiographic and clinical remission at the same time.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2882

**THU0096**

**MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) IS ASSOCIATED WITH THE PROGRESSION OF STRUCTURAL BONE DAMAGE IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION**

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1University of Erlangen-Nuremberg, Erlangen, Germany; 2University Medical Center Freiburg, Rheumatology and Clinical Immunology, Freiburg, Germany; 3St.Vincent Hospital, Vincenza Group Study, Medical University of Vienna, Vienna, Austria; 4Institute of Rheumatology, Sao Paulo, Brazil

**Background:** Due to an increasing number and an earlier use of effective disease modifying anti-rheumatic drug (DMARD) therapy a growing number of rheumatoid arthritis (RA) patients reaches a state of clinical remission of disease. Whether clinical remission completely protects from structural bone damage, however, is still a matter of debate as conventional radiographic methods have their limitation in the sensitivity to characterize bone damage. Furthermore, residual activity of inflammation associated with the generation of inflammatory markers may characterize a subset of RA patients in remission, associated with higher prevalence and/or progression of bone damage.

**Objectives:** To test whether residual systemic inflammation is associated with structural bone damage and the progression of structural bone damage in RA patients in sustained remission.

**Methods:** RA patients (i) fulfilling the 2010 EULAR/ACR classification criteria of RA, (ii) having a positive anti-citrullinated protein antibody (ACPA) status and (iii) being in DAS28-ESR remission for 6 months were included. High-resolution peripheral quantitative computed tomography (HR-pQCT) of the right hand was done at baseline and after 1 year. Erosion numbers and erosion volumes were assessed in the metacarpophalangeal joints. Vectra-DA tests measuring the serum levels of twelve different inflammation markers (CRP, SAA, IL-6, TNFR1, IL-1RA, MMP-3, EGF, VEGF-A, VCAM-1, YKL-40, leptin and resistin) were performed. In the baseline examinations, MBDA score was calculated according to previously defined algorithms with low MBDA score defined as <30 units and moderate to high scores as ≥30 units (1).

**Results:** 100 ACPA+ RA patients in sustained remission were investigate (mean±SD age: 57±14 yrs; disease duration: 48±9 yrs; DAS28: 1.7±0.5;83% females; 100% MTX treatment, 38%; MTX+TNF treatment), 65 patients had low (<30), 25 patients had moderate (≥30–44 and 10 patients had high (≥44) MBDA scores. Patients in the different MBDA categories had similar age, sex, disease duration, DAS28 scores and DMARD treatment. Baseline HR-pQCT analysis showed that erosion numbers and volumes were significantly (p<0.001) higher in patients with high MBDA scores. Higher erosion numbers (>10) and larger erosions (>10 mm²) were exclusively found in patients with moderate to high MBDA scores. MBDA scores were correlated to erosion numbers (p<0.001) and volumes (p=0.0018). Longitudinal analysis showed significant progression of erosions only in patients with high MBDA scores. Furthermore, progression (>5mm² increase in volume) over 1 year was confined to methotrexate treated patients, while tumor necrosis factor inhibitor treated patients were protected from progression even in case of moderate to high MBDA scores. However there were only 4 patients treated with TNFi that had a high MBDA score.

**Conclusions:** These data show that residual disease activity assessed by MBDA score is associated with structural damage and progression of structural damage in RA patients in sustained remission.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4774
THU0097

CHANGE IN SELF-REPORTED PAIN REFLECTS PSYCHOLOGICAL AND FUNCTIONAL STATE RATHER THAN INFLAMMATORY BURDEN IN UNITED STATES LATINOS WITH ESTABLISHED RHEUMATOID ARTHRITIS

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Background: Pain represents the cardinal complaint in patients with rheumatoid arthritis (RA). It may reflect inflammation, structural damage, or aberrant processing and regulatory mechanisms.

Objectives: We evaluated whether changes in pain reflect inflammatory burden variation or non-inflammatory factors in Latinos with established RA in the United States (US).

Methods: We evaluated 271 patients from a single academic center with complete data on parameters of interest on 2 visits 12 months apart. Demographics, serologies, swollen and tender joint assessments, sedimentation rate, fatigue-VAS (visual analogue scale), pain-VAS, depression assessment (Patient Health Questionnaire-PHQ9), functional disability (Health Assessment Questionnaire, HAQ-DI), presence of erosions and irreversible articular damage (IAD, including subluxation, fusion, arthrodesis, or prosthesis) were recorded. Principal components factor analysis with varimax rotation determined latent variables of symptom change. Multinomial logistic regression modeling with forward stepwise entry determined parameters associated with clinically meaningful change in pain compared to no change.

Results: Two factors met acceptance criteria (Eigenvalues > 1) with values of 2.57 and 1.31 respectively (Table 1). Following rotation, factor 1 loadings comprised changes in fatigue, pain, depression scores, and functional disability, representing non-inflammatory factors. Conversely, factor 2 encompassed changes in tender and swollen joints and IAD, representing inflammation. Clinically relevant improvement in pain significantly correlated with respective improvements in fatigue, depression, functional disability and tender joints (Table 2); worsening pain was negatively associated with change in disability or fatigue.

Table 1: Principal Component factor analysis with change variable loadings

| Fatigue change       | 0.814 | 0.019 |
| Pain change          | 0.757 |
| PHQ9 change          | 0.716 |
| HAQ-DI change        | 0.559 |
| Swollen joint change | 0.495 |
| Tend joint change    | 0.386 |
| Sed rate change      | 0.605 |

Table 2: Factors associated with clinically meaningful change in self-reported pain

<table>
<thead>
<tr>
<th>Worsening</th>
<th>1.000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.437</td>
</tr>
<tr>
<td>TJC change</td>
<td>0.026</td>
</tr>
<tr>
<td>HAQ-DI change</td>
<td>0.495</td>
</tr>
<tr>
<td>Fatigue change</td>
<td>0.223</td>
</tr>
<tr>
<td>Sed rate change</td>
<td>0.605</td>
</tr>
<tr>
<td>Reference category</td>
<td>no change</td>
</tr>
</tbody>
</table>

Conclusions: In Latinos with established RA, change in pain reporting reflects alterations in non-inflammatory parameters such as fatigue, depression and functional disability rather than inflammation. Active screening and consideration of those factors may inform therapeutic interventions, balance patient and physician expectations, and optimize patient satisfaction and clinical outcomes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8813

THU0098

THE NAILFOLD CAPILLAROSCOPY IN RHEUMATOID ARTHRITIS: QUANTITATIVE ANALYSIS AND CLINICAL AND SEROLOGICAL CORRELATION

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Background: Nailfold videocapillaroscopy (NVC) abnormalities have been reported in patients with Rheumatoid Arthritis (RA). Nevertheless, only few studies evaluated the grades of the detected alterations (1,2). In 1994, Hachulla et al., showed microvascular permeability alterations in RA confirming the existence of a microangiopathy (3). In addition, Meyer et al. showed modifications of the normal blood flow velocity and microvascular dysfunction in RA (4).

Objectives: The aim of this study was to evaluate, in RA patients and healthy controls (HC), the microcirculatory abnormalities through NVC, applying a quantitative and qualitative method. We also correlated abnormalities with clinical and immunological features.

Methods: Thirty-five HC (35 females, 7 males, median age 55, range 32–70) and 70 RA patients (61 females, median age 58 years, range 30–75; median disease duration 12 years, range 1–20) consecutively admitted to our outpatient clinic, were examined. All patients underwent a full clinical-serological characterization. Both patients and controls underwent NVC, with optical probes of 200X (VideoCap 2.5). We excluded patients who showed conditions known to compromise microcirculation, such as diabetes, hypertension, overlap with other connective tissue diseases or certain pharmacological treatments. The following NVC parameters were evaluated: with a semi-quantitative method: capillary enlargement (ectasia), microhemorrhages, mean capillary density, capillary tortuosity (5).

Results: NVC alterations were detected in 55 of 70 (68.6%) RA patients: 40 (57%) patient showed ectasic capillaries; 21 (30%) decrease of the mean capillary density; 12 (17%) microhemorrhages; 46 (65.7%) capillary tortuosity. No patient had megacapillaries and/or neoangiogenic abnormalities. A statistically significant difference between HC and RA patients was found for the detection of ectasias (p<0.0001) and for the decrease of the mean capillary density (p<0.001).

No differences emerged in RA patients between NVC pattern and/or immunological (ANA, ACA, Rheumatoid Factor) and/or serological profile (ESR, CRP, lipid profile).

Nevertheless we found a correlation between NVC abnormalities (microhemor- rhages) and activity disease evaluated by DAS28 (p=0.0037).

Conclusions: Our study confirms the presence of a sub-clinical microvascular involvement in RA patients either with or without microvascular clinical manifestations. In our opinion capillaroscopy can be considered a valid technique in inflammatory joint diseases to analyze microvascular circulation. Moreover, the correlation of NVC specific alteration with disease activity suggests the importance of these features in the assessment of RA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8818

THU0099

THE 2010 CLASSIFICATION CRITERIA AND A MORE AGGRESSIVE TREATMENT STRATEGY IMPROVE CLINICAL OUTCOMES IN SEROPOSITIVE BUT NOT SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: Current guidelines recommend an early and intensive treatment in patients diagnosed with rheumatoid arthritis (RA), and the 2010 ACR/EULAR Classification Criteria were developed with the aim of allowing earlier diagnosis and treatment (1,2). Recent studies highlighted some differences in disease activity between seropositive and seronegative RA patients at disease onset (3).

Objectives: To investigate whether the application of the 2010 ACR/EULAR Classification Criteria and a more aggressive treatment strategy improve clinical outcomes in patients with early RA irrespective of the autoantibody status.

Methods: 584 early, treatment-naïve RA patients were recruited in the years 2005–2014. RA diagnosis was made according to the ACR 1987 criteria in 2005–2010, and to the 2010 ACR/EULAR criteria in 2011–2014 (n=224, cohort 2010). Patients were classified if an autoantibody (Ab)-negative rheumatoid factor (RF) or and/or anticitrullinated peptide antibody (ACPA) and Ab-positive (RF and/or ACPA positive). Methotrexate (MTX) was used at the initial dosage of 10 mg/week in cohort 1987, and 15 mg/week in cohort 2010, and progressively increased if low disease activity (LDA) (DAS28<3.2) was not met. The frequency and predictors of LDA and clinical remission (DAS28<2.6) over 6 months were assessed by Cox regression.

Results: In Ab-negative patients, LDA and clinical remission were achieved in 62.8% and 37.2% of the cases, and the 2010 cohort did not show significantly improved outcomes compared to the 1987 cohort (HR [95% CI] 0.86 [0.81–0.93] for LDA). In Ab-positive patients, however, the 2010 cohort had a markedly improved remission rate (HR [95% CI] 1.39 [1.01–1.92]) (Figure 1A, B). In contrast, in Ab-positive patients, the application of the 2010 classification criteria and higher dosages of MTX were associated with increased frequency of LDA after adjustment for confounders (age, sex, prednisone, baseline DAS28, HR [95% CI] 1.39 [1.01] for remission) (Figure 1C). Clinical remission was achieved in 41.3% of the cases, compared to 29.6% in the 1987 cohort (p=0.17) (Figure 1D).

Conclusions: Early diagnosis and a more aggressive treatment strategy with MTX lead to significantly improved outcomes in autoantibody positive RA. The management of seronegative patients remains suboptimal.

References:
IN EARLY INFLAMMATORY ARTHRITIS A LYMPHOID PATHOTYPE SIGNIFICANTLY ASSOCIATES WITH REQUIREMENT FOR BIOLOGIC THERAPY AT 12 MONTHS FOLLOW UP: RESULTS FROM THE PATHOBIOLOGY OF EARLY ARTHRITIS COHORT (PEAC)

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Background: Early aggressive treatment in RA equates to better long term outcomes, however targeting aggressive therapies including biologics to patients with the worse prognosis is critical to deliver acceptable risk/benefit ratios and health economic improvements. Such an approach requires prognostic biomarkers, whether the well recognised heterogeneity in synovial pathobiology and health economic improvements. Such an approach requires prognostic biomarkers, whether the well recognised heterogeneity in synovial pathobiology is currently unknown.

Objectives: The aim of this study was to investigate whether in a treatment naive early inflammatory arthritis cohort, baseline synovial pathotype significantly associates with disease outcome at 12 months.

Methods: 166 consecutive DMARD naïve patients recruited as part of PEAC at Barts Health NHS Trust with synovial tissue suitable for analysis were included. At baseline patients were classified as RA (2010 ACR/EULAR criteria) or undifferentiated (UA). All patients underwent a baseline synovial biopsy of a clinically active joint along with collection of demographic data. Patients were subsequently treated with DMARD +/- steroid therapy with aim for low disease activity (DAS <3.3). At 6 month follow up patients were escalated to biologic therapy if fulfilling UK NICE guidelines. At 12 months patients were classified as: (i) no treatment, (ii) DMARDs, and (iii) Biologic +/- DMARD therapy with aim for low disease activity (DAS <3.3). At 6 month follow up patients were escalated to biologic therapy if fulfilling UK NICE guidelines. At 12 months patients were classified as: (i) no treatment, (ii) DMARDs, and (iii) Biologic +/- DMARDs. Sequentially cut sections of baseline synovial biopsies underwent immunohistochemical staining and semi-quantitative scoring (0–4) to determine the degree of CD20+ B-cells, CD3+ T cells, CD68+ lining (l) and sublining (sl) macrophage and CD138+ plasma cell infiltration. Sections were categorised into 3 pathotypes, (i) Fibroid: (CD68 SL<l), (ii) Myeloid: (CD68SL<2, CD20<1 and or CD3<1) and (iii) Lymphoid: (grade 2–3 CD20+ aggregates, CD20<1). At baseline patients with a lymphoid pathotype had a significantly higher CRP and DAS28 and were significantly more likely to be sero positive for RF and ACPA (p<0.05), suggesting that a lymphoid pathotype is associated with higher levels of disease activity. At 12 months follow up a significantly higher proportion of patients classified as lymphoid vs myeloid or fibroid (58% vs 21% vs 21%) required biologic therapy.

Conclusions: Results demonstrate that in an early inflammatory arthritis cohort a lymphoid pathotype significantly associates with higher disease activity at baseline, sero positivity for RF and ACPA and a requirement for more aggressive therapy at 12 month. This supports a direct role for synovial lymphoid structures in disease pathogenesis and suggests a role as a prognostic biomarker facilitating early stratification of aggressive therapeutic intervention.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5101

THU0101 CARDIOVASCULAR MAGNETIC RESONANCE IMAGING CHARACTERISATION OF CARDIOVASCULAR ABNORMALITIES IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Inflammation is the primary contributor to excess cardiovascular (CV) disease in rheumatoid arthritis (RA), with evidence of subclinical abnormalities observed even in treatment-naïve, early RA [1]. Preliminary reports suggest citrullinated proteins are present in atherosclerotic plaque [2]. It is unclear whether immunological changes of anti-citrullinated protein antibody (anti-CCP+) positive individuals ‘at risk’ of developing RA are associated with CV abnormality.

Objectives: To perform a pilot study to explore whether subclinical CV abnormalities are present in anti-CCP+ individuals at risk of developing RA.

Methods: Sixteen consecutive patients with non specific MSK symptoms but no synovitis, detectable anti-CCP antibody and 30 age-matched healthy controls (HC) underwent a multi-parametric 3.0T (Philips Achieva) cardiovascular magnetic resonance (CMR) study. Neither group had any history of CV disease. At-risk individuals were categorised as low and high absolute risk for RA development (<50% and >50% respectively) according to a published risk model [3]. CMR post-processing was performed using CVI 42 (Circle Cardiovascular Imaging, Canada).

Results: HC and at risk individuals were well matched for baseline characteristics (table 1). Aortic strain values (dissensibility, strain and stiffness index I) were lower, indicating increased aortic stiffness, in at-risk individuals than HC, numerically most pronounced those classified high risk (table 2). There were no differences in LV mass and function, late gadolinium enhancement, myocardial T1 (measure of myocardial composition) or LV S prime (longitudinal LV systolic function) (table 2).

<table>
<thead>
<tr>
<th>N=153</th>
<th>Fibroid (44)</th>
<th>Myeloid (52)</th>
<th>Lymphoid (57)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment (14) n (%)</td>
<td>6 (42%)</td>
<td>6 (42%)</td>
<td>2 (14%)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Biologic +/- DMARD (38) n (%)</td>
<td>8 (21%)</td>
<td>8 (21%)</td>
<td>22 (58%)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: Anti-CCP+ individuals with non-specific MSK symptoms (in particular, a high risk group), exhibit increased aortic stiffness. This suggests presence of CV abnormalities prior to development of RA and implies a role of autoantibody-mediated development of atherosclerosis. These findings warrant further investigation in larger scale studies.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4969

THU0102 CLINICAL DISEASE ACTIVITY MEASURES ARE IMPORTANT DRIVERS OF MAJOR CHANGE IN MEDICAL TREATMENT IN US VETERANS ENROLLED IN THE VETERANS AFFAIRS RHEUMATOID ARTHRITIS (VARA) REGISTRY

G.W. Cannon 1, 2, C.-C. Teng 3, N.A. Accort 2, D. Collerer 4, S. Mehrotra 2, B.C. Sauer 5, 6, 7, Rheumatology; 2Salt Lake City Va Medical Center, Salt Lake City; 3Amgen, Thousand Oaks, United States

Background: Current guidelines encourage the measurement of rheumatoid arthritis (RA) disease activity and direct therapy to achieve a low disease state or remission (treat-to-target). Many RA patients with documented moderate to severe disease activity remain on their current therapy without change. This study investigated Veterans Affairs (VA) clinical data to identify patient factors associated with a major change in RA therapy and to determine that disease state using an area under the curve calculation and compared to the DAS28 at the index date. Patients were categorized as having a worsening or improvement of disease if the DAS28 at index date was 0.6 higher or lower than the average DAS28 during the observation period respectively. Other patients were categorized as no change in DAS28.

Analyses of clinical variables including components of the DAS28 and patient and physician reported measures were compared in patients with and without a major change in therapy.

Results: Of 941 patients who met study criteria, only 388/941 (41.2%) had a major change of therapy. Patients with worsened DAS28 were more likely to have a major change 183/369 (49.5%) than no DAS28 change 170/454 (37.4%) and improved DAS28 35/118 (29.6%) (P<0.001). Clinical variables were strongly associated with changes in therapy among patients with worsening disease activity and not as strongly associated with change in therapy in those with no change disease activity. Clinical variables were not significantly associated with major change in patients with disease improvement, though that group had the smallest sample size. Ten representative clinical variables with the highest association with major change are included below.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation with Major Change</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.15</td>
<td>0.001</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.25</td>
<td>0.001</td>
</tr>
<tr>
<td>RA duration</td>
<td>-0.20</td>
<td>0.001</td>
</tr>
<tr>
<td>RA activity</td>
<td>0.15</td>
<td>0.001</td>
</tr>
<tr>
<td>RA medication</td>
<td>0.10</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: More than half of the patients with moderate disease activity did not have a major change in therapy. The likelihood of a major change in therapy increased with worsening disease activity. The clinical variables assessed were more strongly associated with change in therapy in patients with worsening of disease. Clinical disease activity measures are highly associated with the decision to initiate major changes. Future work could further add value of administrative variables. This work emphasizes the need for methods to systematically collect and utilize clinical disease activity measurements, particularly longitudinally, to improve the treat-to-target strategy.

Acknowledgements: Work Sponsored by VA Specialty Care Centers of Innova-
Background: Factors predictive of relapse need to be identified to aid therapy withdrawal decisions for patients with RA achieving remission with treatment. Aims: To evaluate: MRI, HAQ-DI and DAS28 in patients prior to drug withdrawal. Methods: A total of 172 patients achieving DAS28 remission (DAS28 [CRP] <2.6) at Month 12 in any treatment group were included in the analysis. Numbers of patients who relapsed at Month 18 and Month 24 were 100 and 113, respectively. Of the patient characteristics, disease activity and imaging factors analysed at Month 12, only MRI synovitis, erosion and oedema scores, as well as HAQ-DI scores, were significantly associated (p<0.05) with relapse status at both Month 18 and Month 24 (Table).

Conclusions: MRI and HAQ-DI scores in patients in DAS28 remission predicted relapses following treatment withdrawal decisions for patients with RA achieving remission with treatment.

References:

Disclosure of Interest: None declared
Objectives: Evaluate the feasibility of a simple clinical joint damage score and describe the increment over time in RA patients with varying disease duration.

Methods: Cross-sectional study in all patients with a clinical diagnosis of RA visiting the outpatient clinic in 2015 and 2016. Rheumatologists and nurses from the outpatient department of a large regional hospital received a single training to perform the RAAD score. Scores of 0 (no damage), 1 (mild) or 2 (severe: ankylosis, luxation or joint surgery) were assigned to 35 joints (maximum score: 70) with a disease activity score, and stored in the electronic patient record system. Baseline data including ACR 2010 criteria were also registered.

Results: In 1007 (67.3%) of 1496 RA patients seen over 2 years RAAD-scores were performed. 652 (84.7%) were female, average age (SD, range) was 62.6 (13.1, 19–95), disease duration 9.9 (9.6, 0–65) years. Rheumatoid factor and ACPR were positive in 70.6% and 70.3% respectively. RAAD scores related to disease duration illustrate that at disease onset 86%, and after 20 years 37% of the patients has no joint damage (Table). Distribution over joints shows the classical predominance of damage in MCP, PIP and MTP joints (Image). Structural damage in shoulders or elbows was present in 8.3% and 12.5%, in knees and hips in 10.3% each. Despite current treatment strategies, irreversible joint damage of more than 5 joints is present in 6.3% within 10 years.

Table 1. Accumulation of irreversible joint damage score with disease duration, number (%)

<table>
<thead>
<tr>
<th>RAAD score</th>
<th>1st year (N=699)</th>
<th>2–4 yrs (N=228)</th>
<th>5–9 yrs (N=253)</th>
<th>10–19 yrs (N=239)</th>
<th>≥20 yrs (N=218)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (no joint damage)</td>
<td>59 (86)</td>
<td>158 (68.3)</td>
<td>145 (57.3)</td>
<td>81 (33.9)</td>
<td>80 (36.7)</td>
</tr>
<tr>
<td>1–5</td>
<td>8 (12)</td>
<td>60 (26.5)</td>
<td>92 (36.4)</td>
<td>103 (43.1)</td>
<td>42 (19.3)</td>
</tr>
<tr>
<td>6–10</td>
<td>2 (3)</td>
<td>4 (1.8)</td>
<td>11 (4.3)</td>
<td>34 (14.2)</td>
<td>28 (12.8)</td>
</tr>
<tr>
<td>11–20</td>
<td>7 (10.1)</td>
<td>4 (1.6)</td>
<td>13 (5.4)</td>
<td>36 (15.6)</td>
<td>15 (6.9)</td>
</tr>
<tr>
<td>&gt;20</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td>8 (3.3)</td>
<td>32 (14.7)</td>
<td>8 (3.7)</td>
</tr>
<tr>
<td>Average (range)</td>
<td>0.4 (0–6)</td>
<td>0.9 (0–23)</td>
<td>1.6 (0–37)</td>
<td>2.2 (0–18)</td>
<td>9.0 (0–59)</td>
</tr>
</tbody>
</table>

Conclusions: Clinical assessment of joint damage is a feasible parameter of long term outcome in RA. Reflecting overall joint damage, the RAAD-score provides a broader view than radiographic scoring of hands and feet and is easy to apply in routine care. Given the slow increase a single assessment per 5 years may suffice to compare structural joint damage across cohorts of patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4437

THU0108

SUBCLINICAL CENTRAL NERVOUS SYSTEM DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS: DISEASE ACTIVITY AND CYTOKINES

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Background: We aimed in this study to investigate blood-brain barrier (BBB) dysfunction in RA patients who had no neurological symptoms, and were receiving synthetic DMARD treatment.

Objectives: We investigated correlations between cranial MRI images and brain specific proteins (S100 Beta, GFAP), cytokines (IL-1 beta, IL-17) in plasma which had important roles in disease activity.

Methods: In our study, 57 patients (46 females and 11 males) were included in RA group, and 34 patients (24 females and 10 males) in the control group. All of RA patients were receiving synthetic DMARD treatment. Demographic characteristics of all patients were recorded. Disease activity was evaluated by using DAS-28. Mini-mental test (MMT) was used for evaluation of cognitive functions, and Fazekas scale was used to evaluate cranial MR lesions. S100 beta, GFAP, claudin, IL-17, and IL-1 beta levels were measured in peripheral blood of both groups.

Results: Demographic characteristics were similar between the groups, and there was no statistically significant difference in gender, age, and body mass index (BMI) between patient and control groups (p<0.05). S100 beta, and GFAP levels were significantly higher in RA group (p<0.05). No difference was determined in hypointense lesions diagnosed in cranial MR between patient and control groups (p>0.05). There were positive correlations between IL-17, S100 beta and GFAP, and IL-1 beta and S100 beta.

Conclusions: In our study, we have shown that blood-brain barrier may be damaged subclinically in RA patients, brain specific proteins related to BBB dysfunction may be increased in the peripheral blood, and BBB dysfunction may be related to cytokines which play an important role in disease activity. In conclusion, cytokines which circulate in the peripheral blood in RA may cause subclinical BBB damage. Further large scale studies with long-term follow-up are required which will support this hypothesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2313

THU0109

UPDATED ESTIMATION OF THE EQSD QUALITY OF LIFE QUESTIONNAIRE UTILITY VALUES THROUGH HAQ-DI MAPPING FOR SPAIN

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Background: Rheumatoid arthritis (RA) deeply affects the quality of life (QoL) of patients. The preferred approach to evaluate treatment efficiency is to value health as patient preferences known as utilities, and subsequently, calculate Quality-Adjusted Life Years gained. A new 5-level of severity EQSD has recently released for Spain (Ramusio et al, Ann Rheum Dis 2016:75:1063–7). Although OQL questionnaires are not of routine use in clinical practice, it is possible to estimate it using the Health Assessment Questionnaire Disability Index (HAQ-DI)

Objectives: To develop a function that allows the estimation of EQSD-5L utility values from HAQ-DI updated to the newest proposed tariff for Spain

DHU-0109
Methods: Patients with RA from two teaching hospitals, participating in a prospective observational study completed the HAQ-DI and EQ-5D-5L at 0–6–12 month follow-up visits. Inclusion criteria: ACR RA diagnosed patients, on biologic treatment and whose disease activity remained stable at least for 3 months. EQ-5D-5L is a standardized, generic instrument for describing and valuing health and is described in a five-dimensional descriptive system (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale. A country-specific tariff converts patient’s answer to a 0–1 (full health) utility index. HAQ-DI is a self-completed questionnaire used to assess the functional ability using 20 items, distributed across 8 dimensions and resulting in a four-level disability index. REM duration has been shown to affect structural progression.

Results: Participants were 77 patients. Mean (SD) age was 57.0 (12.9), 87% women, at diagnosis 13.7 (7.3), mean DAS28 2.72 (1.00) and HAQ-DI 0.77 (0.60). Baseline EQ-5D index: 0.786 (0.182). All the OLS estimation models resulted in the interval limits defined by the index, so Tobit models were not considered. Considering the linear model we obtained the best results with the HAQ-DI term and its third power: logit(EQ_01) = 2.5821 − 1.1165 * HAQ (AIC = 444.4; MAE = 0.0691; RMSE = 0.0958). Considering the AIC and the residuals together, we obtained the best fitting model with beta regression, with neither age nor sex.

Conclusions: So far, only a utility function using HAQ-DI and an old EQ-5D-3L version was available for Spain (Carreño, 2011). This updated utility function can be used as a practical approach to predict RA patients’ QoL and EQ-5D utility score for Spain when clinicians/researchers need them for clinical practice or cost-effectiveness analyses and generic QoL measurements are not available. 

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4836

THU0110 THE IMPORTANCE OF SUSTAINED REMISSION FOR LONGTERM OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In patients (pts) with rheumatoid arthritis (RA), the long-term impact of sustained versus (vs) transient clinical remission (REM) has not been assessed thoroughly, although REM duration has been shown to affect structural outcomes. The relationship of different definitions of clinical remission with functional and structural integrity has not been assessed.

Objectives: To explore the importance of sustained REM or disease control for long-term outcomes, and assess various definitions of REM in adalimumab (ADA) long-term trials.

Methods: Data are from 2 trials of ADA in early RA pts; In PREMIER, pts received ADA, methotrexate (MTX) or ADA+MTX for 2 years (yrs), after which they could enter an open label (OL) period for upto 8 yrs. In OPTIMA, pts received ADA+MTX or placebo (PBO) +MTX for 26 weeks (wks). Based on whether or not pts achieved DAS28-CRP <2.6 at 26 wks, pts were assessed. Analysis was continued on PBO+MTX, ADA+MTX or OL ADA+MTX until Wk 78. For this analysis, non-sustained REM/disease control was defined as meeting one of the following at 6 months but not yr: DAS28-CRP >2.6; simplified disease activity index (SDAI) >3.3; clinical disease activity index (CDAI) >2.8. Sustained REM/disease control was defined as meeting these criteria at both months 6 and 1 yr. The mean change from baseline in health assessment questionnaire-disability index (△HAQ-DI), or modified total Sharp score (△mTSS), and the number of pts without clinical worsening of HAQ-DI (△<0.22) were assessed over 78 wks for OPTIMA, or 5 yrs for PREMIER. NRI and LOCF were used for binary and continuous variables, respectively.

Results: In OPTIMA, by any of the REM criteria, pts in sustained REM had larger mean △HAQ-DI over time (Fig 1A) vs pts in non-sustained REM. Pts with non-sustained DAS28-CRP >2.6 vs non-sustained CDAI REM had numerically smaller mean △mTSS at Wk 52. Over time, more pts in sustained vs non-sustained REM using DAS28-CRP >2.6 (but not CDAI or SDAI criteria) did not have clinical worsening of HAQ-DI, possibly due to more suppression of inflammatory components upon achieving CDAI REM but not DAS28-CRP <2.6 in these early RA pts (Fig 1B). At Wk 78, △mTSS at Wk 78 was smaller for pts in sustained vs non-sustained REM using DAS28-CRP >2.6, and similar for sustained and non-sustained CDAI REM (Fig 1C). Somewhat fewer pts at Wk 78 may have contributed to some variability. Trends were similar in PREMIER (not shown).

Conclusions: Pts who were in sustained disease control/REM had better clinical, functional and radiographic outcomes over the long-term, vs pts in a
Stress and depression are common in patients with inflammatory polyarthritis (IP). There is little research on long-term patterns of depression and stress or how these variables, disability and disease activity, interact with each other. 

Objectives: To describe the natural history of stress and depression over five years and to assess the association of baseline, one year prior and current disease activity, disability and pain with longitudinal stress and depression.

Methods: Patients recruited to the Norfolk Arthritis Register (NOAR) (inclusion criteria: ≥2 swollen joints for ≥4 weeks) from 2005–2008 were included in this analysis. Demographics, medication use, 50 swollen/tender joint counts (SJC51/TJC51), pain visual analogue scale, HAQ, comorbidities and the Arthritis Impact Measurement Scales 2 (AIM2S) depression and stress subscales (range 0–1; high score = worse health status) were collected at baseline and years 1, 2, 3 and 4. RF, anti-cyclic citrullinated peptide antibodies (anti-CCP2) and C-reactive protein (CRP) were measured in baseline blood samples. ACR/EULAR 2010 RA criteria were applied to baseline characteristics. Depression and stress over five years were described using descriptive statistics. Multivariate random effects models were applied to assess the association of baseline disease activity (SJC51/TJC51), pain and depression with disease activity and stress over time adjusting for baseline age, gender, RF, anti-CCP2, CRP, sDMARD use, comorbidities, depression and stress. Similar methods were used to assess one year prior and current disease activity, pain and disability’s association with stress and depression. Missing data were imputed using multiple imputation.

Results: 509 patients were included (median (IQR) age: 57 (45, 68) years; 321 (63.1%) female; 305 (59.9%) ACR/EULAR RA). Baseline median (IQR) depression and stress were 2.5 (1.5, 4.5) and 4.0 (2.5, 5.5) respectively and remained constant over five years. Baseline SJC51, TJC51, pain and HAQ were not independently associated with depression or stress over five years. Current HAQ and pain, but not SJC51/TJC51, were independently associated with depression and stress (per unit increase in HAQ: depression β 0.83, 95% CI 0.69, 0.97; stress β 0.76, 95% CI 0.61, 0.90; per 1cm increase in pain: depression β 0.09, 95% CI 0.06, 0.12; stress β 0.09, 95% CI 0.05, 0.12). Higher HAQ was independently associated with increased depression and stress one assessment later (per unit increase in HAQ: depression β 0.21, 95% CI 0.09, 0.32; stress β 0.21, 95% CI 0.10, 0.33) but not pain, SJC51 or TJC51.

Conclusions: There were no associations between measures of disease activity and depression or stress. Prospectively higher HAQ scores were associated with worse psychological health a year later. This may have implications for holistic management of IP.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3432

THU0112

STRESS AND DEPRESSION IN PATIENTS WITH EARLY INFLAMMATORY POLYARTHRITIS: NATURAL HISTORY AND ASSOCIATIONS WITH DISEASE ACTIVITY, DISABILITY AND PAIN OVER FIVE YEARS

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Background: Stress and depression are common in patients with inflammatory polyarthritis (IP). There is little research on long-term patterns of depression and stress or how these variables, disability and disease activity, interact with each other.

Objectives: To describe the natural history of stress and depression over five years and to assess the association of baseline, one year prior and current disease activity, disability and pain with longitudinal stress and depression.

Methods: Patients recruited to the Norfolk Arthritis Register (NOAR) (inclusion criteria: ≥2 swollen joints for ≥4 weeks) from 2005–2008 were included in this analysis. Demographics, medication use, 50 swollen/tender joint counts (SJC51/TJC51), pain visual analogue scale, HAQ, comorbidities and the Arthritis Impact Measurement Scales 2 (AIM2S) depression and stress subscales (range 0–1; high score = worse health status) were collected at baseline and years 1, 2, 3 and 4. RF, anti-cyclic citrullinated peptide antibodies (anti-CCP2) and C-reactive protein (CRP) were measured in baseline blood samples. ACR/EULAR 2010 RA criteria were applied to baseline characteristics. Depression and stress over five years were described using descriptive statistics. Multivariate random effects models were applied to assess the association of baseline disease activity (SJC51/TJC51), pain and depression with disease activity and stress over time adjusting for baseline age, gender, RF, anti-CCP2, CRP, sDMARD use, comorbidities, depression and stress. Similar methods were used to assess one year prior and current disease activity, pain and disability’s association with stress and depression. Missing data were imputed using multiple imputation.

Results: 509 patients were included (median (IQR) age: 57 (45, 68) years; 321 (63.1%) female; 305 (59.9%) ACR/EULAR RA). Baseline median (IQR) depression and stress were 2.5 (1.5, 4.5) and 4.0 (2.5, 5.5) respectively and remained constant over five years. Baseline SJC51, TJC51, pain and HAQ were not independently associated with depression or stress over five years. Current HAQ and pain, but not SJC51/TJC51, were independently associated with depression and stress (per unit increase in HAQ: depression β 0.83, 95% CI 0.69, 0.97; stress β 0.76, 95% CI 0.61, 0.90; per 1cm increase in pain: depression β 0.09, 95% CI 0.06, 0.12; stress β 0.09, 95% CI 0.05, 0.12). Higher HAQ was independently associated with increased depression and stress one assessment later (per unit increase in HAQ: depression β 0.21, 95% CI 0.09, 0.32; stress β 0.21, 95% CI 0.10, 0.33) but not pain, SJC51 or TJC51.

Conclusions: There were no associations between measures of disease activity and depression or stress. Prospectively higher HAQ scores were associated with worse psychological health a year later. This may have implications for holistic management of IP.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3432

THU0113

SERUM CALPROTECTIN MAY REFLECT INFLAMMATORY ACTIVITY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE NORMAL C-REACTIVE PROTEIN

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Background: About a half of patients with rheumatoid arthritis (RA) have normal or low C-reactive protein (CRP) levels. Serum calprotectin is a promising and probably more specific biomarker of disease activity than conventionally used acute phase reactants.

Objectives: The aim of this study was to analyse levels of serum calprotectin in RA patients with clinically active disease and with low CRP (<10 mg/L).

Methods: A total of 160 RA patients and 32 healthy subjects were enrolled in this study. All patients underwent clinical examination (DAS28). The levels of calprotectin were analysed in patients with moderate to high disease activity with low CRP levels and in healthy subjects. The discriminatory capacity of calprotectin was assessed using ROC curves.

Results: Out of all RA patients, 74/160 (46.3%) had low CRP and were in remission or had low activity at the same time. However, 51/160 (32%) had low CRP levels despite moderate to high disease activity according to DAS28. In these patients, calprotectin levels were significantly higher compared with low CRP in remission or with low disease activity at the same time (mean 2.7±1.5 vs. 2.1±1.2 μg/mL, p=0.043) and differed from that in healthy subjects (mean 2.7±1.5 vs. 1.9±1.2 μg/mL, p=0.011) (Figure 1). The discriminatory capacity for calprotectin to distinguish clinically active vs. inactive patients in spite of low CRP

Conclusions: RA patients with antibodies to citrullinated peptides only have lower baseline erosions and less radiographic progression over 12m compared to those with a wider autoantibody repertoire. Baseline differences in erosion suggest that these antibodies may be pathogenic during the pre-RA disease process. Radiographic progression increases with autoantibody repertoire suggesting ongoing immune activation.

Disclosure of Interest: J. Nijjar: None declared, F. Morton: None declared, A. Gilmour: None declared, C. Paterson: None declared, H. Bang Employee of: Orgentec Diagnostiske GmbH and holds patent for mutated citrullinated vimentin as diagnostic tool, D. van der Heijde Employee of: Director of Imaging Rheumatology, K. Raza: None declared, C. Buckley: None declared, D. Porter Grant/research support from: Pfizer co-funded the SERA cohort, I. McNines: None declared DOI: 10.1136/annrheumdis-2017-eular.2844
EFFECTS OF SMOKING ON BARICITINIB EFFICACY IN RA patients where CRP fails to do so.

References:


DOI: 10.1136/annrheumdis-2017-eular.1341

THU0114 EFFECTS OF SMOKING ON BARICITINIB EFFICACY IN PATIENTS WITH RHEUMATOID ARTHRITIS: POOLED ANALYSIS FROM TWO PHASE 3 CLINICAL TRIALS

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Background: The efficacy of some rheumatoid arthritis (RA) therapies is reduced among patients who are smokers.

Objectives: This post-hoc analysis of two phase 3 studies assessed the effects of patient smoking status on the response to baricitinib treatment in patients with RA.

Methods: In RA-BEAM (NCT01710358), patients with inadequate response to methotrexate were randomized to placebo once-daily (QD) (N=488), baricitinib 4 mg QD (N=487), or adalimumab 40 mg biweekly (N=330). In RA-BUILD (NCT01721057), patients with inadequate response to conventional synthetic disease modifying antirheumatic drugs (csDMARDs) were randomized to placebo (N=228) or baricitinib (2 mg, N=229; or 4 mg, N=227) QD. Patients continued background csDMARD therapy in both studies. This post-hoc analysis was conducted in the placebo (N=716) and baricitinib 4 mg (N=714) patients. Patient-reported smoking status was categorized as current smokers or non-smokers (non-smokers).

Results: Among 1,430 evaluable patients who received placebo or baricitinib 4 mg, 290 (20.3%) were smokers. Smoking status at baseline did not affect the clinical outcomes of treatment with baricitinib for 24 weeks; smokers who received placebo were numerically less likely than non-smokers receiving placebo to achieve most clinical outcomes (Table). Baricitinib’s effect on modified total Sharp score was more pronounced among nonsmokers (interaction p-value =0.07). ACR20/50/70≥20%, 50%, and 70% improvement in American College of Rheumatology criteria; CDAI=Clinical Disease Activity Index; DAS28-hsCRP=Disease Activity Score 28-high sensitivity C-reactive protein; HAQ-DI=Health Assessment Questionnaire-Disability Index; mTSS=modified total Sharp score; SDAI=Simple Disease Activity Index.

Conclusions: This analysis of smokers and non-smokers in two RA trials demonstrated that the beneficial effect of baricitinib treatment versus placebo was similar on all clinical endpoints, but may differ for structural damage progression.

Table 1: Efficacy outcomes at week 24 with data up to rescue

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Smoker (N=716)</th>
<th>Non-Smoker (N=714)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20</td>
<td>44 (31.7)</td>
<td>44 (31.7)</td>
</tr>
<tr>
<td>ACR50</td>
<td>24 (17.3)</td>
<td>24 (17.3)</td>
</tr>
<tr>
<td>ACR70</td>
<td>8 (5.8)</td>
<td>8 (5.8)</td>
</tr>
<tr>
<td>SDAI ≤3.3</td>
<td>5 (3.6)</td>
<td>9 (6.5)</td>
</tr>
<tr>
<td>SDAI ≤11</td>
<td>24 (17.3)</td>
<td>24 (17.3)</td>
</tr>
<tr>
<td>CDAD &lt;2.8</td>
<td>4 (2.9)</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>CDAD &gt;2.6</td>
<td>9 (6.5)</td>
<td>9 (6.5)</td>
</tr>
<tr>
<td>DAS28-hsCRP ≤3.2</td>
<td>24 (17.3)</td>
<td>24 (17.3)</td>
</tr>
<tr>
<td>DAS28-hsCRP &gt;2.6</td>
<td>9 (6.5)</td>
<td>9 (6.5)</td>
</tr>
<tr>
<td>HAQ-DI ≤0.3</td>
<td>22 (15.8)</td>
<td>22 (15.8)</td>
</tr>
<tr>
<td>HAQ-DI &gt;0.22</td>
<td>61 (43.9)</td>
<td>61 (43.9)</td>
</tr>
<tr>
<td>mTSS change</td>
<td>68/96 (70.8)</td>
<td>70/96 (70.8)</td>
</tr>
</tbody>
</table>

Data are n (%). *mTSS data are from RA-BEAM only.
are additionally controlled for age, sex, smoking (y/n), drinking alcohol (y/n), sport (y/n).

Conclusions: This study showed that HAQ and SF-12 were related to adherence and health literacy. This finding highlights the importance of patient education and counseling in order to increase both, medical understanding and adherence to therapy.

Acknowledgements: The TRACE-Study was sponsored by an unrestricted grant from Chugai.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5415

THURSDAY, 15 JUNE 2017

Rheumatoid arthritis - comorbidity and clinical aspects

THU0116 EUROPEAN MULTICENTRE PILOT SURVEY TO ASSESS VITAMIN D AND CLINICAL STATUS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Vitamin D (25(OH)D) deficiency seems a distinct risk factor influencing prevalence and severity of several autoimmune diseases. Several studies suggest that low serum concentrations of vitamin D are frequent in rheumatoid arthritis (RA) patients, and an inverse relationship exists between several countries. Vitamin D serum concentrations negatively correlate with the clinimetric indexes for disease activity, disability and quality of life in the present cohort of RA European patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5977

THU0117 INDEPENDENT ASSOCIATIONS OF DISEASE CHARACTERISTICS AND CARDIOVASCULAR RISK FACTORS WITH LEFT VENTRICULAR DIASTOLIC FUNCTION IN RHEUMATOID ARTHRITIS

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Background: Heart failure contributes to the excess mortality experienced by patients with rheumatoid arthritis (RA) (1). Impaired diastolic function represents a pre-clinical cardiac alteration which is highly predictive of cardiac events and often progresses to heart failure. Diastolic dysfunction is the most common cause of heart failure in patients with a preserved ejection fraction. Whereas RA is associated with an increased prevalence of impaired diastolic function (2,3), the pathophysiological mechanisms that mediate this comorbidity await further elucidation.

Objectives: This study aimed to identify potential determinants of ventricular (LV) diastolic function in patients with RA.

Methods: LV diastolic function was determined in 176 patients with RA: 9 patients had established cardiovascular disease. LV diastolic function was determined by echocardiography from the ratio of early-to-late transmitral blood flow velocity (E/A), the ratio of E to the mean of the lateral and septal wall myocardial tissue lengthening at the mitral annulus (e’/E’/e’), and the lateral e’. Relationships of comprehensively evaluated traditional cardiovascular risk factors and RA characteristics with markers of LV diastolic function were determined in confounder adjusted multivariate regression models.

Results: Disease duration (partial r=0.23, p=0.00), rheumatoid factor status (partial r=0.16, p=0.04) and erythrocyte sedimentation rate (partial r=0.16, p=0.04) were associated with lower logarithmically transformed (log) E/A. Upon further adjustment for left ventricular mass index or relative wall thickness, these relationships remained significant (p<0.05). Diastolic blood pressure was related to log E’ (partial r=0.16, p=0.04); this association was no longer significant after additional adjustment for left ventricular mass index (p=0.06) or relative wall thickness (p=0.06). Disease duration (partial r=0.32, p=0.00), waist-to-hip ratio (partial r=0.29, p=0.00) and triglycerides (partial r=0.17, p=0.03) were related to log lateral e’. These relationships remained significant upon further adjustment for left ventricular mass index (for all p=0.00) or relative wall thickness (for all p=0.00). In sensitivity analysis among RA patients without established cardiovascular disease (n=167), the results were not materially altered.

Conclusions: Modifiable traditional cardiovascular disease risk factor and disease characteristics are consistently associated left ventricular diastolic function in RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4205
WHAT IS THE ROLE OF STEROIDS IN INDUCING DIABETES MELLITUS IN PATIENTS WITH RHEUMATOID ARTHRITIS? AN OBSERVATIONAL COHORT STUDY

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Background: Patients with Rheumatoid Arthritis (RA) are at increased risk of Diabetes Mellitus (DM) probably due to immune system activation or RA treatment with steroids.[1] However the pathology of DM in RA is not fully understood.

Objectives: To define the prevalence of DM in our RA patients population. Furthermore, to clarify the role of steroid treatment to induce DM in the RA patients.

Methods: All patients with diagnosis of RA who were registered in Danish Danbio Registry at time of study, Nov 2016, were included. To find the concurrent DM, patients’ medical records including past medical history and lab tests (Hemoglobin A1c and Blood Sugar) were reviewed. In addition, year of DM as well as RA diagnoses were extracted from Fyns Diabetes Database and Danbio respectively to the extent that data were available. Patients’ drug histories were searched for information about steroid treatment if diagnosis of RA was made prior to diagnosis of DM.

Results: Of 1035 patients with diagnosis of RA, 104 (10%) patients had DM. Of 104 RA patients with DM, data regarding the year of diagnosis for both RA and DM was found in 55 patients which of them 15 patients were diagnosed with RA before DM, one patient was diagnosed with both DM and RA at the same year and 39 patients were diagnosed with RA after DM. However, only one patient, of those who were firstly diagnosed with RA, was prescribed prednisolone during the time period between diagnoses of RA and thereafter DM. Of 15 patients with prior diagnosis of RA to DM, 13 patients were diagnosed according to 1987 classification criteria (Old) for RA and 2 patients were diagnosed according to 2010 classification criteria (New). Out of 39 patients where DM was diagnosed before RA, 10 patients was diagnosed based on the old criteria and 29 patients was diagnosed based on the new RA criteria [Fig 1A and 1B]. Patients with firstly diagnosed DM were more often diagnosed according to the new RA criteria and, on the contrary, patients with latterly diagnosed DM were more often diagnosed with old RA criteria (p<0.001).

Conclusions: The prevalence of DM in this RA population (10%) was about twice of Danish population (5.7%). The role of steroid treatment in which to what extent increases the risk of DM is not clear, however in this study it was negligible, why we propose that the pathology of DM in RA patients most importantly deals with the role of immune system activation namely Tumor Necrosis Factor alpha and not the treatment modality i.e. steroids.

References:

Disclosure of Interest: We thank Mrs. Maryam Moussavi for her contribution to data collection.

THU0119 ASSESSMENT OF RHEUMATOID CACHEXIA AND ITS ASSOCIATION WITH CLINICAL, FUNCTIONAL AND THERAPEUTIC OUTCOMES

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Background: Rheumatoid arthritis (RA) is a chronic and inflammatory disease that besides articular symptoms leads to loss of muscle mass in presence of stable or increased fat mass (FM), condition defined as rheumatoid cachexia (RC), associated with a worse prognosis, but it is still overlooked in clinical practice.

Objectives: To evaluate the prevalence of rheumatoid cachexia (RC) in patients with rheumatoid arthritis (RA) and determine its correlation with the features of RA, the level of physical activity and with the current therapy.

Methods: Ninety one RA patients in a cross-sectional study underwent total body dual-energy x-ray absorptiometry (DXA) for measurement of total and regional fat mass index (FM; Kg/m²), lean mass index (LMI; Kg/m²), bone mineral content (BMC; Kg/m²) and fat free mass index (FFMI; Kg/m²) to assess the prevalence of RC. The associations of measures of body composition with RA features – age, diagnosis time, Health Assessment Questionnaire (HAQ), Disease Activity Score in 28 joints (DAS 28), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) – level of physical activity (measured by International Physical Activity Questionnaire – IPAQ) and current therapy were explored.

Results: Mean age was 56.8±7.3, disease duration 9 years (3 – 18), DAS28 3.65±1.32, HAQ 1.12 (0.25 – 1.87) and use of biological agents was 25 months (17.8 – 52.5). 17% of the patients had FMI below the 10th percentile and FM above the 25th percentile of a reference population and 33% of the patients had FFMI below the 25th percentile and FMI above the 50th percentile, condition known as RC, according to the more recently used definitions. FMFI correlated negatively only with age (r=-0.219; p=0.037) and disease duration (r=-0.214; p=0.042). FMFI correlated positively with CRP (r=0.229; p=0.029) and ESF (r=0.235; p=0.025), DAS 28 (r=0.273; p=0.026) and HAQ (r=0.297; p=0.004). Among patients under biologics, 3.8% (n=1) had RC versus 23% (n=15) of those not taking biologics (p=0.033), according to the stricter definition.

Conclusions: The prevalence of RC was considerable and deserves additional research. Besides that, patients under biological therapy had lower prevalence of RC, suggesting a protective effect of biological agents.

References:

Disclosure of Interest: None declared.

THU0120 PREVALENCE OF CHRONIC KIDNEY DISEASE IN REUMATOID ARTHRITIS PATIENTS AND IT’S ASSOCIATION WITH MULTIMORBIDITY

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Background: RA pts commonly present with multiple concurrent chronic disease. The great importance is attached to cardiovascular diseases due to their proven association with high frequency of morbidity and death. Much attention has been paid to the potential role of high-grade systemic inflammation and classical modifiable CVD risk factors – such as hypertension, dyslipidaemia, insulin resistance/metabolic syndrome, obesity, physical inactivity and smoking. A recent meta-analysis has shown that renal impairment is a strong independent cardiovascular risk factor in the general population [1].

Objectives: To assess the prevalence and clinical presentations of CKD in RA pts (ACR/EULAR 2010y.) and relate with pts multimorbid background. RA activity and duration.

Methods: 209 RA pts (F-70.6%, mean age 67,0±11,3y), admitted to rheumatology division from 1999 to 2015, were included into analysis. RA duration was 19

Conclusions: The prevalence of CKD in this RA population (10%) was about twice of Danish population (5.7%). The role of steroid treatment in which to what extent increases the risk of CKD is not clear, however in this study it was negligible, why we propose that the pathology of CKD in RA patients most importantly deals with the role of immune system activation namely Tumor Necrosis Factor alpha and not the treatment modality i.e. steroids.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3167


DOI: 10.1136/annrheumdis-2017-eular.5167
Conclusions: The results confirm and expand prior knowledge that MSUS can represent a reliable tool for the diagnosis of CTS [1]. However, its role in the diagnosis of CTS in patients with RA has been poorly investigated.

Objectives: The aim of this study is to evaluate the US findings at carpal tunnel level in a cohort of patients with RA, focusing on those with a clinical diagnosis of CTS.

Methods: Patients with RA fulfilling the ACR/EULAR 2010 classification criteria were consecutively enrolled. The diagnosis of CTS was made according to American Academy of Neurology practice parameter for CTS [2]. The MSUS assessment was carried out using a MyLab Twice (Esaote SPA) US system American Academy of Neurology practice parameter for CTS [2].

The segmentation procedure is fully automated but allows for manual corrections of wrongly segmented areas. Multimodal registration of the muscle segmentation masks to MR Dixon Fat Fraction images was used for fat quantification. Outcome parameters were absolute hand and muscle volume ($V_{abs}$ resp. $V_{rel}$), relative muscle volume ($V_{rel}$, resp. $V_{rel}$) and absolute and relative fat content ($V_{fat}$ resp. $V_{fat}$).

Student’s tests were performed for gender discrimination. Linear regression was used to model dependence on predictors BMI, RA disease duration, DMARD treatment duration, HAQ, DAS28, RF, ESR and CRP after age adjustment. Dixon sequences were not available for all patients, therefore fat analysis could only be done in 17 females.

Results: $V_{fat}$ in males was significantly higher than in females (p<0.001, means: 63 cm$^3$ vs. 29 cm$^3$). Similar results were obtained for $V_{rel}$ (p<0.001, means: 243 cm$^3$ vs. 163 cm$^3$) and $V_{rel}$ (p=0.02, means: 0.256 vs. 0.239). The table shows the results of the linear regression analysis for significant predictors of males and females, respectively. The figure shows age dependence of $V_{fat}$ and $V_{fat}$.

References:


Disclose of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6839

THU0122 QUANTITATIVE ASSESSMENT AND ANALYSIS OF HAND MUSCLE VOLUME

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by bone, cartilage and muscle loss. While bone and cartilage damage have been extensively studied in the past, the effects of RA on volume and composition of hand muscles have not yet been studied. This situation is surprising, since visible hand muscle atrophy is a hallmark of RA and quantification of muscle composition is of growing interest.

Objectives: Quantitative assessment of hand muscle volume and fat using MRI.

Methods: A random forest based method was used to segment hand muscle in T1 weighted MR scans of 76 RA patients (37 males, 26–87 years, mean 61 years). The segmentation procedure is fully automated but allows for manual corrections of wrongly segmented areas. Multimodal registration of the muscle segmentation masks to MR Dixon Fat Fraction images was used for fat quantification. Outcome parameters were absolute hand and muscle volume ($V_{abs}$ resp. $V_{rel}$), relative muscle volume ($V_{rel}$, resp. $V_{rel}$) and absolute and relative fat content ($V_{fat}$ resp. $V_{fat}$).

Student’s tests were performed for gender discrimination. Linear regression was used to model dependence on predictors BMI, RA disease duration, DMARD treatment duration, HAQ, DAS28, RF, ESR and CRP after age adjustment. Dixon sequences were not available for all patients, therefore fat analysis could only be done in 17 females.

Results: $V_{fat}$ in males was significantly higher than in females (p<0.001, means: 63 cm$^3$ vs. 29 cm$^3$). Similar results were obtained for $V_{rel}$ (p<0.001, means: 243 cm$^3$ vs. 163 cm$^3$) and $V_{rel}$ (p=0.02, means: 0.256 vs. 0.239). The table shows the results of the linear regression analysis for significant predictors of males and females, respectively. The figure shows age dependence of $V_{fat}$ and $V_{fat}$.

References:


Disclose of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6804
NEW PERSPECTIVES IN DIAGNOSIS OF INTERSTITIAL LUNG DISEASE RELATED TO RHEUMATOID ARTHRITIS. VALIDATION STUDY OF AN ELECTRONIC STETHOSCOPE AND AD HOC SOFTWARE FOR DETECTION OF PULMONARY CRACKLES

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial joint swelling and tenderness, secondary to the immune-system dysfunction, often complicated by extra-articular manifestations. Among them, lung involvement is very frequent and interstitial lung disease (ILD) represents one of the deleterious complications of RA with impact on both therapeutic approach and overall prognosis. Nevertheless, diagnosis of ILD often remains missing or delayed.

Objectives: To preliminarily evaluate the predictive value of pulmonary sound recorded by an electronic stethoscope (ES) and elaborated by an ad hoc software in identification of RA-ILD diagnosed by mean of high resolution computed tomography (HRCT) in a multicenter study.

Methods: RA patients who underwent HRCT in the last 12 months were enrolled. They were all auscultated with the ES (Littmann 3200 TM 3M, USA), bilaterally, at dorsal level, in at least 3 pulmonary fields (medium and basal). All tracks recorded were analyzed by a suitably developed software capable of recognizing pathological crackles in lung sounds. Results were compared with radiological findings detected in a blind manner by an expert radiologist.

Results: One hundred and six RA patients were enrolled (M/F: 1/2.5, mean age 68.7±10.3); among them 45 (42.5%) showed ILD at HRCT. Three patients were excluded because of diagnosis of another ILD. Despite preliminary these data suggest an important role of ES in clinical practice for an early diagnosis of ILD in RA patients and a significant reduction of inappropriate prescription of HRCT. Since very different types of ILD can occur in course of RA, with different radiologic features and localization, proper development of the measurement setup (ES and ad hoc software for the detection of PO) could further increase its predictive value, in particular to avoid incorrect diagnosis of ILD. The algorithm showed a sensitivity and specificity of 72.1% and 84.4%, respectively and a positive/negative predictive value of 89.1% and 63.8%, respectively.

Conclusions: Despite preliminary, these data suggest an important role of ES in clinical practice for an early diagnosis of ILD in RA patients and a significant reduction of inappropriate prescription of HRCT. Since very different types of ILD can occur in course of RA, with different radiologic features and localization, proper development of the measurement setup (ES and ad hoc software for the detection of PO) could further increase its predictive value, in particular to avoid incorrect diagnosis of ILD. The algorithm showed a sensitivity and specificity of 72.1% and 84.4%, respectively and a positive/negative predictive value of 89.1% and 63.8%, respectively.

Acknowledgement: Airborne agents are considered important environmental triggers of rheumatoid arthritis (RA) among genetically susceptible individuals. Due to the known association between silica dust and RA, we wanted to study the association between RA and another silicate mineral: asbestos.

Objectives: The aim of this study was to estimate the risk of RA from ever occupational asbestos exposure as well as years with exposure among men and women.

Methods: The study base consisted of men and women living in Sweden from 1968 until 2012. RA patients were identified from the National Patient Register, the Swedish Rheumatology Register (SRR), the Swedish population-based nested-control study EIRA or the Swedish Prescribed Drug Register. We matched ten controls from the national population register per case on age, county and sex. Data on occupational histories were collected from the national population and housing censuses carried out in 1960, 1970, 1975, 1980 and 1990. A job-exposure matrix (JEM) containing historical exposure estimates from 1955–1995 to asbestos was applied to the study participants’ occupational histories. We used unconditional logistic regression to assess the odds ratios (ORs) and 95% confidence intervals (CIs) of RA associated with ever exposure and years of exposure to asbestos. ORs were adjusted to contextual dust, which was also generated from a JEM. One of the data sources (EIRA) contained self-reported information on potential confounders. Analyses on this data source were carried out to estimate the confounding effect from pack-years of cigarette smoking and alcohol use.

Results: 1,437 persons in 1 and 701 200 controls were included in the analysis. The proportion of participants who had ever worked with asbestos was 38% among male cases, 35% among male controls, 3% among female cases and 3% among female controls. Ever vs. never asbestos exposure resulted in an OR of 1.15 (95% CI: 1.13–1.17) among men and 1.00 (95% CI: 0.98–1.04) among women. The ORs decreased to 1.09 (95% CI: 1.07–1.12) and 1.00 (95% CI: 0.98–1.04) for men and women respectively after adjusting for silica exposure. Asbestos exposed men were more likely than women to have worked with asbestos for a longer period of time, but the risk of RA did not appear to increase with years with the exposure. Male participants with 30 or more years of asbestos exposure at work had an OR of 1.10 (1.02–1.19) after adjustment for silica exposure.

Conclusion: Asbestos exposure is associated with RA among men, and mainly the ACPA- RA subtype. The increased risk remained after adjustments for potential confounders.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5804

PROGRESSION OF SUBCLINICAL ATHEROSCLEROSIS OVER ELEVEN YEARS IS INCREASED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have an increased mortality and morbidity due to cardiovascular disease (CVD).

Objectives: In this prospective follow up over eleven years, we investigated the relation to traditional CVD risk factors and inflammation, in patients with early RA compared to controls.

Methods: Patients from northern Sweden diagnosed with early RA are consecutively recruited into an ongoing prospective study. A subgroup aged 60 years (n=54) was consecutively included for ultrasound measurements of IMT of a. Carotis communis at inclusion (T0), and after 11 years (T11). 31 age-sex-matched controls were included. The patients were clinically assessed, SCORE, Reynolds Risk Score and Larsen score were calculated and blood samples drawn from all individuals at T0 and T11. Data and results presented in this abstract are preliminary.

Results: Patients with RA as well as controls had a significant aggravation in IMT over 11 years (0.52 at T0 and 0.68 at T11 in RA: p<0.001; 0.54 at T0 and 0.63 at T11 in controls; p<0.05; IMT in RA vs controls at T0 and at T11: p<0.05). The patients with RA had a significantly higher progression in IMT from T0 until T11 (0.16 vs 0.08, p<0.001). In simple linear regression analyses among RA-patients, the IMT at T11 was significantly associated with several variables at T0: age, systolic blood pressure, SCORE, Reynolds Risk Score, iPA, L-selectin (inversely), MCH, MCV and Larsen score. The progression in IMT over 11 years was associated with age and Larsen score at T0.

Conclusions: In this prospective study, the progression of sub-clinical atherosclerosis over 11 years was significantly higher in patients with RA than in controls. The IMT at T11 was associated with several traditional cardiovascular risk factors, as well as disease severity, at time of diagnosis.

Disclosure of Interest: None declared


THE EFFECT OF GLUCOCORTICOIDS ON BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: The role of glucocorticoids (GCs) in the treatment of rheumatoid arthritis (RA) is widely debated. GCs stimulate bone resorption and impair bone formation (1). Inflammatory cytokines also stimulate bone resorption, and patients with RA have a high risk of osteoporosis (OP) and fragile fractures (2). However, in patients with RA, impairment of bone formation by GCs may be counter-balanced by reduced systemic inflammation and increased physical activity.

Objectives: This systematic review aims to assess the effect of oral prednisolone and prednisone on bone mineral density (BMD) in patients with RA analyzed in randomized, controlled trials (RCT).

Methods: We performed a systematic literature search and identified double-blinded RCTs comparing prednisolone or prednisone with placebo and measuring...
BMD dual-energy absorptiometry at baseline and at least once thereafter. Two authors independently reviewed references, extracted data and assessed risk of bias. We assessed quality of evidence using the GRADE methodology. Primary outcomes were mean change in BMD at the hip and lumbar spine. Secondary endpoints included RA disease activity and radiographic progression. Results: 30 studies. Studies differed regarding study population and intervention. Risk of bias was considered low for BMD outcomes. Data completeness was low in some studies. We found no statistically significant difference in change in BMD from 0 to 24 months neither at the lumbar spine (Standard Mean Difference (SMD) 0.02 (95% CI -0.16, 0.12)) nor at the hip [SMD 0.02 (95% CI -0.12, 0.16)]. Disease activity was significantly lower in the GC groups (mean difference in DAS28 -0.32 (95% CI -0.52, -0.11). Concomitant treatment of RA differed between studies, as did OP prophylaxis. However, sensitivity analyses excluding a study with different distribution of OP prophylaxis between GCs or placebos did not alter the estimates. Quality of evidence was rated moderate for BMD outcomes.

Conclusions: In this group of double-blinded RCT studies we found no difference in change in BMD in patients with RA who received GCs compared to those who received placebo. The interpretation of this is difficult as it challenges the well-established fact that GCs negatively impact BMD. However, our findings suggest that in a population with early RA, followed for two years, the dampening of inflammation as well as increased physical activity may outweigh the inherent effects of GCs. This concurs with our finding of lower disease activity in the groups receiving GCs.


Disclosure of Interest: None declared, D. Veltishchev: None declared, O. Seravina: 2 Ultrasound Department, Lugansk Clinical Regional Hospital, Lugansk, Ukraine

Background: Now it is proved that the leading reason for the decline in life expectancy in patients with rheumatoid arthritis (RA) are cardiovascular (CV) disease. The increase in CV risk in patients with RA is associated with increased progression of atherosclerotic vascular lesions. Autoimmune inflammatory process in RA affects the vascular endothelium contributing to the appearance of CV events in patients with RA. It is known that when SHTD levels increased levels of proinflammatory cytokines. Also, when there is an increase SHTD thickness complex intra-media (CIM).

Objectives: To study the characteristics of ultrasound dopplerography in patients with RA with SHTD.

Methods: The observation 139 patients with RA. The I group consisted of 91 patients with RA and SHTD, the II - 48 patients with RA without SHTD. Patients in group I and II did not differ significantly by age and duration of RA. Detection of endothelial dysfunction was performed using ultrasound dopplerography vessels in accordance with international guidelines.

Results: In the study of endothelial regulation of vascular tone in both groups of patients revealed the presence of disturbances, as determined signs of reduced function of SHTD patients with RA leads to a significant increase in the risk of developing CVD. This requires a more careful study of RA patients with SHTD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5750

THU0127 THE DYNAMICS OF MENTAL DISORDERS FREQUENCY IN COMPLEX DMARDs, BIOLOGICS AND ANTIDEPRESSANTS TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS

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Background: mental disorders (MD) (anxiety/depressive (ADD) and cognitive (CD)) occur in rheumatoid arthritis (RA) patients (pts) very often, they are usually stress-related and, probably, have common pathogenesis chains with RA. In this connection the disease-modifying anti-rheumatic drugs (DMARDs) and biologics drugs treatment may be effective in ADD in RA-pts.

Objectives: to determine the frequency of MD dynamics during DMARDs, biologics and antidepressants treatment of RA-pts in prospective 5yrs study.

Methods: 128 RA-pts were enrolled in this study. All of them met the full ACR criteria. 86% RA-pts were women with a mean age of 47,4±10,0 (M±m) yrs. RA- activity was assessed by DAS28 and was high (5,25±0,70 (M±m)) in the beginning of the study. 67% RA-pts were taking prednisone (5±2,7 mg/day). 80% RA-pts were taking biologics and antidepressants treatment of RA-pts in prospective 5yrs study. Major depressive disorder (MDD) was found in 41(32%), minor depressive disorder (MinDD) – in 50 (39%) and anxiety disorders (AD) – in 30 (23,4%) of RA-pts.

Table 1

<table>
<thead>
<tr>
<th>Indicators</th>
<th>I group (n=48)</th>
<th>II group (n=91)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1, cm</td>
<td>76.1 (71.6; 79.6)</td>
<td>70.8 (62.6; 76.6)*</td>
<td>0.002</td>
</tr>
<tr>
<td>V1, Vm</td>
<td>56.2 (54.2; 58.2)*</td>
<td>56.2 (54.2; 58.2)*</td>
<td>0.16</td>
</tr>
<tr>
<td>V1, CNS</td>
<td>10.6 (10.2; 10.9)</td>
<td>10.6 (10.2; 10.9)</td>
<td>0.9</td>
</tr>
<tr>
<td>V1, EIVD</td>
<td>15.4±1.5</td>
<td>15.4±1.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Note: *p<0.05.

It is also a distinction between the two groups in terms of the thickness of the CIM (Z=9.7, p<0.001), exceeding in group II. Determined a significant decrease in the coefficient of sensitivity to endothelial shear stress (C) in patients with RA, who was in I group of 0.45 (0.34; 0.71), and in II - 0.26 (0.18; 0.46) that there was a statistical difference in this index between the groups of patients (Z=3.6, p<0.001) due to a significant reduction in patients of group II.

The performed analysis of variance indicated that there SHTD influence on the development of disorders of vascular endothelial function in motor RA patients. The SHTD presence in group II patients significantly affected the reduction EIVD, EIVD, C (H=13.8, p<0.001; H=14.5, p<0.001; H=10.2, p<0.001).

Conclusions: The analysis indicated the presence of influence SHTD on the development of disorders of vascular-motor endothelial function in RA patients. These data show that the presence SHTD patients with RA leads to a significant increase in the risk of developing CVD. This requires a more careful study of RA patients for early detection and correction of comorbidities that worsen the clinical course of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3238

HYPOTHYROID DYSFUNCTION

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Background: It is known that when SHTD levels increased levels of proinflammatory cytokines. Also, when there is an increase SHTD thickness complex intra-media (CIM).

Objectives: To study the characteristics of ultrasound dopplerography in patients with RA with SHTD.

Methods: The observation 139 patients with RA. The I group consisted of 91 patients with RA and SHTD, the II - 48 patients with RA without SHTD. Patients in group I and II did not differ significantly by age and duration of RA. Detection of endothelial dysfunction was performed using ultrasound dopplerography vessels in accordance with international guidelines.

Results: In the study of endothelial regulation of vascular tone in both groups of patients revealed the presence of disturbances, as determined signs of reduced function of SHTD patients with RA leads to a significant increase in the risk of developing CVD. This requires a more careful study of RA patients with SHTD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3759
CD8+CD28- T-lymphocytes are associated with subclinical atherosclerosis in patients with rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) have an increased mortality and morbidity due to atherosclerotic vascular disease. We evaluated the association between subclinical atherosclerosis, markers of CD8+CD28- T-lymphocytes and T-lymphocytes expressing CX3CR1.

Patients and Methods: To study the association between subsets of T-lymphocytes, subclinical atherosclerosis assessed by intima-media thickness (IMT) and antibodies against CMV in patients with RA.

Results: The percentage of CD8+T-lymphocytes lacking the co-stimulatory molecule CD28 (CD8+CD28-) was significantly (standardized beta coefficient 0.39, p-value 0.018) associated with IMT at T11 in a linear regression model including T0 variables smoking, systolic blood pressure and cholesterol. No association with IMT was seen for CD4+CD8- T-lymphocytes. CX3CR1 was expressed in 71% of CD8+CD28- T-lymphocytes, compared with 8.2% of CD4+CD8- T-lymphocytes. The prevalence of immunoglobulin G seroconversion of CMV was 47/70 (67%), 42/66 (63%) and 34/56 (61%) at T0, T5 and T11, respectively. Patients with constantly positive CMV serologies (T0, T5 and T11) had a significantly higher percentage of CD8+CD28- T-lymphocytes, compared with CD4+CD8- T-lymphocytes expressing CX3CR1.

Also the proportion of cells expressing CX3CR1 was in both CD4+ and CD8+ T-lymphocytes associated with constantly positive serovars for CMV.

Conclusions: Subclinical atherosclerosis in patients with RA was associated with CD8+CD28- T-lymphocytes in a regression model adjusted for traditional cardiovascular risk factors. Positive serologies for CMV was associated with an increased proportion of CD8+CD28- T-lymphocytes and T-lymphocytes expressing CX3CR1.

Disclosure of Interest: B. Wahlin: None declared, A. Fath Employee of: Novartis Sweden AB, K. Karp: None declared, K. Lejon: None declared, A. Södergren: None declared, S. Wållberg-Jonsson: None declared

DOI: 10.1136/annrheumdis-2017-eular.4364

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease that can affect any joint in the body. Treatment options vary widely, and each patient's response to therapy is unique. The efficacy of a treatment can be assessed by monitoring the resolution of symptoms, improvements in physical function, or changes in disease activity measures. However, the mechanisms underlying these changes are not fully understood. It is believed that treating RA in its early stages can lead to better outcomes, but the optimal time for initiating therapy is uncertain. The goal of this study was to investigate the early response to sirukumab, a human monoclonal antibody that selectively binds to interleukin-6 (IL-6), a cytokine involved in the inflammatory process, in patients with RA.

Methods: This was a post-hoc analysis of two Phase III, randomized, double-blind, placebo-controlled trials evaluating efficacy and safety of sirukumab in the treatment of RA. The results of these trials were previously published.

Objectives: The main objective was to assess the early response to sirukumab in patients with RA. Early response was defined as the changes in treatment of premature and other CHD.

Results: Among 1235 RA patients recorded in the database, 12 (21%), 20 (35,1%) and 25 (43,9%) CHD patients, respectively. There was no statistical difference in treatment of premature and other CHD.

Conclusions: Our findings are consistent with previous results from a phase II RA study. Periperal anti-IL-6 cytokine treatment is associated with improvement in depressive symptoms in RA patients, possibly supporting a role for IL-6 dysfunction in depression.

References:


Background: Patients with rheumatoid arthritis (RA) are at increased risk of coronary heart disease (CHD) overall, as well as death from CHD. A direct impact of chronic inflammation on the vascular system, secondary effects of physical inactivity and some drugs used in the management of RA are shown as the reasons for the increase in this comorbidity.

Objectives: We aim to determine the frequency of CHD in the RA patients who receive biological agents.

Methods: Hacettepe University Biologic Registry (HUR-BIO) includes demographic and clinical data of patients treated with biological agent since 2005. By August 2016, 1235 RA patients were recorded in the database. Smoking status, comorbidities, current and previous treatments were analysed in 1000 patients. Disease activity was estimated by the 28-joint activity calculator (DAS28-ESR) and DAS28-CRP. Functional assessment was evaluated by the Health Assessment Questionnaire (HAQ). Premature CHD should be defined if chronic CHD or sudden death is documented in male younger than 55 years of age and in female younger than 65 years of age.

Results: Overall 1000 patients (79.8% female) were enrolled in this study. Mean age was 53,1±12,6 years old, mean disease duration was 12,3±9,3 years. CHD was detected in 57 (5,7%) patients and female/male was 38/19. Premature CHD was observed in 38 (66,7%) patients. CHD patients had more frequently male, older, higher classical risk factors, higher baseline ESR level and higher functional disability (Table). HAQ score also remained high in CHD group at last visit. Clinical course of RA, vascular risk factors, seropositivity, disease activity score and HAQ score were similar in the premature and other CHD group. Coronary artery stenting, coronary artery bypass surgery and medical treatment was applied in 12 (21%), 20 (35,1%) and 25 (43,9%) CHD patients, respectively. There was no statistical difference in treatment of premature and other CHD.

Table 1. Characteristic of patients who have or not CHD

<table>
<thead>
<tr>
<th>CHD (n=577)</th>
<th>No CHD (n=943)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female n (%)</td>
<td>36 (66,6)</td>
<td>19 (60,6)</td>
</tr>
<tr>
<td>Hypertension n (%)</td>
<td>38 (66,6)</td>
<td>27 (29,7)</td>
</tr>
<tr>
<td>Diabetes Mellitus n (%)</td>
<td>11 (19,3)</td>
<td>9 (10,3)</td>
</tr>
<tr>
<td>Smoking (current/past) n (%)</td>
<td>30 (52,6)</td>
<td>37 (39,2)</td>
</tr>
<tr>
<td>Baseline Erythrocyte sedimentation rate (SD)</td>
<td>64 (9,9)</td>
<td>62 (12,4)</td>
</tr>
<tr>
<td>Baseline ESR (SD)</td>
<td>45,7 (30,3)</td>
<td>36,1 (24,6)</td>
</tr>
<tr>
<td>Last HAQ mean (SD)</td>
<td>1,27 (0,64)</td>
<td>1,02 (0,62)</td>
</tr>
<tr>
<td>Last HAQ mean (SD)</td>
<td>0,84 (0,6)</td>
<td>0,66 (0,58)</td>
</tr>
</tbody>
</table>

CHD: Coronary heart disease. HAQ: Health Assessment Questionnaire.

Conclusions: As a result of CHD were detected in 5,7% of RA patients who are receiving biological agents. Importantly, two third of these patients have
THU0132 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE FOR PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 2-YEAR FOLLOW UP

Background: Comorbid infections have significant impact on morbidity and mortality, especially in autoimmune diseases. Prevention of infection is an integral part of supervision of these patients.

Objectives: To investigate immunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine in patients with rheumatoid arthritis (RA) treated with drugs modifying anti rheumatic drugs (DMARDs) and biologic diseases modifying anti rheumatic drugs (bDMARDs) during the 2-year follow-up.

Methods: Out of 110 subjects (81 females (73.6%), 29 males (26.4%) aged 23–76 years) included into the study, 79 were RA patients and 31 were controls with a history of ≥2 episodes of lower respiratory tract infections (bronchitis, pneumonia). 52 patients with RA were on methotrexate (MTX), 14 were on leflunomide (LEF), 13 were on tumor necrosis factor alpha inhibitors (TNF-α) + MTX. One dose (0.5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously without discontinuation of MTX/LEF or 28–30 days prior to initiation of TNF-α. Totally four study visits were preplanned: initial vaccination visit and 3 control visits in 1, 3 and 12 months after vaccination in 110 patients. 39 RA patients were followed up for 2 years (24 months). Routine evaluation during each visit included physical exams and laboratory tests. Levels of antibodies to pneumococcal capsular polysaccharide were measured using VacciYmeTM PCCpig 2 kit (The Binding Site Group Ltd, Birmingham, UK). Post-immunization response coefficient was calculated for each participant as the ratio of AB levels during visits II, III, IV and V to baseline AB level at Visit I.

Results: Not a single case of clinicoradiologically confirmed pneumonia was documented during the follow up period. Pronounced positive immune reaction after administration of the vaccine under investigation was documented in RA patients during different therapies, i.e., significant post-immunization response coefficient increase. There were 61% responders among RA patients and 70% responders among the controls during one-year follow-up. Dynamics of post-immunization response coefficient in RA patients during 2-year follow-up are presented in the Table. RA patients and the control group are marked more than 2-fold significant increase in the content of antibodies in 3 months after the vaccination. Despite the decline in their concentration to 12 months, it remained at the proper level and was increased to 24 month follow-up. Good tolerability of the vaccine was documented in 65% of cases, satisfactory (injection site pain, swelling and hyperemia of the skin up to 2 cm in diameter and subblebivelief) in 35% of cases. As these reactions had no causal relationship with current RA therapy, and fully resolved within 24 hours without additional treatment, no RA therapy modification was required. Pronounced DAS28 positive dynamics in RA patients (4.27 and 2.68 at Visit I and Visit V, respectively, p < 0.001) indicates the absence of any negative impact of vaccination on disease activity.

Conclusions: Thus, all given prove the sufficient immunogenicity and safety of 23-valent pneumococcal vaccine in RA patients, getting different therapeutic regimens during the 2-year follow-up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4269

THU0133 SERUM PENTRAxin-3 IN THE ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS
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Background: Rheumatoid arthritis (RA) is associated with the increased cardiovascular (CV) morbidity and mortality due to accelerating, progressive atherosclerosis. The chronic, systemic inflammatory process is responsible for both joint damage and increased CV risk in RA patients. Pentraxin 3 (PTX3) is an inflammatory marker, a member of long pentraxin superfamily, supposed to be involved in inflammatory process as well as in atherosclerosis.

Objectives: The goal of the study was to assess the role of PTX3 as an inflammatory marker in patients with RA and to evaluate the relationship between PTX3 and CV risk markers [carotid intima-media thickness (cIMT), QTc distance (dQTc), lipid profile].

Methods: The study group consisted of 72 consecutive RA patients, 60 (83.3%) female and 12 male (16.7%), with the mean (SD) age 53.4 (10.29) (range 21–71) and disease duration 16.8 (10.3) years (range 2–49). The activity of RA was evaluated by clinical examination with the disease activity score in 28 joints (DAS28). Remission or low disease activity was observed in 35 (48.6%) patients; moderate or high disease activity (DAS28 > 3.2) in 37 (51.4%) patients. Disease modifying antirheumatic drugs (DMARDs) used in the treatment included: methotrexate (11 (84.7%), leflunomide 4 (5.6%), cyclosporine 1 (1.4%) patient. The majority of patients 54 (75%) were treated with biological DMARDs, currently or in the past.

Results: The mean (SD) PTX3 concentration in RA patients was 4.57 (2.83) mg/l (range 1.43–16.07), in the control group 2.55 (1.37) mg/l (SD 0.99) mg/l. PTX3 concentration was significantly higher in patients with moderate/high RA activity in comparison with remission/low disease activity [5.56 (3.29) vs 3.48 (1.71) mg/l, p=0.001] and in patients anti-CCP positive compared with anti-CCP negative [4.57 (2.58) vs 3.32 (0.85) mg/l, p = 0.04]. The mean (SD) PTX3 concentration was significantly higher in patients with definite atherosclerosis (cIMT > 0.9 mm) than in patients with subclinical or no atherosclerosis [5.77 (3.02) vs 3.99 (2.58) mg/l, p=0.04], as well as in patients with atherosclerotic plaques in comparison with no plaques (6.18 (2.83) vs 4.02 (2.64) mg/l, p=0.0007).

There was a negative correlation between PTX3 and dQTc (R = -0.33, p = 0.007).

Conclusions: The results of the study suggest a twofold role of PTX3: 1. an inflammatory marker of the joint disease activity 2. a biomarker indicating intensity of atherosclerosis, estimated by greater cIMT value and the presence of atherosclerotic plaques. The negative correlation between PTX3 and dQTc suggests the increased risk of sudden cardiac death due to shortening of dQTc.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3303

THU0134 INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS. MULTICENTER STUDY WITH TOCILIZUMAB
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Background: Interstitial Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA). AntiTNFα drugs and conventional disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) have been involved in the development of ILD. IL6 has been implicated in the pathogenesis of ILD (Kobayashi J et al). However, a fatal case of exacerbation of ILD has been involved in the development of ILD. IL6 has been implicated in the pathogenesis of ILD (Kobayashi J et al). However, a fatal case of exacerbation of ILD has been described with tocilizumab (TCZ) (Kawashiri SY et al at).

Methods: Multicenter study of RA patients with ILD treated with TCZ. ILD was diagnosed by high-resolution computed tomography (HRCT), TCZ was used at standard dose (8 mg/iv/4 weeks). We have analyzed the following variables: a) change in the degree of ILD according to the Modified Medical Research Council (MMRC); b) Forced Vital Capacity (FVC) improvement ≥10%; and improvement ≥10% in DLCO; c) HRCT, and d) joint assessment (DAS28 score).

Results: We studied 12 patients (9 women/3 men) with ILD related to RA,
The mean age SD was 57.1±16.1 years. The mean evolution of RA was 9±5.8 years. The patients had previously received the following DMARDs: MTX (n=12), leflunomide (LFN) (8), sulfasalazine (SSZ) (3), hydroxychloroquine (HCQ) (1), azathioprine (AZA) (2), gold salts (2). In addition, 11 patients had previously received biological drugs: adalimumab (4) anakinra (1), etanercept (4), rituximab (4), infliximab (1), certolizumab (1), abatacept (1). RA was severe in 11 cases (92%). Besides HRCT, the diagnosis of ILD was confirmed by biopsy in 4 patients. In 2 patients ILD was drug-related: MTX (n=2). TCZ was prescribed in monotherapy (n=8) or combined with other DMARDs (4). These DMARDs were: LFN (2), MTX (1), AZA (1). In many patients the dyspnea and DLCO remain stabile (Table). After a follow-up of 12 months, 2 patients withdrew TCZ, 1 patient for ILD worsening and 1 patient for joint inefficacy.

Table 1

| MRC, n (%) | 11 | 8 | 11 |
| Improvement | 0 | 2 | 18 |
| Worsening | 0 | 1 | 12 |
| FVC, n (%) | 2 | 5 | 9 |
| No change | 2 (100) | 5 (100) | 6 (67) |
| Improvement | 0 | 0 | 2 (23) |
| Worsening | 0 | 0 | 4 (44) |
| DLCO, n (%) | 2 | 4 | 9 |
| No change | 1 (50) | 3 (75) | 9 (100) |
| Improvement | 0 | 0 | 0 |
| Worsening | 1 (50) | 1 (25) | |
| HRTG, n (%) | 2 | 3 | 10 |
| No change | 1 (50) | 2 (70) | |
| Improvement | 0 | 0 | 0 |
| Worsening | 1 (50) | 0 (0) | 0 |

Conclusions: In our knowledge, this is the largest series that assess the EPID

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3580

THU0135 THE COURSE OF LOWER EXTREMIT Y FUNCTION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS OVER THE FIRST FIVE YEARS

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Background: Rheumatoid arthritis (RA) frequently involves joints of the feet and the knees. Disability related to arthritis in the lower extremities has a major impact in many patients, but has not been extensively studied.

Objectives: To investigate lower extremity function in early RA, using validated tests, and to assess its relation to other disease parameters.

Methods: Consecutive patients with early RA (symptom duration ≤12 months) in an inception cohort from a well-defined area were followed according to a structured protocol, with visits at inclusion and after 1, 2, and 5 years. Lower extremity function was investigated using the Index of Muscle Function (IMF) (1), a validated battery of tests by which the patient's general ability, muscle strength, muscular endurance, and balance are assessed by a physiotherapist. The scores on the subscales are added for a total IMF score (IMF total) of 0–40. A subscore of the Health Assessment Questionnaire Disability Index (HAQ-DI), based on 10 questions that are mainly dependent on function of the lower extremities (the HAQ-DI-LE) is on the only three HAQ-DI domains in which all activities related mainly to the lower extremities. Changes in the IMF total score and subtest scores between visits were analyzed using the Wilcoxon signed rank test. Correlations between disease parameters were assessed using Spearman's rank test.

Results: A total of 106 patients (67% women, mean age 61 years, mean baseline DSAS 28 4.4, median baseline HAQ-DI LE 0.75) were included. Data on IMF total were available for 100, 89 and 67 patients at the 1, 2 and 5-year visits. Lower extremity function improved from baseline to the 1-year visit (IMF total median 4.1 (IQR 2–6) vs 3 (IQR 2–6); p=0.001) and for balance/coordination (median 2 (IQR 1–6) vs 5 (IQR 2–9); p=0.001) and for balance/coordination (median 2 (IQR 1–6) vs 5 (IQR 2–9); p=0.001). There were significant correlations between IMF total and HAQ-DI-LE, HAQ-DI-LE and HAQ-DI at all time points, but no significant correlations for IMF total with CRP and DSAS28 at the 2-year visit.

Conclusions: HAQ-DI-LE improvement in lower extremity function during the first year, followed by a gradual decline, possibly explained by lack of complete disease control and aging. Tests of muscular function in the lower extremities may reveal aspects of RA disease severity that are not fully captured by standard disease activity measures, and may add important information regarding functional loss.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular-4223

THU0136 NESFATIN-1 EXPRESSION IS ASSOCIATED WITH REDUCED Atherosclerotic disease risk in patients with Rheumatoid Arthritis

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Background: Nesfatin-1 comprises a peptide that is involved in appetite suppression, energy homeostasis and fluid regulation, and was recently documented to participate in a range of cardiometabolic pathways (1,2). There is currently a need for the identification of novel biomarkers in the elucidation of CVD risk and its stratification in patients with rheumatoid arthritis (RA). The role of nesfatin-1 in cardiovascular disease risk among RA patients is uncertain.

Objectives: We investigated the potential impact of nesfatin-1 on subclinical cardiovascular disease manifestations in patients with RA by determining the associations of nesfatin-1 concentrations with atherosclerosis and circulating levels of matrix metalloproteinases (MMP-2) that mediates plaque stability and those of MMP-3 and MMP-9 that cause plaque vulnerability.

Methods: Nesfatin-1 concentrations were measured in 236 (114 black; 122 white) RA patients. Relationships of nesfatin-1 concentrations with ultrasound determined carotid intima-media thickness (cIMT) and plaque and MMP levels were identified in confounder adjusted multivariable regression models.

Results: Nesfatin-1 concentrations were inversely associated with c-IMT (β(SE) = -0.022 (0.008), p =0.00) and directly with MMP-2 levels (β(SE) = +0.117 (0.031), p =0.00). After adjustment for conventional risk factors and RA characteristics, these associations persisted (c-IMT: β(SE) = -0.022 (0.008), p =0.00) and directly with MMP-2 levels (β(SE) = +0.117 (0.031), p =0.00). By contrast, the Disease Activity Score in 28 joints (DAS28) and Clinical Disease Activity Index impacted the nesfatin-1-cIMT relation (interaction p=0.7). Contrast, the Disease Activity Score in 28 joints (DAS28) and Clinical Disease Activity Index impacted the nesfatin-1 to-cIMT relation (interaction p=0.04 and 0.02, respectively). Nevertheless, in stratified analysis, nesfatin-1 concentrations were related to those of MMP-2 in patients with no or mild disease activity (β(SE) = +0.148 (0.054), p=0.00) and moderate or high disease activity (β(SE) = -0.086 (0.041), p=0.04) as determined by DAS28 (cut-off value 3.6) as well as by CDAl (cut-off value ≤10) (β(SE) = +0.130 (0.048), p=0.00 and 0.107 (0.046), p=0.02, respectively).

Conclusions: Nesfatin-1 concentrations are consistently associated with a reduced atherosclerosis burden and increased MMP-2 levels in patients with RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4586

THU0137 IMPACT OF PERIODONTAL AND RHEUMATIC DISEASE MARKERS ON FIRST-DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) and periodontal disease (PD) have been independently associated with atherosclerosis burden and increased plaque vulnerability.
DAS 28 CORRELATED POORLY WITH THE OBJECTIVE EVIDENCE OF INFLAMMATION AS DETECTED BY ULTRASOUND (US) EXAMINATION OF HANDS AND FEET IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS (RA)

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Background: The Disease Activity Score including 28 joint count (DAS-28) is the most widely used outcome measure in RA. However, despite evidence that articular Doppler signal, erosions and osteophytes. Information about demographics, disease duration, current treatment, inflammatory markers, and DAS-28 scores was captured. The hereby-obtained assessment questionnaires including the health assessment questionnaire (HAQ), and matched controls.

Objectives: To evaluate PD markers in first-degree relatives (FDR) of consan- guinity individuals with patients with rheumatoid arthritis to compared with controls and to establish an association to rheumatic activity according to age groups.

Methods: 201 FDR and 201 controls were included. Statistical evaluation of rheumatologic and periodontal condition was performed. P gingivalis, P. gingivalis IgG1 and IgG2, ESR, CRP, RF, ACPAs, painful and swollen joints were assessed. A frequencies analysis, comparisons and a logistic regression model were made. The study was approved by local ethics committees.

Results: 32% of the controls and 10.1% of patients. Subjects with more than one swelling joint were 21 subjects <30 years, 5 between 31–40, 5 between 41 to 50 subjects and 9 subjects over 50, for more one painful joint were 73. The RF was present in 8.0%, APCA in 13%, RA33 in 1%, 67.3% had a disease of PD. 81.6% had a moderate-severe p=0.003. P gingivalis was in 47.9%, and P. gingivalis IgG1 were in 54.7%. It was evident that 25.3% patients presented BMI <30, where 81.8% had periodontitis p=0.006. Regression analysis on the whole group shows a risk to present BMI >25 (OR 1.67 IC-95% 1.02−2.74 p=0.042), ACPAs (OR 3.7 IC-95% 1.34−10.22 p=0.02), at least one pain join (OR 5.1 IC-95% 1.42−4.44 p=0.001), and gingival index (OR 4.57 IC-95% 1.76−11.80 p=0.002) in FDR individuals. Based on age the risk to develop PD was increasing: individuals among 30 to 40 years shows OR 2.76 (IC-95% 1.24−6.18, p=0.013); among 41 to 50 years, OR 4.72 (IC-95% 1.81−12.32, p=0.001); and for >50 years individuals OR 6.22 (IC-95% 2.05−15.1, p=0.001). The disease activity scores by age rank shows the FDR individuals 20 years (n=47) exhibited high risk to have at least one pain join (OR 3.84 IC-95% 1.28−11.47 p=0.016). In subjects among 30 to 40 years (n=46), the risk was associated with periodontal pocket (OR 4.4 IC-95% 1.05−4.98 p=0.021), one or more pain join (OR 3.56 IC-95% 1.00−12.02) which it was maintained until 50 years old individuals (n=35) (OR 3.2 IC-95% 1.11−6.78 p=0.004), individuals >50 years (n=53) show high risk to present BMI >25 (OR 4.00 IC-95% 1.46−10.45 p=0.007).

Conclusions: Obesity, ACPA and periodontitis can be considered as relevant conditions associated with the development of RA in FDRs. However, the analysis based on age group shows that periodontal markers do not appear early in FDR individuals; however, clinical rheumatologic variables are manifested and maintained over time.

References:

Disclosure of Interest: None declared


THU0139 DEPRESSIVE SYMPTOMS AND VITAMIN D IN PATIENTS WITH EARLY ARTHRITIS

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Background: There is a high prevalence of depression in patients with rheumatic diseases, especially in rheumatoid arthritis (RA). It is one of the most prevalent co-morbidities with 16% to 38%. Vitamin D (VD) deficiency is one of the known risk factors for depressive disorders. On the other hand, a VD deficiency has often been detected in rheumatic diseases. A possible correlation between these co-morbidities has not been investigated so far in patients with early arthritis (EA).

Objectives: The aim of this study was to examine the association between VD deficiency and depression and/or anxiety disorders in patients who have presented themselves for the first time in the EA clinic.

Methods: Patients with a suspected EA (at least one swollen joint without previous trauma or joint infection with a symptom duration of 6 weeks to 12 months) received a screening date within five work days. The VD status (25-hydroxy-VD) was obtained during the first EA clinic consultation. In addition, each patient completed questionnaires on the disease history, as well as evaluated self-assessment questionnaires including the health assessment questionnaire (HAQ) and the Hospital Anxiety and Depression Scale (HADS). The hereby-obtained results of disease activity, VD-status and HADS-scores were investigated. In the observation period from June 2012 to March 2015, 75 patients fulfilled the inclusion criteria of complete results which resulted in questionnaires as well as a disease duration of less than 12 months.

Results: The mean age of this EA cohort was 51.7±16.9 years (±65.3%, mean disease duration: 4.0±3.0 months). The prevalence of VD deficiency (<75 mol/l) was 73.3%. 48.0% of EA patients showed a positive global distress score (≥13). The most prominent VD status global distress score ≥1 in sufficient patients was 10.2±6.6 vs. 13.3±6.9 in deficient patients. The observed difference was not statistically significant. There was neither an association between gender, age and VD status nor was there any difference in the laboratory parameters (e.g. C-reactive protein, rheumatic factor, anti citrullinated peptide, hemoglobin) or assessment of functional status (e.g. HAQ, disease activity score by 28 joints).

Conclusions: The prevalence of VD deficiency is higher in EA patients with 73% than in the general German population (vs. 60%). The prevalence of positive distress with 50% is also higher. Interestingly, no association of deficient VD status and negative distress scores with 90% was observed in the HAQ, disease activity score by 28 joints. This might be explained by the early stage of disease, but further studies are necessary to evaluate this new insight.

References:


Discussion of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4351

THU0140 SPECKLE TRACKING ECHOCARDIOGRAPHY EVALUATION OF CORONARY TERRITORIES IN MEXICAN MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The main cause of death in patients with rheumatoid arthritis (RA) is atherosclerotic cardiovascular disease. Speckle Tracking Echocardiography (STE) is an imaging technique that analyses the local and global myocardial function by assessing the myocardial deformation (strain). This technique is useful in addressing early alterations in ischemic pathologies (1,2).

Objectives: The aim of this study was to analyze if longitudinal strain abnormalities correspond with vascular territories, and compare the results between RA-patients and matched controls.

Methods: An observational cross-section case-control study was designed. Patients that fulfilled the 1987 ACR and/or 2010 ACR/EULAR classification criteria for RA, were 40–75 years old, with no overlap syndromes and no history of atherosclerotic cardiovascular disease were included. The control group was formed by age- and sex-matched subjects, with no rheumatologic or cardio-vascular diseases. A standard transthoracic echocardiogram was performed by a
board-certified echocardiographer. Affection of coronary territories was compared between groups using longitudinal strain by speckle tracking according to the European Society of Cardiology and the American Society of Echocardiography recommendations.

Results: A total of 53 RA-patients and 24 control subjects were included. Demographic and clinical characteristics for each group are shown in Table 1. There was no statistical difference in global longitudinal strain between RA-patients and controls (-20.86±2.82 vs -21.19±2.46, p=0.62). Comparison of longitudinal strain values of the three vascular territories evaluated between RA-patients and controls did not reach statistical difference (Table 2).

Conclusions: Contrary to previous published evidence (1, 2), there was no statistical difference in global longitudinal strain between RA patients and controls. Further studies with a larger cohort are necessary to determine the usefulness of strain in the evaluation of subclinical cardiovascular disease.

References:

DOI: 10.1136/annrheumdis-2017-eular.5669

**THU0141** CAN WE PREDICT THROMBOTIC TENDENCY IN RHEUMATOID ARTHRITIS: A THROMBOELASTOGRAPHIC ANALYSIS

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Background: Arterial and venous thromboembolism were proven to be increased in cases with rheumatoid arthritis (RA) [1]. It would be interesting to predict thrombosis in these patients by a laboratory test. Rotational thromboelastography (ROTEM) is a viscoelasticomographic test to evaluate the kinetics of clot formation and fibrinolysis which provides global information on cellular and soluble procoagulant/anticoagulant protein interactions.

Objectives: Our aim was to determine the thrombosis predisposition in RA patients by thromboelastography and to identify the possible clinical and laboratory risk factors for thrombotic tendency in RA patients.

Methods: 85 RA patients (mean age: 54.12±13 yrs; female: 66 (77.6%)) diagnosed based on 2010 ACR/EULAR classification criteria were sequentially recruited. Patients were receiving either conventional synthetic disease modifying antirheumatic drugs (csDMARD) or were receiving biological treatments. Age- and gender matched 35 healthy individuals were enrolled as a control group. Complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were measured and DAS-28 scores were calculated. ROTEM was applied at the same time and clotting time (CT, seconds), clot formation time (CFT, seconds), and maximum clot firmness (MCF, mm) were determined. A shorter CT and/or CFT values and/or a higher MCF levels imply tendency towards hypercoagulability.

Results: RA patients with a higher disease activity were found to have a shorter I-CFT and a higher I-MCF (p values p<0.020, p=0.033, respectively). Correlation analysis revealed shorter I-CFT and E-CFT and higher I-MCF and E-MCF in those with more active disease, hence indicating a higher tendency to thrombosis.

Conclusions: Disease activation in RA patients may lead to hypercoagulability, independent of the ongoing medication of patients. Considering the fact that the predictive value of ROTEM parameters for further thrombosis, additional studies are needed whether pro-thrombotic state in RA may herald thrombosis in the presence of inflammation.

References:

Disclosure of Interest: None declared


**THU0142** MATRIX METALLOPROTEINASE-3 AND ANTIBODIES (IGG) AGAINST OXIDIZED LOW-DENSITY LIPOPROTEIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with an unexplained increased cardiovascular risk. Matrix metalloproteinase-3 (MMP-3) is the most important disease related factor in RA patients which may play a role in the development of cardiovascular events. Antibodies against oxidized low-density lipoprotein (oxLDL) are known to be involved in the development of inflammation and atherosclerosis. Specific role of MMP-3 and antibodies against oxLDL in cardiac pathology in RA patients (pts) is not well investigated.

Objectives: To compare MMP-3 and oxLDL-IgG antibody levels, as well as lipid profiles in pts with active RA and healthy controls.

Methods: Thirty nine RA pts (33 women and 6 men, median age 56.5 [49; 65] years), with active arthritis (disease duration 96 [48; 190] months; DAS28 5.8 [5.3;6.3]) and 29 healthy controls were studied. Twenty three pts (59%) received methotrexate, 5 (13%) – the combination of methotrexate with oral glucocorticoids, 10 (26%) - oral glucocorticoids monotherapy. The control group consisted of 29 volunteers (21 women and 8 men, median age 58.5 [53; 62] years). Serum MMP-3 and oxLDL-IgG levels were measured by enzyme-linked immunosorbent assay (ELISA). Results: Elevated MMP-3 levels were detected more frequently in RA pts (31/39 (79%)) vs healthy controls (2/29 (7%), p<0.0001), MMP-3 concentrations were higher in RA pts (57.0 [36.6, 114.9] mU/ml) vs the control group subjects (13.4 [9.9, 20.4]mU/ml, p<0.0001), MMP-3 levels demonstrated significant correlation with ESR (r =0.64, p<0.05) and CRP (r =0.52, p<0.05) values.

OxLDL-IgG levels in RA pts and healthy controls did not differ significantly (290.3 [111.3, 608.6] mU/ml and 228.1 [125.1, 338.8] mU/ml, respectively p>0.05). Rates of dyslipidemia were similar in RA pts (23/39 (59%) and control group subjects (15/29 (52%). Concentrations of lipids were also similar in both groups and were as follows: total cholesterol was 5.2 [4.9, 6.2] mmol/l in RA pts and 6.3 [5.1, 6.6] mmol/l in the control group; HDL cholesterol - 1.7 [1.4, 2.0] mmol/l and 1.7 [1.5, 2.1] mmol/l; LDL cholesterol - 3.3 [2.8, 4.0] mmol/l and 3.6 [3.0, 4.0] mmol/l, triglycerides - 1.3 [1.0, 1.6] mmol/l and 1.4 [1.1, 1.8] mmol/l, the atherogenic index - 2.4 [1.8, 2.8] and 2.4 [1.9, 3.0], respectively. Showed no correlation between the levels of oxLDL-IgG and lipids in both groups. In the RA group, concentrations of HDL cholesterol were negatively correlated with MMP-3 (r =–0.5, p<0.05), C-reactive protein (r =–0.53, p<0.05), and DAS28 (r =–0.4, p<0.05).

Conclusions: RA pts exhibited higher serum MMP-3 levels than healthy individuals. OxLDL-IgG levels were similar in RA pts and healthy subjects. Obtained results suggest that MMP-3 and CRP may produce a negative impact on HDL-cholesterol levels in patients with active RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3807

**THU0143** CHOLESTEROL EFFLUX CAPACITY OF HDL IS OTHERWISE IMPROVED BY DIFFERENT BIOLOGIC-DMARDS IN RHEUMATOID ARTHRITIS

F. Cacciapaglia 1, S. Perniola 1, J. Härdfeldt 2, M. Nivuori 1, O. Magazzino 1, M.G. Giannotta 1, M. Giannini 1, M.G. Anelli 1, A. Moschetta 2, F. Iannone 1

1DETO - Unit of Rheumatology; 2DIM - Clinica Medica “Cesare Frugoni”, University of Bari, Bari, Italy

Background: Rheumatoid arthritis (RA) patients have an increased mortality that cannot be completely explained by impaired cholesterol levels or other traditional CV risk factor (1). Target therapy with effective control of systemic inflammation have been demonstrated to improve articular outcomes, but the effect on CV risk is still under investigation (2). The ability of high-density lipoprotein (HDL) to accept cholesterol from macrophages (HDL cholesterol efflux capacity – HDL-EC) is a key property of HDL, with significant consequences on incident atherosclerotic CV disease (3), but this marker in RA have still alternate evidence (4,5).

Objectives: To assess the effects of different biological DMARDS on HDL-EC in RA

References:

Methods: Disease activity data and blood samples from 40 patients with RA before and up to 12 months after starting a biologic therapy were collected. The study included patients starting intravenously administered Abatacept (ABA, n=10), Infliximab (INF, n=10), Tocilizumab (TCZ, n=10), and Rituximab (RTX, n=10), at approved dose regimens for RA treatment. HDLc-EC was measured on paired samples at baseline, after 6 months of treatment, and after 12 months of treatment. ANOVA was used to compare paired continuous data, and Pearson’s r value was calculated for correlations.

Results: Disease activity assessed by DAS28-CRP and CDAI significantly dropped during all treatments. No significant changes in total and high or light density cholesterol fractions were detected. HDLc-EC at baseline was 22±3% with a statistically significant increase up to 25±3% and 27±4% after 6 and 12 months of treatment, respectively (P<0.001) [Figure A]. Patients treated with INF and RTX demonstrated the higher rise in HDLc-EC, already after 6 months and lastingly up to 12 months of treatment. ABA and TCZ treated patients after 6 months had a slight HDLc-EC rising, with a subsequent plateau. We observed an opposite correlation between HDLc-EC and disease activity by DAS28-CRP and CDAI (r=−0.2, P=0.01) [Figure B]. Finally, no CV events were detected during the study follow-up.

Conclusions: Our results indicate that disease activity of RA and aging contribute to cognitive impairment, but there was no association between cognitive function and subclinical carotid atherosclerotic changes in RA patients.


Disclosure of Interest: None declared 
DOI: 10.1136/annrheumdis-2017-eular.3942

THU0145 IMPACT OF DIFFERENT FORMULATIONS OF “PATIENT GLOBAL ASSESSMENT” ON REMISSION CLASSIFICATION BY DISEASE ACTIVITY INDICES IN RHEUMATOID ARTHRITIS

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Background: Patient global assessment (PGA) of disease activity is included in a large number of composite indices of disease activity and definitions of remission in Rheumatoid Arthritis (RA). However, the actual question is formulated in a variety of different ways according to the instrument considered.

Objectives: To evaluate how 6 different formulations of PGA affect patient estimates and impact upon disease activity and remission rates as assessed by 4 Disease Activity Indices.

Methods: Consecutive RA patients followed in a Rheumatology outpatient department were included in this cross-sectional study. Data collection comprised 28 joint counts (tender and swollen), C-reactive protein (CRP) and 6 different PGA formulations. The chosen formulations were the ones stated in the: v1) Portuguese National Registry Reuma.pt, the locally used formulation; v2) ACR/EULAR provisional definition of remission (considered in this study as the “standard”); v3) CDAI and SDAI; v4) Disease Activity Score (DAS28) assessment of general health; v5) DAS28 assessment of disease activity (the currently used); v6) one, exploratory, developed by the investigators, including idiomatic cultural expressions. ACR/EULAR Boolean criteria, CDAI, SDAI, and DAS28-CRP (v4) were used to test how these 6 PGA formulations change the rates of remission.

PGA differences were assessed by descriptive analyses (including patients with PGA ≤ 10 and >20mm) and Bland-Altman test.

Results: In total, 193 patients were included (92% female, mean (SD) age of 59 (13) years, mean disease duration of 12 (9) years and 31% under biologics). The average PGA ranged from 42.3 (25.3) to 48.1 (27.7)mm as measured in different formulations. The ACR/EULAR (v2) formulation yielded the largest proportion of patients in remission (82%).

Table 1. Descriptive statistics of the 6 PGA’s formulations (n=193)

<table>
<thead>
<tr>
<th>PGA Formulation</th>
<th>Mean (SD)</th>
<th>PGA below cut-off n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>v1 Reuma.pt</td>
<td>47.5 (28.0)</td>
<td>26 (13.5)</td>
</tr>
<tr>
<td>v2 ACR/EULAR</td>
<td>43.5 (27.7)</td>
<td>31 (16.7)</td>
</tr>
<tr>
<td>v3 CDAI/SDAI</td>
<td>47.2 (25.9)</td>
<td>23 (11.9)</td>
</tr>
<tr>
<td>v4 DAS28-GH</td>
<td>42.9 (25.3)</td>
<td>27 (14.0)</td>
</tr>
<tr>
<td>v5 DAS28-DA</td>
<td>42.3 (25.3)</td>
<td>28 (14.5)</td>
</tr>
<tr>
<td>v6 Investigators</td>
<td>48.1 (26.7)</td>
<td>22 (11.4)</td>
</tr>
</tbody>
</table>

Conclusions: Our results indicate that disease activity of RA and aging contribute to cognitive impairment, but there was no association between cognitive function and subclinical carotid atherosclerotic changes in RA patients.
Quality of life in patients with rheumatoid arthritis - demographic and socio-economic associations

H. Baharuddin 1, N. Zainudin 2, H. Mohd Yusoof 2, I.S. Lau 2.

Background: The primary goal of treating patients with rheumatoid arthritis (RA) is to maximise long-term HRQoL. Quality of life (QoL) in patients with RA may be substantially impacted by their inability to perform daily activities, a shift in family roles, more restricted employment opportunities, increased financial burden and social dependency and reduced recreational activities.  

Objectives: To investigate the QoL among RA patients and its association with demographic and socioeconomic details.  

Methods: This is a cross-sectional study conducted in a rheumatology outpatient clinic in Malaysia. Patients who fulfilled 2010 ACR/EULAR classification criteria for RA were asked to answer WHOQOL-BREF questionnaire and specific questions on demographics and socio-economic details, during their attendance to rheumatology clinics. WHOQOL-BREF is a self-report quality of life questionnaire on individual's perception of quality of life and health, physical health, psychological, social relationships and environment domains.  

Data was analysed using SPSS 20. Student’s t-test was used to analyse the mean difference between two groups and chi-square test was used to analyse between 2 categorical data. Pearson correlation was used to analyse correlation between two groups of continuous data. P<0.05 was considered significant.  

Results: The mean age of patients in this study was 53.10±14.3 years, with majority being females (80.4%) and married (70.6%). Half of the patients were Malays (49.0%). 51.0% rated overall quality of life as good and 41.2% rated it as poor, with non-Malays (53.1±18.2) in the social relationship domain; t (49) =2.58, p=0.01. There were significant differences in the transformed scores for Malay (65.5±15.9) and 58.2 (±15.2) in environment domains.  

Conclusions: There were no differences in heart rate (HR), QTc interval duration, and for education at secondary level and above (65.9±14.6) and primary level (48.0±16.6), t(49)=3.87, p=0.003 and more frequently positive for rheumatoid factor (RF) (25/7 ([%6.2] vs 77/121 (%63.3), p=0.003) than patients without ILD. ILD was detected before beginning of biologics in 11 (37.9%), patients and during biologic treatment in 18 (62.1%) patients. Honeycombing was seen in 10 (34.5%) patients. First choice of biologic agent was RTX in 10 (34.5%) and TNFi in 19 (65.5%) patients. In ILD patients, mean follow-up duration was 51±31 months and first biologic was switched to another in 16 (55.2%) of patients. At the last follow-up visit 19 (65.5%) patients were on rituximab, 3 (10.3%) patients were on abatacept and 7 (24.1%) were on TNFi. Small airway disease was detected in 19 (9.3%) patients. History of smoking was present in only 4 (21.0%) of patients with small airway disease.

Table 1. Distribution of thorax CT findings

<table>
<thead>
<tr>
<th>Thorax CT finding</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Intestinal thickening</td>
<td>13 (6.4)</td>
</tr>
<tr>
<td>Reticular densities</td>
<td>31 (15.3)</td>
</tr>
<tr>
<td>Ground glass opacities</td>
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<tr>
<td>Traction bronchiectasis</td>
<td>17 (8.4)</td>
</tr>
</tbody>
</table>

Conclusions: Bronchiectasia, rheumatoid nodules, small airway disease and ILD were the most frequent CT findings of RA patients. Rituximab was the choice of first biologic treatment in one third of patients, however two-thirds of patients were on rituximab therapy at the last follow-up visit. Lung involvement stands out as an important factor in selection of biologic therapies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4076

Increase of night QT-interval duration in rheumatoid arthritis patients treated with tofacitinib during 12-month follow-up


Objectives: to evaluate dynamic of ECG parameters in RA pts treated with tofacitinib (TOFA) during 12-month follow-up.  

Methods: After 12-month follow-up the ECG parameters by 12 lead ECG and 24h ECG was assessed in 28 RA pts treated with TOFA (22 women, median age 54 [40;62] years, disease duration 39.5 [16.5;60.0] m, moderate to high activity (DAS28≥5.1 [4.6;6.0], SDAI=26 [21;34], positive for ACCP (75%)/RF (79%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs and bDMARDs. TOFA therapy was started in all pts with dose 5 mg BID per os followed by the dose escalation to 10 mg BID in 8 (29%) pts. TOFA used in combination with MTX in 27 (96%) pts, leflunomide in 4 (14%). Low dose oral corticosteroids (<10 mg/day prednisolone or equivalent) were received by 9 (35%) pts. Remission or LDA was achieved in 55% pts (DAS28,  

Results: Among 1229 patients (78.8%) female, mean age was 53.3±12.9 and disease duration was 11.4±7.9. Thorax CT had been performed in 203 (16.5%) patients. Distribution of pathologic findings in thorax CT was represented in Table 1. 29 patients (%2.4) were diagnosed as ILD with regard to CT findings. Patients with ILD were older (64.5±6.7 vs 60.6±10.1, p=0.039) and more frequently positive for rheumatoid factor (RF) (25/7 ([%6.2] vs 77/121 (%63.3), p=0.003) than patients without ILD. ILD was detected before beginning of biologics in 11 (37.9%), patients and during biologic treatment in 18 (62.1%) patients. Honeycombing was seen in 10 (34.5%) patients. First choice of biologic agent was RTX in 10 (34.5%) and TNFi in 19 (65.5%) patients. In ILD patients, mean follow-up duration was 51±31 months and first biologic was switched to another in 16 (55.2%) of patients. At the last follow-up visit 19 (65.5%) patients were on rituximab, 3 (10.3%) patients were on abatacept and 7 (24.1%) were on TNFi. Small airway disease was detected in 19 (9.3%) patients. History of smoking was present in only 4 (21.0%) of patients with small airway disease.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4076
QRS duration measured by 12-lead ECG in RA pts treated with TOFA (table 1). However, an increase in PQ interval duration was observed (p<0.04). There were significantly decrease of mean HR (p<0.003), increase of QRS duration (p<0.03), QTC (p<0.03), night QTC (p<0.02) in 24 h ECG ambulatory recording. HR, PQ, QTC duration were changed independently of beta-blockers therapy. The number of RA pts treated with tocilizumab (TCZ) during 12-month follow-up. An increase in QTc duration correlated negatively with dynamics of DAS 28, SDAI (r=-0.04, p<0.05), DM (r=0.5, p<0.02), dBiP (r=-0.4, p<0.04). There were also significantly increase number of ventricular premature beats (p<0.03).

Table 1. ECG characteristics of pts with RA treated with TOFA

<table>
<thead>
<tr>
<th>ECG Parameter</th>
<th>Baseline</th>
<th>After 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>71 [64;81]</td>
<td>70 [64;84]</td>
</tr>
<tr>
<td>PQ, ms</td>
<td>133 [120;150]</td>
<td>132 [120;149]</td>
</tr>
<tr>
<td>QRS, ms</td>
<td>83 [79;89]</td>
<td>84 [80;91]</td>
</tr>
<tr>
<td>QTc, ms</td>
<td>421 [406;434]</td>
<td>410 [398;420]</td>
</tr>
<tr>
<td>24 h ECG Heart rate, bpm</td>
<td>78 [70;84]</td>
<td>74 [65;80]*</td>
</tr>
<tr>
<td>QRS, ms</td>
<td>82 [73;91]</td>
<td>85 [73;92]*</td>
</tr>
<tr>
<td>QTc, ms</td>
<td>409 [402;425]</td>
<td>415 [406;427]*</td>
</tr>
<tr>
<td>QTc-night, ms</td>
<td>414 [404;434]</td>
<td>420 [405;437]*</td>
</tr>
<tr>
<td>WPB, n (%)</td>
<td>18 (66)</td>
<td>22 (78)</td>
</tr>
<tr>
<td>Ventricular premature beats, n</td>
<td>14 (7.50)</td>
<td>280 [15;3423]*</td>
</tr>
</tbody>
</table>

Data are presented in median values and IQR (unless otherwise noted), *p<0.05 before and after TOFA treatment (nonparametric paired Wilcoxon test).

Conclusions: A significant decrease in HR and an increase in QRS, night QTc interval duration, number of ventricular premature beats by 24 h ECG were observed in RA pts treated with tocilizumab (TCZ) during 12-month follow-up. An increase in QTc duration correlated with dynamic of disease activity, DM type 2 and diastolic BP.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5119

THU0149 A CLINICAL AND PATHOLOGICAL CHARACTERIZATION OF METHOTREXATE-ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Nakano 1, A. Nawata 2, S. Nakayama 3, I. Ishida 4, K. Hanami 1, S. Kubo 4, I. Miyagawa 1, M. Yoshikawa 1, K. Saito 1, Y. Tanaka 1, 1The First Department of Internal Medicine, 2Department of Pathology, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Background: Methotrexate (MTX) is used as an anchor drug for the treatment of rheumatoid arthritis (RA). Patients with RA have a modestly increased risk of developing lymphoproliferative disorders (LPD). Furthermore, although sometimes spontaneous regression occurs after withdrawal of MTX, LPD developed during the treatment with MTX is broadly defined as MTX-associated LPD (MTX-LPD).

Objectives: To characterize the risk factors concerning MTX-LPD and to consider optimal treatment after occurrence of LPD in patients with RA.

Methods: We retrospectively evaluated 51 RA patients with LPD from 2006 to 2015 in our institution. MTX-LPD patients were divided into two groups; regressive LPD after MTX cessation (N=27) and persistent LPD though MTX was tapered (N=24), and the clinical characteristics, pathology and treatment outcomes were compared. EBV infection and IL-6 receptor (IL-6R) expression were analyzed by in situ hybridization and immunohistochemistry.

Results: There was no significant difference in disease duration, stage, disease activity of RA, the positive rate of Epstein-Barr virus-encoded small RNAs, EBERs (42.7 vs 50.0%) and treatment with TNF-inhibitors (40.7 vs 45.8%) between regressive LPD and persistent LPD. Age of LPD onset (59.1 vs 68.3), CRP (2 vs 5 mg/dl) and the weekly MTX dose (10.9 vs 8.4 mg/w) significantly differed between the groups. Of note, IL-6R was highly expressed in both group (75.0 vs 66.7%). Among regressive LPD, 3 patients developed DLBCL later.

Conclusions: The LPD development of RA is not only related to MTX treatment but also linked with EBV infection and IL-6R expression.

THU0150 OPTIMIZING COMORBIDITY RISK MANAGEMENT IN RA BY TRANSLATING A NURSE-LED INTERVIEW INTO AN EASILY INTERPRETABLE TRAFFIC LIGHT SYSTEM

K. Krüger 1, R. Eder 2, C. Müller 2, R. Hecker 3, 1Rheumatologisches Praxiszentrum St. Bonifatius, München; 2Rheumapräxis am Spitator, Deggendorf; 3AbbVie Deutschland GmbH & Co. Kg, Wiesbaden, Germany

Background: Due to its inflammatory nature, rheumatoid arthritis (RA) is associated with a variety of comorbidities and individual risk factors [1]. The benefit of a nurse-led programme on RA comorbidity management has been reported recently [2].

Objectives: To describe a new assessment tool for patient risk management and report the difference between structured versus expert guided assessment following standard of care in a construct-validation cohort.

Methods: The ongoing cluster randomized multicentre study ERIKO is longitudinally assessing individual risk profiles of patients with RA in Germany. The aim of this study is to test the benefit of applying a nurse-led scoring algorithm for individual risk profiles followed by a structured patient consultation (active arm) as compared to local standard of care.

The ERIKO-Score was calculated by rating validated assessment tools and treatment guidelines and translating their outcome into a three-level ordinal score defined by the categories low, intermediate or high risk, including nominal weights for risk management (e.g. condition is being treated with goals achieved or not).

Scores were interpreted numerically by rating categories with 0, 1 and 2 points, respectively.

We included cardiovascular (CV) risk (ESC-guideline), infection risk (RABBIT risk calculator), vaccination status (guideline), fracture risk (FRAX), tooth status (PSI), depression (PHQ-9) and health-related quality of life (hQoL, RAID). The same risk category was prioritized in all centres at the screening visit without providing the rating tools.

This analysis compares SOC ratings from the screening visit (month zero) with the baseline ERIKO-scores at month three in the active arm. No statistical hypothesis testing was performed in this analysis.

Results: This analysis included 283 patients from 31 centres specialized in rheumatology care randomized to the active study arm. 82.3% were female with a mean age of 57.8 years (sd 12.1) and a mean DAS28 of 2.6 (sd 1.1). The mean total ERIKO-Score was slightly higher at baseline as compared to applying the scoring algorithm on SOC ratings at the screening visit (5.33 ± 1.95 vs. 4.32 ± 2.61, respectively, table 1). The discrepancy was mainly driven by CV risk, vaccination status, tooth status and depression risk, that were more often rated worse by applying the ERIKO score than by SOC, while infection- and fracture risk were more frequently rated lower by the ERIKO-Score (table 2). The strongest discrepancy between SOC ratings and ERIKO-Score (± =2 points) were observed for tooth status (N=54), CV risk (N=25) and vaccination status (N=25) (table 2).

SOC ratings were strongly based on expert opinion with the most frequently cited tools being vaccination guidelines (38.9%), bone mineral density measurement (BMD) (39.6%) and RABBIT-infection risk-score (23.1%).

THU0150 Table 1 ERIKO Score at baseline visit (3 moches)

<table>
<thead>
<tr>
<th>Dimension</th>
<th>ERIKO-Score [n=283]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact</td>
<td>3 (0,0)</td>
</tr>
<tr>
<td>Risk</td>
<td>4 (1,4)</td>
</tr>
<tr>
<td>Overall</td>
<td>7 (2,4)</td>
</tr>
</tbody>
</table>

THU0150 Table 2 Discrepancy between ERIKO Score and ratings following SOC (baseline vs. screening)

<table>
<thead>
<tr>
<th>Dimension</th>
<th>SOC Impact</th>
<th>SOC Risk</th>
<th>SOC Overall</th>
<th>ERIKO Impact</th>
<th>ERIKO Risk</th>
<th>ERIKO Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV risk</td>
<td>50.0</td>
<td>44.1</td>
<td>49.1</td>
<td>50.0</td>
<td>44.1</td>
<td>49.1</td>
</tr>
<tr>
<td>Vaccination status</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Depression</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Conclusions: A nurse-led comorbidity risk assessment in rheumatology practices seems feasible. Applying the ERIKO-Score based on validated tools led to a
ACPA ARE ASSOCIATED WITH LOW BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS


Background: Several studies have related ACPA with the presence of bone disease of 5 years. Demographic and clinical variables were collected.

Methods: Case-control study of 73 RA patients (2010 CULAR criteria) and a long standing disease of 5 years. Demographic and clinical variables were collected. BMD values using densitometry at the lumbar (LCL, hip) and femoral neck (CF) were collected. The presence of low bone mineral density (osteopenia: T-score: ≤ -1) and ACPA levels were compared using logistic regression analysis, adjusting variables related to BMD: age, sex, menopause, body mass index (BMI), smoking habit, corticoids, disease duration, disease modifying drugs, methotrexate treatment and inflammatory activity (DAS28).

Results: A group of 73 patients were included (41 men) with a mean age of 66.45±10.41 years, mean body mass index 28.48±5.22 kg/m², mean long standing disease of 2.28±1.75 years and mean DAS 28 of 3.71±1.8. A total of 29 patients were negative for ACPA compared to 44 patients that were positive for ACPA. Osteopenia in lumbar spine was found in 82.2% of patients 65.8% hip and 75.3% in femoral neck. Logistic regression was performed without finding statistically significant association between osteopenia and inflammatory activity (DAS28), vitamin D levels and positive rheumatoid factor, adjusted for variables that can modify BMD. ACPA Positive (any titer) were associated with the presence of lumbar spine osteopenia (OR 7.19, 95% CI 1.77–29.17) (p=0.006), hip (OR 15.17, 95% CI 3.96–58.18) (p=0.001) and femoral neck (OR 3.76; 95% CI 1.20–11.82) (p=0.023). In addition, a simple variance analysis (ANOVA) was performed to compare T scores and ACPA levels divided into three categories: ≤25μL, 25–300μL and ≥300μL. ACPA group ≤25μL differed in mean T score values in lumbar spine, hip and femoral neck. No differences were found between ACPA positive patients with low and high levels for T score values.

Conclusions: In RA is associated with an increased risk of osteopenia in lumbar spine, hip and femoral neck independently of other variables that may modify bone mineral density. These data suggest that ACPA may play a role in bone remodeling.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4422

THU0153 VASCULAR MORBIMORTALITY IN RHEUMATOID ARTHRITIS (RA) PATIENTS AND ITS RELATION WITH VASCULAR STUDY


Background: RA patients have a higher risk of vascular events, especially cardiovascular ones. Besides, mortality in these patients is 54% higher than the general population. Nowadays, we have non-invasive techniques that allow us to detect subclinical vascular damage.

Objectives: To describe subclinical vascular affection in a sample of RA patients and to explore its relationship with mortality and with the development of vascular events.

Methods: Ambispective observational study with analytical components. We included, consecutively, RA patients controlled in a tertiary hospital. We gathered demographic (sex, age, body mass index (BMI), clinical (traditional vascular risk factors, previous vascular events), and analytical variables (atherogenic index, glomerular filtration [GF] [MDRD], CRP, ESR). Other variables were collected retrospectively from the electronic medical record. We estimated the modified SCORE. We explored the extracranial branches of the carotid artery with an Esate MyLab70XVG ultrasound device with a linear probe (7–12mHz) and an automated program measuring intima media thickness (IMT) by radiofrequency ("Quality intima media thickness in real-time, QIMT"), and the presence of atheroma plaques, as per the Mannheim consensus, was registered. We also determined pulse wave velocity (PWV) by a validated MobiGraph® device. We considered an IMT ≥1.8 and a PWV >10m/s as pathologic values. We prospectively collected mortality and the development of new vascular events over three years. Statistical analysis was performed using SPSS 17.0 software.

Results: We included 198 patients, excluding 13 because of previous vascular events. The mean age was 68.8 years (DE 13.3) and most of them were women (76.2%). The mean BMI was 27.28 (4.48), 27% were smokers, 42.7% hypertensive, 46.7% dyslipemic and 10.8% were diabetic. The mean duration of RA was 17.37 years. 74.6% of patients were seropositive (RF and/or ACPA) and 75.5% had erosions. 74.6% received glucocorticoids, 58.4% NSAIDs, 98.9% DMARDs, 65.7% other immunosuppressants. The mean CRP and ESR were 4.0 mg/L (DE: 3.32) and 14.04mm/h (DE:14.46), respectively. The mean modified SCORE was 1.81 (DE: 1.79).

Regarding the vascular study, 48.6% of the patients had atheroma plaques, 31.7% had a pathologic PWV with a mean value of 9.13 (DE: 2.12), and 16.7% had a pathologic IMT with a mean value of 7.64 (DE: 1.42).

During 3 years of follow up, we registered 26 (14.1%) vascular events: 9.7% cardiac, 2.1% cerebral and 2.2% peripheral. There were 5 deaths: 3 vascular, 1 infectious and 1 respiratory. The development of vascular events was related with the presence of atheroma plaques (p = 0.008) and with pathologic PWV (p
0.028, as well as with the presence of erosions, GF, HTA and dyslipidaemia. The appearance of cardiac events was related also, with the use of NSAID (p 0.041). The presence of a pathologic IMT (p 0.032) and HTA (p 0.044) were the only variables related with death from any cause.

**Conclusions:** A combination of carotid ultrasonography and arterial stiffness study can help us to best identify patients with RA who have an increased risk of dying or developing a vascular event.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3469

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### Table 1. Relation between plasma lipids, disease activity and PCSK9 levels

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>21.86</td>
<td>0.004</td>
</tr>
<tr>
<td>LDL-C</td>
<td>12.03</td>
<td>0.356</td>
</tr>
<tr>
<td>VLDL</td>
<td>11.04</td>
<td>0.484</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>22.34</td>
<td>0.005</td>
</tr>
<tr>
<td>HDL-C</td>
<td>21.22</td>
<td>0.059</td>
</tr>
<tr>
<td>TC-HDL ratio</td>
<td>6.28</td>
<td>0.074</td>
</tr>
<tr>
<td>DAS28 (low vs. high disease activity)</td>
<td>45.284</td>
<td>0.029</td>
</tr>
</tbody>
</table>

**Corrected for age and gender.**

**Conclusions:** PCSK9 levels in RA are similar to the general population. RA patients with active disease had higher PCSK9 levels compared to patients with low disease activity. Altogether, PCSK9 inhibitors could be an alternative treatment for dyslipidaemia in RA patients who have experienced side effects of statins, albeit that a formal trial still has to be conducted in this category of patients.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2121

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### Table 1. Baseline demographics of patients with Psoriatic Arthritis (PsA), Rheumatoid Arthritis (RA), and Spondyloarthritis (SpA)

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA (n=214)</th>
<th>PsA (n=208)</th>
<th>SpA (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>51.1±13</td>
<td>51.3±12</td>
<td>54.2±11</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>407 (64)</td>
<td>136 (65)</td>
<td>78 (37)</td>
</tr>
<tr>
<td>Normal weight (BMI ≤25), n (%)</td>
<td>278 (44)</td>
<td>84 (40)</td>
<td>111 (52)</td>
</tr>
<tr>
<td>Overweight (BMI &gt;25 ≤30), n (%)</td>
<td>242 (28)</td>
<td>78 (37)</td>
<td>64 (30)</td>
</tr>
<tr>
<td>Obese (BMI &gt;30), n (%)</td>
<td>115 (18)</td>
<td>46 (22)</td>
<td>39 (18)</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>79.8±92</td>
<td>69.9±123</td>
<td>72.8±75</td>
</tr>
</tbody>
</table>

**mRDCI, n (%)**

<table>
<thead>
<tr>
<th>Value</th>
<th>RA (n=214)</th>
<th>PsA (n=208)</th>
<th>SpA (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>302 (48)</td>
<td>87 (42)</td>
<td>92 (43)</td>
</tr>
<tr>
<td>1</td>
<td>128 (21)</td>
<td>44 (21)</td>
<td>33 (15)</td>
</tr>
<tr>
<td>2</td>
<td>88 (14)</td>
<td>34 (16)</td>
<td>30 (14)</td>
</tr>
<tr>
<td>3</td>
<td>53 (8.3)</td>
<td>15 (7.0)</td>
<td>15 (7.0)</td>
</tr>
<tr>
<td>4</td>
<td>30 (4.7)</td>
<td>12 (5.8)</td>
<td>12 (5.6)</td>
</tr>
<tr>
<td>5</td>
<td>13 (2.0)</td>
<td>7 (3.3)</td>
<td>1.0 (0.5)</td>
</tr>
<tr>
<td>6</td>
<td>9 (1.4)</td>
<td>6 (2.8)</td>
<td>1.0 (0.5)</td>
</tr>
<tr>
<td>7</td>
<td>9 (1.4)</td>
<td>3 (1.4)</td>
<td>1.0 (0.5)</td>
</tr>
<tr>
<td>8</td>
<td>3 (0.5)</td>
<td>1 (0.5)</td>
<td>1.0 (0.5)</td>
</tr>
</tbody>
</table>

Values are the mean 1 SD unless otherwise indicated. BMI = Body Mass Index; mRDCI = modified Rheumatic Diseases Comorbidity Index.

**Conclusions:** This study provided evidence that baseline mRDCI negatively impacts the persistence on biologic treatments and the clinical outcomes in patients with RA, SpA, and PsA in real-life settings.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1502
ARTHRITIS: DATA FROM THE CHIKARA STUDY
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2Department of Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan

Background: Sarcopenia is an age-related loss of muscle mass and strength. It is associated with a higher risk of falls, fractures, and death in patients with rheumatoid arthritis (RA). However, the incidence of sarcopenia in RA patients undergoing biological therapy has not been well characterized.

Objectives: To evaluate the incidence of sarcopenia and its correlation with disease activity in RA patients treated with biological therapy.

Methods: A total of 39 patients with RA were enrolled. Sarcopenia was defined as a muscle mass index (MMI) of less than 7.37 kg/m². Disease activity scores (DAS28-ESR), muscle mass (MMI), and body mass index (BMI) were measured. The correlation between sarcopenia and disease activity was analyzed using the Mann-Whitney U test.

Results: The incidence of sarcopenia was 28% (11/39). Patients with sarcopenia had significantly higher values for tendon count (TJC) and swollen joint count (SJC) compared to those without sarcopenia. In the RA non-FM group, GS and PD-US7 correlated with the joint count criteria for FM, after the study of Pollard et al. [2].

Conclusions: The percentage of sarcopenia was 28% in RA patients. Low BMI, high body fat mass, and high MMP-3 represented independent risk factors for sarcopenia. A relationship between MMP-3 and sarcopenia was indicated by this study.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2334

IMMUNE RESPONSE EFFICIENCY AFTER VACCINATION IN RA AND SPA PATIENTS TREATED WITH BIOLOGICS AND IMMUNOSUPPRESSIVE AGENTS: A SYSTEMATIC LITERATURE REVIEW
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Background: One of the most effective strategies to prevent infections is vaccination, especially in patients treated with biologics and immunosuppressive (IS) agents. Nevertheless, the effectiveness of the resulting immune response in these patients is not well known.

Objectives: To perform a systematic literature review aiming to assess evidence regarding immune response efficiency (IRE) and the ideal schedule for vaccination in RA and SpA patients treated with Methotrexate (MTX), TNF inhibitors (TNFi), anti-CD20 (rituximab, RTX), anti-IL1b (tocilizumab, TCZ), and anti-TNF (adalimumab, ADA).

Methods: A systematic literature review was conducted by searching in PubMed all studies with the MeSH terms ["Rheumatoid Arthritis" OR "Spondyloarthritis"] AND ["vaccination" OR "vaccines"] AND ["Methotrexate" OR "Abatacept" OR "Golimumab" OR "Infliximab"] with no limitation regarding time of publication. Only studies evaluating the IRE were included. Case reports, general reviews and meta-analysis were excluded.

Results: Of 35 studies (out of 60 studies retrieved), 27 studies compared IRE between RA and SpA patients, receiving different IS agents. The anti-meningococcal vaccine was the most used (n=24), followed by the tetanus vaccine (n=12), the hepatitis A vaccine (n=6), and the influenza vaccine (n=4). The prevalence of patients having an IRE ≥70% for tetanus, hepatitis and influenza was similar in RA and SpA patients. The anti-pneumococcal vaccine was less efficient in RA and SpA patients than in healthy controls.

Conclusions: The IRE consequences of vaccination in RA and SpA patients treated with IS are different for each vaccine and are dependent on the type of IS used.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2391

RELATIONSHIP OF MATRIX METALLOPROTEASE 3 TITER AND SARCOPIENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE CHIKARA STUDY
M. Tada, Y. Yamada, K. Mandai, N. Hidaka. Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan

Background: Patients with rheumatoid arthritis (RA) show a lower muscle mass and higher prevalence of sarcopenia than healthy individuals. A prospective observational study (CHIKARA study, registration number: UMIN000023744) was started to clarify the influence of changes in disease activity for sarcopenia.

Objectives: We investigated the relationship between sarcopenia and disease activity at baseline in patients with RA.

Methods: We analyzed baseline data from the CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis). Sarcopenia was diagnosed using the criteria of the Asian Working Group on Sarcopenia. Muscle mass, body fat mass, total body water, bone mass, and basal metabolic rate were measured using a body composition analyzer (MC-780A; TANITA, Tokyo, Japan). We investigated correlations between sarcopenia and disease activity (DAS28-ESR, SDAI, physical function (HAQ), and laboratory data using uni- and multivariate analyses.

Results: Participants comprised 100 patients with RA (females, 78%; mean age, 66.1 years). Mean disease duration was 5.5 years. DAS28-ESR was 3.55, and the percentage of subjects with sarcopenia was 28%. Table 1 shows risk factors for sarcopenia. Sarcopenia correlated with weight, body mass index (BMI), body fat mass, muscle mass, basal metabolic rate, Steinbrocker stage, CRP bone mass, and matrix metalloproteinase (MMP-3) on univariate analysis. Glucocorticoid dosage, rheumatoid factor, and anti-CCP antibody showed no correlation with sarcopenia. BMI, body fat mass, and MMP-3 were identified as independent risk factors on multivariate analysis. MMP-3 over 90.7 ng/ml was a risk factor for sarcopenia by ROC curve analysis (odds ratio, 3.09; p=0.023).

Table 1. Risk factors for sarcopenia in patients with RA

<table>
<thead>
<tr>
<th>Uniivariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>P</td>
</tr>
<tr>
<td>Weight</td>
<td>-0.421</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.490</td>
</tr>
<tr>
<td>Body fat mass</td>
<td>-0.219</td>
</tr>
<tr>
<td>Muscle mass</td>
<td>-0.325</td>
</tr>
<tr>
<td>Basal metabolic rate</td>
<td>-0.419</td>
</tr>
<tr>
<td>Steinbrocker stage</td>
<td>0.206</td>
</tr>
<tr>
<td>CRP</td>
<td>0.201</td>
</tr>
<tr>
<td>Bone mass</td>
<td>-0.374</td>
</tr>
<tr>
<td>MMP-3</td>
<td>0.238</td>
</tr>
</tbody>
</table>

Conclusions: The incidence of sarcopenia was 28% in patients with RA. Low BMI, high body fat mass, and high MMP-3 represented independent risk factors for sarcopenia. A relationship between MMP-3 and sarcopenia was indicated by this study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2391
THU0159 RHEUMATOID ARTHRITIS MAY NOT INFLUENCE EATING BEHAVIOURS CHARACTERISTICS

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of obesity and cardiovascular disease compared with the general population (1). Eating behaviours may play an important role in obesity and cardiovascular disease.

Objectives: We hypothesised that RA patients have impaired eating behaviours that may have a role in obesity. For evaluating this hypothesis, we compared eating behaviours of patients with RA, osteoarthritis (OA) and healthy controls.

Methods: One hundred and fifty-seven RA patients (M/F: 23/134) who fulfilled the 2010 American College of Rheumatology (ACR) RA classification criteria, 31 hand OA patients (M/F: 1/30) who fulfilled 1990 ACR hand OA criteria and 60 healthy controls (M/F: 9/51) were enrolled to the study who applied to Kartal Dr. Lutfi Kirdar Training and Research Hospital Rheumatology outpatient clinic. Eating behaviours was assessed by the Three-Factor Eating Questionnaire (TFEQ). Demographic data, smoking status, co-morbidities, anthropometric measurements, VAS pain score, were analyzed.

Results: There were no differences between three groups in demographic features and anthropometric measurements (table1). Moreover, there were no differences between three groups in cognitive restraint and emotional eating scores. Although, healthy controls had significantly higher uncontrolled eating scores than the RA group (p=0.05), uncontrolled eating scores of all three groups were lower than Turkish people average scores (2) (table2).

Table 1. Demographic and Anthropometric features of study groups

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>OA (n=31)</th>
<th>Healthy controls (n=60)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>51.00 (40.00–57.50)</td>
<td>50.00 (46.75–62.00)</td>
<td>48.00 (39.25–53.75)</td>
<td>0.06</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>23/134</td>
<td>23/130</td>
<td>23/130</td>
</tr>
<tr>
<td>Education (year)</td>
<td>5.00 (5.00–10.00)</td>
<td>5.00 (5.00–11.00)</td>
<td>5.00 (5.00–11.00)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>24.2</td>
<td>23.3</td>
<td>20.7</td>
</tr>
<tr>
<td>Co-morbid disease</td>
<td>55.8</td>
<td>64.5</td>
<td>49.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>160.00</td>
<td>157.00</td>
<td>160.50</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.150 (25.50–33.20)</td>
<td>31.100 (27.12–35.07)</td>
<td>27.550 (23.87–32.77)</td>
</tr>
</tbody>
</table>
| Training and Research Hospital Rheumatology outpatient clinic. Eating behaviours were assessed by the Three-Factor Eating Questionnaire (TFEQ). Demographic data, smoking status, co-morbidities, anthropometric measurements, VAS pain score, were analyzed.

Table 2. Eating behaviours of study groups

<table>
<thead>
<tr>
<th>RA (n=157)</th>
<th>OA (n=31)</th>
<th>Healthy controls (n=60)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled eating scores</td>
<td>10.00 (8.00–12.00)</td>
<td>10.00 (8.00–13.00)</td>
<td>11.00 (9.00–14.00)</td>
</tr>
<tr>
<td>Cognitive restraint scores</td>
<td>16.00 (13.00–18.00)</td>
<td>16.00 (14.00–19.00)</td>
<td>14.00 (11.25–18.00)</td>
</tr>
<tr>
<td>Emotional eating scores</td>
<td>5.00 (3.00–8.00)</td>
<td>5.00 (3.75–11.00)</td>
<td>4.00 (3.00–7.00)</td>
</tr>
</tbody>
</table>

Conclusions: This was the first study using the TFEQ in patients with RA. In our study, we found that disease features of RA may had no effect on eating behaviors.


SYNDECANS ARE CORRELATED WITH HIGH TITRES OF ANTIBODIES AGAINST CITRULLINATED PROTEINS (ACPAs) IN SERA FROM ACTIVE RHEUMATOID ARTHRITIS


Background: Syndecans include a group of proteins from the cell-surface heparin-sulfate proteoglycan family, with a relevant role in chronic inflammation of synovial tissue in patients with rheumatoid arthritis (RA) participating in the cell-matrix and cell-cell interactions. Syndecans are differentially expressed in the synovial tissue: syndecan-1 (SDC-1) is expressed mainly in mononuclear cells, syndecan-3 (SDC-3) is mainly expressed by synovial endothelial cells and syndecan-4 (SDC-4) is expressed by B lymphocytes regulating B cell development and survival. Currently, there is strong evidence that antibodies directed to citrullinated protein antigens (ACPAs) are associated with a more severe disease in RA. Nevertheless, to date, there is a lack of information about the relation between serum syndecan levels and serum concentrations of rheumatoid factor (RF) and ACPAs.

Objectives: To evaluate the association between serum SDC-1, SDC-3 and SDC-4 levels with serum concentrations of RF and ACPAs.

Methods: Eighty-one patients with RA were included. We assessed clinical characteristics including disease activity by DAS-28, functioning by HAQ-DI. Serum concentrations of RF were measured by nephelometry, two ACPAs were measured: anti-CCP2 and anti-mutated citrullinated vimentin (anti-MCV) antibodies using ELISA. Serum levels of SDC-1, SDC-3 (ng/mL) and SDC-4 (pg/mL) were measured by ELISA. We compared the serum levels of MCV syndecans in the ACPA+ group (group 1) versus ACPA- group (group 2) with Student t-test. A correlation analysis (Pearson tests) was performed to identify the strength of association between concentrations of syndecans with concentrations of ACPAs and other variables.

Results: Patients with RA had a mean age of 50±11 yrs, 75% were RF+ and 64% were ACPA+. In patients with ACPAs+ were observed higher serum concentrations of SDC-3 (p<0.003) and SDC-4 (p<0.001). SDC-1 correlated significantly with anti-MCV (r=0.53, p<0.001). Serum concentrations of SDC-3 correlated significantly with anti-CCP titres (r=0.53, p<0.003) and anti-MCV (r=0.46, p<0.001), whereas SDC-4 levels correlated significantly with anti-CCP titres (r=0.61, p<0.001) and RF (r=0.53, p<0.003). Additionally, serum SDC-1 levels correlated with decrement in response to treatment with synthetic DMARDs (r=-0.25, p=0.026). SDC-1 did not correlate with serum SDC-3 (p=0.8) and SDC-4 (p>0.8), whereas serum SDC-3 and SDC-4 had a strong correlation (r=0.8, p<0.001).

Conclusions: Serum SDC-3 and SDC-4 are increased in ACPA-positive RA patients. These data suggest that syndecans might be useful as serum biomarkers for discriminate a group of patients with RA and more severe disease.

References:

Disclosure of Interest: N. Rodriguez-Jimenez: None declared, E. Cardona-Muñoz: None declared, J. Gamez-Nava: None declared, E. Perez-Guerrero: None declared, M. Ponce-Guarneros: None declared, E.Y. Vera-Navairete: None declared, A. Nava-Zavala: None declared, T. Garcia-Cobian: None declared, M. Salazar-Paramo: None declared, L. Gonzalez-Lopez Grant/research support declared, A. Nava-Zavala: None declared, T. Garcia-Cobian: None declared, N. Rodriguez-Jimenez: None declared, E. Cardona-

THU0163 THE ASSOCIATION BETWEEN INFAMMATORY JOINT DISORDERS AND CORONARY HEART DISEASE: NATIONWIDE REGISTER STUDY IN 50 444 PATIENTS

P Mulull1, V. Rantalalto2,3, H. Kautiainen4,5, L. Virts6, K. Puolakkala7

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Background: Inflammatory joint disorders (IJD) are associated with cardiovascular (CV) problems, including coronary heart disease (CHD). This association is best known for rheumatoid arthritis (RA); but also for ankylosing spondylitis and psoriatic arthritis (PsA) associated with a constant generation of citrullinated proteins, and it lead to a proportional hPAD enzymatic production.

Objectives: The aim was to demonstrate the association between serum levels of hPAD4 and severe Periodontitis in patients with rheumatoid arthritis.

Methods: Patients with RA (n=127) matched with healthy controls (n=120) were included. Patients with RA and volunteers were measured: anti-CCP2 and anti-mutated citrullinated vimentin (anti-MCV) antibodies using ELISA. Serum levels of hPAD4 were measured by ELISA.

Results: A significant correlation was found between levels of hPAD4 with the DAS28 ESR score (p<0.002). The high score of HAG-DI (>2.0) correlated with hPAD4 levels (p<0.001). The group of people with higher HAG-DI score and at the same time with greater severity of CP (n=12) showed increased levels PAD4 (p<0.025).

Conclusions: hPAD4 levels correlate with the severity of CP independent of the RA presence and in RA subjects with high score of disability and activity disease.

The hPAD4 could be proposed as a serological marker of clinical severity in chronic diseases such as RA and CP. This project was supported by a grant from the Foundation Annemarie Sohlberg.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3538
SUBCLINICAL ATHEROSCLEROSIS AND CARDIOVASCULAR RISK OF HERPES ZOSTER IN PATIENTS WITH RHEUMATOID ARTHRITIS

Results:

Out of 1176 patients, 217 (18%) showed evidence of subclinical atherosclerosis: ischemic transitory attack, 7 stroke), too this figure is lower than that re-

Conclusions:

This is the first Italian multicenter study on subclinical and clinical

OR:2.117, CI95%:1.35–3.32) were significantly associated with the presence

Background: A high incidence of herpes zoster (HZ) in patients with rheumatoid arthritis (RA) has been reported (1). According to our previous report on the incidence of HZ in Japanese patients with RA enrolled in the IORRA (Institute of Rheumatology, Rheumatoid Arthritis) cohort from 2005 to 2010, the standardized incidence rate (SIR) of HZ per 1,000 patient-years was 9.1 (95% confidence intervals [95 Cis]: 6.2–12.9) (2). In that study, 3.0% of patients used biologics at baseline. Subsequently, the use of biologics has increased, and many new potent disease-modifying antirheumatic drugs (DMARDs) have been introduced. The treatment strategy for RA has progressed in recent years; thus, it is important to investigate whether there is a change in the HZ incidence rate and the risk factors for HZ with the expanded use of biologics.

Objectives: To elucidate the incidence of HZ and risk factors for HZ in RA patients in the IORRA cohort.

Methods: The IORRA cohort is a large, single institute-based, observational cohort of RA patients established at the Institute of Rheumatology, Tokyo Women’s Medical University, in 2000. Among patients with RA enrolled in the IORRA surveys from 2010 to 2015, the incidence of HZ was extracted based on patients’ self-report and confirmed by the medical records. The SIR with 95 CIs was calculated and risk factors for HZ were analyzed using a Cox regression analysis.

Results: For 7,815 patients with RA (female, 84.7%) who were analyzed, the median [interquartile range (IQR)] age was 61.0 [49.7–68.9] years, and disease duration was 10 [4–18] years. Baseline drugs (median dose [IQR]) included prednisolone (PSL, 4 [2–5] mg/day) in 36.8%, methotrexate (MTX, 8 [6–10] mg/week) in 70.4%, and biologics in 14.7% of patients. Among 7,815 patients with RA (female, 84.7%) who were analyzed, the

CIs was calculated and risk factors for HZ were analyzed using a Cox regression analysis.

References:


Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.4733

THU0165 RISK OF HERPES ZOSTER IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE BIOLOGICS ERA BASED ON THE IORRA COHORT

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Background: A high incidence of herpes zoster (HZ) in patients with rheumatoid arthritis (RA) has been reported (1). According to our previous report on the incidence of HZ in Japanese patients with RA enrolled in the IORRA (Institute of Rheumatology, Rheumatoid Arthritis) cohort from 2005 to 2010, the standardized incidence rate (SIR) of HZ per 1,000 patient-years was 9.1 (95% confidence intervals [95 Cis]: 6.2–12.9) (2). In that study, 3.0% of patients used biologics at baseline. Subsequently, the use of biologics has increased, and many new potent disease-modifying antirheumatic drugs (DMARDs) have been introduced. The treatment strategy for RA has progressed in recent years; thus, it is important to investigate whether there is a change in the HZ incidence rate and the risk factors for HZ with the expanded use of biologics.

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Results: For 7,815 patients with RA (female, 84.7%) who were analyzed, the median [interquartile range (IQR)] age was 61.0 [49.7–68.9] years, and disease duration was 10 [4–18] years. Baseline drugs (median dose [IQR]) included prednisolone (PSL, 4 [2–5] mg/day) in 36.8%, methotrexate (MTX, 8 [6–10] mg/week) in 70.4%, and biologics in 14.7% of patients. Among 7,815 patients with RA (female, 84.7%) who were analyzed, the

CIs was calculated and risk factors for HZ were analyzed using a Cox regression analysis.

References:


Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2027

Background: Patients with rheumatoid arthritis (RA) have a higher risk of comorbidities such as infections 1, cardiovascular diseases2, and fractures3 than general population. To understand the risk of these comorbidities in RA more precisely, it is needed to compare the risk between RA and other chronic diseases. A Dutch study4 showed that patients with RA had comparable risk of infections, cardiovascular diseases and stroke with DM cases using Japanese health insurance database.

Methods: This retrospective longitudinal population-based study was conducted using claims data provided by the Japanese Medical Data Center Co., Ltd. We defined individuals as RA cases if they met all of the following: 1) had at least 6 months of continuous enrollment in the health insurance database; 2) had at least one RA diagnosis code and at least one prescription of disease-modifying antirheumatic drugs between January 2005 and December 2013; and 3) were ≥50 years old (RA group, n=3,607). Among individuals who met above criteria 1) and had at least DM diagnostic code and at least one prescription of drugs for DM, but did not meet 2), we selected age- (±5 years), gender-, calendar year of the observation start, and observation length-matched DM cases at 1:3 ratio (RA: DM) (DM group, n=10,821). Each comorbidity was defined as follows: HIs, at least one ICD10 code and one prescription of drugs for infections; CVDs, at least one ICD10 code and one prescription of drugs or medical procedures for CVDs with hospitalization; fractures, at least one ICD10 code for fractures. We calculated incidence rates (IR) with 95% confidence interval (CI) of each comorbidity in the two groups up to 10 years and adjusted odds ratio (OR) of RA compared with DM for each comorbidity using generalized estimating equations (GEE).

Results: The median age was 58, and 75.1% were female in the both groups. The IR [95% CI] of HIs, CVDs, and fractures was 2.8 [2.5–3.2] per 100 patient years, 9.2 [7.4–11.4] per 1,000 PY, 16.7 [14.2–19.6] per 1,000 PY in the RA group, 2.8 [2.6–3.0] per 100PY, 26.3 [24.4–28.3] per 1,000PY, 10.3 [9.1–11.6] per 1,000PY in the DM group respectively. The OR (95% CI) of RA (vs. DM) for HIs, CVDs, fractures was 0.5 [0.8–1.1], 0.4 [0.3–0.6], 1.3 [1.0–1.7] after adjusting for baseline characteristics.

Conclusions: This study revealed that patients with RA had significantly lower risk of CVDs than and similar risk of HIs and fractures to those with DM using health insurance database for the first time in Asia.

References:

Acknowledgements: This work was supported by the research grant from the Ministry of Health, Labour, and Welfare, Japan.


DOI: 10.1136/annrheumdis-2017-eular.4558

THU0167

ASSOCIATION OF BIOLOGIC ANTIRHEUMATIC THERAPY WITH THE RISK OF DEVELOPING TYPE 2 DIABETES IN ADULTS WITH RHEUMATOID ARTHRITIS: NEW EVIDENCE FROM REAL-WORLD DATA


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Background: While rheumatoid arthritis (RA) has been associated with the increased risk of developing type 2 diabetes mellitus (T2DM), few basic science studies have indicated the possible beneficial role of some biologic disease-modifying antirheumatic drugs (bDMARDs), including the interleukin-6 (IL-6) based DMARDs, on insulin resistance in patients with RA.

Objectives: To evaluate the impact of treatment with bDMARDs, including the IL-6 inhibitors, on the probability of developing T2DM in a real world setting.

Methods: From the Centricity Electronic Medical Records of GE Healthcare, a longitudinal cohort of 192,509 US adults (age 18 years) with diagnosis of RA from January 2000 to April 2016 was selected. Patients were excluded if they had a prior history of diabetes, cancer and micro- or macro-vascular diseases at diagnosis of RA. Four mutually exclusive antirheumatic treatment groups (TGs) were identified by diagnosis date (Dx) and treatment initiation date (ID): tocilizumab (TCZ, n=843), TCZ+Other bDMARDs (TCZ+obDMARD, n=2489), non-TCZ other bDMARDs (obDMARD, n=45,262) and no bDMARD (n=143,915). Within the treatment groups, 142,225 patients had a minimum 6 months of exposure before development of T2DM or end of follow-up. Treatment-effects models were used to estimate the probabilities (95% CI) of developing T2DM during follow-up in the 4 TGs after adjusting and balancing with inverse-probability-weighted regression for various factors including age, sex, smoking status, body mass index, use of non-biologic DMARDS, use of statins, anaemia status and follow-up time post ID.

Results: At diagnosis, the 142,225 patients were on average 55 years old, 22% male, 71% white Caucasian, 13% with anaemia, and 32% obese with mean BMI of 29 kg/m². About 28%/42% were using statins/MTX at diagnosis or during follow-up before development of T2DM. During mean 4.6 years of follow-up from Dx, 2.6%/2.6%/5.5%/5.8% developed T2DM in the TCZ/TCZ+obDMARD/obDMARD/no bDMARD TGs. The adjusted probability of developing T2DM was 0.05 (95% CI: 0.04, 0.05) in no bDMARD group; with significantly lower probability of developing T2DM in TCZ [0.02 (95% CI: 0.01, 0.04)], TCZ+obDMARD [0.03 (95% CI: 0.02, 0.04)] and obDMARD [0.01 (95% CI: 0.01, 0.02)] groups (Table). Hypertension, higher BMI and Statin use were associated with significantly higher probability of developing T2DM by 0.25% (95% CI: 0.16, 0.35), 0.08 (95% CI: 0.07, 0.08) and 0.36 (95% CI: 0.27, 0.47) respectively. Patients with a prior history of diabetes had an 8% higher likelihood of developing T2DM (p=0.13). Among those who received any bDMARD, those who ever received TCZ had significantly lower probability of developing T2DM (0.024, 95% CI: 0.02, 0.03), compared to those who were never exposed to TCZ therapy.

Table: The probability of developing T2DM, adjusted by age, sex, BMI, anaemia, balanced on hypertension, follow-up, obDMARDs and statin usage.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Probability (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No bDMARD</td>
<td>0.046 (0.045, 0.048)</td>
</tr>
<tr>
<td>obDMARD Only</td>
<td>0.041 (0.039, 0.044)</td>
</tr>
<tr>
<td>TCZ Only</td>
<td>0.023 (0.016, 0.031)</td>
</tr>
<tr>
<td>TCZ+obDMARD</td>
<td>0.018 (0.01, 0.026)</td>
</tr>
<tr>
<td>Among those who received any bDMARDs</td>
<td>0.046 (0.041, 0.049)</td>
</tr>
<tr>
<td>TCZ</td>
<td>0.023 (0.017, 0.029)</td>
</tr>
</tbody>
</table>

Conclusions: This study indicates the possible beneficial role of IL-6 inhibitors (TCZ) in reducing the likelihood of developing T2DM among adults without major co-morbidities at diagnosis of RA.

Acknowledgements: Funding by F. Hoffmann-La Roche/Genentech.


DOI: 10.1136/annrheumdis-2017-eular.5222
CONCLUSIONS: People who are uncertain about how to attribute illness events are less likely to adhere within the first six months of starting MTX therapy. Encouraging patients to actively monitor their progress with therapy and providing them with support to understand likely effects of MTX may help optimise DMARD use.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2463
Objectives: To evaluate outcomes of rapid dose escalation regimen of MTX compared with conventional treatment.

Methods: We implemented a randomized, controlled trial that enrolled patients with RA who fulfilled all of the following criteria: 20 to 70 years-old, disease duration ≤2 years, SDAI ≤11, and without prior use of MTX, tacrolimus (TAC) or biologics. Patients were randomized into rapid escalation (RE) group or conventional treatment (CT) group at 1:1 ratio. In RE group, doses of MTX were escalated up to 0.25 mg/kg/wk within 8 weeks after start of MTX and increased maximum tolerable dose or 16 mg/wk until wk 12. If a patient achieved SDAI remission at wk 12, MTX was continued at the same dose. If a patient did not achieve SDAI remission at wk 12 or showed intolerance to MTX, use of TAC or TNF inhibitor (TNFi) were allowed. In CT group, patients were treated with either MTX, TAC, salazosulfapyridine, or bucillamine by the discretion of physicians until wk 12. If a patient achieved SDAI remission at wk 12, same treatment was continued. If a patient did not achieve SDAI remission at wk 12, treatment was allowed. Patients were treated by the discretion of physicians at wk 24 and onward. We set two primary endpoints; the percent of patients achieving SDAI remission and Boolean remission at wk 24. We planned to enroll 120 patients per arm based on expected SDAI remission rates at wk 24, alpha and beta errors and dropout rates.

Results: Enrollment was terminated prematurely and all patients were followed for 48 wks. Of 115 enrolled patients, 57 were randomly assigned to RE group and 58 to CT group. Baseline demographics were similar between the two groups. The median baseline values (RE vs. CT) were 23.2 and 25.9 for SDAI, 0.64 and 0.61 for EO-SD, respectively. At wk 24, the percentages of patients achieving remission in RE and CT groups were 42% and 28% by SDAI criteria (p=0.1, \( \chi^2 \) test), and 35% and 17% (p=0.03, \( \chi^2 \) test) by Boolean criteria, respectively. Median values of HAQ at wk 24 in RE and CT groups were 0 and 0.04, respectively. Ten patients (2% of RE group and those of EO-SD were 0.78 and 0.77 (p=0.12, M-W U test, respectively. At wk 48, these values were not statistically different between the two groups. There were no significant differences between the two groups with incidence of severe adverse events.

Conclusions: The rapid dose escalation regimen of MTX provided significantly higher remission rate and tendency to provide superior SDAI remission than conventional treatment in patients with early RA in the short term.


DOI: 10.1136/annrheumdis-2017-eular.3335

THU0172 IMPROVEMENT OF DISEASE ACTIVITY IN A 5-YEAR COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS AND A MULTISPECIALTY CARE MODEL RECEIVING CONVENTIONAL DMARD THERAPY

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Background: Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA), this strategy has become recognized as a standard of good practice embodying the principle that rapid attainment of remission, or low disease activity, can halt joint damage and maintain good quality of life.

Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 5 year period in patients with conventional DMARD therapy in a large cohort of patients from a Colombian specialized in RA center with multidisciplinary care model (MCM).

Methods: A descriptive dynamic cohort study was performed. Records of patients using conventional DMARD treatment from specialized in RA center were reviewed; those patients were followed-up under T2T standards. Clinical follow-up was according to DAS28 as follows: every 3–5 weeks (DAS28 ≤5.1), every 7–9 weeks (DAS28 >5.1 and ≤7.1), and every 11–13 weeks (DAS28 >7.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. MCM model means that every patient is seen by other specialties involved in conventional DMARD therapy in a large cohort of patients from a Colombian specialized in RA center with multidisciplinary care model (MCM).

Results: We included 1443 patients, 84% were women and 16% were men. Mean age was 62±11 years; mean DAS28 at beginning was 4.0±1; regarding disease activity 57% were in moderate disease activity and 17% in severe disease activity. Clinical follow-up was according to DAS28 as follows: every 3–5 weeks (DAS28 ≤5.1), every 7–9 weeks (DAS28 >5.1 and ≤7.1), and every 11–13 weeks (DAS28 >7.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. MCM model means that every patient is seen by other specialties involved in conventional DMARD therapy in a large cohort of patients from a Colombian specialized in RA center with multidisciplinary care model (MCM).

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3668
patients receiving only conventional DMARDs therapy, treated and followed under T2T strategy recommendations and a MCM model.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5592

THU0173 LONG TERM SAFETY AND EFFICACY OF FILGOTINIB IN A PHASE 2B OPEN LABEL EXTENSION STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS UP TO 144 WEEKS


Background: Filgotinib (GLP00634, GS-6034) is an oral JAK1 selective inhibitor with a favorable safety and efficacy profile in two 24-week Phase 2b studies as add-on to methotrexate (DARWIN 1) or as monotherapy (DARWIN 2) in patients with active rheumatoid arthritis (RA). Three daily doses were tested (50mg, 100mg or 200mg) in comparison to placebo.

Objectives: To assess long term safety and efficacy of filgotinib 200mg daily in patients from the DARWIN 3 Phase 2 open-label extension study.

Methods: Patients who completed DARWIN 1 or 2 and enrolled in DARWIN 3 received filgotinib 200mg once daily or 100mg twice daily, depending on prior treatment assignment. The DARWIN 3 data cut off was when the last patient reached end point Week 60. For safety, all data from the first intake of filgotinib in DARWIN 1/2/3 were analysed (up to 144 weeks).

Results: 877 patients participated in DARWIN 1 or 2, 790 completed and 739 entered DARWIN 3 from 22 countries (82% females, mean age 53y), 559 patients (75.6%) completed Week 60, 9.3% discontinued due to positive quantitative, 7.8% due to other adverse events, 6.8% for other reasons and 0.3% due to insufficient response. Overall exposure to filgotinib was 1314 patient-years (PYE).

Treatment-emergent adverse events (157.7/100PYE), serious adverse events (5.3/100PYE) and serious infections (1.9/100PYE) occurred at similar rates compared to the core studies, however infections decreased on a percentage basis from 15% (109/739, W0–12) to 5% (25/549, W85–96). 16 cases of Herpes zoster were reported (1.2/100PYE), 6 cases of malignancy (excl. NMSP) (0.5/100PYE) and 1 case of MACE (0.1/100PYE). There was no active case of tuberculosis. Three fatalities were reported (0.2/100PYE).

Mean change from baseline (CBF) at Week 96 and CTCAE toxicity grading in lab parameters of special interest are shown in table 1.

Table 1. Mean CBF at Week 96 and CTCAE toxicity grading in selected lab parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CBF at Week 96 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>+6.5 g/L</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>−1.37 giga/L</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>−0.19 giga/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>+8.2 µm/L</td>
</tr>
<tr>
<td>ALT</td>
<td>+6.1 U/L</td>
</tr>
<tr>
<td>LDL</td>
<td>+13%</td>
</tr>
<tr>
<td>HDL</td>
<td>+23%</td>
</tr>
<tr>
<td>Tot chol/HDL</td>
<td>−4%</td>
</tr>
<tr>
<td>NK cells</td>
<td>−0.02 g/L</td>
</tr>
</tbody>
</table>

Based on an observed case analysis 84% (505/601), 65% (389/601), 44% (265/601) and 51% (298/587) of patients reached ACR20, ACR50, ACR70 and DAS28(CRP) remission at Week 60 respectively.

Conclusions: With 1314 patient-years of exposure, the safety profile of filgotinib appears consistent with that of previously reported double-blind studies and the clinical response appears durable.

References:


Disclosure of Interest: R. Alten Grant/research support from: Galapagos, R. Westhoven Grant/research support from: Roche, Consultant for: Galapagos, Speakers bureau: BMS, A. Kavanagh Consultant for: Galapagos, Pfizer, AbbVie, Amgen, Celgene, Janssen, Novartis, Eli Lilly, UCB, M. Genovese Grant/research support from: Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, Consultant for: Galapagos, Gilead, Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, K. Winthrop Grant/research support from: BMS, Pfizer Consultant for: pfizer, BMS, Lilly, Abbvie, Roche, UCB, Galapagos, M. Greenwald Grant/research support from: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Galapagos, Gilead, Lilly, Merck, Pfizer, UCB, Consultant for: Lilly, Pfizer, L. Ponce: None declared, F. Enriquez: None declared, M. Stanislavchuk: None declared, M. Mazur: None declared, A. Spindler: None declared, R. Cseuz: None declared, N. Nikulenkova: None declared, M. Glowacka-Kulesz: None declared, I. Szombati: None declared, A. Dudek: None declared, L. Meuleners Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, P. Harrison Employee of: Galapagos NV, A. Van der Aa Employee of: Galapagos NV

DOI: 10.1136/annrheumdis-2017-eular.5460

THU0174 DRUG RETENTION OF TOFACITINIB VERSUS BIOLOGIC ANTI-RHEUMATIC AGENTS IN RHEUMATOID ARTHRITIS: OBSERVATIONAL DATA FROM THE SWISS SCQM REGISTRY

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Background: The oral Janus kinase inhibitor tofacitinib (Tofa) was licensed in Switzerland in 2013 for the treatment of moderate to severe rheumatoid arthritis (RA) patients having failed methotrexate. Besides Tofa, rheumatologists in Switzerland have the choice between 7 alternative bDMARDs licensed with similar indications, including 5 TNFi inhibitors (TNFi) and 2 bDMARDs with other mechanisms of action (OMA-bDMARDs).

Objectives: To compare the drug retention rate of three alternative treatment options licensed with a similar indications, namely Tofa, TNFi and OMA-bDMARDs, using data from the Swiss registry.

Methods: This is an observational cohort study within the Swiss Clinical Quality Management registry (SCQM). All therapies with Tofa, TNFi, and OMA-bDMARDs initiated in adult RA patients between August 1, 2013 and Dec 1, 2016 were considered. The exposure of interest was treatment with Tofa vs TNFi and vs OMA-bDMARDs (Abatacept or Tocilizumab). The primary outcome was drug retention defined as the time from initiation to discontinuation of treatment. We used Kaplan Meier curves to display drug retention and Cox proportional hazard models stratified by seropositivity to analyze the hazard for treatment discontinuation. We adjusted for potential confounders, including gender, age, disease duration, seropositivity, BMI, smoking status, DAS28(CRP) and the total number of previous bDMARDs. We applied multiple imputation to account for missing baseline covariate data.

Results: A total of 1996 therapies were initiated during the study period (376 Tofa, 928 TNFI, 692 OMA-bDMARDs). Some differences in disease and treatment characteristics existed between the 3 groups, in particular TNFi tended to be used in patients with fewer previous bDMARDs experience, younger age and shorter disease duration. The crude overall drug retention was similar between the 3 these drug groups (p=0.24) (Figure 1A). The adjusted analysis demonstrated a slightly higher hazard of drug discontinuation with TNFi compared to Tofa [HR 1.27 (95% CI: 1.02 – 1.57, p=0.03)], while no difference was observed for OMA-bDMARDs compared to Tofa or TNFi. There was no active case of tuberculosis. The results of this observational study suggest that Tofa is a valuable alternative to treatment options in RA, with Tofa drug retention at least comparable to other available bDMARDs.

A. Ciurea: None declared, R. Mueller: None declared, P. Hasler: None declared, P. Exer: None declared, J. van Muelenhien: None declared, D. Kyburz: None declared, C. Gabay: None declared, R. Zuffery: None declared.

Disclosure of Interest: Investigator Initiated Research grant supported by Pfizer.

Disclosure of Interest: A. Finckh Grant/research support from: BMS, Speakers bureau: Abbvie, BMS, Pfizer, Roche, UCB, L. Herzog: None declared, A. Scherer: None declared, J. Dudler: None declared, B. Moeller: None declared, A. Ciurea: None declared, R. Mueller: None declared, P. Hasler: None declared, P. Exer: None declared, J. van Muelenhien: None declared, D. Kyburz: None declared, C. Gabay: None declared, R. Zuffery: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6804
THU0175

INFLAMMATION DETECTED WITH MODERN SENSITIVE MRI ANALYSIS DEMONSTRATES THAT THERAPEUTIC RESPONSE AS EARLY AS ONE MONTH PREDICTS 12-MONTH RADIOGRAPHIC PROGRESSION: DATA FROM A STUDY USING TOFACITINIB AND METHOTREXATE IN METHOTREXATE-NAIVE PATIENTS WITH EARLY RA

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Objectives: To determine if early changes in RAMRIS were predictive of subsequent MRI and radiographic damage progression in a study of tofacitinib for the treatment of early RA in methotrexate-naive patients with minimal radiographic progression.

Methods: We used data from an exploratory, Phase 2 randomised controlled trial comparing tofacitinib, methotrexate and the combination (n=109) in methotrexate-naive patients with early active RA.1 All patients met ACR classification criteria for active RA. MRI was performed at baseline and at 1, 3, 6 and 12 months. A single centralised reader read all MRI data; data for each patient were randomised by time point and read in the same sitting. We examined changes in synovitis, osteitis and erosions for RAMRIS and RAMRIQ at 1 and 3 months and performed univariate analyses on their relationship to RAMRIS, RAMRIQ and radiographic progression (modified Total Sharp Score [mTSS]) at 12 months.

Results: Reduction in RAMRIQ synovitis and osteitis at 1 and 3 months were significantly associated with reduction in RAMRIS erosion progression at 12 months (Table). Improvement in RAMRIS synovitis and osteitis at 1 and 3 months were also associated with reduction in radiographic progression at 12 months, while RAMRIS erosions at 1 and 3 months were not significantly associated with radiographic progression (Table). Early changes in RAMRIS erosion at 1 and 3 months were associated with radiographic progression at 12 months (Table). Treatment with tofacitinib alone or in combination with methotrexate was also associated with reduced progression in RAMRIS erosions (p=0.017 and p=0.007, respectively).

Conclusions: These data suggest that sensitive automated detection of early changes in synovitis and osteitis, as well as erosions for RAMRIS and RAMRIQ at 1 and 3 months is associated with reduced radiographic progression and that treatment with tofacitinib alone or in combination with methotrexate is associated with reduced progression in RAMRIS erosions.

Table. Univariate analyses of the relationship between RAMRIS and RAMRIQ measurements at Month 1 and 3 and RAMRIS erosion and radiographic progression at Month 12.

<table>
<thead>
<tr>
<th>p value</th>
<th>RAMRIS erosion progression (mTSS; Month 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in RAMRIQ synovitis</td>
<td>Month 1: 0.04</td>
</tr>
<tr>
<td>Change in RAMRIQ osteitis</td>
<td>Month 1: 0.001</td>
</tr>
<tr>
<td>Change in RAMRIQ erosions</td>
<td>Month 1: 0.001</td>
</tr>
</tbody>
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Disclosure of Interest: None declared

THU0176

EFFICIENCY AND SAFETY OF RAPAMYCIN COMBINED WITH LOW-DOSE IL-2 TREATMENT COMPARED WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The molecular target rapamycin (mTOR) signaling can regulate between effector and regulatory T cell lineage commitment and to be a new therapy for several autoimmune diseases, such as systemic lupus erythematosus [2].

Objectives: To evaluate whether rapamycin is beneficial in patients with Rheumatoid Arthritis (RA), and compared with Methotrexate in efficiency and safety.

Methods: Fifty-eight DMARD-naive RA patients were enrolled, thirty-eight were treated with Rapamycin (0.5 mg every 2 days, combined with IL-2 500 IU per day for 5 days), the others with Methotrexate (10 mg per week) taken as control. Clinical improvement and immunological assessments were performed at baseline, 1 and 12 weeks. Treatment group assessed CD4+ T cell subsets by flow cytometry at baseline, 1 and 12 weeks.

Results: We enrolled 58 patients. At baseline, patients had a mean DAS28 of 3.34 (0.87) in the Rapamycin group and Methotrexate group included 38 and 20 patients, respectively, with no significant differences in baseline characteristics. At 1 week, the mean DAS28 after Rapamycin treatment (2.43 [0.77]) and Methotrexate (2.25 [0.86]) was not significantly different (P=0.43). Same as ESR (24.74 [24.53], 21.76 [24.27], P=0.69). The dose of glucocorticoid during hospitalization of rapamycin treatment (720.8 [554.3]) was lower than Methotrexate (1202.3 [943.1], P=0.042). The length of hospital stay of Rapamycin (14.5 [3.9]) was lower than Methotrexate (21.0 [3.8], P<0.001). Rapamycin administration resulted in an increase in the absolute counts of Treg cells from a median of 36.82 cell/ul (at week 0) to 99.80 cell/ul (at week 1) (P<0.001). The ratios of Th17/Treg cells showed a reduction from a median of 0.16 to 0.09, and the difference was significant (P=0.047). At 12 week, 5 patients treated with Rapamycin dropped out because of non-compliance. the mean DAS28 was not significantly different (2.36 [0.97], 2.16 [0.86], P=0.51). The same as the daily dose of glucocorticoid (10.21 [32.9], 9.16 [40.1], P=0.804). The absolute counts of Treg cells increased from a median of 36.82 cell/ul (at baseline) to 43.26 cell/ul after Rapamycin administration (P=0.028). The ratios of Th17/Treg had no significant difference from a median of 0.16 at baseline to 0.12 at week 12 (P=0.937). Liver enzyme elevations occurred in 2 patients after Methotrexate therapy for 1 week. However, there were no serious adverse events observed during the 12-week period of rapamycin treatment.

Conclusions: Rapamycin combined with low-dose IL-2 appears to be a safe and effective therapy for RA, by a rapid increase of Treg cells and a correction of the ratio of Th17/Treg cells, which has gotten a same response compared with Methotrexate.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4575

THU0177

ABT-494 PHARMACOKINETICS FOLLOWING ADMINISTRATION OF THE ONCE-DAILY EXTENDED-RELEASE TABLET FORMULATION BEING UTILIZED IN THE ONGOING RHEUMATOID ARTHRITIS PHASE 3 TRIALS

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Background: ABT-494 is a selective Janus Kinase 1 inhibitor, in two Phase 2b clinical trials, 6 mg and 12 mg twice-daily (BD) doses of ABT-494 immediate-release formulation achieved optimal benefit-risk profiles. To enhance patients’ compliance, an extended-release formulation was developed targeting to achieve comparable exposures with the 6 mg and 12 mg BD of the immediate-release formulation with once-daily (QD) administration.
Objectives: The objective of this work was to characterize the pharmacokinetics of ABT-494 with the extended-release formulation that is currently being utilized in Phase 3.

Methods: Comparison of ABT-494 pharmacokinetics from the immediate-release and extended-release formulations was conducted following multiple-dose administration to healthy subjects. Two cohorts of subjects were evaluated. In the first cohort, healthy subjects (N=12) received multiple 15 mg QD doses of the extended-release tablet formulation and multiple 6 mg BID doses of the immediate-release capsule formulation for 7 days. In the second cohort, healthy subjects (N=12) received multiple 30 mg QD doses of the extended-release tablet formulation and multiple 12 mg BID doses of the immediate-release capsule formulation for 7 days. Both evaluations were conducted following an open-label, randomized, 2-period, 2-sequence, crossover design under fasting conditions. ABT-494 plasma concentrations were measured and pharmacokinetic parameters were calculated using non-compartmental analyses.

Results: At steady-state, ABT-494 AUC_{0–24} ratio (and [90% confidence interval]) was 0.94 [0.84 – 1.05], C_{max} ratio was 0.91 [0.74 – 1.12] and C_{min} ratio was 1.09 [0.85 – 1.40] for the 15 mg QD regimen of the extended-release formulation relative to the 6 mg BID regimen of the immediate-release formulation. Similarly, ABT-494 mean AUC_{0–24} ratio was 0.97 [0.87 – 1.09], C_{max} ratio was 0.90 [0.73 – 1.11] and C_{min} ratio was 0.87 [0.75 – 1.02] for the 30 mg QD regimen of the extended-release formulation relative to the 12 mg BID regimen. All evaluated regimens were well-tolerated by healthy subjects.

Conclusions: ABT-494 regimens of 15 mg QD or 30 mg QD of the extended-release formulation, currently being utilized in Phase 3 RA studies, provide similar exposures to 6 mg BID and 12 mg BID, respectively of the immediate-release capsule formulation previously shown to provide optimal benefit-risk profiles in RA Phase 2 trials.


DOI: 10.1136/annrheumdis-2017-eular.3224

THU0179 INCIDENT OF DEEP VEIN THROMBOSIS AFTER TOTAL HIP REPLACEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS


Background: The purpose of this study was to compare incidences of VTE in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) after total hip arthroplasty, different strategies for prevention of VTE and evaluate their efficiency.

Objectives: To evaluate the efficiency of prevention of VTE in patients with RA and osteoarthritis and arthritis after hip replacement surgery under comparable conditions.

Methods: A one-year prospective cohort study was performed on 173 primary THA patients operated in V.A. Nasonova Research Institute of Rheumatology for the period 2016. Of these, 91 patients with RA (52.6%) and 82 patients with OA (47.4%). For a comparative analysis of the efficiency of anticoagulant therapy, each patient group was divided into 2 subgroups by type of drug therapy. The first - nadroparin calcium (the drug therapy was started for 12 hours after the operation at a dose of 0.1 ml per 10 kg of body weight time one per day), the second - nadroparin calcium with transfusion to dabigatran etexilate (the first stage of 4 hours after the operation was started therapy by nadroparin calcium, and then after the removal of the epidural catheter moved to the dabigatran etexilate), Doppler ultrasonography (DUS) was routinely performed preoperatively and on postoperative day 7, 14, then 1 time a month for diagnosing a deep venous thrombosis (DVT). Time of observation was 6 months.

Results: DVT were reported in 8 (4.8%) patients, 2 of them (1.2%) with RA and 6 (3.4%) with OA. Distal DVT developed on 8 and 17 days after total hip replacement in RA patient's group. They received nadroparin calcium only. 5 patients with VTE after surgery from OA group used nadroparin calcium and 1 patient was on combined drug therapy. Of the 8 cases of VTE - 6 (75%) were asymptomatic and 2 (25%) with development of clinical and laboratory picture. All cases of thrombosis in a group of RA was asymptomatic. In a perioperative period of clinically significant bleeding was not seen.

Conclusions: Cases of VTE in patients with RA, despite the large number of risk factors, under comparable conditions is significantly lower than patients with OA. The number of asymptomatic DVT dominates symptomatic both comparison groups. In patients with RA and OA who were from the first group have reported 6 cases of VTE and only 1 case of VTE have reported in patients who were from second group. Prevention of VTE by combination of LMWH and NOACs was more effective and safety in RA and OA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6422

THU0180 SYSTEMS BASED INVESTIGATION OF THE ANTI-INMUNOGENIC POTENTIAL OF DMARDS FOR RHEUMATOID ARTHRITIS USING HUMAN PRIMARY CELL-BASED BIOMAP® PHENOTYPIC PROFILING

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1BioMAP Division, DiscoverX Corporation, South San Francisco, United States; 2Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, United Kingdom

Background: Biologics represent a rapidly growing class of approved and investigational drugs routinely used to treat multiple diseases, including inflammatory and rheumatic diseases. Unfortunately, the success of such therapeutics is
undertaken by their immunogenicity and the development of anti-drug antibodies (ADA) associated with treatment failure and hypersensitivity reactions2. Methotrexate (MTX) has been shown to reduce the generation of an ADA response3. The ability of other conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs) to mitigate unwanted immunogenicity, and prolong efficacy in patients who cannot tolerate methotrexate, is less clear.

**Objectives:** We previously reported that MTX markedly inhibited the production and release of soluble immunoglobulin (sIgG) by human primary B cells cocultured with PBMC (BT system) in the in vitro BioMAP® phenotypic screening panel2. MTX also had anti-proliferative effects on human primary tissue and immune cell types4. We evaluated other csDMARDs to determine if they were broadly active or, were similar to MTX in selectively blocking sIgG production and therefore would be more likely to reduce ADA associated with biologics.

**Methods:** A series of csDMARDs (sulfasalazine, hydroxychloroquine, cyclosporine, leflunomide, azathioprine) were profiled at the concentrations across the BioMAP Diversity PLUS™ panel to generate phenotypic activity profiles. In addition to assessing sIgG production, effects on a broad scope of disease-relevant readouts related to primary cell activation and proliferation, inflammation, wound healing, tissue remodeling and fibrosis, and were also evaluated.

**Results:** Similar to MTX, cyclosporine, leflunomide and azathioprine strongly inhibited sIgG production at all tested concentrations. In contrast, treatment with sulfasalazine or hydroxychloroquine did not decrease sIgG indicating these compounds may not mitigate the immunogenicity of biologics. In contrast to MTX, several csDMARDs were broadly active in many BioMAP systems. Bioinformatics analysis was used to identify distinct mechanistic signatures for these agents in the BioMAP Panel.

**Conclusions:** The results support application of the BioMAPs in vitro assay suite in preclinical drug discovery, to determine the suitability of csDMARDs as anti-immunogenic co-treatments to extend the clinical efficacy of biologics. Clinical studies are needed to confirm these results, however, in inflammatory bowel diseases and to a less extent in rheumatoid arthritis, azathioprine has been shown to reduce immunogenicity of biologics5.

**References:**

**Acknowledgements:** We acknowledge the contributions of BioMAP operations, bio-analysts and support staff to this work. Thanks to the BioMAP Research Biology team for their analysis and interpretation of BioMAP profiling data.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1942

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**THU0182 MONOTHERAPY WITH THE JAK1-SELECTIVE INHIBITOR FILGOTINIB DISPLAYS AN ANTI-INFLAMMATORY BIOMARKER PROFILE IN RHEUMATOID ARTHRITIS PATIENTS**

**A. Kavanaugh,1  A. Van der Aa,2  C. Jamoul, W. Li, L. Goyal, Y. Pan1,  P. Harrison,2  C. Tasset, J. Tarrant,3  R. Galien,4  P. P. Harrison2, C. Tasset2, J. Tarrant3, R. Galien 4.**

**Background:** Janus kinases (JAKs) are key proteins in the signal transduction of many cytokines and growth factors. The selective JAK1 inhibitor filgotinib (GLPG0634, GS-6034) has been evaluated in a 24-week phase 2B study (DARWIN 2) as monotherapy in active rheumatoid arthritis (RA) patients with inadequate response to methotrexate and has shown a good safety and efficacy profile1.

**Objectives:** To gain insight into filgotinib mode of action as monotherapy in RA patients by analysing the impact of filgotinib on a broad panel of immune modulators in the serum.

**Methods:** RA patients received either placebo (PBO), or filgotinib monotherapy at 50mg, 100mg or 200mg once daily (QD). Serum samples were collected at baseline, week 4 and week 12 and analysed using the 18-plex bead-based immunoassay (HSTCMAG-28SK Merck-Millipore) on BioPLEX 200 instrument to measure cytokine concentration. Median % change from baseline for biomarkers are reported for week 4 and 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups and PBO.

**Results:** Following treatment with filgotinib at 100 mg QD and 200mg QD, there were significant reductions in cytokines important in expansion and activity of multiple T cell subsets and innate immunity compared to PBO (see Table). These changes include decreases in proinflammatory cytokines (IL-6, IL-1β, and TNFα), Th1-related (IL-2, IFN-γ and IL-12), Th2-related (IL-4, IL-5, and IL-13) and Th17-related cytokines (IL-17a, IL-17, IL-21, IL-23 and IL-23) in PBO and filgotinib treated groups. All doses of PBO and filgotinib are presented as a significant higher (mean±SD) at 100mg (P=0.01; ***p<0.001). Table 1. Median percent change of biomarkers from baseline

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>PBO</th>
<th>Filgotinib 50mg</th>
<th>Filgotinib 100mg</th>
<th>Filgotinib 200mg</th>
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<tr>
<td>IL-6</td>
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<td>-11***</td>
<td>-9***</td>
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<td>-11***</td>
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</table>

**P values comparing % changes between filgotinib and PBO groups: NS <p=0.05; *p<0.01; ***p<0.001.**
**THU0184**

**ADHERENCE PROFILES TO METHOTREXATE OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ELIGIBLE FOR BIOLOGICS: TYPOLoGIES FROM FORGET, A CROSS-SECTIONAL SURVEY OF 244 PATIENTS**

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**Background:** Adherence to Methotrexate (MTX) is not optimal in RA patients [1]. The FORGET survey carried out in 2016 aimed to assess the MTX adherence rate of RA patients, insufficient responders to MTX, biologic-naïve, when an initiation of biologics was being considered. Non-adherence was defined as a compliance rate < 80% according to the CQR19 (Compliance Questionnaire for Rheumatology) [2]. The factors tested were socio-demographic characteristics, DAS 28, RAID, CQR responses, beliefs, voluntary or involuntary dose skipping, social and medical support.

**Results:** Of the 244 patients analyzed, the non-adherence rate was 34%. The rather weak correlation between adherence (CQR) and the disease impact (RAID) tended to confirm the hypothesis of different profiles. Four typologies of non-adherence were determined. Groups G1 and G2 were non-adherent patients with high (G1) or lower (G2) impact. Groups G3 and G4 were patients with good adherence with high (G3) or lower impact (G4). Significant adherence factors were found for these 4 groups (p<0.01 (table).

**Conclusions:** Four adherence profiles to Methotrexate have been identified. Among the non-adherent patients, 2 topologies are opposed: 1- patients in state of suffering, with low support from relatives, negative beliefs and significant professional impact. 2-patients with less disease impact, who perceived their treatment with constraints although well tolerated. Detection of patients' profiles may allow targeted strategies to improve or maintain adherence.

**References:**


**Acknowledgements:** This study was funded by Chugai Pharma France.

**Disclosure of Interest:** None declared. V. Hautin-Monteil Employee of: Roche France, M.-C. Ducrot: None declared, R.-M. Filpo: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5523

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**THU0185**

**COMPARISON OF TOFACITINIB SAFETY AND EFFICACY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS, OR TO ONE OR MORE BIOLOGICAL DMARDS**

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**Background:** Tofacitinib is an oral JAK inhibitor for the treatment (tx) of rheumatoid arthritis (RA). Studies have shown diminishing response to tx in RA patients (pts) when cycling through TNF inhibitors. Prior analyses assessed tofacitinib in csDMARD- inadequate response (IR) pts vs overall bDMARD-IR pts.

**Conclusions:** Among the non-adherent patients, 2 topologies are opposed: 1- patients in state of suffering, with low support from relatives, negative beliefs and significant professional impact. 2-patients with less disease impact, who perceived their treatment with constraints although well tolerated. Detection of patients' profiles may allow targeted strategies to improve or maintain adherence.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2182

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**THU0183**

**IMPROVED ADHERENCE TO NEWLY PRESCRIBED DMARDS WITH CO-PRESCRIPTION WITH LOW DOSE STEROIDS IN RHEUMATOID ARTHRITIS PATIENTS ATTENDING CLINIC AT A DISTRICT GENERAL HOSPITAL IN THE UK**

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**Background:** Non-adherence to DMARDS is associated with disease flares and increased disability. Adherence rates to prescribed medicine regimes in people with Rheumatoid Arthritis vary from 30–80% in different studies. Improving adherence to therapy leads to better disease outcome and reduced costs associated with management of RA.

**Objectives:** This study was carried out as a pilot study to look at the effect of co-prescription of steroids on the adherence and side effects to newly prescribed DMARDS in patients with rheumatoid arthritis.

**Methods:** This is a prospective, observational cohort study, for the duration of three months per participant. Patients were selected sequentially from those attending outpatient clinic at Basildon Hospitals with a confirmed diagnosis of rheumatoid arthritis (ACR/EULAR criteria), and had been planned to start on a new DMARD by the treating physician. Baseline data included demographics, disease characteristics and data regarding steroid co-prescription including route, dose and duration. Patients were reviewed at three months to look at DMARD adherence defined by continuation of the DMARD. We looked at the side effect profile as possible contributing factor to non-adherence. The effect of co-prescription with steroids and other demographic data on treatment duration was investigated using Kaplan-Meier survival plots. Logistic regression analysis was used to investigate the effect of co-prescription of steroids on continuation of medication.

**Results:** Fifty one patients were recruited to the study. Median age at the time of enrolment was 61 years (IQR 46–71), 73% were females and 92% were caucasians. Seventy percent of the patients were seropositive and DMARD naïve with a mean DAS CRP at recruitment of 4.13 (1.21). Seventeen (33%) patients were co-prescribed with steroids at the initiation of DMARDS. Out of these 59% (n=10) were DMARD naïve. Thirty patients received a tapering dose of oral prednisolone with a mean starting dose of 13.8mg daily (range 3mg - 20 mg) for a mean duration of 10.8 weeks. Two patients received oral prednisolone 5mg daily for 12 weeks. The mean cumulative dose of oral prednisolone prescribed was 602.2mg. The two remaining patients received 120 mg of depomedrone IM. The non-adherence rate for our cohort was 35%, 6% for patients co-prescribed with steroids versus 50% for patients who were not co-prescribed with steroids. The odds ratio for likelihood of discontinuation for patients who were not co-prescribed with steroids versus patients who were, was 16 (1.94–134.5, p=0.011). At the end of therapy, 25% of the patients who were co-prescribed with steroids versus 32% of the patients who were not co-prescribed with steroids reported side effects to the DMARD initiated. The odds ratio for reporting side effects for steroid co-prescription was 0.28 (0.054–1.438, p=0.12).

**Conclusions:** Co-prescription of low dose steroids with initiation of DMARDS increases the chances of adherence and possibly reduces the side-effect profile.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2182

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**Filgotinib** also reduced the β- and T-cell development cytokine IL-7. In contrast, IL-8 was not affected by filgotinib. Reductions in MIP1α, MIP1β and GM-CSF are in line with a down modulation of innate immune activity.

**Conclusions:** Treatment of RA patients with filgotinib monotherapy resulted in significant reduction in the levels of a broad range of cytokines related to Th1, Th2, Th17 and potentially B cells, as well as innate immunity. This observed anti-inflammatory activity of filgotinib is consistent with its efficacy in RA patients.

**References:**


**DOI:** 10.1136/annrheumdis-2017-eular.5814
Objectives: To compare tofacitinib safety and efficacy in RA pts who have previously failed tx (lack of efficacy and/or safety reasons) with csDMARDs, with pts who failed tx with either 1 or ≥2 prior bDMARDs.

Methods: Data from pts who received ≥1 dose of tofacitinib in 19 RA studies up to 96 months (2 Phase [P] 1; 9 P2; 6 P3; 2 LTE studies [1 LTE ongoing; data as of March 2015]) were used in this analysis. Data were pooled across all 19 studies for safety assessments in the All RA population: csDMARD-IR, n=4377; bDMARD-IR, n=838 (1 bDMARD-IR, n=533; ≥2 bDMARD-IR n=305). Safety was also assessed up to 24 months in pts randomised to tofacitinib 5 or 10 mg BID or placebo (PBO) in a pooled P2/P3 randomised controlled trial (RCT) population (8 P2, 6 P3 studies; csDMARD-IR, n=332; bDMARD-IR, n=782). Incidence rates (pts with events/100 pt-years) were calculated for serious AEs (SAEs), serious infections (SIs) and herpes zoster (HZ). Efficacy was assessed by pts achieving ACR20 response and DAS28-4 (ESR) ≤3.2 at Month (M) 3 in a pooled P3 RCT population (P2/P3 RCT n=2757; ORAL SOLO n=272).

Results: Prior to tofacitinib tx, bDMARD-IR pts had longer RA duration, greater disease burden and more corticosteroid use vs csDMARD-IR pts. SAEs were more common among bDMARD-IR vs csDMARD-IR pts in both the P2/P3 RCT and the All RA populations; SAE rates were not higher in pts failing ≥2 bDMARDs vs 1 bDMARD (Table). Incidence rates for SIs were generally greater in pts with IR to bDMARDs vs csDMARDs in the All RA population, but generally lower in pts with IR to 1 or ≥2 bDMARDs vs csDMARDs in the P2/P3 RCT population; incidence with 5 mg BID was lower for 1 vs ≥2 bDMARDs in the P2/P3 RCT population. Incidence rates for HZ were similar to tofacitinib vs csDMARDs or 1 bDMARD, but appeared numerically greater in pts with IR to ≥2 bDMARDs in both the P2/P3 RCT and the All RA populations. A similar pattern was observed across tofacitinib and PBO groups. Efficacy at Month 3 in the P3 RCT population was greater with both tofacitinib doses vs PBO. Although absolute response was smaller in pts with IR to ≥2 bDMARDs vs csDMARDs, generally similar efficacy was observed in pts with IR to 1 or ≥2 bDMARDs (Table).
activity, HQO-DL, and pain as early as Week 2 (first post-baseline assessment), and improvements in fatigue by M3. Responses were maintained or improved through M3 (monotherapy) or M6 (with background csDMARDs).

References:

Disclosure of Interest: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by AG McCluskey of CMC and was funded by Pfizer Inc.

Disclosure of Interest: D. Aletaha Consultant for: AbbVie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, and UCB, Employee of: Novartis, G. Valenzuela: None declared.

THU0188

EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO DID NOT RESPOND TO SYNTHETIC AND BIOLOGICAL DMARDS IN CLINICAL PRACTICE

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Background: Tofacitinib (TOFA) is so far the only representative of a new class of Jak-inase inhibitors in rheumatology. Despite extensive data on TOFA obtained from 3rd phase studies, for use in clinical practice, the information is limited.

Objectives: To study the efficacy and safety of TOFA in RA in clinical practice.

Methods: Data from two parallel Phase-IV open-label observational clinical trials, modelling clinical practice, conducted by very similar protocols in 11 rheumatology centers in Russia, Inclusion criteria were active RA, methotrexate (MTX) failure, and/or other synthetic or biologic DMARDs failure. In total, 142 pts (26 males, 116 females, age 51.5±12.2 years, disease duration 88.6±78.1 months, 86.6% RF(+), 76.6% ACPA(+), 81.7% with erosive disease, DAS28-ESR 5.89±1.03, SD: 35.7±13.4, HAO 1.59±0.64) were included. 32 (22.5%) pts had biologics in history. TOFA used in the dose of 5 mg BiD for 6 months, with possibility to increase to 10 mg BiD (carried out in 27/pts after 3±2.7 weeks). 115 (81%) pts received TOFA in combined mode (MTX 118±5,4 mg per week), 18 with leflunomide or sulfasalazine, 9 pts used TOFA in monotherapy.

Results: 129 (90.8%) pts successfully completed the six-month period of treatment. TOFA was withdrawn due to lack of response in 6 cases, adverse events (AEs) in 4 (anemia, arterial hypotension, skin vasculitis, mouth ulcers), withdrawal of informed consent – 2, protocol violation – 1. At month 3 SDAI score decreased to 14.6±10.9 (p<0.01), 55 (42.6%) pts achieved SDAI LDA and 22 (17.1%) SDAI remission; HAQ decreased to 0.95±0.61, HAO=0.5 observed in 56 (27.8%) pts. After 6 months, SDAI and HAQ scores decreased to 10.5±8.6 and 0.83±0.64 resp. (p<0.01); 81 (62.8%) pts achieved SDAI LDA and 29 (22.5%) SDAI remission; HAO=0.5 observed in 48 (37.2%) pts. Results of treatment in patients with and without biological DMARDS in history were similar. Pts who needed dose escalation of TOFA had worse results at month 3 compared to others (SDAI 21±10.2 and to 33±10.7 resp., p=0.02), but after increase of the dose to 10 mg BiD at month 6 they showed a slightly better result (SDAI 9.5±7.1 and to 10.7±8.9 resp., p=0.54). Only 2 serious AEs (anemia and skin vasculitis) observed. We didn’t see any case of Herpes zoster in our group.

Conclusions: TOFA was effective in patients with severe RA who did not respond to both synthetic and biological DMARDS (achievement of SDAI LDA in 42.6% of pts at month 3 and in 62.8% at month 6). Dose escalation to 10 mg BiD can be useful in 1/4 of patients who do not respond to standard dose of TOFA. TOFA has shown a good safety profile.

Acknowledgements: This scientific study was supported by grant from Pfizer.

Disclosure of Interest: E. Luchikina Grant/research support from: Pfizer, Bio- cad, Speakers bureau: Abbvie, Pfizer, Tirupharm, D. Karateev Grant/research support from: Pfizer, Consultant for: Pfizer, Tirupharm, Biocad, Egis, R-Pharm, Novartis, Speakers bureau: Abbvie, Pfizer, Bristol Myers Squibb, Roche, Tirupharm, Biocad, R-Pharm, Novartis, Egis, MSD, UCB, A. Misuyuk: None declared, N. Demidova: None declared, G. Loukina: None declared, D. Abdulganieva: None declared, A. Baranova: None declared, A. Babaeva: None declared, L. Evstigneeva: None declared, O. Ivanova: None declared, V. Mazurov: None declared, O. Semagina: None declared, A. Sizikov: None declared, V. Sorototskaya: None declared, E. Nasonoval: None declared.


THU0189

SAFETY OF FOUR TREATMENT REGIMENS IN EARLY RHEUMATOID ARTHRITIS

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Objectives: To compare safety data in patients (pts) with early (≤ 2 years duration) RA who were randomised in the four treatment regimens (MTX, MTX + BiD, MTX + a csDMARD, MTX + a csDMARD + BiD).

Methods: One hundred forty-one pts with RA of less than 2 years duration (122 women, mean age 51 years, mean disease duration 24 weeks, mean DAS 28 5.9; 84% RF-positive,59% ACPA-positive) were randomly allocated to receive one of the following treatment regimens: methotrexate (MTX, up to 20 mg/week,
DERMATOLOGICAL GUIDELINES FOR MONITORING METHOTREXATE TREATMENT REDUCE DRUG-SURVIVAL COMPARSED TO RHEUMATOLOGICAL GUIDELINES

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Background: Methotrexate (MTX) is widely used in the treatment of psoriasis and psoriatic arthritis (PsA). To prevent MTX-induced adverse events dermatological MTX guidelines advise a higher number and frequency of blood tests than rheumatological guidelines (1,2). These differences are not based on evidence indicating a higher risk for patients with psoriasis compared to PsA.

Objectives: Compare the effects of MTX monitoring strategies by rheumatologists and dermatologists.

Methods: Patients with psoriasis or PsA in a Dutch teaching hospital. Inclusion criteria: start methotrexate (MTX) between 2006 and 2012 and scheduled follow-up by dermatologist or rheumatologist. Exclusions: incomplete availability of lab data. Start and stop dates and dosing of MTX and folinic acid, reasons for withdrawal of MTX, numbers and results of laboratory tests performed for MTX safety, occurrence of any serious adverse event (SAE) were retrieved from electronic records.

Results: PsA patients used higher initial and maximum doses of MTX and folinic acid, but psoriasis patients had a higher frequency of abnormal liver function tests, resulting in a striking difference in withdrawal of MTX (Table). In PsA MTX was more often withdrawn for remission, and less frequently for ineffectiveness leading to longer drug survival in the first course of treatment. There were no differences in the occurrence of SAE or death between these groups. Hospital admissions related to infection were recorded in 6 (3.1%) PsA vs 4 (2.1%) psoriasis patients.

Conclusions: In most cases side effects were moderate or minimal. The most serious side effects, leading to the discontinuation of the therapy, were registered in LEF group. There was no withdrawal of treatment in MTX-P group. Safety profile was the same in all groups.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6717

THU0190

[Table 1. MTX dose, lab results, and reasons for withdrawal]

THU0191

EFFECTS OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, ON PATIENT-REPORTED OUTCOMES IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Improvements in patient-reported outcomes (PROs) have been reported in the global population of the Phase (P)2, P3 and long-term extension (LTE) tofacitinib studies.

Objectives: To explore the effect of tofacitinib on PROs in Japanese patients (pts) with RA.

Methods: In this post hoc analysis, data from Japanese pts with RA were obtained from two 12-week randomised dose-finding P2 studies in methotrexate (MTX) inadequate responder (IR) and DMARD-IR pts (NCT00603512; A3921039 and NCT00687193; A3921040), one 24-month P3 study in MTX-IR pts (ORAL Scan; NCT00847619; A3921044) and an open-label LTE study in pts who completed a qualifying P2 or P3 study (NCT01661661; A3921041; completed April 2014). Pts received tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO) (P2 and ORAL Scan; no PBO in LTE). In ORAL Scan, non-responder BID pts advanced to tofacitinib at Month 3; all remaining pts were advanced at Month 6. PROs included: mean change from baseline in Pts Global Assessment of Arthritis (PGA; visual analogue scale [VAS]), Physician's Global Assessment of Arthritis (PGA; VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Pain (VAS), Functional Assessment of Chronic Illness Therapy - Fatigue (FACT-F), Medical Outcomes Study (MOS) Sleep Scale and Short-Form Health Survey (SF-36) domain scores. Significance was declared for p ≤ 0.05 for the P2 and P3 studies reported here.

Results: The analysis included 238 pts from P2 studies, 118 pts from ORAL Scan and 486 pts from the LTE study. Demographics and baseline characteristics were similar between treatment groups for all studies. In P2 studies at Week 12, tofacitinib 5 and 10 mg BID demonstrated significantly greater improvements from baseline vs PBO in PGA, PGA, HAQ-DI, Pain, FACT-F, MOS Sleep Scale and in 4 (Functional Physич [F]), Role-Physical [RP], Bodily Pain [BP] and General Health [GH]) of the 8 SF-36 domain scores (Table). Significant improvements in PGA, PGA, HAQ-DI, Pain and FACT-F vs PBO were seen as early as Week 2. In ORAL Scan at Month 3, statistically significant improvements from baseline in PGA, PGA, HAQ-DI and Pain were seen for both tofacitinib 5 and 10 mg BID vs PBO (Table) and these were maintained to Month 24. Significant improvements vs PBO as early as Month 1 were seen for PGA (tofacitinib 10 mg BID) and Pain (both doses). In the LTE study, mean changes from LTE study baseline in PGA, PGA, HAQ-DI and Pain were -32.5, -40.8, -0.5 and -32.9, respectively, for all tofacitinib doses at Week 2, and -40.7, -50.2, -0.7 and -42.4, respectively, at Week 168. Mean changes from baseline in SF-36 domain scores at Week 12 and
Conclusions: Tofacitinib 5 and 10 mg BD significantly improved PROs in Japanese pts with RA enrolled in the P2, P3, and LTE studies.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Haines of CMC and was funded by Pfizer Inc.


DOIs: 10.1136/annrheumdis-2017-eular.1402

THU0192 INFORMING PATIENTS ABOUT METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS WITH PATIENTS IN THE UNITED KINGDOM – A SURVEY OF RHEUMATOLOGISTS STRATEGIES

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Background: Rheumatologists are the primary prescribers of methotrexate (MTX) for the treatment of rheumatoid arthritis (RA) in the United Kingdom (UK), however rheumatologists’ views on their clinical practices are largely unknown. The aim of this study was to conduct a qualitative sub-study in a UK cohort that highlighted a number of factors that contributed to their ability to discuss and commence MTX, which included how emotionally and cognitively prepared patients were to discuss treatments.

Objectives: The aims of this study were: 1) To establish the views of rheumatologists about MTX for the treatment of rheumatoid arthritis (RA), 2) To examine if rheumatologists’ views influenced discussing or commencing MTX during the initial consultation.

Methods: An online survey was designed and subsequently refined based on interviews with rheumatologists in the UK. The survey asked rheumatologists about their clinical setting, and their views and practices with respect to treating RA with MTX. Rheumatologists were asked how often specific pieces of MTX information were discussed during a consultation to commence MTX (5 = Always to 1 = Never). They were also asked to identify the barriers to discussing these issues.

Results: Ninety-six rheumatologists were included in the study (58% of eligible respondents), representing a broad range of specialties across the UK, including those based in teaching hospitals and/or in the private sector. The questionnaire was structured to follow the patient journey of initiating MTX therapy, with questions being asked about different stages of the process: the patient’s readiness for commencing MTX, the rheumatologist’s views on whether MTX information was discussed, and any barriers to discussing these topics.

Conclusions: Currently UK rheumatologists convey a large amount of information to patients during early consultations. Almost half of rheumatologists identified the need to communicate large amounts of information in clinical consultations as a barrier to discussing MTX therapy. These data reflect the challenge clinicians face in trying to execute effective shared decision-making practices. Strategies to address patients’ emotional responses to their diagnosis and being overloaded with MTX information are needed. Staggering presentation of information during clinical consultations may benefit some patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2429

THU0193 REESTABLISHMENT OF EFFICACY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN RHEUMATOID ARTHRITIS PATIENTS AFTER TEMPORARY DISCONTINUATION


Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: To assess the efficacy and safety of tofacitinib after temporary discontinuation and reinstitution of therapy in RA patients (pts).

Methods: Data were collected from a randomised, parallel-group (grp), controlled, open-label, multicentre, double-blind placebo-controlled, 2-phase, 2-treatment, 3-treatment, 18-month, randomized, double-blind extension (LTE) study (NCT00413699). Pts were ≥18 years of age with active RA and had received tofacitinib 10 mg BD for ≥3 months. The sub-study included 2 treatment (tx) grps: "continuous tx" (tofacitinib 10 mg twice daily [BID] as monotherapy or with methotrexate [MTX]) and "interrupted tx" (tofacitinib withdrawn for 2
weeks post-randomisation [Day 1–Day 15; Visits 1–3], then tofacitinib 10 mg BD reintroduced as monotherapy or with MTX at Visit 3); randomisation was stratified by MTX use. Pneumococcal and influenza vaccines were administered to all pts on Day 8 (Visit 2; vaccine titers reported previously)\(^1\). Blood samples were taken on Days 8, 15 (Visit 3) and 43 (Visit 4). Efficacy endpoints included change from baseline in C-reactive protein (CRP), Health Assessment Questionnaire Disability Index (HAQ-DI) and Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR]) at each visit. A mixed-effects model with repeated measures was used to evaluate treatment effect at each visit. Analyses for efficacy were exploratory, with no multiplicity adjustment for comparisons.

Results: Of the 199 pts in this analysis (continuous, n=100; interrupted, n=99), 117 received concomitant MTX. At LTE study baseline (BL) in the continuous and interrupted grps, respectively: 81.8/83.8% of pts were white, 84.8/86.9% were female and mean age was 55.0/53.9 years. BL (Day 1) values for CRP, HAQ-DI and DAS28-4[ESR] were generally similar between groups. At Day 8, mean CRP and DAS28-4[ESR] significantly increased from BL for interrupted vs continuous tx; HAQ-DI values were similar between grps (Figure). As expected at Day 15, mean CRP, HAQ-DI and DAS28-4[ESR] significantly increased from BL for interrupted vs continuous tx. After tofacitinib re-introduction for 28 days (Day 43), changes in CRP, HAQ-DI and DAS28-4[ESR] were similar between grps and approached BL levels. Adverse events (AEs) were experienced by 35.4% and 49.5% of pts receiving interrupted and continuous tx, respectively. The most frequent treatment-emergent AEs were bronchitis and upper respiratory tract infection (each AE: 6 pts) and vaccination-related immunisation reaction, myalgia and rash (each AE: 5 pts). Serious AEs occurred in 3 pts (3%) in each grp. In total, 1 pt (1%), in the interrupted tx grp, discontinued due to a study-drug related AE; no pts discontinued due to disease flare.

Figure. LS mean change from BL in RA efficacy endpoints over time from a vaccine sub-study with temporary tofacitinib dose interruption

Conclusions: Efficacy of tofacitinib 10 mg BD can be re-established following loss of efficacy during temporary (2 weeks) tx discontinuation in pts with RA. Pts receiving continuous tx maintained efficacy throughout the study. Further investigations are required.

References:

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Haines of CMC and was funded by Pfizer Inc.

Disclosure of Interest: was provided by K Haines of CMC and was funded by Pfizer Inc.

Acknowledgements:

Disclosure of Interest: was provided by K Haines of CMC and was funded by Pfizer Inc.
score ranged from 6.2–6.5. Tofacitinib 5 and 10 mg BID achieved higher ACR responses and greater changes from baseline in DAS28-4(ESR) and HAQ-DI scores vs PBO at Month 3 in both populations (Table). Numerically higher proportions of non-MTX csDMARD-IR pts achieved efficacy outcomes vs 2nd-line population. CIRs for SAECs, DAs due to AEs and AEs of special interest were generally similar across groups. CIRs for TEAEs were higher with PBO vs tofacitinib. AE frequency was generally lower in the non-MTX csDMARD-IR population vs non-MTX csDMARD-IR POP.

Table: Efficacy outcomes of Month 3 and safety outcomes to Month 24

<table>
<thead>
<tr>
<th>Tofacitinib 5 mg BID</th>
<th>Tofacitinib 10 mg BID</th>
<th>PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-MTX csDMARD-IR</td>
<td>45.1%</td>
<td>55.9%</td>
</tr>
<tr>
<td>Non-MTX csDMARD-IR</td>
<td>57.3%</td>
<td>63.2%</td>
</tr>
<tr>
<td>MTX-IR</td>
<td>7.4%</td>
<td>8.2%</td>
</tr>
<tr>
<td>MTX-IR</td>
<td>9.1%</td>
<td>11.6%</td>
</tr>
</tbody>
</table>

Methods: Incidence rates (IR; pts with events per 100 pt-years [pyrs] exposure) were calculated using pooled data from randomised controlled trials (RCT) and long-term extension (LTE) studies. Two Phase (P) 1 studies, 9 P2 trials 105 months of observation.

Results: The tofacitinib P123LTE dataset included 6194 pts with a total exposure of 19 385 pt-yrs. A total of 64 bDMARD articles were retrieved for analysis, representing 58 unique studies and approximately 27 000 pts. Study populations were generally consistent. LTE studies were typically more than 5 yrs age and estimated mean percentage of pts who were female was 74–84% and mean baseline C-reactive protein level was 20–30 mg/L. The IR (95% confidence interval [CI]) of malignancy for tofacitinib in the P123LTE dataset was 0.89 (0.76, 1.04) (Figure). Estimated IRs (95% CI) of malignancy were 0.75 (0.55, 1.01) for abatacept, 1.06 (0.41, 2.74) for rituximab, 1.02 (0.69, 1.52) for tocilizumab and 0.95 (0.79, 1.14) for tumour necrosis factor inhibitors (adalimumab, certolizumab, etanercept, golimumab and infliximab) (Figure).

Conclusions: This analysis indicates that tofacitinib is associated with similar efficacy and safety outcomes compared with established treatments for RA. Tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background disease-modifying antirheumatic drugs (DMARDs) was generally well tolerated with similar AEs as placebo. Tofacitinib may be considered for rheumatoid arthritis patients who have a contraindication to or refuse treatment with traditional DMARDs.
modifying antirheumatic drugs (DMARDs). Primary endpoints were adverse events (AEs) and confirmed laboratory safety data. Secondary endpoints included clinical efficacy measures (American College of Rheumatology [ACR] 20/50/70 response rates, Disease Activity Score using 28 joint counts and erythrocyte sedimentation rate [DAS28-4(ESR)], Health Assessment Questionnaire-Disability Index [HAQ-DI]) and clinical disease activity index (CDAI). Safety data were included up to Month 105 and efficacy data up to Month 90 (n=100 at Month 96).

**Results:** A total of 4967 patients were treated (mean [±SD]: 1215 [3182] days). Total tofacitinib exposure was 16,117 patient-years; 77.4% of patients maintained their initial dose. In total, 2370 patients (47.7%) discontinued (AEs: 1131 [22.8%]; insufficient clinical response: 175 [3.5%]). The most common AE classes were infections and infestations (68.9%) and musculoskeletal/connective tissue disorders (39.0%). The most common AEs were nasopharyngitis (18.7%), upper respiratory tract infection (17.2%), bronchitis and urinary tract infection (12.2%) each. Serious AEs occurred in 28.6% of patients and serious infection events (SIEs) in 8.8% of patients. Malignancies, excluding non-melanoma skin cancer, were reported in 3.0% of patients. Incidence rates (IR; patients with events per 100 patient-years) for AEs of interest (with 95% confidence intervals [CIs]) and laboratory observations are provided in Table 1. IRs for SIEs and malignancies through Month 105 did not increase compared with reported data through Month 96. No new safety risks were identified. Clinical responses were sustained from Month 1 to Month 90 (Table 2).

**Conclusions:** In patients with RA who remained in the LTE studies, tofacitinib (5 or 10 mg BID) with or without background DMARDs was associated with consistent safety through Month 105 and sustained clinical efficacy through Month 90.

**References:**


**Comparison of Efficacy Between Combination Therapy with IGRATIMOD and SULFASALAZINE with RHEUMATOID ARTHRITIS: PROPENSITY SCORE ANALYSIS**

**Background:** Igratimod (IGU) is a small-molecule disease-modifying antirheumatic drug (DMARD) that has been shown to suppress inflammation via the inhibition of nuclear factor-kappa B activation in vitro. The efficacy of combination therapy with IGU and methotrexate (MTX) has been demonstrated in comparison with that of placebo in rheumatoid arthritis (RA). However, its efficacy in comparison with other DMARDs such as sulfasalazine (SSZ) has not been elucidated.

**Objectives:** To clarify the efficacy of combination therapy with IGU in comparison with that of SSZ with MTX in typical clinical practice.

**Methods:** We analyzed data from 16,825 RA patients registered in a large database (NinJa; National Database of Rheumatic Diseases by IR-net in Japan) from April 2001 to March 2015 (1). In this study, we compared the two groups who received IGU or SSZ in addition to methotrexate in the earlier year. We excluded patients who started receiving biologic DMARDs, IGU or SSZ the year prior to the study period, and those whose regimes were changed to other DMARDs such as tocilizumab and b-cellululamine. Baseline characteristics were compared using the t-test, Wilcoxon rank-sum test, or chi-square test. Fisher analysis was conducted for both outcomes. The predicted probability of IGU treatment was calculated by fitting a logistic regression model using all clinically relevant variables as presented in Table 1. Moreover, to reduce the effect of treatment-selection bias and potential confounding in this observational study, we performed rigorous adjustment for significant differences in the baseline characteristics of patients with propensity-score matching using the following algorithm: 1:1 optimal match with a ±0.15 caliper and no replacement. We used the standardized difference to measure covariate balance, whereby a standardized mean difference of ≤0.1 represents meaningful imbalance. The outcome was remission rate with disease activity score 28 CRP (DAS28-CRP) in the year after initiation of IGU or SSZ therapy.

**Results:** The group that received IGU in addition to MTX included 66 patients; the other group that received SSZ in addition to MTX included 163 patients. Table 1 shows the results of the pre- and post-propensity score matching of patients' characteristics. Sixty-six patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 77.2% (44/57 patients) and 71.7% (38/53 patients; P=0.52) in the IGU and SSZ groups, respectively.

**Conclusions:** Combination therapy with IGU or SSZ and methotrexate for rheumatoid arthritis did not show a significant difference in disease activity. Further studies are needed.

**References:**
Tofacitinib improves left ventricular mass and cardiac output in patients with rheumatoid arthritis

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Background: Rheumatologists need to develop primary prevention strategies for cardiovascular disease (CVD) in rheumatoid arthritis (RA) patients. We reported tofacitinib (Tofa) improved arterial stiffness in RA patients. RA is associated with an increased left ventricular mass index (LVMI), a strong marker of cardiovascular mortality. There is no evidence that Tofa affects on left ventricular (LV) morphology and function.

Objectives: To study the effect of Tofa plus methotrexate (MTX) on LV morphology and function in MTX resistant active RA patients, in a cohort study design.

Methods: Patients eligible if they had at least disease despite treatment with MTX. All patients have no steroids, and no previous history of CVD. Consecutive 28 patients with moderate to severe active RA patients (DAS28≥3.2) despite MTX were received Tofa plus MTX. LV morphology and function was assessed with cardiac-MRI at baseline and 24 weeks follow-up. Cardiovascular risk factors and clinical data were collected at regular visits.

Results: 24 patients completed 24 weeks. Left ventricular mass index (LVMI) was attenuated significantly by Tofa (week 0-week24, -12.4±5.4 g/m²; p<0.0002).

Cardiac output (CO) was attenuated significantly by Tofa (week 0-week24, -0.87±0.21/min). DAS28 and CRP improved significantly by Tofa (week 0-week24; DAS28: -2.26±0.91; CRP: 14.1±8.7 mg/dl) (p<0.05). LVMI and CO in this study. Observationally, 4 cases significantly improved right ventricular mass as well as left ventricular mass (20% improved right ventricular mass index from baseline).

Conclusions: Tofa improved LVMI and CO in active RA despite MTX. TCZ improves LVMI and CO independently of its effects on disease activity. Tofa might improve right ventricular mass. JAK-STAT pathway blocking, may prevent cardiovascular morbidity and mortality in RA.

References:


Acknowledgements: Thanks for Noriko Kukawa to calculate data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1098
**BACKGROUND:** In the developing world rheumatologists and their patients are struggling to implement target therapy in established Rheumatoid Arthritis (RA) which means they can hardly establish remission and low disease activity which is the mainstay of the RA treatment. The main reason is the lack of conventional synthetic and biological (c and b) DMARDs in the therapeutic armamentarium as well as their high cost which increases already difficult burden of RA.

**OBJECTIVES:** The aim of the study is to evaluate the RA treatment and treatment expenses in a group of patients with established RA in FYROM including the availability of DMARDs.

**METHODS:** We have conducted a cross-sectional study at the University Rheumatology Clinic in Skopje, including 100 patients with established RA, who fulfilled RA classification criteria from 2010. Physical examination, laboratory analyses and BASDAI were performed and all patients filled a questionnaire with 13 questions about treatment expenses and availability.

**RESULTS:** There were 82 females and 18 males, with mean age of 59 and disease duration of 8.3 (SD 7.3) years and moderate disease activity DAS28 3.9±1.47 and 75% of seropositive RA (double positive 30%, Anti-CCP positive 30%, RF positive 15%) with mean CRP of 21.5 mg/L. They spend from 10 to 100 Euros monthly (on average 27.1±17.6) for the c DMARDs therapy. Almost 85% think that the c DMARDs therapy is too expensive for them and 100% of them could not afford to pay or co-pay for b DMARDs. Most of the patients (49%) are using single c DMARDs. Double and triple c DMARD therapy is used by 32% vs 17%, respectively. Even though it is highly effective, patients consider triple c DMARD therapy expensive and with very low compliance because of the high costs and low tolerability. Only 2% of the patients are using b DMARDs using rituximab, the only available biologic DMARD therapy in FYROM. Around 70% are taking low dose prednisolone. Almost 50% of the patients cannot take the c DMARD therapy with a prescription and have to buy their DMARDs without any coverage from the insurance fund and the same percent have problems to find the c DMARDs with prescription because it is not available. Almost half of the patients have heard about the b DMARDs, most of them from their rheumatologist and 54% of them would like to receive it. The patient’s reasons for taking b DMARDs are presented in Graph 1.

**CONCLUSIONS:** High expenses and low availability of c DMARDs on prescription and the urgent need for b DMARDs are adding the burden of RA in developing countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars conventional DMARDs and at least partial coverage of biologic DMARDs, countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars conventional DMARDs on prescription because it is not available. Almost half of the patients have heard about the b DMARDs, most of them from their rheumatologist and 54% of them would like to receive it. The patient’s reasons for taking b DMARDs are presented in Graph 1.

**REFERENCES:**
2. O’Dell JR. Therapies for active rheumatoid arthritis after methotrexate failure might be highly appreciated in the future, especially anti-TNF agents by the insurance companies. The use of biosimilars conventional DMARDs and at least partial coverage of biologic DMARDs, countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars conventional DMARDs and at least partial coverage of biologic DMARDs, countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars conventional DMARDs and at least partial coverage of biologic DMARDs, countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars conventional DMARDs and at least partial coverage of biologic DMARDs, countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars
EFFECTS OF THE JAK1-SELECTIVE INHIBITOR FILGOTINIB ON MULTIBIOMARKER DISEASE ACTIVITY SCORES IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE


Objectives: To evaluate the effect of filgotinib compared to placebo on a multi-biomarker disease activity score (MBDA score) that measures 12 disease-related biomarkers of inflammation and joint injury in RA patients taking background MTX.

Methods: RA patients treated with filgotinib in combination with MTX had significant reductions in the MBDA score that was driven by key RA biomarkers encompassing both inflammation and joint injury. These findings are consistent with the filgotinib efficacy observed in RA patients over 12 weeks.

Results: RA patients treated with filgotinib compared to placebo had statistically significant reductions in the median MBDA score and subcomponents. These reductions were observed as early as week 4, with the largest reductions in YKL-40 and MMP-3. Median percent changes from baseline for biomarkers are reported. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups vs. placebo.

Conclusions: Filgotinib in combination with MTX for 12 weeks was associated with statistically significant reductions in multiple markers of inflammation linked to various pathologic cell types and processes in rheumatoid arthritis patients.


DOI: 10.1136/annrheumdis-2017-eular.5738

THU0206 THE JAK1-SELECTIVE INHIBITOR FILGOTINIB REDUCES MULTIPLE MARKERS OF INFLAMMATION LINKED TO VARIOUS PATHOLOGIC CELL TYPES AND PROCESSES IN RHEUMATOID ARTHRITIS PATIENTS


Background: JAK1, 2, 3 and TYK2 are cytoplasmic tyrosine kinases that mediate intracellular signaling of many cytokines and growth factors. Filgotinib (GLP00634, GS-6034) is a JAK inhibitor with high selectivity for JAK1 over other JAK family members. Filgotinib has a favorable safety and efficacy profile in two Phase 2B studies in active rheumatoid arthritis (RA) patients who were MTX-inadequate responders. These findings are consistent with the filgotinib efficacy observed in RA patients over 12 weeks.

Methods: Serum samples from RA patients who were on a stable dose of MTX and received either placebo (PBO) or filgotinib 100mg or 200mg once daily (QD), were tested for MBDA components (Crescendo Biosciences, CA, US) at baseline, week 4 and week 12. Median % change from baseline for MBDA score and individual components are reported for week 4 and week 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups vs. PBO.

Results: Baseline MBDA scores and component values (median; interquartile range) were similar in PBO (55; 45–64), 100mg QD (58; 42–66), and 200mg QD (59; 50–67.5) treatment groups. Filgotinib treated patients had reductions in the MBDA score comparable to baseline at the 100mg and 200mg QD dose levels, but not in the PBO group. At both weeks 4 and 12, these reductions in the filgotinib treated groups were significantly different from the PBO group. Most of the individual components contributed to the decrease in MBDA score, but the largest reductions were observed for serum amyloid A (SAA), C-reactive protein (CRP), interleukin-6, and the biomarkers of joint-damage, matrix metalloproteinase 3 (MMP3), MMP1, vascular endothelial growth factor (VEGF), and YKL40 (human cartilage glycoprotein 39). There was an increase in leptin and no change in epidermal growth factor (EGF) concentrations.

Conclusions: Filgotinib treatment induced a dose-dependent and significant decrease
in a variety of biomarkers implicated in RA pathogenesis including inflammation (IL-1), IL-6, TNFα and SAA), matrix degradation and cartilage destruction (MMP1 and MMP3), immune cell trafficking (CXCL10, ICAM-1 and VCAM-1) and angiogenesis (VEGFC). Cytokines involved in T1f (IFNγ, IL-2, IL-12) and T17 (IL-17A, IL-21, IL-23) cell subset differentiation and activity were significantly differentially expressed. Additionally, decrease in the B-cell chemoattractant CXCL13 and the myeloid growth factor GM-CSF supports the anti-inflammatory effects of filgotinib treatment.

Table 1. Median percent change of biomarkers at week 12 from baseline for PBO and 200mg QD dose

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PBO</th>
<th>Filgotinib 25mg</th>
<th>Filgotinib 100mg</th>
<th>Filgotinib 200mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAFF</td>
<td>-2</td>
<td>-8</td>
<td>-6</td>
<td>0</td>
</tr>
<tr>
<td>CRP</td>
<td>-8</td>
<td>-23</td>
<td>-21</td>
<td>0</td>
</tr>
<tr>
<td>IL-17A</td>
<td>0</td>
<td>-26</td>
<td>-28</td>
<td>0</td>
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<tr>
<td>IL-10</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IL-12</td>
<td>-7</td>
<td>-27</td>
<td>-26</td>
<td>0</td>
</tr>
<tr>
<td>IL-17</td>
<td>-2</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>INFP1</td>
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<td>IL-6</td>
<td>0</td>
<td>-5</td>
<td>-6</td>
<td>0</td>
</tr>
<tr>
<td>IL-13</td>
<td>1</td>
<td>-5</td>
<td>-9</td>
<td>0</td>
</tr>
<tr>
<td>IL-17A</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IL-18</td>
<td>2</td>
<td>-26</td>
<td>-26</td>
<td>0</td>
</tr>
</tbody>
</table>
| p-values comparing changes between filgotinib and PBO groups: NS, p>0.05; *p<0.05; **p<0.01; ***p<0.001.

Conclusions: Treatment with filgotinib decreased several factors that have key roles in RA for matrix degradation, cartilage destruction, angiogenesis, leukocyte adhesion and recruitment. The changes were accompanied by decreases in cytokines that promote and activate T H1, T H17, B-cells and myeloid cells that are important in RA. These findings provide insights into filgotinib mechanism of action and are consistent with its efficacy observed in RA patients.

Disclosure of Interest: P. Tseng: Consultant for: Galapagos NV, Pfizer, Lilly. UCB, GSK, R. Westhovens: None declared, A. Van der Aa Employee of: Galapagos NV, C. Jamoul Employee of: Galapagos NV, W. Li Employee of: UCB, GSK, R. Westhovens: None declared, A. Ohishi: None declared, M. Shinohara: None declared, G. Tsuji: None declared, Shinko Institute for Medical Research; 2Center for Rheumatic Diseases, Shinko Hospital; 2Graduate School of Medicine, Kobe University, Kobe, Japan

Background: Detection of the intracellular levels of polyglutamated MTX (MTX-PGn) can predict response of MTX or possibly its adverse effects. As efficacy and toxicity of MTX differs among individual patients, we had proposed a predictive model for MTX efficacy consisting of 9 SNPs (2015 EULAR). In the present study, we measured erythrocyte MTX-PGn in RA patients with low disease activity for long time receiving a stable dose of MTX, investigated their associations with genetic polymorphisms, and speculated MTX dose required to reach effective MTX-PGn levels.

Objectives: To investigate if erythrocyte MTX-PGn concentration is associated with the 9 SNPs in 7 genes reportedly related to MTX-efficacy in RA patients with low disease activity.

Methods: The study was cross-sectional using 121 adult patients with RA in Shinko Hospital. All patients enrolled had received a stable dose of MTX (mean 8.9±0.3mg/week), and kept lower disease activity (DAS28-CRP 2.06±0.79 mg/L) for at least 3 months. Concentrations of MTX-PG with 1-5 glutamate residues (PG1-PG5) in erythrocytes were quantitated by LC-ESI-MS/MS as described by den Boer et al. Nine SNPs in 7 genes previously found to associate with efficacy of MTX by us were genotyped by RT-PCR (Applied Biosystems, Inc.). First, association of the 9 SNPs with concentrations on MTX-PGn was analyzed by one-way layout (Wilcoxon signed-rank test). Secondly, multivariate logistic regression analyses were performed to estimate roles of MTX dose and polymorphisms in concentrations of MTX-PGn.

Results: Total PGn concentrations were 82.1±31.7 nmol/L (m±SD) and positively correlated with MTX dose (Rs=0.4104, p<0.001), but range of concentration was rather wide even if the dose was same. By one-way layout, GGH c.452C>A, EPHX1 c.357G>A, SLC19A1 c.80G>A, SLC28A3 c.267G>A, and SLC28A3 c.267G>T were related to MTX doses. Next, we investigated roles of MTX dose and 9 SNPs in maintenance of MTX-PGn concentrations as by multiple regression analyses. As PG1 levels were related to GGH c.452C>T but not to MTX dose, PG1 levels were 38.2±19.6 and 54.8±21.5 nmol/L in CC and CT genotypes, respectively (P=0.0291). MTX dose was strongly associated with PG3 levels as well as with those of PG4. MTX-PG3 levels were regulated as follows; MTX-PG3 (nmol/L) = -0.035 +2.04 * MTX dose [2.34 * SLC19A1 c.80G>A +2.04 * SLC28A3 c.267G>A] when upper and lower limits of them were defined, we can speculate MTX dose to reach the effective levels for individual patients. However, the ranges of effective levels were rather wide, suggesting that effectiveness of MTX may depend on not only concentrations of MTX-PG but also responsiveness to MTX-PG.

Conclusions: We measured erythrocyte MTX-PGn in RA patients with low disease activity and investigated for their associations with MTX dose and genetic polymorphisms. We could speculate MTX dose required to reach possible effective MTX-PG levels in individual patient.

LYMPHOCYTE SUBSETS IN BIOPSY SPECIMEN ARE ASSOCIATED WITH SPONTANEOUS REGRESSION OF LYMPHOPROLIFERATIVE DISORDERS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE

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Background: Patients with rheumatoid arthritis (RA) have a high risk for lymphoproliferative disorders (LPDs). An LPD in a patient treated with methotrexate (MTX) is known as MTX-associated LPD (MTX-LPD), which is classified among immunodeficiency-associated lymphoproliferative disorders (ID-LPD) as “other interstitial lymphoproliferative disorder” in the 2016 World Health Organization Classification of Haematopoietic and Lymphoid Tissues (1). We previously reported that MTX is an independent risk factor for LPD onset in Japanese patients with RA (2).

In MTX-LPD, MTX withdrawal can result in spontaneous regression of LPD. In addition, limited evidence indicates that Epstein–Barr virus infection is related to spontaneous regression of MTX-LPD. No biomarker has been identified that predicts spontaneous regression of MTX-LPD.

Objectives: To identify a biomarker that predicts spontaneous regression of MTX-LPD in RA patients.

Methods: We enrolled RA patients from Kagawa Prefecture, Japan, who developed MTX-LPD during the period from June 2010 through December 2016. RA was diagnosed in accordance with the American College of Rheumatology 1987 classification criteria and was treated with disease-modifying antirheumatic drugs, including MTX. The patients were divided into two groups: those followed-up after discontinuation of MTX alone (MTX withdrawal group) and those who received chemotherapy at 1 month or later after MTX discontinuation (chemotherapy group). The following variables were compared between groups: change in peripheral lymphocyte subsets after MTX discontinuation, serum soluble interleukin-2 receptor, and lymphocyte subsets and Epstein–Barr virus–encoded RNAs in a biopsy specimen from a lesion.

Results: We enrolled 43 MTX-LPD patients (29 in the withdrawal group and 14 in the chemotherapy group) and 22 for analysis of lymphocyte subsets in a lesion specimen (11 each in the withdrawal group and chemotherapy group). Peripheral lymphocyte counts were significantly higher after MTX discontinuation in the withdrawal group. Analysis of lymphocyte subsets from lesion specimens revealed significantly higher CD8-positive lymphocyte counts in the chemotherapy group than in the withdrawal group.

Conclusions: Lymphocyte count differed before and after MTX discontinuation, and a higher CD8-positive lymphocyte count in a lesion specimen was associated with spontaneous regression of MTX-LPD. These findings may help identify a predictive marker for MTX-LPD treatment and management.

References:

Disclosure of Interest: None declared.
DOI: 10.1136/annrheumdis-2017-eular.4683

CHANGES IN HEMOGLOBIN LEVELS UPON TREATMENT WITH ABT-494, A SELECTIVE JAK-1 INHIBITOR, AND RELATION TO BASELINE LEVELS OF C-REACTIVE PROTEIN

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Background: Patients with rheumatoid arthritis (RA) often have inflammation-related anemia of chronic disease, partially due to IL-6 and its induction of hepcidin. High levels of the inflammatory marker C-reactive protein (CRP) are largely induced by IL-6. Treatment with JAK inhibitors has been associated with both rise and fall in hemoglobin (Hb) levels, possibly due to inflammation control and inhibition of JAK2 (which is involved in erythropoiesis), respectively 1, 2.

Objectives: To examine the association of changes in Hb upon treatment with ABT-494 with baseline (BL) CRP levels.

Methods: This post hoc analysis used data from two phase 2b randomized controlled trials (RCT) of ABT-494 in RA pts with inadequate responses to TNF inhibitors (TNF-IR, BALANCE-1) 3, and in pts with inadequate responses to methotrexate (MTX-IR, BALANCE-2) 4. The analyses included pts receiving ABT-494 at 8 or 12 mg. Pts were subgrouped by quartiles of BL CRP. For each RCT, and for the pooled data from both, changes from BL in Hb (g/dL) were determined after 12 weeks (wk) of treatment with ABT-494, for the overall population and for pts who achieved ACR20 or DAS28-CRP ≤ 3.2 responses at Wk 12. For ACR20 and DAS28-CRP ≤ 3.2, non-responder imputation was used. For changes in Hb, data are as observed. Significance was determined by ANCOVA.

Background: In pooled data from 110 and 100 pts from BALANCE-1 and -2 respectively, higher BL CRP was associated with smaller mean decreases in Hb at Wk 12 (p < 0.074). In the MTX-IR trial, pts in the highest CRP quartile had a mean increase from BL in Hb (+0.28 g/dL) vs pts in the lower quartiles who had mean decreases in Hb (p < 0.01). In both RCTs, ACR20 or DAS28-CRP ≤ 3.2 responders had smaller decreases in Hb vs non-responders at Wk 12. Among DAS28-IR-p<3.2 responders, pts in the higher CRP quartiles had significantly smaller mean decreases in Hb vs pts in the lower quartiles (p<0.01 for MTX-IR and p<0.05 for TNF-IR pts). Responders in the highest BL CRP quartile also had a mean increase in Hb (+0.31 and +0.54 g/dL for MTX-IR ACR20 and DAS28-IR ≤ 3.2 responders respectively) + 0.15 g/dL for TNF-IR DAS28-IR ≤ 3.2 responders (Fig. 1A–D). While similar trends between BL CRP levels and changes in Hb at Wk 12 were observed among ACR20 or DAS28-IR ≤ 3.2 non-responders, the differences in Hb levels between the quartiles were not significant. Despite the small mean changes, the mean Hb values remained within the normal range for females (lower limit of normal 11.5 g/dL).

Conclusions: Upon treatment with ABT-494, pts with the highest CRP (a potential surrogate for IL-6) at BL had a mean increase in Hb compared to decreases in those with lower CRP. This effect was more apparent in pts with clinical responses. This suggests that effective treatment of RA-associated inflammation with ABT-494 may counterbalance the small Hb reduction associated with JAK inhibition.

References:

Acknowledgements: AbbVie: Study sponsor, involved in study design, data collection, analysis, and interpretation, and in publication writing, review, and final approval. Medical writing: Naina Barretto, of AbbVie.

Disclosure of Interest: V. Strand Consultant for: AbbVie, Afferent, Amgen, Biogen Idec, Bioventus, BMS, Carbylan, Celgene, Celltrion, CORONa, Crescendo, Genentech/Roche, GSK, Hospira, Iroko, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, SKK, Takeda, UCB, Vertex, M. Genovese Grant/research support from: AbbVie, Lilly, Astellas, Vertex, Pfizer, Galapagos, Gilead, Consultant for: AbbVie, Lilly, Astellas, Vertex, Pfizer, Galapagos, Gilead, J. Kremer Grant/research support from: AbbVie, Lilly, Novartis, Pfizer, MedImmune, Sanofi, and Regeneron, Consultant for: AbbVie, Lilly, Novartis, Pfizer, MedImmune, Sanofi, and Regeneron, Employee of: CORONA, M. Schiff Consultant for: AbbVie, Speakers bureau: AbbVie, Y. Li Employee of: AbbVie, J. Sokolove Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.3216
THU0211

META-ANALYSIS OF SERIOUS INFECTIONS WITH BARICITINIB, TOFACITINIB AND BIOLGIC DMARDS IN RHEUMATOID ARTHRITIS

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Background: Tofacitinib is an oral Janus kinase (JAK) inhibitor for the treatment of rheumatoid arthritis (RA). Baricitinib is a JAK inhibitor being investigated for RA. Serious infection events (SIEs) have been reported in RA randomised controlled trials (RCTs) but limited head-to-head data are available to directly compare rates of these events for tofacitinib vs biologic (b)DMARDs and baricitinib.

Objectives: We provide an updated meta-analysis of published RCTs and corresponding long-term extension (LTE) studies to contextualise the risk of SIEs with tofacitinib and baricitinib and extend this work to include the JAK inhibitor baricitinib.

Methods: An initial systematic literature search (Medline, Embase, PubMed and regulatory submission documents) was conducted for SIEs with tofacitinib and bDMARDs (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab). A subsequent systematic literature review of RCTs was conducted using Medline, BIOSIS, Embase and conference abstracts to evaluate SIEs with baricitinib. Incidence rates (IRs; patients per event per 100 patient-years) were calculated for each agent vs control across RCTs up to rescue of patients randomised to receive placebo using the random effects Mantel-Haenszel method. Between-study variances. Risk ratios and risk differences were calculated for each agent vs control across RCTs up to rescue of patients randomised to receive placebo using the random effects Mantel-Haenszel method.

Results: Six RCTs with baricitinib were included in this updated analysis. In the original analysis, 70 RCTs and 18 LTE studies met inclusion criteria for tofacitinib and bDMARDs. The table provides a summary of the meta-analyses conducted for SIE IRs (with and without LTE), risk ratios and risk differences relative to control for both doses of baricitinib, which is consistent with analyses of tofacitinib and bDMARDs. There were limited data to evaluate SIE incidence for baricitinib (4 mg) monotherapy vs in combination with methotrexate (MTX); the RA-BEGIN study showed IRs of 3.77 (1.7, 8.4) and 2.33 (0.97, 5.59), respectively; when administered in combination with MTX, the IRs were 3.44 (2.41, 4.76) and 3.42 (2.42, 4.70) for 5 and 10 mg BID monotherapy respectively; when administered in combination with MTX, the IRs were 3.44 (2.41, 4.76) and 3.42 (2.42, 4.70) for 5 and 10 mg BID monotherapy respectively.

Table: Serious infection incidence rates, risk ratios and risk differences for tofacitinib and biologic DMARDs and baricitinib

<table>
<thead>
<tr>
<th>Drug</th>
<th>Incidence rate (IR) per 100 pt yr</th>
<th>Risk ratio (95% CI)</th>
<th>Risk difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tofacitinib</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baricitinib 4 mg</td>
<td>3.46 (2.38, 5.04)</td>
<td>0.72 (0.59, 0.87)</td>
<td>-0.01 (0.06, 0.05)</td>
</tr>
<tr>
<td>Baricitinib 10 mg</td>
<td>3.83 (2.60, 5.60)</td>
<td>0.59 (0.50, 0.70)</td>
<td>-0.01 (0.06, 0.05)</td>
</tr>
</tbody>
</table>

Conclusions: The results from these meta-analyses suggest that the risk of SIEs (IRs, risk ratios and risk differences) with tofacitinib is comparable with published rates for bDMARDs and baricitinib in patients with severe RA.

References:

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Nicholson and C Viegelmann of CMC and funded by Pfizer Inc.


THU0212

THE IMPROVEMENT OF ULTRASONOGRAPHIC FINDINGS FOR 24 WEEKS MAY PREDICT REMISSION AT 52 WEEKS IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS TREATED WITH IGuratIMOD THERAPY

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Background: Iguratimod (IGU) suppressed tumor necrosis factor alpha-induced production of interleukin (IL)-6, IL-8, and monocyte chemotactractor protein 1 via inhibition of nuclear factor kappa B activation in cultured human synovial cells and human acute monocytic leukemia cells. We reported the clinical efficacy of IGU at ACR2014 and EULAR2015. However there is still few studies of improvement of ultrasonographic findings in rheumatoid arthritis (RA) treated with IGU.

Objectives: To evaluate the efficacy of IGU therapy in patients with RA using ultrasonography (US).

Methods: Participants comprised 54 Japanese RA patients who had recently received IGU. All patients had a diagnosis of RA according to the 2010 ACR/EULAR criteria. Patients underwent clinical and laboratory assessments from baseline to 52 weeks. US assessments at baseline, 12, and 24 weeks. Clinical findings related to RA were as follows: tender and swollen joint count, patient's and physician's global assessment of disease activity, ACR/EULAR criteria. Patients underwent clinical and laboratory assessments from baseline to 52 weeks.

Results: The patients included 16 males and 38 females. The mean age was 65.4±11.6 years; the mean disease duration was 9.3±10.8 years; and the number of MTX combination, other DMARD excluded combination, IGU monotherapy and Biological combinations were each 32, 10, 8 and 4 cases.

Clinical findings related to RA were as follows: tender and swollen joint count, patient’s and physician’s global assessment of disease activity, ACR/EULAR criteria. Patients underwent clinical and laboratory assessments from baseline to 52 weeks.

Conclusions: The AUC and PD score at each time point for remission achievement at 52 weeks were each 0.643 and 0.648 from week 0 to 24 weeks as were follows: AUC score: -3.7±0.8 vs 0.16±6.8 (p=0.068) at 12 weeks and -5.8±7.7 vs -0.4±9.8 (p=0.008) at 24 weeks and PD score: -2.4±5.6 vs -1.1±5.2 (p=0.05) at 12 weeks and -9.5±6.3 vs -1.2±6.1 (p=0.013) at 24 weeks (Fig.1). Areas under the receiver operating characteristic curves for the AUC and PD score at each time point for remission achievement at 52 weeks were each 0.643 and 0.648 from week 0 to 24 weeks. The mean PD score changed from 7.6±6.8 at baseline to 5.8±6.0 (p=0.053) and 5.3±5.5 (p=0.05) at week 12 and 24. In the achieved remission for DAS28-ESR at Week52 (n=16) and not achieved or discontinued IGU patients (n=38), the respective changes in GS and PD scores from baseline to 12 or 24 weeks were as follows: Δ GS score: -3.7±0.8 vs 0.16±6.8 (p=0.068) at 12 weeks and -5.8±7.7 vs -0.4±9.8 (p=0.008) at 24 weeks and Δ PD score: -2.4±5.6 vs -1.1±5.2 (p=0.05) at 12 weeks and -9.5±6.3 vs -1.2±6.1 (p=0.013) at 24 weeks (Fig.1). Areas under the receiver operating characteristic curves for the Δ GS and PD score at each time point for remission achievement at 52 weeks were each 0.643 and 0.648 from week 0 to 24 weeks.

Disclosures: All authors have declared no conflicts of interest.
Conclusions: The IGU therapy improved not only the disease activity not also the inflammatory synovitis. The present study provides evidence supporting the improvement of GS and PD score from baseline to week24 may predict whether the achieved remission or not at Week 52.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6948

THU0213 | COMPARATIVE EFFICACY AND SAFETY OF BARICITINIB 2 MG AND 4 MG IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Baricitinib is a potent, selective JAK1 and JAK2 inhibitor. Baricitinib has been investigated in phase II and phase III studies of active patients with rheumatoid arthritis (RA), who showed an inadequate response to disease-modifying antirheumatic drugs (DMARDs), including methotrexate (MTX) and biologics. However, due to the lack of adequate multiple comparisons, the comparative efficacy and safety of baricitinib in various treatment regimens with different dosages or in combination with DMARDs or MTX remains unclear.

Objectives: This study aimed to assess the relative efficacy and safety of once-daily baricitinib 2 mg and 4 mg administration in patients with active RA.

Methods: We performed a literature search using MEDLINE, EMBASE, the Cochrane Controlled Trials Register, and the EULAR and ACR conference proceedings. In this network meta-analysis, randomized controlled trials (RCTs) examining the efficacy and safety of baricitinib in patients with active RA were included. A Bayesian network meta-analysis was conducted to combine the direct and indirect evidence from the RCTs.

Results: Seven RCTs involving 3,461 patients met the inclusion criteria. There were 10 pairwise comparisons, including 7 direct comparisons and 5 interventions. The ACR20 response rate was significantly higher in the baricitinib 4 mg arm compared with placebo. The ACR50 response rate was significantly higher in the baricitinib 4 mg arm compared with placebo. The ACR70 response rate was significantly higher in the baricitinib 2 mg arm compared with placebo. The change in DAS28-CRP from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in HAQ-DI from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in VAS from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in SF-36 from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in EQ-5D from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in WLA from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in Form-36 from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in Work Limitations Questionnaire from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo. The change in patient assessment of disease activity from baseline to week24 was significantly lower in the baricitinib 2 mg arm compared with placebo.

Conclusions: Efficacy of IGU in RA patients who had intolerance of MTX dose escalation or usage of biologics was observed. Although biological DMARDs is effective in RA patients, the cost is very expensive. IGU is comparative cheap (99,200/month) and suitable for RA patients with economical difficulties. As IGU decreased TNF-alpha production via inhibition of NF-kB, MTX+IGU may have similar mode of action with MTX+TNF inhibitor. Drug continuation rates were decreased over time and escape of efficacy may occur in some patients. Otherwise, IGU was very effective in some cases. Some of RA patients with high disease activity decreased disease activity greatly to remission state at 2 years after initiation of IGU.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4852
10 mg BID). There were no major differences in demographics or baseline characteristics between treatment groups. At Month 3, tofacitinib resulted in significantly greater changes in HAQ-DI (5 mg BID, p < 0.05; 10 mg BID, p < 0.001), PtGA (5 mg BID, p < 0.05; 10 mg BID, p < 0.001), Pain (5 mg BID, p < 0.01; 10 mg BID, p < 0.001) and SF-36 Physical Component Summary (PCS) scores (5 mg BID, p < 0.05; 10 mg BID, p < 0.001) vs PBO (Figure). Numerical improvements in FACIT-Fatigue, SF-36 Mental Component Summary (MCS) [Figure] and EQ-5D health state profile (utility scores) were observed at Month 3 with tofacitinib vs PBO. There were no improvements in WLOQ observed at Month 3 with tofacitinib vs PBO. Improvements were generally maintained at 6 and 12 months (Figure). The proportion of patients achieving HAQ-DII improvement ≥ 0.22 from baseline at Month 3 was significantly higher with tofacitinib vs PBO (5 mg BID, p < 0.05; 10 mg BID, p < 0.05).

Conclusions: Tofacitinib 5 and 10 mg BID administered with csDMARDs significantly improved PROs including SF-36 PCS, PtGA, physical function and pain vs PBO. These improvements were maintained for up to 12 months in Chinese patients with RA.

References:

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by C Evans of CMD and was funded by Pfizer Inc.


DOI: 10.1136/annrheumdis-2017-eular.2273

Thursday, 15 June 2017

SLE, Sjögren’s and APS - etiology, pathogenesis and animal models

THU0216 Urinary Neuropilin-1: A New Biomarker Approach in the Prognosis of Lupus Nephritis

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Background: Lupus nephritis (LN) affects up to 50% of patients with SLE and is a major cause of morbidity, despite modern therapeutic approaches [1,2]. To date, renal biopsy is still the gold standard for diagnosing and classifying the degree of renal inflammation and scarring, but its invasiveness makes it unsuitable for serial monitoring. A novel biomarker to predict the evolution of renal inflammatory injury is still needed. Neuropilin-1 (NRP-1) has important functions in adult tissues, being involved in axonal guidance, vascular endothelial sprouting, regeneration and organ repair and immunosuppression [3].

Objectives: Evaluate the protein and expression levels of NRP-1 at the time of the renal flare in patients with lupus nephritis and determine whether they could predict the disease progression.

Methods: Urine and serum of 70 patients with LN with nephrotic proteinuria, 25 patients with chronic non-lupus related nephopathy, and 25 healthy controls were analyzed by pQPCR-RT and ELISA to determine the levels of mRNA/protein of NRP-1. Immunohistochemistry of protein levels were done in renal biopsy (N=5). Urine and serum from 39 other patients with LN with nephrotic proteinuria were collected prospectively during two years.

Results: Increases in mRNA expression and protein concentration of NRP-1 were identified in urine samples of LN patients in flare compared with the different control groups. However, significant NRP-1 levels were found in LN patients that gone into remission compared with patients in non-remission after one year of treatment (p < 0.0001). Urinary VEGFA, VEGFR1, VEGFR2 and SEMA3A mRNA and protein levels were also determine. Results were confirmed with immunohistochemistry in renal biopsies (N=5). We observed a strong correlation with NRP-1 protein levels and VEGFA protein levels (r=0.466, p < 0.0001). Areas under the receiver operating characteristic curve of urinary NRP-1 and VEGFA protein levels to distinguish between remission and non-remission patients were 0.8384 and 0.7706, respectively (Figure 1). In a prospective study (N=39), urinary protein NRP-1 and VEGFA levels decreased in LN patients going to complete remission; but no those with non-response that maintain their low levels during all the follow-up.

Conclusions: For first time, we demonstrate that urinary levels of NRP-1 might reflect the evolution of renal inflammatory injury and could be used as novel biomarker to predict the recovery of LN.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5729

THU0217 DNA Methylation Analysis in Multiple Cellular compartments Demonstrates a Universal DNA Methylation Interferon Signature in Multiple Cellular compartments and Predominant B-Cell Hypermethylation in Twins with Systemic Lupus Erythematosus

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune
CIRCULATING MICRORNAS AS BIOMARKERS FOR AUTOANTIBODY PROFILE OF CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A TERTIARY CARE CENTRE IN NORTH INDIA

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Background: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune inflammatory muscle disorder that can result in severe disability or death. Children with JDM can have autoantibodies in their sera like other autoimmune diseases [1]. Over the last few years, few novel Myositis Specific Antibodies (MSA) have been identified. Some phenotypical associations have been described with these autoantibodies like anti p-140 (anti NXp2) has been shown to have correlation with calcinosis in children with JDM [1–2].

Objectives: To study autoantibody profile and to look for phenotypical associations of autoantibodies in JDM.

Methods: Cross-sectional retrospective study. All children diagnosed to have JDM, registered from 1995 to 2015 in Pediatric Rheumatology Clinic at Post Graduate Institute of Medical Education and Research Chandigarh, India and who were tested for autoantibodies were included in the study. Clinical findings, autoantibodies (ANAs), autoantibody for MSA and myositis associated autoantibodies (MAAs) were noted. Some phenotypical associations have been described with these autoantibodies like anti p-140 (anti NXp2) has been shown to have correlation with calcinosis in children with JDM [1–2].

Results: Anti nuclear antibody (ANA) testing was done in 97 patients. Forty six (47.4%) tested positive. In addition, MSA and MAAs were assessed. Anti-SRP antibodies were present in 4 (11.4%) children, anti-MDA5 in 3 (8.6%), anti-Mi2 in 1 (2.9%) and 1 patient tested positive for anti-SSA/Ro52 antibodies. All 4 children with anti-SRP were girls, had polycyclic course and 2 of them developed calcinosis. All 3 children with anti-MDA5 had predominant skin involvement, less severe muscle disease and followed a monocular course. Two of them had arthritis/arthralgia at the time of presentation. The only patient with anti-Mi2 had normal muscle strength/endurance at the time of follow up. None of the patients had anti MSA and anti MAA were present in any of the patient. Thus anti p-140 had anti SS-A/Ro52 antibodies have been done by Immunodot. Evaluation for anti p-140 or Nuclear Matrix Protein (NXp2) and anti 200/100 or 3-Hydroxy-3-Methylglutaryl-Coenzyme (HM-CoA reductase) was done using ELISA.

Conclusions: Prevalence of autoantibodies in children with JDM in our study is similar to what has been described previously. Type of autoantibodies, though, is not similar. This may be due to ethnic differences of the population. Autoantibodies were tested in children while they were on treatment. This may have resulted in lower positivity. Evaluation of autoantibody profile at the time of diagnosis may assist in predicting the course of disease and response to treatment.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6090

THU0219
AUTOANTIBODY PROFILE OF CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A TERTIARY CARE CENTRE IN NORTH INDIA

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Background: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune inflammatory muscle disorder that can result in severe disability or death. Children with JDM can have autoantibodies in their sera like other autoimmune diseases [1]. Over the last few years, few novel Myositis Specific Antibodies (MSA) have been identified. Some phenotypical associations have been described with these autoantibodies like anti p-140 (anti NXp2) has been shown to have correlation with calcinosis in children with JDM [1–2].

Objectives: To study autoantibody profile and to look for phenotypical associations of autoantibodies in JDM.

Methods: Cross-sectional retrospective study. All children diagnosed to have JDM, registered from 1995 to 2015 in Pediatric Rheumatology Clinic at Post Graduate Institute of Medical Education and Research Chandigarh, India and who were tested for autoantibodies were included in the study. Clinical findings, autoantibodies (ANAs), autoantibody for MSA and myositis associated autoantibodies (MAAs) were noted. Some phenotypical associations have been described with these autoantibodies like anti p-140 (anti NXp2) has been shown to have correlation with calcinosis in children with JDM [1–2].

Results: Anti nuclear antibody (ANA) testing was done in 97 patients. Forty six (47.4%) tested positive. In addition, MSA and MAAs were assessed. Anti-SRP antibodies were present in 4 (11.4%) children, anti-MDA5 in 3 (8.6%), anti-Mi2 in 1 (2.9%) and 1 patient tested positive for anti-SSA/Ro52 antibodies. All 4 children with anti-SRP were girls, had polycyclic course and 2 of them developed calcinosis. All 3 children with anti-MDA5 had predominant skin involvement, less severe muscle disease and followed a monocular course. Two of them had arthritis/arthralgia at the time of presentation. The only patient with anti-Mi2 had normal muscle strength/endurance at the time of follow up. None of the patients had anti MSA and anti MAA were present in any of the patient. Thus anti p-140 had anti SS-A/Ro52 antibodies have been done by Immunodot. Evaluation for anti p-140 or Nuclear Matrix Protein (NXp2) and anti 200/100 or 3-Hydroxy-3-Methylglutaryl-Coenzyme (HM-CoA reductase) was done using ELISA.

Conclusions: Prevalence of autoantibodies in children with JDM in our study is similar to what has been described previously. Type of autoantibodies, though, is not similar. This may be due to ethnic differences of the population. Autoantibodies were tested in children while they were on treatment. This may have resulted in lower positivity. Evaluation of autoantibody profile at the time of diagnosis may assist in predicting the course of disease and response to treatment.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6090

THU0220
SELECTASIS, A NOVEL SELECTIVE PI3Kδ INHIBITOR WITH THERAPEUTIC POTENTIAL IN INFLAMMATION AND AUTOIMMUNITY

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Background: PI3Kδ is predominantly expressed in lymphocytes; the role it plays in immune disease has encouraged the development of inhibitors targeting
DOWNGRADED EXPRESSION OF MR200B-5P IN MINOR SALIVARY GLANDS (MSG) OF PATIENTS WITH SJÖGRÖN’S SYNDROME (SS) ASSOCIATED LYMPHOMA

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Background: The miRNAs of the miR-200 family are critical regulators of oncogene and tumor suppressor genes. Preliminary data from a limited number of patients with SS-associated lymphoma suggested that the expression of miR200b-5p in MSGs may be downregulated in lymphoma.

Objectives: To validate whether low miR200b-5p levels are associated with SS-related lymphomas and if they are deregulated before lymphoma development, suggesting a possible diagnostic value.

Methods: miR200b-5p expression was analyzed by quantitative real-time PCR in total RNA from MSG tissue obtained from 77 SS patients and 9 patients with non-SS sialadenitis associated with sarcoidosis, HIV infection (4 each) or HBV (1) who was also diagnosed with MALT lymphoma, and 28 SS patients without lymphoma and non-SS sialadenitis associated with sarcoidosis, HIV (4 each) or HBV infection (1) who was also diagnosed with MALT lymphoma. Non-SS sialadenitis included 4 cases of sarcoidosis, 2 cases of HCV infection, and 1 case of HBV infection.

Results: In a group of 77 SS patients, miR200b-5p levels were significantly down-regulated in MSG tissues of prelymphoma and lymphoma SS patients (mean relative expression±SE: 0.37±0.10 and 0.26±0.06, respectively) compared to SS patients without lymphoma (0.67±0.07; p<0.05 and p<0.0001, respectively). Interestingly, low miR200b-5p levels were detected in HBV patient that had MALT lymphoma (0.17). The expression of miR200b-5p was not found to differ between patients with SS without lymphoma and non-SS sialadenitis, or SS-associated prelymphoma and lymphoma. The analysis of the 15 cases of SS patients that had sequential samples before and after lymphoma diagnosis revealed that miR200b-5p levels do not significantly change over transition to lymphoma. The miR200b-5p expression levels were negatively correlated with the biopsy focus score (r=-0.6550, p<0.0001), whereas they were not associated with the site or the number of involved sites, the type or the stage of lymphoma.

Conclusions: The significantly low levels of miR200b-5p in MSG tissues of patients with SS-associated prelymphomas and lymphomas suggest that miR200b-5p deregulation is implicated in SS-lymphomagenesis. The downregulation of miR200b-5p in prelymphoma samples and the lack of change over transition to lymphoma suggest that miR200b-5p serves as a biomarker for future lymphoma development. The prognostic value of miR200b-5p in SS-associated lymphomas, the expressing cell types and affected molecular pathways are under investigation.

Acknowledgements: Funded by the Hellenic College of Rheumatology

Disclose of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5132

ELEVATED MTORC1 SIGNATURE IN B CELLS FROM SJÖGRÖN’S SYNDROME PATIENTS CORRELATES WITH B CELL HYPERACTIVITY THAT IS ABROGATED BY MTOR INHIBITION: A NOVEL THERAPEUTIC STRATEGY TO HALT B CELL HYPERACTIVITY IN PSS?

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Background: A hallmark feature of primary Sjögren’s syndrome (pSS) is B cell hyperactivity, including presence of autoantibodies, aberrant presence of B cells and plasma cells in the salivary glands, elevated serum IgG levels and increased risk of lymphoma development. The mTOR pathway is essential for cell growth,
**THU0224** ASSOCIATION OF IRAK-M WITH NEUROPSYCHIATRIC SYMPTOMS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS  
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**Background:** Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease where a breakdown in immune tolerance leads to sustained inflammation and autoimmunity. Patients with SLE suffer from a diverse range of symptoms that include arthritis, nephritis, neuropsychiatric events and dermatological complaints. Interleukin-1 receptor-associated kinase M (IRAK-M), a negative regulator of toll-like receptor (TLR) signalling has previously been associated with SLE in a murine study. [1] Deficiency of IRAK-M was observed to exacerbated disease in a SLE model in C57BL/6-lpr/lpr mice. [2]. Deficiency of IRAK-M has been associated with SLE in a murine study. [1]. Deficiency of IRAK-M was shown to exacerbated disease in a SLE model in C57BL/6-lpr/lpr mice [2]. Deficiency of IRAK-M has been associated with SLE in a murine study [1]. Deficiency of IRAK-M was shown to exacerbated disease in a SLE model in C57BL/6-lpr/lpr mice [2].  

**Objectives:** To study the IRAK-M pathway in B cells of SSc patients as a potential therapeutic target to inhibit B cell hyperactivity.  

**Methods:** Expression of IRAK-M pathway genes (MTOR, RPTOR, RICTOR, DEPTOR, AKT1, IGF1R, IGF1, PTEN) were assessed on an OpenArray platform in purified peripheral blood B cells and monocytes from SSc patients (n=12), non-Sjögren’s sicca patients (n=17) and healthy controls (HC, n=9). Correlations with clinical parameters including lymphocytic focus score, ESSDAI and serum IgG levels were assessed. Flow cytometry analysis for B cell subset distribution was performed to assess potential effects of B cell subset distribution on gene expression.  

**Results:** Total IRAK-M expression was significantly increased in B cells of the SSc group compared to HC and non-SSc patients (p=0.019 and p=0.018, respectively) and correlated with serum IgG levels (r=0.429, p=0.020, and r=-0.462, p=0.012). Differences in expression of IRAK-M pathway genes were not found in monocytes. To indicate the MTOR signature a cumulative MTORC1 score was calculated consisting of Z scores (AI) of MTOR, RICTOR, RICTORR, AKT1, IGF1R, Mkk1, Mkk2, Mkk3, Mkk4. MTORC1 score was significantly elevated in pSS (p=0.027), correlating with serum IgG levels (r=0.463, p=0.011). Frequencies of memory and naïve B cells did not differ between SSc patients and HC in this cohort (p=0.415). Activation of B cells in culture resulted in phosphorylation of S6, which indicates increased mTORC1 activity, in accordance with both SSc patients (n=12) and HC in this cohort, and Correlations with serum IL-35 level were assessed by qRT-PCR and by ELISA and a multiplex kit for IL-12 and IL-23.  

**Conclusions:** Presence of an MTORC1 signature in B cells from SSc patients correlated with B cell hyperactivity indicates a role for MTORC1 in B cell activation in this disease. That B cell proliferation and IgG production is effectively inhibited by rapamycin suggests that MTOR inhibition represents a potential therapeutic strategy for SSc.  

**Disclosure of Interest:** None declared  

**DOI:** 10.1136/annrheumdis-2017-eular.1618

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**THU0225** ROLE OF THE IL-12/IL-35 BALANCE IN SJÖGREN’S SYNDROME  

**Methods:** The genetic study involved 673 patients with pSS from 2 French pSS cohorts and 585 healthy French controls. Functional studies were performed on sorted monocytes, stimulated or not, IL-12A/mRNA and IL-12 and IL-35 protein levels were assessed by qRT-PCR and by ELISA and a multiplex kit for IL-12 and IL-12, respectively.  

**Results:** We confirmed the association of the IL-12A rs485497 polymorphism and pSS and found an increased serum protein level of IL-12p70 in pSS patients carrying the risk allele (p=0.016). Serum level of IL-12p70 was greater in patients than controls (p=0.0001), especially patients with more active disease (p=0.05); conversely IL-35 level was decreased in patients (p=0.001) especially in patients with a more active disease (p=0.05).  

**Conclusions:** Our findings emphasize the involvement of the IL-12/IL-35 balance in the pathogenesis of pSS. Serum IL-35 was associated with low disease activity, in contrast to serum IL-12p70 level, which was rather associated with a more active disease.  

**Acknowledgements:** We thank Dr Odile Devergne (Université Paris Descartes, AP-HP, Hôpital Necker, Paris) for her expertise on the IL-35 ELISA kit to ensure the quality and reproducibility of this test.  

The authors thank the following investigators of the ASSESS cohort prospective cohort of patients with Sjögren’s syndrome (all in France) who recruited the patients and conducted follow-up: A. L. Fauchais (Limoges), S. Rist (Orléans), V. Le Guern (Rennes), P. Hayem (Paris), J. Sibilia (Strasbourg), J. Morel (Montpellier), A. SARAA (Brest), A. Perdriger (Rennes), X. Puechail (Le Mans), E. Hachulla (Lille) and V. Goebr (Rouen).  

The authors thank Dr Benessiano, S Tubiana and all staff members of the Bichat Hospital Biological Resource Center (Paris) for their help in centralizing and managing biologic data collection from the French ASSESS.  

**Disclosure of Interest:** None declared  

**DOI:** 10.1136/annrheumdis-2017-eular.5386

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**THU0226** DIFFERENTIAL SUSCEPTIBILITY OF TH17 AND T REGULATORY CELLS TO APOPTOSIS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS – THE MODULATORY EFFECTS OF STATIN  
J. Sun, J. Frostegard, A. Liu, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden  

**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder. Patients with SLE have accelerated cardiovascular disease. Recent studies show there are more Th17 while less T regulatory (Treg) cells in the SLE patients. Th17/Treg imbalance may contribute to the pathogenesis of SLE.  

**Objectives:** To investigate the underlying mechanisms of Th17/Treg imbalance, we test the proportion and susceptibility of Th17 and Treg to apoptosis, and the modulatory effects of statin in the SLE patients.  

**Methods:** Totally 17 SLE patients and 20 gender- and age-matched control subjects were enrolled for this study. Peripheral blood mononuclear cells were isolated, either analyzed ex vivo, or cultured in the conditions to induce Th17 and/or Treg differentiation. The proportions of Th17, Th17/Treg and Treg/Teff cells and frequency responding to apoptosis were analyzed by multiple color flow cytometry. Cytokines in cell culture supernatants and plasma were tested by ELISA, T cell polarization-related transcription factors were detected by quantitative real time PCR.  

**Results:** The proportion of Th17 (CD4+IL-17+) cells were higher in SLE patients, capacity to resolve inflammation. This was reflected in the elevated cytokine production observed from SLE monocytes. Thus, low expression of IRAK-M in SLE monocytes is linked to elevated inflammatory cytokine production and may be a biomarker for neuropsychiatric symptoms in SLE patients.  

**References:**  

**Acknowledgements:** Study funded by Brighton and Sussex Medical School.  

**Disclosure of Interest:** None declared  

**DOI:** 10.1136/annrheumdis-2017-eular.6201
both in ex vivo and in the Th17-polarizing cultures. While the frequencies of Treg (CD4+CD25+CD127dim+) cells were lower in the corresponding populations. Higher levels of IL17 and IL6 were detected in plasma of SLE patients. Responding to CD95-induced apoptosis the frequency of CD4+IL17+ cells from SLE patients was substantially lower, but that of CD4+CD25+CD127dim+ cells from Treg-polarizing cultures was considerably higher. With treatment of atorvastatin, CD4+IL17+ cell population in cultures derived from SLE patients showed an increased susceptibility to CD95-induced apoptosis. However, the CD4+CD25+CD127dim+ cell population had reduced response to apoptosis. Accordingly, the ratio of transcription factor ORC5/FOXJ3 decreased in T cell cultures of SLE patients.

Conclusions: Th17 cells were more resistant than Treg cells to CD95-induced apoptosis in SLE as compared to control subjects. Statins counteracted the dysregulated susceptibility of SLE T cells to apoptosis. Our findings reveal a novel mechanism underlying the imbalance of Th17/Treg and show a potential interest to the treatment of the patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6193

THU0227 GENOME-WIDE ASSOCIATION META-ANALYSIS IDENTIFIES FIVE NEW LOCI FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Recent genome-wide association studies (GWAS) have identified more than 50 loci associated with systemic lupus erythematosus but they explain less than 30% of the heritability of the disease. Meta-analysis including new populations can contribute to identify additional genetic risk factors.

Objectives: The aim of the present study was to identify additional genetic risk loci for SLE.

Methods: We performed a meta-analysis using data from a recent large scale GWAS from 4,036 cases and 6,959 controls from Caucasian European ancestry [1] and a newly genotyped cohort of 907 SLE patients and 1,524 healthy controls from Spain. Genetic association was tested at the single-marker level using linear regression and at the pathway-level using Fisher’s modified method.

Results: Combining the two cohorts we identified genome-wide significant association (P<5E-8) at five new loci: three SNPs at intronic regions and two intergenic loci at chromosomes 7q11.23 (Manhattan plot for chromosome 7 is shown in Figure; new SLE risk region SNPs highlighted in green) and 17q21.31.

Several of the new associated genes are functionally associated with B cell regulation. After multiple test correction, B Cell Receptor signaling, Biopeptides and Cell surface interactions at the vascular wall pathways were also significantly associated with SLE risk.

Conclusions: In conclusion, we have identified five new risk loci for SLE through a meta-analysis including a new GWAS.

References:

Acknowledgements: We would like to thank the clinical researchers and patients participating in the IMID Consortium for their collaboration. We would also like to thank the international SLE consortium for access to the data.

Disclosure of Interest: None declared


THU0228 INTRA-RENAL ACTIVATION OF ADAPTIVE IMMUNE EFFECTORS IS ASSOCIATED WITH HIGHER DISEASE SEVERITY IN LUPUS NEPHRITIS

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Background: Chronic renal impairment remains a feared complication of lupus nephritis (LN). Yet, little is known about mechanisms and markers of disease severity in the lupus kidney.

Methods: We performed high-throughput transcriptomic studies (Illumina HumanHT12 v4 Expression Beadchips) on archived (≥80 degrees) kidney biopsies from 32 SLE patients and 8 controls (pre-transplant donors). Unsupervised clustering and differential gene expression studies were performed using GeneSpring software. Pathway analyses were carried on using DAVID and GSEA. Clinical and biological data were retrieved from the patients’ medical records. Immunohistochemistry experiments (CD3, CD20, CD34) were performed on the same samples, and on an additional cohort of 37 SLE kidney biopsy specimens. Syndecan-1 (SDC1) was used as a marker of renal tubular cell response to stress.

Results: Compared to controls, LN samples overexpressed transcripts involved in interferon signature, apoptosis, chemokines, antigen presentation, T and B cell activation.

Unsupervised clustering studies isolated 14 SLE samples based on their gene expression features. These samples were characterized by a significantly lower estimated GFR at the time of biopsy (T0) (50.7 versus 97.4 ml/min/1.72m2), but also at follow-up (49.1 versus 85.8 ml/min/1.72m2) compared to the other SLE samples. Yet, apparent renal disease duration at T0, disease duration at last follow-up (median 91.5 versus 86 months), double-stranded DNA antibody titers, proteinuria, numbers of subsequent flares were not different between both groups.

From a transcriptomic point of view, these 14 samples were characterized by the overexpression of transcripts and pathways involved in adaptive immune responses: antigen presentation, T cell differentiation and B cell activation. Immunohistochemistry studies confirmed a significant association between the expression of CD3 and CD20 positive cells in the interstitial space and lower estimated GFR at baseline in the same, but also in an independent set of samples. The presence of CD3 and CD20 positive cells was also associated with lower SDC1 expression on renal tubular cells. Low SDC1 expression on renal tubular cells was strongly associated with impaired kidney function at baseline.

Conclusions: LN kidney biopsy samples from patients with lower estimated GFR are characterized by the overexpression of transcripts pointing to the activation of a local antigen-dependent immune response. Activation of “second wave” immune effectors in the LN kidney is a known feature of the disease, and impacts kidney function through alterations in the function of renal tubular cells.

Acknowledgements: The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115565, resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007–2013) and EFPIA companies’ in kind contribution

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3427
DNA HYPMETHYLATION AND DECREASED HYDROXYMETHYLATION IS ASSOCIATED WITH DECREASED ANTIOXIDANT RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS

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Background: Systemic lupus erythematous (SLE) shows increased DNA demethylation. An intermediate step to DNA demethylation is the DNA hydroxymethylation, where 5-mC is oxidized into 5-hmC. Hydroxymethylation is not completely understood and it may be related to oxidative stress in SLE patient.

Objectives: To analyze the association between the hydroxymethylation and demethylation, with the antioxidant response and SLE pathophysiology.

Methods: We analyzed in 142 SLE patients and 34 healthy controls the serum concentration of glutathione (GSH) and glutathione disulfide (GSSG) by UPLC-MS/MS, superoxide dismutase (SOD) and total antioxidant capacity (TAC) by colorimetric method. 5-mC and 5-hmC levels were measured by colimetric methods. Complete blood-test was made and clinical data by personal interview was collected. Biostatistical analysis with R (3.3.2.) was performed.

Results: There is a correlation between the methylation and hydroxymethylation rate (P<0.001) and between 5-mC levels and GSH, GSSG or GSH/GSSG ratio. Higher demethylation is associated to vascular symptoms (defined by RELESSER score) and lupus anticoagulant (AL) positivity (P<0.04; P<0.001), and lower hydroxymethylation (P<0.001; P<0.001). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P<0.001; P<0.001). We did not observe any association between hydroxymethylation and SOD or TAC levels. Lower SOD and TAC values are associated with higher demethylation and lower hydroxymethylation rates (P<0.001; P<0.001). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P<0.001; P<0.001). We did not observe any association between SOD or TAC levels and 5-mC or 5-hmC levels. GSH and GSSG concentrations were higher in patients (P=0.001), but TAC did not show significant differences. Higher demethylation is associated to lower TAC values in patients and healthy controls (P=0.005; P=0.01). Reduced demethylation and decreased GSH and GSSG concentrations were associated to increased long-term renal failure, cardiovascular disease, and to increased mortality rate. SOD levels were associated to vascular symptoms.

Conclusions: In SLE patients, lower SOD values are associated with higher disease duration (P<0.001; P=0.007), and lower SOD values with longer disease duration (P<0.001). We did not observe any association between hydroxymethylation and SOD or TAC levels. Lower SOD and TAC values are associated with higher demethylation and lower hydroxymethylation rates (P<0.001; P<0.001). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P<0.001; P<0.001). We did not observe any association between hydroxymethylation and SOD or TAC levels. Lower SOD and TAC values are associated with higher demethylation and lower hydroxymethylation rates (P<0.001; P<0.001). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P<0.001; P<0.001). We did not observe any association between hydroxymethylation and SOD or TAC levels. Lower SOD and TAC values are associated with higher demethylation and lower hydroxymethylation rates (P<0.001; P<0.001). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P<0.001; P<0.001). We did not observe any association between hydroxymethylation and SOD or TAC levels. Lower SOD and TAC values are associated with higher demethylation and lower hydroxymethylation rates (P<0.001; P<0.001). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P<0.001; P<0.001).

Disclosure of Interest: None declared
 DOI: 10.1136/annrheumdis-2017-eular.2905
antibody were determined by ELISA. Histopathological evaluation of renal lesions was undertaken by HE, PAS, PASM and Masson staining under light microscopy. Podocyte foot processes were assayed by the transmission electron microscopy. Depositions of C5a, C5b-9, and MBL were detected by immunohistochemistry assay. Immunofluorescence was utilized to detect the expression of C5aR1, IgG, IgM, IgA, C3, C1q, and properdin in the glomeruli.

**Results:** At the end point, proteinuria in mice of the former three groups was significantly reduced when compared with the control mice, and renal function was also improved in both MSCT and CTX groups. Plasma level of C3 was significantly elevated in mice of MSCT and C5aRA groups. Furthermore, mice in MSCT group appeared a remarkably decreased C5a in the circulation. Compared to control mice, no significant difference was found in plasma levels of anti-dsDNA and SC5b-9, although there were decline trends in other three groups. Pathological analysis showed that the proliferation of glomerular cells and foot process fusion were significantly inhibited in MSCT treated mice. Immunohistochemistry showed that deposits of C5a and C5b-9 were significantly decreased in the MSCT group. Immunofluorescence examination showed that the expression of IgG, C3, C1q, and properdin was significantly decreased in MSCT treated mice, meanwhile, the expression of MBL was also significantly reduced in these mice.

**Conclusions:** The activation of the complement system was obviously involved in the glomerulonephritis in lupus mice. Allogeneic UC-MSC transplantation can effectively improve the clinical outcome of lupus mice. Possible mechanism of MSCT might be related to inhibit the activation of complement C5 in the circulation and local kidney via interrupting the classical, alternative, and lectin pathways. The potential involved contributors of UC-MSC are currently under study.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2559

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**THU0233** IN VITRO INDUCED REGULATORY T-CELLS CAN AMELIORATE SEVERITY OF PRISTANE INDUCED LUPUS (PIL) H. Leiss, B. Jacobs, I. Gessl, A. Puchner, J. Smolen, G. Stummvoll. Rheumatology, Medical University Vienna, Vienna, Austria

**Background:** Pristane induced lupus (PIL) is a well-established murine model for environmentally induced systemic lupus erythematosus (SLE). Mice develop specific autoantibodies and show symptoms of SLE including arthritis, diffuse proliferative immune complex glomerulonephritis and haemorrhagic pulmonary capillaritis.

**Objectives:** To investigate the therapeutic effects of in vitro-induced regulatory T cells (iTreg) in the murine model of PIL.

**Methods:** BALB/c mice were injected i.p. with either 0.5ml of pristane (PIL) or PBS (controls). Naive CD4+ thymocytes were sorted and cultured and cell suspensions with >80% of CD4+Foxp3+ cells (iTreg) were injected intravenously (i.v) once when PIL was induced (5x10^6 iTreg i.p., 2 times) or (ii) every 4 weeks (1x10^6 iTreg, i.p., 3 times). Animals were monitored for paw swelling and grip strength. After 12 weeks, histopathological analysis evaluated for cartilage degradation, number of osteoclasts and the extent of inflammation and bone erosion. Glomerulonephritins and pneumonitis were quantified using the kidney biopsy score and a newly adapted histomorphometric image analysis system; inflammatory tissue was further analyzed by tissue cytometry. Serum levels of anti-dsDNA, anti-histone and anti-nuclear antibodies were measured by ELISA.

**Results:** Monthly injections of 1x10^6 iTreg reduced the clinical as well as the histological severity of PIL-arthritis, seen by a higher mean grip strength (2.96±0.02 vs. 2.73±0.06, p<0.01), less mean paw swelling (0.04±0.02 vs. 0.36±0.07, p<0.001) and retardation of the symptom onset (Figure A). 62% of iTreg-mice and 33% of iTreg-rep mice had erosive arthritis. There was a significant reduction of arthritis severity in all histological parameters (inflammatory area in mm^2 0.19±0.06 vs. 0.69±0.11; erosive area in mm^2 0.01±0.01 vs. 0.70±0.02; number of osteoclasts 2.1±1.3 vs. 9.1±4.2; cartilage degradation in mm^2 0.06±0.01 vs. 0.19±0.03, all p<0.01, Figure B). The single boost of 5x10^6 iTreg could not prevent joint manifestations. However, a slight retardation in ‘loss of grip strength’ and a significantly less erosive area was observed. In regards to the cellular composition of the inflammatory tissue in paws, a significantly increased relative amount of CD4+Foxp3+ cells was found in the iTreg-rep group compared to the PIL-group (Figure C). Correspondingly, serum levels had significantly lower levels of disease-associated auto-antibodies (Figure D).

**Conclusions:** Repeated injections of iTreg ameliorate the clinical and histological severity of PIL- manifestations. A single boost of iTreg at the time of disease induction does not prevent manifestations, but retards the onset of symptoms. Thus iTreg have significant positive effects on PIL, which may have consequences for future approaches in treating SLE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3020

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**THU0234** EPIGENETIC CELL COUNTING: A NOVEL TOOL TO QUANTIFY IMMUNE CELLS IN SALIVARY GLANDS DETECTS ROBUST CORRELATIONS OF TFH CELLS WITH IMMUNOPATHOLOGY J.A. van Roon 1,2, F.M. Moret 1,2, S.L. Blokland 1,2, A.A. Kruize 2, B. Bouma 3, A. van Maurik 4, S. Olek 4, U. Hofmann 4, T.R. Radstake 1,2, 1Laboratory of Translational Immunology; 2Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands; 4Immunoinflammation TAU, GlaxoSmithKline, Stevenage, United Kingdom; 5Epiontis GmbH, Berlin, Germany

**Background:** Histological analysis of salivary glands for decades has been a valuable tool in the characterization of patients with primary Sjögren’s syndrome (pSS) and non-Sjögren’s sicca (nSS) patients. However, understanding the immunopathology of sicca patients is challenging.

**Objectives:** To investigate whether epigenetic cell counting can serve as a novel reliable tool to quantify immune cells in salivary glands of sicca patients.

**Methods:** DNA was isolated from frozen tissue sections of 13 nSS, 12 probable SS, 29 pSS and 7 overlap SS patients. Bisulfite conversion of demethylated DNA sites was followed by qPCR on a qPCR machine that was used to calculate the percentage of cell subsets related to the total number of cells quantified by housekeeping gene expression. Percentages of epigenetically counted cells were correlated to gene expression generated by RNA-Seq analysis of matched salivary gland tissue and histological and clinical parameters (LFS, %IgA+ plasma cells, serum IgG3, SSA positivity).

**Results:** Strongly increased percentages of epigenetically quantified percentages of CD3, CD4, CD8, B cells, T follicular helper (Tfh) cells and Treg cells in pSS vs nSS patients were observed (all p<0.001, CD8 p<0.01). These inflammatory cell types were strongly correlated with LFS (all at p<0.001) and local B cell hyperactivity (% IgcA+ cells, all p<0.01, except CD8 p=0.06 and B cells, p=0.127) and systemic B cell hyperactivity (all at p<0.01, except CD8 p=0.051). Th17 cells were not significantly different between nSS and pSS patients. Only CD6 T cells were significantly increased in probable SS patients compared to nSS patients (p=0.03). Percentages of CD3 and B cells positively correlated with CD3 and CD19 RNA expression (r=0.608, p=0.0001; r=0.597, p=0.0001), respectively. Interestingly, percentages of Tfh cells correlated with CXCL13 (r=0.789, p=0.0001), IL7R, CXCR3 and ICOS RNA expression (all p=0.001) and were strongly associated with autoimmunity (SSA positivity; p<0.001).
Conclusions: Epigenetic cell counting is a promising novel tool to reproducibly and easily quantify immune cells in the (inflamed) labial salivary gland of sicca patients with relatively low amount of tissue needed (≤1 mm³). Considering the potential of this technique to include a huge number of (cell-specific) biomarkers we believe this opens up new standardized ways for salivary gland analysis with high relevance for patient classification, understanding of immuneopathology and clinical trials.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4933

EXOSOME-DELIVERED MIR-146A REGULATES SENESCENCE OF BONE MARROW- MESENCHYMAL STEM CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS THROUGH TARGETING IRAK1 AND TRAF6

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Background: Exosomes are membrane nano-vesicles secreted by a multitude of cells that harbor biological constituents such as proteins, lipids, mRNA and microRNA. Recent study suggests that microRNAs can be transferred between cells and mediate target gene repression. Our research group revealed the senescence of bone marrow-mesenchymal stem cells from systemic lupus erythematosus patients, which participated in the development of SLE. However, the relationship between senescence of MSCs and miRNAs remains unclear.

Objectives: In this study, we investigated whether exosomes act as intercellular messengers delivering microRNA that modulate the senescence of BM-MSCs from SLE patients and its possible mechanism.

Methods: Twelve female SLE patients and healthy subjects were enrolled in the study. All patients were females, and their age distribution was similar to that of the cases. Serum were collected from these persons. All BM-MSCs were isolated by density gradient centrifugation. Serum-derived exosomes were extracted by Total Exosome Isolation Reagent and confirmed by transmission electron microscopy. They were then used to challenge MSCs from both groups. Internalization of exosomes was detected by immunofluorescence. QRT-PCR was used to distinguish the difference of expression of miR-146a in exosomes between normal group and SLE group. Different exosomes stimulated normal BM-MSCs, then detecting expression of miR-146a by qRT-PCR. Activating expression of IRAK1 and TRAF6 by WB, observing the activity of β-gal of cells, the changes of cytoskeletal structure by F-actin staining and the distribution of cell cycle by flow cytometry. We used miRNA mimics and miRNA inhibitor to interfere the expression of miR-146a.

Results: Serum-derived exosomes could be taken up by BM-MSCs through the plasma membrane due to treatment of BM-MSCs with exosomes. After stimulation of exosomes in normal MSC, miR146a was decreased, but, IRAK1 and TRAF6 was activated. And, the cell volume and the number of SA-β-gal positive in SLE BM-MSCs was increased. The organization of cytoskeleton was nearly disordered. The rate of cell proliferation was decreased. The miR-146a mimics in SLE BM-MSCs can significantly reverse the senescence.

Conclusions: Exosomes-delivered miR-146a in the serum of SLE patients can promote the senescence of BM-MSCs through targeting IRAK1 and TRAF6. Exosomes play an important role in the pathogenesis of SLE.

Acknowledgments: This research was supported by grants from the National Natural Science Foundation of China (81471603).

WHOLE TRANSCRIPTOME ANALYSIS OF APL TREATED HUEVCs MAPS PROINFLAMMATORY AND PROCOAGULANT PATHWAYS

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Background: Antiphospholipid syndrome is an autoimmune thrombophilia characterized by recurrent thromboembolism and or pregnancy morbidity in the presence of antiphospholipid antibodies (aPL). j2GPI which is the major autoantigen in the syndrome forms complexes with anti-b2GPI autoantibodies that activate platelets, monocytes and endothelial cells. Previous studies have shown that anti-j2GPI-j2GPI complexes activate TRLR4 and TLR6 on endothelial cells leading to NFκB, MAPK activation and Tissue Factor and proinflammatory cytokine expression.1,2

Objectives: To evaluate the whole transcriptome of endothelial cells that have been stimulated with aPL-b2GPI complexes.

Methods: Human umbilical Vein Endothelial cells (HUEVCs) were isolated from 2 APL patients and 4 Healthy control women upon delivery. Healthy donor HUEVC were stimulated with aPL from APS patients with high aPL titers and healthy individuals in the presence of b2GPI. Consequently total mRNA was isolated, CDNA libraries were created and whole transcriptome sequencing (RNASeq) was performed. Gene expression data were validated in protein levels with immunohistochemistry in placenta tissues from APS patients and healthy individuals.

Results: Whole transcriptome analysis of HUEVCs stimulated with aPL-j2GPI complexes and IgG from healthy individuals revealed 680 differentially expressed genes, among which 377 were upregulated and 303 downregulated in the aPL stimulated endothelial cells. Characteristic examples of the upregulated genes are IL-6, IL-8, VCA1M, SELE and TGFβ2 and TGFBR1. Bioinformatics analysis revealed that the upregulated genes belong mainly to the cytokine-cytokine receptor interaction (hsa03323), MAPK signaling pathway (hsa04010), TNF signaling pathway (hsa04668) and NOD-like receptor pathway (hsa04662). Characteristic examples of the downregulated genes include the CX34, CX8X, BOCR and HDAC7 genes. Interestingly some of the proteins encoded by these genes play role in the epigenetic modification of DNA. Immunohistochemical staining on placenta biopsies from APS patients and healthy individuals for IL-6, IL-8, IL-18, NF-κB, TGFβ1 and TGFβ2 showed increased intensity in the signal of endothelial cells on APS specimens validating thus the RNASeq results in the tissues.

Conclusions: RNASeq of endothelial cells treated with aPL and b2GPI reveals a thoroughly analysed proinflamatory and procoagulant phenotype. Moreover differential expression of DNA modifying proteins suggests the possible epigenetic regulation of gene expression on endothelial cells in APS syndrome. Ongoing experiments aim to analyze histone acetylation and methylation status of the promoters of the selected genes that were shown to be differentially expressed.

References:

ANTIBODIES TOWARDS ATP-BINDING CASSETTE TRANSPORTER ABCA1: A NEW MECHANISM FOR AHEROSCLEROSIS IN SLE?

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Background: Systemic Lupus Erythematosus (SLE) is considered an indeﬁnite risk factor for cardiovascular disease and patients with SLE have an increased burden of atherosclerotic vascular disease. High-density lipoproteins (HDL), the plasma lipoproteins responsible for reverse cholesterol transport2, are the plasma lipoproteins that moderate HDL protective effect on cardiovascular disease is attributed to the cholesterol efflux capacity as well as to its anti-oxidant and anti-inﬂammatory properties. Dyslipidemia is frequent amongst patients with SLE that have higher damage, measured by SLICC classification criteria. Future studies will determine their pathogenic role and the potential use of a standardized ELISA to detect anti-ABCA1 antibodies in clinical practice.

Methods: Patients with SLE were divided in two groups: group A, with low damage (based on less than 4 SLICC criteria), and group B, with high damage (based on the presence of at least 4 SLICC criteria). Groups A and B were compared with a control group. 48 patients were enrolled (13 in group A and 35 in group B), and 18 age and gender-matched healthy controls were included in the control group. IgG anti-ABCA1 and anti-HDL antibodies were assessed by home-made ELISAs, using commercially available ABCA1 synthetic peptide and HDL from healthy donors.

Results: There were no differences between group A and the control group. Group B had higher titers of anti-ABCA1 antibodies when compared with group A (p=0.02) and the control group (p=0.022). For positivity we considered values superior to 3 standard deviations above the mean of healthy controls. Four patients showed positive anti-ABCA1 titers (11.4%).

Conclusions: This is the first time that naturally occurring antibodies against ABCA1 are detected by ELISA. These antibodies are increased in patients with SLE that have higher damage, measured by SLICC classification criteria. Future studies will determine their pathogenic role and the potential use of a standardized ELISA to detect anti-ABCA1 antibodies in clinical practice.

References:

WHOLE TRANSCRIPTOME ANALYSIS OF APL TREATED HUEVCs MAPS PROINFLAMMATORY AND PROCOAGULANT PATHWAYS

THU0235

THU0237

None declared

DOI: 10.1136/annrheumdis-2017-eular.7013

THU0236

None declared


Abstracts

Thursday, 15 June 2017

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P-GLYCOPROTEIN MONOCLONAL ANTIBODY IMPROVES LUPUS-LIKE SYMPTOMS IN MRL/PLR MICE

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Background: Preventing steroid resistance and maintaining disease control are significant challenges in treating SLE patients.[1] P-glycoprotein (P-gp) of membrane transporters, a product of the multiple drug resistance (MDR)-1 gene, is known to play a pivotal role in the acquisition of drug resistance to chemotherapy in autoimmune diseases.[2] Inhibition of P-gp could overcome such drug resistance.[3,4] So we observed the effect of P-gp monoclonal antibody on MRL/lpr lupus mice.

Objectives: To investigate the efficacy of P-glycoprotein monoclonal antibody in the treatment of the MRL/lpr mice.

Methods: Twenty-four 14-week-old MRL/lpr female mice were divided into three groups: Group 1 (G1) were treated with P-glycoprotein monoclonal through caudal vein, group 2 (G2) were treated with P-glycoprotein monoclonal three times and group 0 (G0) were treated with 0.5 ml normal saline as a control. Twenty-four-hour proteinuria and body weight were assessed every two weeks. Enzyme-linked immunosorbent assay (ELISA) was used to measure the levels of anti-dsDNA antibodies. The histopathology changes of the kidneys were observed.

Results: From the 22th week, the body weight of groups G1 and G2 increased significantly than that of the group G0 (p < 0.05). At the 22th week, the 24-hour proteinuria in group G1 (1.9±1.1) mg and G2 (1.4±0.9) mg was decreased than that in group G0 (3.1±1.9) mg (p < 0.05). During the 26th week, the levels of anti-dsDNA antibodies in group G1 (0.11±0.05) μg/ml and G2 (0.09±0.01) μg/ml were both significantly lower than those of the group G0 (0.37±0.19) μg/ml (p < 0.001) and at the 26th weeks the difference between group G2 (35±32)×10⁹ U/ml and G0 (59±35)×10⁹ U/ml was statistically significant. The nephron crescent formation in group G1 (0.11±0.05)μg/ml and G2 (0.09±0.01)μg/ml was significantly lower than that of group G0 (0.23±0.07)μg/ml (p < 0.05) and that of group G2 was significantly less than that of group G1 (p < 0.05).

Conclusions: P-glycoprotein monoclonal antibody is very effective in treating MRL/lpr mice. It is safe and free of rejection reactions.

References:

Acknowledgements: We thank prof. Guofeng GAO's assistance in editing the manuscript.

Disclosure of Interest: M. Wang Grant/research support from: NO, P. ZENG Consultant for: NO, G. ZOU Employee of: NO, J. LV Paid instructor for: NO, Q. WANG Grant/research support from: NO, Speakers bureau: NO

DOI: 10.1136/annrheumdis-2017-eular.5880

THU0239
SERUM HMGB1 AND TL4 LEVELS AS NOVEL BIOLOGICAL MARKERS FOR THE ACTIVITIES OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) is a severe complication of SLE, including a variety of neurological and psychiatric features. Previous studies have demonstrated the close relationship between NPSLE and TLR4-NF-κB signaling pathways. The HMGB1-TLR4 pathway is the upstream pathway of NF-κB, which could upregulate the expression of various cytokines and other inflammatory mediators.

Objectives: The objective of the study was to explore the potential mechanism of HMGB1/TLR4 axis in SLE.

Methods: The study population consisted of 107 SLE patients and 43 age- and sex-matched healthy controls. 73 SLE patients had active disease. 36 of these had NPSLE. The serum anti-NR2A antibodies levels were measured by ELISA. Clinical and serological parameters were assessed according to routine procedures. HMGB1 and TL4 levels were measured by ELISA. Statistical analyses were performed by using the chi-square test and the t-test.

Results: CNS manifestations accounted for 94% (34/36 patients), while involvement of the PNS was 6% (2/36 patients). The majority of the manifestations were Seizure disorders (n=17; 47.2%), Headache (n=12; 33.3%), and Cognitive dysfunction (n=10; 27.8%). Psychoses (n=6; 22.2%) within the group of active patients those with NP manifestations had higher HMGB1 levels (0.451 (0.292 to 0.583)) compared to active patients with non-NP manifestations (0.356 (0.098 to 0.436)). In patients with NP (0.429 (0.313 to 0.526)) and non-NP (0.375 (0.196 to 0.478)) manifestations during active periods of the disease, TL4 levels significantly increased in comparison to the controls. TL4 levels were significantly higher in active patients (0.401 (0.196 to 0.526)) compared to quiescent patients. There was a significant positive correlation between levels of HMGB1 and TL4 in the total patients group (P < 0.0001, r=0.939). We observed a correlation between HMGB1 levels and SLEDAI (P < 0.0001, r=0.804). Also, TL4 levels showed a significant correlation with SLEDAI (P < 0.0001, r=0.809). HMGB1 levels correlated with anti-dsDNA levels (P < 0.0001, r=0.558). Similarly, TL4 showed a correlation with anti-dsDNA levels (P < 0.0001, r=0.322). We observed a negative correlation in the total SLE group between C3, C4 and HMGB1 levels (P < 0.001, r=-0.545 and P < 0.0001, r=-0.270 respective. Also, TL4 showed a significant negative correlation with C3 and C4 (P < 0.0001, r=-0.559 and P < 0.0001, r=-0.285 respectively).

Conclusions: Our data suggest that HMGB1-TLR4 axis plays an important role in the pathogenesis of SLE as well as NPSLE.

Acknowledgements: This work was supported by The President Foundation of Nantong Hospital, Southern Medical University (NO. 2014C009, NO.2015C021).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1730

THU0240
DEFECTIVE REGULATION BY ATP-GATED IONOTROPIC P2X7 RECEPTOR DRIVES T FOLLICULAR HELPER CELL EXPANSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune...
DECREASED CIRCULATING CXCR3+CCR9+ TH CELLS ARE ASSOCIATED WITH INCREASED LEVELS OF THEIR LIGANDS CXCL10 AND CCL25 IN THE SALIVARY GLAND OF PATIENTS WITH SJÖGREN’S SYNDROME TO POTENTIALLY FACILITATE CONCERTED MIGRATION

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Background: Primary Sjögren’s syndrome (pSS) is characterized by dryness and lymphocytic infiltration in the salivary glands. Both CXCR5+ T follicular helper (TFH) cells and CCR9+ Th1-like cells and their specific chemotactic ligands CXCL13 and CCL25 are present at increased levels in the salivary glands of pSS patients. Recently, we and others found that CCR9+ Th cells are elevated in pSS peripheral blood and co-express CXCR3 and other chemokine receptors, known to be important for TFH cell survival. Our group also showed that CCR9+ Th cells play an important role in mucosal immunity and have been shown to produce high levels of IFN-γ, like CXCR3+ Th1 cells. Since ligands of CXCR3 (CXCL9/10/11) are abundantly expressed in the salivary glands of pSS patients the potential role of this receptor in conjunction with CCL25 was studied in comparison with other chemokine (Th) receptors.

Methods: To study potential chemokine interactions causing enhanced migration of CCR9+ T cells into the salivary glands in pSS.

Methods: CXCL10, CCL25, CXCL13, CCL17 and CCL20 mRNA and protein expression in the submandibular glands of pSS patients and non-pSS patients was assessed (mRNA: n=9 vs n=9 and protein: n=26 vs n=34, respectively). Frequencies of CXCR3, CCR9, CXCR5, CCR4 and CCR6 expressing Th cells in blood of pSS patients and healthy controls were assessed by flow cytometry (n=11 vs n=11). Chemokinesis assays (n=3 HC, n=5 pSS) were performed to study migration induced by CXCL10 and CCL25. Results: CCL25, CXCL10 and CXCL13 expression were increased in pSS compared to nSS patients, both at mRNA and protein level (all p<0.05). CXCL17 and CCL20 expression were low and detectable in only few patients. Protein levels of CXCL10 and CXCL13 correlated with lymphocytic focus scores and all 3 chemokines correlated with serum IgG levels in pSS (all p<0.05). CCL25 protein levels strongly correlated with CXCL10 (r=0.545, p<0.004) but not with CXCL13. A relative decrease of CXCR3+ cells was found in the CCR9+ Th subset in the peripheral blood of pSS patients (p=0.04), which was most pronounced in the effector and effector memory subsets (84% vs 26%, p=0.03 and 51% vs 27% (both respectively). CXCR4 or CCR6-expressing CCR9+ Th cells and CXCR5 or CCR6-expressing CCR4+ Th cells were not decreased. To test the hypothesis that CXCR4 ligands and CCL25 facilitate migration, co-migration of lymphocytes in response to CXCL10 and CCL25 was studied. CXCL10 and CCL25 induced synergistic Th cell chemotaxis in vitro (p<0.02 and p<0.01 as compared to CCL25 or CXCL10 only, respectively).

Conclusions: The decreased frequency of CXCR3+CCR9+ Th cells in blood of pSS patients may be due to a concerted action of overexpressed ligands at the site of inflammation. Elevated expression of ligands CXCL10 and CCL25 in the salivary gland and the synergetic effect on chemotaxis in vitro indicate a potential role for these chemokines in formation of lymphocytic infiltrates in exocrine glands of pSS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3914
CAN THE INCREASE OF LOBULES / FOCI RATIO BE
HISTOPATHOLOGICAL EVIDENCE OF PRIMARY SJÖGREN'S SYNDROME

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Background: Minor salivary gland biopsy from the lip region is commonly used for primary Sjögren’s syndrome’s (SS) diagnosis. It is accepted that changes of histopathology is the most important component of diagnostic criteria. In this study, we analyzed the relationship between histopathological changes and laboratory findings/clinical features in SS patients and control group.

Objectives: The aim of this study was to determine the histopathological changes in minor salivary tissue for SS diagnosis

Methods: A total of 69 minor salivary gland biopsies (29 Sjögren’s syndrome and 40 controls) were included in the study. Biopsies were evaluated by a blind pathologist unaware of the diagnosis. Histopathological findings were noted as ductal dilatation, fat tissue percentage (<10% or >10%), acinar atrophy, ductal/ acinar ratio and lobules/foci ratio. It was evaluated whether there was a relationship between histological changes and age, gender, ANA, anti-SSA, anti-SSB, RF and Chisholm scores.

Results: The lobules/foci ratio of patients with Sjögren’s syndrome was significantly higher than the control group (p<0.001). The cutoff value of the lobules/foci ratio for SS diagnosis was 0.8. Furthermore, there was a significant correlation between the lobules/foci ratio greater than 0.8 and antibodies (ANA, RF, anti-Ro) positivity and Chisholm score (p<0.01). Other histopathological findings such as ductal dilatation, fat tissue percentage, acinar atrophy, and ductal/atherine ratio do not distinguish SS from non-SS.

Conclusions: The results of this study revealed that only the lobules/foci ratio from histopathological changes has a strong relation with SS diagnosis. It can be important for pathologists to distinguish SS.

Disclosure of Interest: None declared


THE ROLE OF STEM CELL-LIKE MEMORY T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The stem cell-like memory T (Tscm) cell, a special subset of memory T cell, has a potential to self-renew and differentiate into wide spectrum of T cells1. However, the role of Tscm in autoimmune disease such as systemic lupus erythematosus (SLE) remains to be unknown.

Objectives: To investigate the levels of Tscm cells in SLE patients compared with healthy controls and to understand the functional characteristics of the Tscm cells from SLE patients.

Methods: Fifty two SLE patients and 57 healthy controls (HCs) were enrolled. To detect Tscm cells which are designated as CD3+ CD4+ CD8+ CD45RA- CCR7+ CD62L- CD45RA+ CD27+ CD28+ CD127+ CD122+ CD95+1, flow cytometry was performed after stimulating peripheral blood mononuclear cells (PBMCs, 1x10^7 cells/mL) with fluorescence-conjugated antibodies. To ascertain the differentiation ability of Tscm cells, different subsets of T cells including naive-like T, central memory T, effector memory T and follicular helper T cells (Tfh) were evaluated after stimulating the isolated Tscm cells with anti-CD3/CD28 antibodies for 6 days. To investigate the function of the Tfh cells derived from Tscm cells, secreted IgG antibodies were measured from the supernatants by ELISA after incubating Tfh –containing differentiated Tscm cells with autologous B cells and SEB for 6 days.

Results: Among the naive-like T (CD3+ CD4+ CCR7+ CD45RA- CD45RA+ CD62L-), the proportion of CD4+ and CD8+ Tscm cells was significantly higher in SLE patients than HCs (for CD4+ T cells, 2.9±0.22 (SLE) vs 1.1±0.13 (HC), p-value<0.001; for CD8+ T cells, 5.36±0.63 (SLE) vs 3.41±0.44 (HC), p-value=0.013). Among the total CD4+ T cells, the ratio of Tscm to CD4+ T cells was higher in SLE patients than in healthy controls (0.63±0.10 (SLE) vs 0.40±0.04 (HC), p-value=0.035) (Fig 1). SLE and HC Tscm cells could differentiate into naive-like T, central memory T, effector memory T cells and renewed themselves in response to α-CD3/CD28 stimuli. In addition, in response to the same stimuli, SLE Tscm cells could differentiate into more Tfh cells than HC Tscm cells could (for CXCR5+ ICOS+ PD-1+ T cells in CD4+ T cells, 9.30% (SLE) vs 5.41% (HC) and for Bcl-6+ cells in CD4+ T cells, 34.29% (SLE) vs 19.20% (HC)). Tscm-derived Tfh cells could help B cells produce antibodies in vitro (12007.81±4457.54 (SLE) vs 2082.18±517.82 (HC)).

Conclusions: Proportions of Tscm cells among T cells is increased in SLE patients compared with HCs and the Tscm cells may help maintain SLE by its ability to differentiate into Tfh cells.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2116

Figure 1. Minor salivary gland biopsy pictures with different stainings of mTOR. (a) positive staining (b) negative staining (c) and score 2 (d) and TGF-β1 (negative staining (e) and score 3 (f)).
The impact of classifying SLE patients with the presence of anti-Ro and anti-La antibodies is associated with poor renal outcomes in lupus nephritis (LN) independently of glomerular pathology. Specific antibody profiles associated with LN have not been identified. Unlike glomerular damage, TID is not associated with anti-dsDNA or complement levels. An association between TID and the presence of anti-Ro/La antibodies has been proposed in Sjogren’s syndrome. Whether these antibodies are associated with TID in LN is not known.

Objectives: To study an association between anti-Ro/La antibodies and moderate-to-severe TID in LN.

Methods: We identified all patients who fulfilled ACR and/or SLICC criteria for SLE. Patients were included if they had an index renal biopsy consistent with LN between January 2005 and July 2015 and had complete data on TID and anti-Ro/La. Medical history, demographic and laboratory data were ascertained from chart review. TID was defined as the presence of moderate or severe tubular atrophy or interstitial fibrosis from the renal biopsy reports.

Results: Of the 157 LN patients, 39 (25%) had moderate/severe TID (Table). As expected, moderate/severe TID was associated with older age, class III/IV LN and lower estimated glomerular filtration rate (eGFR) by biopsy. Anti-Ro antibodies were present in 54% of patients with none/mild TID and 17% of patients with moderate/severe TID (p=0.047). Both anti-Ro and anti-La antibodies were present in 19% of patients with none/mild TID vs 11% of patients with moderate/severe TID (p=0.003). In the logistic regression model adjusted for age, eGFR and LN class, the presence of both anti-Ro and anti-La antibodies was associated with a 3-fold increase in the odds of TID. OR 3.1, 95% CI (1.1–9.1), p=0.04.

Baseline characteristics by TID (none/mild vs moderate/severe).

None/Mild TID
Moderate/Severe TID
p-value

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(n=118)</th>
<th>(n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), years</td>
<td>26 (17, 37)</td>
<td>41 (25, 53)</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>21 (18)</td>
<td>10 (26)</td>
</tr>
<tr>
<td>Malar rash, n (%)</td>
<td>55 (47)</td>
<td>22 (56)</td>
</tr>
<tr>
<td>Hispanic ethnicity, n (%)</td>
<td>41 (40)</td>
<td>12 (38)</td>
</tr>
<tr>
<td>Charlson comorbidity index, median (IQR)</td>
<td>3 (1, 4)</td>
<td>3 (1, 4)</td>
</tr>
<tr>
<td>Creatinine (mg/dl), median (IQR)</td>
<td>0.8 (0.6, 1.2)</td>
<td>1.6 (1, 2.6)</td>
</tr>
<tr>
<td>eGFR mL/min/1.73m², median (IQR)</td>
<td>91 (61, 127)</td>
<td>42 (26, 75)</td>
</tr>
<tr>
<td>Protein/Creatinine ratio (mg/mg), median (IQR)</td>
<td>2.2 (1.0, 4.9)</td>
<td>2.1 (1.5, 5.5)</td>
</tr>
<tr>
<td>LN class n (%)</td>
<td>0.038</td>
<td></td>
</tr>
<tr>
<td>I/II</td>
<td>10 (9)</td>
<td>0</td>
</tr>
<tr>
<td>III/IV</td>
<td>71 (61)</td>
<td>34 (87)</td>
</tr>
<tr>
<td>V</td>
<td>35 (30)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Low C3, n (%)</td>
<td>83 (75)</td>
<td>23 (70)</td>
</tr>
<tr>
<td>Low C4, n (%)</td>
<td>76 (70)</td>
<td>22 (67)</td>
</tr>
<tr>
<td>Elevated dsDNA, n (%)</td>
<td>70 (68)</td>
<td>21 (66)</td>
</tr>
<tr>
<td>Anti-Ro, n (%)</td>
<td>55 (47)</td>
<td>17 (44)</td>
</tr>
<tr>
<td>Anti-La and anti-Ro, n (%)</td>
<td>11 (9)</td>
<td>11 (28)</td>
</tr>
</tbody>
</table>

Conclusions: The presence of anti-Ro and anti-La antibodies is associated with moderate/severe TID of the LN. Other baseline characteristics were not significantly different between the two groups.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2237
Objectives: The objective of this study was to investigate the association between SLE and Bipolar Disorder (BD) using big data analysis methods.

Methods: Patients with SLE were compared with age- and sex-matched controls regarding the proportion of BD in a cross-sectional study. Chi-square and t-tests were used for univariate analysis and a logistic regression model was used for multivariate analysis after adjustment for confounders. The study was performed utilizing the chronic disease registry of Clalit Health Services medical database.

Results: The study included 5,018 SLE patients and 25,090 matched controls. BD was found in a higher proportion among SLE patients compared to controls (0.62% vs. 0.26%, respectively, p<0.001). BD patients had a greater proportion of smokers compared to non-BD patients (62.5% vs 23.5%, respectively, p<0.001). In a multivariate analysis, smoking and SLE were both found to be significantly associated with BD.

Multivariate logistic regression model of covariates associated with Bipolar disorder

<table>
<thead>
<tr>
<th>OR</th>
<th>CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01</td>
<td>1.00, 1.02</td>
</tr>
<tr>
<td>Gender: Female</td>
<td>1.63</td>
<td>0.96, 2.97</td>
</tr>
<tr>
<td>SES: Medium vs. Low</td>
<td>1.06</td>
<td>0.66, 1.69</td>
</tr>
<tr>
<td>High vs. Low</td>
<td>1.17</td>
<td>0.67, 1.98</td>
</tr>
<tr>
<td>Smoking</td>
<td>3.16</td>
<td>3.73, &lt;0.001</td>
</tr>
<tr>
<td>SLE</td>
<td>1.74</td>
<td>1.11, 2.66</td>
</tr>
</tbody>
</table>

SLE: Socioeconomic status, SLE: Systemic lupus erythematosus.

Conclusions: SLE was found to be independently associated with BD. These findings may imply that an autoimmune process affecting the central nervous system among lupus patients facilitates the expression of concomitant BD.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3687

THU0249
SUBCLINICAL HAND ARTHROPATHY IN PATIENTS WITH SYSTEMIC LUPUS ERITEMATOSUS

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Background: As well as other systemic inflammatory diseases with joint compromise, there is an interest to identify the presence of synovitis in systemic lupus erythematosus (SLE) patients, in every follow up consultation. In SLE, the research about subclinical synovitis (that, which is clinically unnoticed but demonstrable by means of image studies) is quiet limited. The majority of studies non selected patients so many of them counted with patients with chronic synovitis or even deformities. Due to that their results are difficult to compare and the real prevalence of subclinical synovitis is still unknown.

Objectives: To determine the prevalence of synovitis in a selected cohort of patients without clinical evidence of arthritis or synovitis.

Methods: We performed a prospective study on 96 SLE patients grouped as follows: Group 0 (20) without any historical or present joint symptoms, Group 1 (34) with intermittent joint pain and Group 2 (42) with intermittent arthritis without deformities or erosions. A systematic US study of the carpal, 2nd and 3rd MCP joint of the non dominant hand were performed to all patients. US findings were expressed according to the nomenclature EULAR recommendations for synovitis, power Doppler signal and composite synovitis index.

Results: Six patients from group 0 showed any grade of synovitis (30%), 13 from group I (38.2%) and 18 from group II (42.8%). From the whole group of subjects, those with at least a synovitis finding was 37 (38.5%). Into the 2nd MCP joint, 4 patients (20%) from group 0 showed any grade of synovitis, one of them (5%) with power Doppler (PD) signal. The composite index of synovitis and PD signal (CSI) was 0.3 DE 0.36. In group 1, 9 patients (26.5%) showed any grade of synovitis, 4 of them also showed PD signal (11.8%). The CSI for this group was 0.44 DE 0.48. In group 2, 15 patients (14.3%) showed any grade of synovitis and 6 of them also showed PD signal (14.3%). The CSI for this group was 0.59 DE 0.55. Globally, we detected synovitis in 28/96 patients (29.2%) and PD signal in 11 (11.5%).

Conclusions: We performed a prospective study on 96 SLE patients grouped as patients without clinical evidence of arthritis or synovitis. Due to that their results are difficult to compare and the real prevalence of subclinical synovitis is still unknown. The majority of studies non selected patients so many of them counted with patients with chronic synovitis or even deformities. Our findings may imply that an autoimmune process affecting the central nervous system among lupus patients facilitates the expression of concomitant BD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2210

THU0250
EFFECT OF FETAL UMBILICAL ARTERY DOPPLER ON PREDICTION OF ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Pregnancies in women with SLE resulted in an increase of adverse pregnancy outcomes (APOs). The predictive value of fetal umbilical artery Doppler examinations for APOs has been reported, while not widely be assessed in SLE pregnant women.

Objectives: To ascertain the predictive value of fetal umbilical artery Doppler for fetal APOs in SLE pregnancies.

Methods: A fetal Doppler ultrasound examination was performed on all fetuses during the third trimester (28–36 weeks of gestation) and the term pregnancy (37–42 weeks of gestation). The Doppler flow parameters of umbilical arteries were recorded, including pulsatility parameter (PI), resistance index (RI), the peak value of umbilical arteries at end-diastole (Vmax, also abbreviate as S) and the peak value of umbilical arteries at end-diastole (Vmin, also abbreviate as D). The value of S/D was automatically calculated. Clinical data and pregnancy outcomes were analyzed retrospectively.

Results: In total, 109 cases of pregnant SLE women performed fetal umbilical artery Doppler at the third trimester and 82 at the term pregnancy. Among the 109 cases, 65 resulted in one or more APOs, including 45 with premature delivery, 23 with intrauterine growth restriction (IUGR), 16 with fetal distress, 8 with neonatal lupus (NLE) and 3 with congenital malformation. Fetuses with APOs had higher S/D values compared with fetuses without APOs (2.9±0.9 VS. 2.4±0.5, p=0.001). In addition, other Doppler indexes did not differ significantly across groups. The positive and negative predictive values were 83.3% and 52.1%, respectively. Among the 82 cases with term pregnancy, 23 resulted in APOs, including 11 with IUGR, 15 with fetal distress, 4 with NLE and 1 with congenital malformation. All of the Doppler indexes (S/D, PI, RI, Vmax and Vmin) in fetus with APOs were higher than those without APOs, but no statistical significance were found between the 2 groups.

Conclusions: Umbilical artery Doppler was a good monitor method for APOs in pregnancies complicated by SLE. Women with more 2.8 S/D could start strict monitoring to rapidly identify and treat obstetric complications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2210

THU0251
DIFFERENT RESPONSES TO INDUCTION THERAPY IN TWO ONSET CATEGORIES OF LUPUS NEPHRITIS

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Background: We previously reported different clinical features, serological profiles and activities in two onset categories of lupus nephritis (LN): LN that
developed as a flare of systemic lupus erythematosus (SLE) after treating the prior non-renal SLE conditions successfully (delayed, D-LN) and LN manifesting at the time of SLE onset (early, E-LN). More frequent flares and higher serum titers of anti-dsDNA antibody during the LN flares were observed in D-LN than E-LN, suggesting that D-LN may reflect intractable SLE conditions. However, we had not analyzed whether there is a difference in the response to treatment between the two groups.

**Objectives:** This study investigated possible differences in the response to induction therapy between E-LN and D-LN.

**Methods:** We retrospectively examined 95 LN (48 E-LN, 47 D-LN) patients who attended our hospital between January 1991 and May 2016. All of them were diagnosed with SLE according to the American College of Rheumatology criteria and were shown to have LN on renal biopsy. First, we compared the clinical features of E-LN and D-LN, such as sex, age at SLE and LN onset, urinary protein, serum creatinine, serum anti-dsDNA titer, serum Ca, prevalence of serum anti-Sm, renal biopsy histological types and induction therapy options at LN onset. Then we compared the response to therapy at 24 weeks for LN onset and flares between the two groups. The response to treatment was classified into complete response (CR), partial response (PR), and “scleroderma-like pattern”. Higher serum C3 (56.4±22.4 vs. 46.5±22.7 mg/dl, p=0.03) were observed in D-LN groups. The proportion of histological types (I or II/III or III/I-V or IV-V or IV-V) was 6/7/6 in E-LN vs. 4/5/6/12 (p=0.77) and induction therapy options at LN onset were similar between the two groups. However, the response to therapy for LN onset was better in E-LN than D-LN (CR/PR/IR: 37/10/1 vs. 24/17/6, p=0.02) (Fig). Univariate Cox regression analysis indicated that severe proteinuria, elevated serum creatinine, class IV or IV-V on renal biopsy and D-LN were associated with non-CR (PR+IR) to induction therapy for LN onset (p<0.05). Multivariate Cox regression analysis including variables identified as significant in univariate analyses showed that severe proteinuria (hazard ratio [HR]: 1.35, p=0.007) and D-LN (HR 4.96, p=0.003) were independent predictors of non-CR to the induction therapy. LN flares were observed in 13/48 E-LN and 20/47 D-LN patients, and IR was observed in 15.4% (2/13) of E-LN and 40.0% (8/20) of D-LN patients.

**Conclusions:** In this study, the relatively poorer treatment response was observed in D-LN compared with E-LN patients and D-LN was a predictor of poorer treatment response independent of renal histology and the severity of nephritis at LN onset.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2694

**THU0252**

**NAILFOLD CAPILLAROSCOPY IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND CRITICAL APPRAISAL**

S. Wijnant1, F. Ingegnoli2, K. Melsens3, F. De Keyser1,3, K. Thevissen3, F. De Keyser1,3,

**Background:** Systemic lupus erythematosus (SLE) is a rheumatic disease with common vascular involvement. Nailfold capillaroscopic changes have been described in SLE. Although, until today there is no clear role yet for capillaroscopy in classifying or staging the disease.

**Objectives:** To systematically review and critically appraise the literature on capillaroscopic changes described in SLE.
COMPARISON OF URBAN VERSUS RURAL ENVIRONMENT
ASSOCIATED SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RISK AND CLINICAL FEATURES

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Background: SLE originates from the complex interplay between genetic, epigenetic and environmental factors but the effects of the latter remain elusive. Very few studies have examined the impact of the place of residence (urban/rural) on SLE clinical profile and outcomes.

Objectives: To evaluate the effect of rural versus urban place of residence with regards to: i) SLE occurrence; ii) delay in diagnosis; iii) clinical manifestations, severity and non-reversible organ damage; iv) comorbidities and hospitalizations.

Methods: We employed data from the Lupus Epidemiology & Surveillance project in Crete (750 adult SLE patients with ≥4 ACR-1997 classification criteria). Crete is a Mediterranean island with genetically stable and homogenous population in ethnicity and sociodemographic characteristics, with no significant inequalities regarding access to healthcare facilities; 61% of the inhabitants live in rural (-10,000 people) and 47% in urban areas (-10,000 people). Demographics and residency history were retrieved from face interviews. In 200 patients with exclusively urban or rural residence, a subanalysis was performed in relation to disease risk, diagnosis age, disease severity, renal and neuropsychiatric involvement, and organ damage (SLICC damage Index [SDI]).

Results: SLE prevalence (December 2013) varied across the four geographical prefectures of Crete (Figure 1) and was significantly higher in urban (165/105) vs rural (123/105) areas (p<0.001). The relative risk of SLE in urban versus rural regions was 2.0 (95% Confidence Interval 1.5–2.9). Notably, patients in urban regions had lower age of diagnosis (38±13.4 vs. 44±14.8 years, p<0.005) and female-to-male ratio (6.5:1 vs. 11:1) than those in rural regions. Delay ≥2 years between symptoms onset and SLE diagnosis occurred in 42% of patients from rural areas as compared to 32% of those from urban areas (p<0.01). Acute cutaneous lupus was more prevalent in the rural environment (83.9% vs. 72.6%, p<0.05) whereas the opposite trend was noted for discoid rash (2.3% vs. 16.8%, p<0.001). Nephritis occurred less frequently (10.3% vs. 12.4%) and nephropathic disease was more prevalent (14.9% vs. 10.6%) in rural than urban patients albeit non-significantly. Prevalence of mild, moderate, and severe disease was 42%, 40%, and 18% in patients from rural areas, the respective figures being 55%, 28% and 18% in those from urban areas (p<0.012). Hospitalization due to active lupus did not differ between the two groups. At last follow-up, 45.3% of the patients living in urban and 51.9% of patients in rural areas had no organ damage (p=0.89). Concurrent allergic diseases were more frequent in urban patients (30.9% vs. 14.3%, p=0.045), particularly allergic rhinitis (8.8% vs. 2.3%, p=0.05).

Conclusions: SLE may be more prevalent in urban than rural regions and urbanization is associated with increased risk of SLE and earlier age of disease onset. Our results suggest an important effect of the environment on SLE occurrence and characteristics, which warrants further investigation.

Disclosure of Interest: None declared

THU0255 COMPARISON OF REMISSION AND LUPUS LOW ACTIVITY STATE AS PREDICTORS OF ORGAN DAMAGE

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Background: Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage.

Objectives: We assessed whether two recently proposed disease activity outcomes were predictive of future damage.

Methods: For each month of follow-up in a large SLE cohort, we determined whether the patient was in Clinical Remission (as defined by the DORIS work group) or low lupus disease activity state (LLDAS) (as defined by Franklyn et al.). Clinical Remission was defined as a PGA<0.5, clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone~<5mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI ≤4, PGA ≤1.0, no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone ≤7.5 mg/d and immunosuppressants. Damage was defined using the SLICCA/ACR index.

Results: There were 81,118 person-months observed among 2,026 patients (92% female, 53% Caucasian, 39% African-American). Table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS.

Table 1. Rates of new damage, in subgroups defined by past level of disease activity

<table>
<thead>
<tr>
<th>Percentage of prior months in:</th>
<th>Number of person-months observed</th>
<th>Number of months with an increase in SLICC/ACR damage</th>
<th>Rate of damage per 100 person-months</th>
<th>Rate ratios</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>35,772</td>
<td>406</td>
<td>1.13</td>
<td>1.0 (Ref)</td>
<td></td>
</tr>
<tr>
<td>Not none, but ≤25%</td>
<td>14,358</td>
<td>102</td>
<td>0.71</td>
<td>0.60 (0.48, 0.75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>25% to 50%</td>
<td>6573</td>
<td>50</td>
<td>0.76</td>
<td>0.66 (0.46, 0.94)</td>
<td>0.023</td>
</tr>
<tr>
<td>50% to 75%</td>
<td>3845</td>
<td>27</td>
<td>0.70</td>
<td>0.63 (0.42, 0.97)</td>
<td>0.035</td>
</tr>
<tr>
<td>75%+</td>
<td>1,641</td>
<td>10</td>
<td>0.61</td>
<td>0.58 (0.30, 0.95)</td>
<td>0.12</td>
</tr>
<tr>
<td>Clinical Remission on Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>16,491</td>
<td>250</td>
<td>1.52</td>
<td>1.0 (Ref)</td>
<td></td>
</tr>
<tr>
<td>Not none, but ≤25%</td>
<td>20,169</td>
<td>170</td>
<td>0.84</td>
<td>0.54 (0.44, 0.67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>25% to 50%</td>
<td>14,344</td>
<td>103</td>
<td>0.72</td>
<td>0.46 (0.36, 0.67)</td>
<td>0.0001</td>
</tr>
<tr>
<td>50% to 75%</td>
<td>8,396</td>
<td>54</td>
<td>0.64</td>
<td>0.43 (0.30, 0.60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>75%+</td>
<td>2,789</td>
<td>18</td>
<td>0.65</td>
<td>0.45 (0.27, 0.75)</td>
<td>0.0019</td>
</tr>
</tbody>
</table>

LLDAS                           |                                  |                                             |                                   |            |         |
| None                          | 30,366                           | 343                                         | 1.13                              | 1.0 (Ref)  |         |
| Not none, but ≤25%            | 10,890                           | 106                                         | 0.97                              | 0.86 (0.69, 1.07) | 0.18 |
| 25% to 50%                    | 5,012                            | 40                                          | 0.80                              | 0.70 (0.51, 0.98) | 0.037 |
| 50% to 75%                    | 8,494                            | 60                                          | 0.71                              | 0.63 (0.48, 0.83) | 0.0001 |
| 75%+                          | 7,527                            | 46                                          | 0.61                              | 0.54 (0.40, 0.73) | <0.0001 |

Damage rates were relatively low when LLDAS was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least 50% of the time.

Conclusions: The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment >50% of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.

Disclosure of Interest: None declared

THU0256 DEVELOPMENT AND VALIDATION OF A SCORE TO PREDICT THE RISK OF SEVERE INFECTION IN SLE

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Background: Infection is a major cause of morbidity and mortality in SLE patients. It would be helpful to have a tool to predict the risk that an individual patient with SLE will develop serious infection.

Objectives: To develop a predictive risk calculation algorithm (SCORE) that...
assesses the probability of serious infection (i.e. leading to hospitalization) in SLE patients and to test it in an independent cohort.

**Methods:** The SCORE was developed using data from the RELESSER (Spanish Society of Rheumatology Lupus Registry) cohort of 3658 SLE patients. A Cox regression model for repeated events (Andersen-Gill) was applied to assess which demographic and clinical factors were independently associated with increased risk of developing serious infection (Table 1). The SCORE was then validated using retrospective data from the UCLH (University College London Hospital) cohort including 699 SLE patients. Median SCORE values were compared between sub-groups of patients using the U-Mann-Whitney test.

**Results:** Among 699 SLE UCLH patients, 98 (14%) developed serious infection. We compared these patients with 111 SLE controls who have never suffered serious infection. The characteristics of both groups are summarized in Table 2. The infection group were more likely to have suffered previous infection (P<0.001) and/or hospitalized for SLE (P<0.001) and had renal and joint disease (P<0.005). Over a quarter of the infection group died from their infection. Median (Md) SCORE at diagnosis in SLE patients with infection was 4.27 (IOR 3.18) which was significantly higher than in the control group (Md 2.55, IQR 3.79; P=0.0008). Md SCORE before infection in patients was 5.3 (IQR 3.68) which was significantly higher than at diagnosis (P<0.001; P<0.001) in those patients. By ROC analysis, we defined three possible cut-offs to distinguish patients with and without infection. The area under the ROC curve was 0.66 (CI 95% 0.56 to 0.71). A cut-off for SCORE at diagnosis >3.18 identified patients who would develop serious infection with sensitivity (S)76.5% and specificity (SPC) 50.5%. For SCORE>3.75, S was 64.3% and SPC 57.7%. For SCORE >4.24, S was 64.3% and SPC 60.4%.

**Table 1 – FACTORS INCLUDED IN THE SCORE**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>B</th>
<th>P-value</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (&gt;44 years old)</td>
<td>0.1163</td>
<td>0.001</td>
<td>1.12</td>
</tr>
<tr>
<td>Latin ethnicity</td>
<td>0.437</td>
<td>0.001</td>
<td>2.40</td>
</tr>
<tr>
<td>Corticosteroids (mg/day) at time of calculating SCORE</td>
<td>0.2678</td>
<td>0.001</td>
<td>1.33</td>
</tr>
<tr>
<td>Seemal score</td>
<td>0.3692</td>
<td>0.0003</td>
<td>1.49</td>
</tr>
<tr>
<td>Previous hospitalization (yes/no)</td>
<td>1.0049</td>
<td>&lt;0.00001</td>
<td>2.73</td>
</tr>
<tr>
<td>Keto index</td>
<td>0.062</td>
<td>0.002</td>
<td>1.06</td>
</tr>
<tr>
<td>Prior infection at any time</td>
<td>0.8759</td>
<td>&lt;0.0001</td>
<td>2.40</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SLE-infection (n=98)</th>
<th>SLE-non infection (n=111)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Females: 90 (91.9)</td>
<td>Females: 103 (92.8%)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>Males: 8 (8.2%)</td>
<td>Males: 8 (7.2%)</td>
<td></td>
</tr>
<tr>
<td>Mean age (years old) of SLE</td>
<td>30.5 (27)</td>
<td>31 (18)</td>
<td>ns</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian 49 (49%)</td>
<td>Caucasian 72 (64.9%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Latin American 3 (3.6%)</td>
<td>Latin American 2 (1.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>African/Caribbean 28 (28.6%)</td>
<td>African/Caribbean 20 (18.02%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian 7 (7.1%)</td>
<td>Asian 6 (5.4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other 12 (12.2%)</td>
<td>Other 12 (10.8%)</td>
<td></td>
</tr>
<tr>
<td>Median length of follow-up (IQ)</td>
<td>9.5 (14) yrs</td>
<td>14 (9) yrs</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous treatment</td>
<td>Steroids at any time 89 (90.8%)</td>
<td>Steroids at any time 61 (55%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>MMF 25 (25.5%)</td>
<td>MMF 23 (20.7%)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>AZA 46 (47%)</td>
<td>AZA 29 (26.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide 20 (20.4%)</td>
<td>Cyclophosphamide 13 (11.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Biological treatment 24 (24.5%)</td>
<td>Biological treatment 22 (19.8%)</td>
<td>ns</td>
</tr>
</tbody>
</table>

**Conclusions:** We have developed a SCORE for predicting risk of serious infection in SLE and validated it in an independent cohort. Given the potential mortality from such infections, this SCORE could be clinically useful though the moderate sensitivity and specificity necessitate caution and further prospective studies.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4130

**THU0257 ENHANCED ACTIVATION OF NLRP3 INFLAMMASOMES IN PATIENTS WITH SJÖGREN’S SYNDROME**

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**Background:** There has been data about pathogenic role of NLRP3 inflammasome in Sjögren’s syndrome. However, linkage between their clinical features and NLRP3 inflammasome has not been clearly defined.

**Objectives:** The aim of this study is to identify the association of NLRP3 inflammasome with clinical features in patients with primary Sjögren’s syndrome.

**Methods:** A total 25 female patients with Sjögren’s syndrome and gender-matched 25 healthy controls were consecutively enrolled. The mRNA expression for target genes including NLRP3, ASC, caspase-1, IL-1β, and IL-18 in peripheral blood mononuclear cells (PBMCs) were measured using real-time polymerase chain reaction. Serum IL-1β and IL-18 expression were also measured by ELISA method. Clinical information and disease activity and damage for Sjogren’s syndrome such as EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI) and Sjögren’s Syndrome Disease Damage Index (SSDDI) were collected at the time of enrolment. Statistical analysis were applied including Spearman’s correlation coefficient and Mann-Whitney t-test.

**Results:** Patients with Sjögren’s syndrome was found to be highly expressed in mRNA IL-1β and its protein, compared to controls (p<0.001 and p<0.001, respectively). The mRNA levels of caspase-1 and ASC were significantly higher than those in controls (p<0.02 and p=0.008, respectively), but not mRNA level of NLRP3. The mRNA level of IL-1β is closely related with mRNA level of NLRP3 and ESR (r=0.549, p<0.001 and r=0.577, p=0.003, respectively). Serum IL-1β protein expression in Sjögren’s syndrome was found to be associated with mRNA level of caspase-1. Based on SSDDI, patients with SSDDI >1 was older and had higher IL-1β and NLRP3 mRNA expression, compared to those with SSDDI =0 (p=0.035, p=0.005, and p=0.016, respectively).

**Conclusions**: This study confirmed that activation of NLRP3 inflammasome might implicated the pathogenesis of Sjögren’s syndrome.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3068

**THU0258 SERUM PARAOXONASE 3 ACTIVITY IS REDUCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHROMATOMATOSIS AS COMPARED TO HEALTHY CONTROLS**


**Background:** Premature atherosclerosis is a well recognised comorbidity in patients with SLE (1). Elevated levels of circulating Oxidised Low Density Lipoprotein (OxLDL) have been described in SLE patients, especially in those with a history of cardiovascular disease (2). Paraoxonase 3 (PON3) is believed to play a role in prevention of atherosclerosis by contributing towards the anti oxidant activity of high density lipoprotein (HDL).

**Objectives:** To determine serum PON3 levels and PON3 activity in patients with SLE and compare them with healthy controls.

**Methods:** Serum PON3 levels and PON3 activity were determined in 100 patients of SLE with no prior history of coronary artery disease and they were compared with those of 50 healthy controls who did not have diabetes, hypertension or coronary artery disease. Serum PON3 concentration was determined by enzyme-linked immunosorbent assay (ELISA) using anti-PON3 antibody specific for human PON3. PON3 activity was estimated using Spectrophotometric assay which quantified the hydrolysis of dihydrocholesterin at 270 nm (3).

**Results:** PON3 levels were lower in SLE patients (P<0.001) and PON3 activity was reduced (p<0.001) compared to healthy controls. In subgroup analysis of SLE patients, PON3 activity and levels did not correlate with disease activity. On Univariate analysis, serum creatinine (r=0.06, p=0.002), age (r=0.03, p=0.035), and SLE status (r=-0.27, p<0.001) contributed to PON3 levels. On Univariate analysis, serum creatinine (r=0.15, p=0.001), AST (r=0.04, p=0.01), ALT (r=0.16, p<0.001) and SLE status (r=-0.77, p<0.001) contributed to PON3 levels. On multivariate analysis, only SLE status predicted PON3 levels (P<0.001) and PON3 activity (p<0.001).

**Conclusions:** PON3 levels are reduced and PON3 activity is decreased in patients with SLE as compared to healthy controls, the difference was attributable to the disease itself. This may contribute to premature atherosclerosis in these patients.

**References:**


Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3459

THU0259 RESPIRATORY SYMPTOMS IN PRIMARY SJÖGREN’S SYNDROME, A CROSS-SECTIONAL STUDY OF THE OASIS COHORT

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Background: In previous studies, 5 to 35% of patients with primary Sjögren’s syndrome (pSS) are reported to have respiratory symptoms (RS). Pulmonary involvement varies from a dry cough due to airway dryness to life-threatening interstitial lung disease.

Objectives: To evaluate RS prevalence in patients with pSS and compare characteristics of pSS patients with and without RS to those in patients without pSS suffering from ocular or oral dryness.

Methods: Cross-sectional study of patients at the time of their inclusion in the OASIS cohort between 2014 and September 2016. This UK prospective research includes patients with suspected pSS or known pSS and aims to collect long-term high quality data with regular clinical, dental and ophthalmological assessments. We asked systematically all the patients if they had any RS. In case of clinically significant RS, pulmonary function tests (PFTs) were requested, and if needed, a high-resolution chest tomography (HRCT) was performed. We included in the analysis only patients fulfilling the AECG (2002) criteria for pSS and excluded patients with secondary Sjögren’s syndrome. Characteristics of pSS patients with and without and non-pSS patients with sicca symptoms were compared. For HRCT and pulmonary function tests, we used unpaired t test, Mann-Whitney test, Fisher’s exact test and Chi-square test when appropriate. P < 0.05 was considered statistically significant.

Results: Among the 157 patients included in the cohort, 70 fulfilled the AECG criteria for pSS and 63 had sicca symptoms without pSS. In the pSS/sicca group, 18% (28/157) of patients had RS, compared to 5% (4/97) of non-pSS patients with sicca symptoms without pSS suffering from ocular or oral dryness. These results were statistically significant.

Conclusions: In conclusion, we found a considerable RS prevalence in pSS patients and a lesser prevalence, but still significant, in patients with sicca symptoms without pSS. We also found that pSS patients with RS had higher ESSDAI and ESSPRI index values but did not differ in terms of objective measurements of tear and saliva production, histological focus scores and auto-immunity profiles.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5757

THU0260 LOW PLASMA CONCENTRATIONS OF APOPOPROTEIN M CORRELATE TO DISEASE ACTIVITY AND ENDOTHELIAL DYSFUNCTION IN SLE

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Background: ApoM is an antiatherogenic and vasculoprotective 25kDa apolipoprotein suggested to play a role in keeping endothelial barrier integrity.

Objectives: The aims of the current study were to determine the impact of SLE disease activity on apoM levels and to investigate if apoM levels reflect endothelial function in SLE.

Methods: Plasma concentrations of apoM were measured in ELISA in two SLE cohorts. All patients fulfilling ACR classification criteria for SLE, and 100 healthy controls (HC). Patients in cohort I had active disease as evaluated with SLEDAI score. In cohort II endothelial function was measured by EndoPAT 2000 and correlated to apoM levels. A low Reactive Hyperemia Index (RHI) value indicated endothelial dysfunction (ED).

Results: In cohort I, the plasma levels of apoM were found to be significantly decreased in SLE (p < 0.0001), and the apoM concentrations correlated inversely to disease activity (SLEDAI, r = -0.29, p = 0.0063). ApoM was also significantly lower in patients with active nephritis, leukaopenia, anti-DNA antibodies or rash compared to patients without these manifestations. In cohort II, using linear regression analysis, there was a positive correlation between apoM levels and the RHI value, indicating endothelial dysfunction, in the younger SLE patients: p = 0.94 CI 95% 0.22,1.65 r=0.32 p = 0.011.

Conclusions: SLE related inflammation may have an impact on lower plasma apoM, which may affect the endothelium and the process towards cardiovascular disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4759
PREVALENCE OF REMISSION AND ITS EFFECTS ON ORGAN DAMAGE AND QUALITY OF LIFE IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: To study the effect of disease remission on organ damage and quality of life in Chinese patients with systemic lupus erythematosus (SLE).

Methods: Patients who fulfilled the ACR classification for SLE were studied. Their remission status at last visit was determined by the European consensus (DORIS definition): (1) Complete remission (clinical SLEDAI=0, serology inactive); and (2) Clinical remission (clinical SLEDAI=0, serology active). These two categories were further divided into those who required ongoing immunosuppressive treatment (corticosteroids ≤ 7.5 mg or other immunosuppressive agents) and who did not. The increase in SLE organ damage (SDI) score since 5 years prior to recruitment was compared between patients who were and were not in remission for ≥5 years. Participants were randomly selected for assessment of quality of life by using both the validated version of SF36 and the LupusPRO (version 1.8) and comparison was made between those who did and did not achieve remission for ≥5 years by the independent Students’ t-test.

Results: 769 SLE patients were studied (92% women; age 46.4±14.6 years, SLE duration 12.6±8.1 years). At last visit, clinical remission was present in 259 (33.7%) patients (median 43 months) and complete remission (clinically and serologically inactive) was present in 280 (36.4%) patients (median 51 months). Clinical/complete remission for ≥5years was achieved in 64 (8.3%) and 129 (16.8%) of the patients, respectively. 53 (6.9%) patients in remission ≥5 years were taken off all medications including HCO (drug-free). Compared with patients who did not remit, those remitted ≥5 years were older (49.8±13.2 vs 45.7±15.6; p=0.004), and had significantly lower prevalence of renal involvement, leucopenia or thrombocytopenia. Significantly fewer patients who remitted for ≥5 years were maintained on prednisone compared to others (31% vs 68%; p=0.001). The increase in SDI scores over the preceding 5 years was 0.17±0.53 in patients who had a prior clinical remission and ongoing therapy (except HCO) for ≥5 years (N=98), 0.25±0.51 in those remitted for ≥5 years but maintained on immunosuppressive medications (N=105), 0.41±0.84 in those remitted for <5 years (N=346) and 0.67±1.10 in those who did not remit (N=230), respectively. The increase in SDI was statistically higher in those remitted for ≥5 years than <5 years (p=0.007) or those who did not remit (p=0.001). Logistic regression showed that patients with remission for ≥5 years or who did not remit had an increase in the risk of new damage accrual as compared to those with remission for ≥5 years (OR 2.42 [1.50–3.98]; p=0.001), adjusted for age, sex, SLE duration, SDI scores 5 years prior to the last visit and the daily dosen of immunosuppressive therapy (except HCO) for ≥5 years (N=453) patients who had QOL assessment, remission for ≥5 years was associated with significantly higher physical component and mental component scores of the SF36 than those who did not remit. Patients with remission for ≥5 years had significantly higher scores in the individual health-related domains (except cognition) of the LupusPRO than those who did not remit.

Conclusions: Durable remission can be achieved in a quarter of patients with SLE. Patients with remission for ≥5 years have significantly less damage accrual and better QOL. Prolonged remission is an appropriate parameter for outcome assessment in SLE.
domains (Lupus Symptoms, Physical Health, Pain-Vitality, Emotional Health and Body Image) were responsive to changes in patient reported and physician assessed health status (disease activity and damage) (Table 1). Procreation and Cognition domains showed responsive trends with patient reported change in health status, while Lupus Medications domain was responsive additionally to changes in Damage.

Conclusions: LupusPRO summary HRQOL and HROQL domains show responsiveness to changes in patient-reported and physician assessed changes in health status in this observational study among Chinese SLE patients. Results support inclusion of LupusPRO into larger clinical trials to allow for robust estimates of responsiveness.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3943

THU0265 IDENTIFYING THE LINKS BETWEEN IRON DEFICIENCY AND FATIGUE IN ADOLESCENTS AND YOUNG ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Between 80–90% of patients with systemic lupus erythematosus (SLE) report fatigue to be the single most troublesome and debilitating symptom of their illness. Recent studies have found that functional iron deficiency and iron deficiency anaemia have been linked with fatigue and decreased cognitive performance. Increased red blood cell distribution width (RDW) is an early indicator of iron deficiency that can be useful in assessing iron stores in patients with SLE who may have an elevated serum ferritin due to underlying inflammation.

Objectives: To investigate the relationship between early iron deficiency (measured by RDW) and fatigue in adolescents and young adults with SLE.

Methods: Adolescent and young adult patients with SLE were recruited prospectively between November 2016 and January 2017. All patients were asked to complete the Functional Assessment of Chronic Fatigue Illness Therapy (FACIT) Fatigue Scale v4, in which a numerical score between 0–52 is generated. Lower scores indicate more fatigue. Standard measures of lupus disease activity including Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Complement C3 levels, anti-double stranded DNA binding (anti-dsDNA) and SLEDAI were recorded. Haemoglobin (Hb) and RDW were also measured. Anaemia was defined by World Health Organisation criteria (male Hb <130g/L and female Hb <120g/L). Non-parametric analysis was performed using Spearman’s rank with a p-value <0.05 felt to be significant.

Results: 33 patients aged between 16.7 and 27.5 years (median age 20) were included. 85% of the patients were female. Their FACIT scores were lower than those published for healthy individuals of the same age group - median 24, IQR 22–44 for SLE vs median 43, IQR 35–48 for healthy. There was no statistically significant correlation between FACIT Fatigue score and SLEDAI score (p=0.92), anti-dsDNA (p=0.36), C3 levels (p=0.37), ESR (p=0.30) or CRP (p=0.85). Interestingly a statistically significant negative correlation between FACIT Fatigue score and RDW was observed (p=0.012; r=-0.43). A correlation between FACIT Fatigue score and Hb was noted although this was not statistically significant (p=0.079). 12 of the 33 patients were found to be anaemic (11 female, 1 male). Analysis of the sub-group of 21 non-anaemic patients found FACIT Fatigue Score and RDW continue to show a statistically significant association (p=0.026; r=-0.49).

Conclusions: Fatigue is a common and debilitating symptom described by young patients with SLE. Standard serological and clinical markers of disease activity did not correlate with the burden of fatigue. Increased RDW has been shown for the first time to correlate with increased fatigue in patients with lupus, suggesting that iron deficiency may play a significant role in the manifestation of this troublesome symptom. A trial of therapeutic iron infusions in the treatment of fatigue in SLE is planned.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2440

THU0266 DAMAGE INDEXES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY ANTIPHOSPHOLIPID SYNDROME: DIAPS VS SLICC/ACR DAMAGE INDEX
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Background: Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are systemic autoimmune diseases that have overlapping irreversible organ damages. Since SLICC/ACR Damage Index (SDI) misses key features of APS, the Damage Index in patients with Thrombotic Antiphospholipid Syndrome (DIAPS) was proposed.

Objectives: To assess the differences in indexes available for measuring organ damage in a cohort of patients with SLE and secondary APS.

Methods: Clinical records of patients with SLE and secondary APS were reviewed. Data on medical history and clinical manifestations were collected. The two damage indexes, SDI and DIAPS, were applied. Comparison between the two indexes was done for each organ system affected.

Results: Sixty-five clinical charts were reviewed, 5 had been excluded for incomplete information. SDI and DIAPS was recorded in 60 patients. Patient’s mean age was 45.05±14.61 years, with mean disease duration of 9.47±6.96 years. Mean SDI in our cohort was 4.15±2.58 and mean DIAPS – 4.06±3.41. SDI correlated significant to DIAPS (R=0.926, p=0.000). Neuropsychiatric manifestations were found in 25 patients (41.7%). Their mean SDI value was 4.92±2.73 and DIAPS value of 5.52±3.47. DIAPS value was higher in the subgroup of patients with neuropsychiatric (p=0.006) and respiratory system damage (p=0.037) This difference was not observed regarding SDI value. DIAPS value correlated significantly to neurological (R=0.397, p=0.002) and pulmonary damage (R=0.364, p=0.004), but not to SDI value. No differences were observed between the two scores regarding peripheral vascular manifestation (DIAPS p=0.221, SDI p=0.136) and renal involvement (DIAPS p=0.082, SDI p=0.078).

Conclusions: SDI may under estimate APS related damage in patients with SLE and secondary regarding neurological and pulmonary organ involvement. Given the implications for high morbidity and mortality, DIAPS may be the appropriate damage score to be used.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4384

THU0267 METABOLIC SYNDROME AND HEALTH-RELATED QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Systemic Lupus Erythematosus (SLE) is associated to a huge prevalence and incidence of cardiovascular diseases (CVDs) due to accelerated atherosclerosis. Several evidences demonstrated that metabolic syndrome (MeS) could contribute to CVDs burden in SLE. In general population, MeS components and, according to some reports, MeS itself are associated to worsened Health related Quality of Life (HR-QoL). In SLE patients, a severe decline of HR-QoL has been widely demonstrated.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4384
Prevalence and features of celiac disease in patients with systemic autoimmune diseases: results of a large multicenter study

E. Bartoloni, A. Alunno, O. Bistoni, L. Cavagna, L. Nalotto, C. Baldini, A. Gabriele, S. De Vita, R. Giacomelli, R. Gerli, G. Nucera, A. Gabrielli, S. De Vita, R. Giacomelli, R. Gerli, L'Aquila, L'Aquila; Rheumatology Unit. Sapienza University, Roma; University of Perugia, Perugia; Department of Rheumatology, University of Pavia, Pavia; Rheumatology Unit, University of Padova, Padova; Rheumatology Unit. University of Pisa, Pisa; Rheumatology Unity, Sapienza University, Roma; Politecnica delle Marche, Ancona; Rheumatology and Clinical Immunology, Spedali Civili, Brescia; Rheumatology Clinic. University of Udine, Udine; Division of Rheumatology, University of L'Aquila, L'Aquila; Rheumatology Unit, Sapienza University, Roma; Rheumatology Clinic. University of Udine, Udine, Italy

Background: Celiac disease (CD) is an inflammatory and immune-mediated gluten-dependent enteropathy occurring in genetically susceptible individuals. CD prevalence may vary, and CD can coexist with other autoimmune diseases, such as autoimmune thyroiditis, rheumatoid arthritis, systemic lupus erythematosus, type 1 diabetes mellitus, and inflammatory bowel disease. The aim of this study was to assess the prevalence of CD in a large cohort of patients with systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and primary Sjögren's syndrome (pSS) with systemic lupus erythematosus-like features.

Methods: Data from consecutive 580 SLE, 354 SSc and 524 pSS patients were collected. Disease-specific features were recorded in patients with known CD. Remaining patients were tested for IgA transglutaminase (UE-IgT®) human IgA new, Eurospital S.p.A., Trieste), Anti-endomyosium (EMA) IgA and IgG were tested in IgA IgT positive and borderline patients. Esophagogastrroduodenoscopy with duodenal biopsy was proposed in IgA IgT+/EMA+, IgA IgT-/EMA+ and IgA IgT-/EMA patients.

Results: CD prevalence was 1.7% in SLE, 7% in pSS and 1.3% in SSc patients. Higher prevalence of elevated liver enzymes was detected in SLE-CD and of herpetiform dermatitis in SSc-CD patients in comparison to the other groups (p<0.05 for both). Interestingly, pSS-CD and SSC-CD patients were younger and had a lower age at diagnosis in comparison to pSS and SSC without CD (p<0.05 for all). Of interest, higher prevalence of CD was detected in SSc patients with diffuse form in comparison to limited SSc (86% vs 14%, p=0.002).

Conclusions: The presence of CD in systemic lupus erythematosus may be considered in younger patients with CD and lower age at diagnosis. The strong association of CD with the diffuse type of SSc is of note and suggests that different, still unexplored, pathogenetic mechanisms may characterize the two subsets of the disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4388
THU0270 | HOMOCYSTEINE, ANTIPHOSPHOLIPID ANTIBODIES AND RISK OF VASCULAR EVENTS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: SLE patients have higher plasma total homocysteine concentrations compared to healthy controls. Hyperhomocysteinemia in SLE is a potentially modifiable, independent risk factor for stroke and thrombotic events, hypertension, and coronary artery calcification.

Objectives: We investigated the association of homocysteine levels with the presence of antiphospholipid antibodies as well as the potentially additive thrombotic risk in patients with antiphospholipid antibodies who have hyperhomocysteinemia.

Methods: To analyze the association between hyperhomocysteinemia and the prevalence of antiphospholip antibodies in SLE, 844 patients with homocysteine measurements were included in the analysis. 237 patients had at least one measurement over 15 umol/L. Patients were followed quarterly after cohort entry. The association of hyperhomocysteinemia with antiphospholip antibodies is detailed in Table 1.

Conclusions: SLE patients with elevated homocysteine were less likely (p<0.05) to have any of the antiphospholip antibodies. Among patients with SLE who have antiphospholip antibodies, elevated homocysteine is associated with a significantly higher prevalence of myocardial infarction and deep vein thrombosis (p<0.05).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6705

Table 1. Homocysteine and antiphospholip antibody positivity

<table>
<thead>
<tr>
<th>Homocysteine (umol/L)</th>
<th>Odd ratios</th>
<th>P value</th>
<th>Adj. Odd ratios</th>
<th>Adj. P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 (%)</td>
<td>&lt;15 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-cardiolipin</td>
<td>0.56 (0.37,0.84)</td>
<td>0.0049</td>
<td>0.54 (0.36,0.81)</td>
<td>0.0033</td>
</tr>
<tr>
<td>Anti-β2 Glycoprotein</td>
<td>0.48 (0.28,0.82)</td>
<td>0.0076</td>
<td>0.46 (0.27,0.8)</td>
<td>0.0054</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>0.6 (0.36,0.98)</td>
<td>0.0040</td>
<td>0.54 (0.33,0.91)</td>
<td>0.0190</td>
</tr>
</tbody>
</table>

To analyze the prevalence of vascular events among SLE patients with antiphospholip antibodies based on homocysteine levels, 571 patients with positive antiphospholip antibodies and at least one homocysteine measurement were included in the analysis. There were 166 patients with at least one homocysteine measurement over 15 umol/L. The lupus anticoagulant was assessed by dRVVT with mixing studies and measurement over 15 umol/L. Patients were followed quarterly after cohort entry.

Results: Table 2. Prevalence of vascular events among SLE patients with antiphospholip antibodies based on homocysteine levels

<table>
<thead>
<tr>
<th>Abnormal Homocysteine &gt;15 umol/L</th>
<th>Normal Homocysteine</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>Superficial Thrombosis</td>
<td>12 (2.86)</td>
<td>0.7176</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>58 (14.36)</td>
<td>0.0257</td>
</tr>
<tr>
<td>Stroke</td>
<td>30 (7.41)</td>
<td>0.3139</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>11 (2.72)</td>
<td>0.0099</td>
</tr>
<tr>
<td>Digital Gangrene</td>
<td>8 (1.98)</td>
<td>0.7523</td>
</tr>
</tbody>
</table>

Conclusions: SLE patients with elevated homocysteine were less likely (p<0.05) to have any of the antiphospholip antibodies. Among patients with SLE who have antiphospholip antibodies, elevated homocysteine is associated with a significantly higher prevalence of myocardial infarction and deep vein thrombosis (p<0.05).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6705
THU0273 PREVALENCE AND FACTORS ASSOCIATED WITH FATIGUE IN FEMALE SLE PATIENTS AT THE HOSPITAL DEL MAR / PARC DE SALUT MAR

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Background: In patients with SLE, subjective parameters are very important as they have a great impact on the quality of life. Among them, fatigue is the most prevalent symptom in SLE, as it occurs in more than 90% of patients (1). Likewise, subjective parameters are independently associated with increased cardiovascular risk and mortality (2). There is a great variability of fatigue measurement scales, some of them being validated for healthy women (3). The aim of this study was to determine the prevalence of fatigue and factors associated with fatigue in female SLE patients.

Methods: A cross-sectional study was carried out including female SLE patients aged 18 and older attending the Rheumatology policlinic of the Hospital del Mar. Patients were considered for inclusion if they had a diagnosis of SLE according to the American College of Rheumatology criteria and were aged 18 and older. Patients were excluded if they had a diagnosis of other chronic diseases or if they were pregnant. A total of 102 patients with SLE of different etiologies and stages were included. All of them were subjected to full medical history and physical examination. A validated questionnaire was used to assess fatigue severity (4). According to the score obtained, the patients were divided into two groups: low fatigue (score <7) or high fatigue (score ≥7) based on the study by York et al. (5).

Results: The study included 102 female patients with SLE. The mean age was 47.8 ± 12.6 years. The prevalence of fatigue was 61.8%, with 27.7% classified as high fatigue. A statistically significant correlation was found between fatigue and age (p=0.008) and BMI (p=0.024). No significant correlations were found with other demographic variables, disease activity, or serological markers. The most commonly used medications were prednisone (89.5%), hydroxychloroquine (84.3%), and methotrexate (73%). The most frequent comorbidities were hypertension (38.2%) and diabetes (22%).

Conclusions: The prevalence of fatigue in female SLE patients is high, and it is associated with age and BMI. Further studies are needed to explore the underlying mechanisms and develop effective strategies to manage fatigue in this population.

References:

THU0274 FOOTPRINTS OF NEUTROPHIL EXTRACELLULAR TRAPS ARE ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Impaired removal of apoptotic debris in patients with systemic lupus erythematosus-SLE has been long known as important factor that trigger autoimmune response. Neutrophil extracellular traps could be another source of extracellular damage in SLE patients. The aim of this study was to compare NETs markers (free DNA, IL-10, IL-18 and TNF-α) in non-obese vs obese SLE patients, as well as to assess their relationship with serological markers of SLE disease activity (C3 and C4 complement components). NETs could be another source of extracellular damage in SLE patients.

Methods: We analysed 111 sera obtained from 84 SEL patients (60 patients had 1 sample and 24 patients had 2 or 3 samples) and 50 healthy blood donors. Serum levels of myeloperoxidase, B-cell activating factor-BAFF, cell free DNA, complement components C3 and C4, antibody to dsDNA by CLIFT and ELISA assays, netotic activity and DNAse I were measured. The group of 35 patients was selected (11 with de novo disease) for which clinical data were recorded.

Results: SLE patients had significantly higher concentration of free DNA (1.69±0.23 vs 1.42±0.31 ng/mL, p=0.0003), messenger RNA of MPO (10.4±6.9 vs 5.8±5.7 mg/mL, p=0.05), anti-MPO antibodies (13.8±4.3 vs 0.9±0.3 U/mL, p=0.001) and myeloperoxidase activity (1607±2353 vs 560.3±1825.2 RU, p<0.05) in comparison to healthy controls. The ability of sera to degrade NETs was similar in both groups. Free DNA, MPO and anti-MPO levels as well myeloperoxidase activity showed significant correlation with anti-dsDNA antibodies measured by ELISA test. None of studied parameters showed correlation with C3 and C4 complement components, C3 and anti-dsDNA antibodies measured by indirect immune fluorescence were independent predictors of SLEDAI score in multivariate analysis, while BAFF and DNAse I were significant in univariate analysis. Free DNA was predictor of SLEDAI score higher than in univariate analysis.

Conclusions: Increased amount of NETs markers found in lupus sera confirms their role in SLE pathogenesis. Determination of NETs markers could be useful serological parameter to follow disease activity in SLE patients.

References:
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4016

THU0277 REASONS FOR DEFICIENCY OF PHYSICAL INACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Systemic lupus erythematosus (SLE) is associated with musculoskeletal complaints, fatigue and reduced quality of life. Physical exercise can play a crucial role in the treatment of rheumatic diseases, optimizing both physical and mental health.

Objectives: To characterize physical activity (PA) and its impact on SLE patients. Methods: 65 SLE outpatients (92% female; age 44.2±12.5; 57.5% with SLEDAI score ≤5, 42.5% with SLEDAI score >5) were included in this study. The following questionnaires were utilized: painDETECT, visual analog scale for pain (VAS 0 - 100 mm), short-form health survey (SF - 36, quality of life), the FACT-P, the Rheumatoid Arthritis Health Assessment Questionnaire (RA-HAQ - D1), PA was assessed for every patient using the long form of International Physical Activity Questionnaire (IPAQ - L) and the Metabolic Equivalent of Task (MET) minutes per week (min/wk) (physiological measurement expressing calories of physical activities). The participants were classified in 3 groups according to the PA levels conforming to the guidelines of IPAQ. Physical inactivity was defined as fewer than 150 min/week spent in moderate or vigorous physical activities, respectively.

Results: 10.6% of SLE patients were physically inactive (525.2±277.3 MET-Min/wk), 31.8% had a moderate physical activity, and 57.6% were physically active. Physical inactivity was associated with higher fatigue (FACT-F, p<0.04) and lower "vitality" (SF-36, p<0.03) scores. Moreover, the subjective impact of fatigue on PA was significantly higher in physically inactive patients compared to physically active patients (the patient’s score: 7.75±1.25 vs. 5.5±0.94, p<0.04). Moderate and severe pain (more than 40 mm VAS) was also associated with physical inactivity (OR 12.38, 95% CI 1.69 to 144.3, p=0.0056). In contrast, HAQ-D1 was not related to levels of PA. Although physical inactivity correlated

Conclusions: Levels of IP-10, but not MCP-1, might be useful as a predictive biomarker for progression to SLE in patients with iSLE, although future prospective longitudinal analyses are needed to confirm this hypothesis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4016

THU0276 INTERFERON-RELATED CHEMOKINE IP-10 IS A POTENTIAL BIOMARKER IN INCOMPLETE SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Incomplete SLE (iSLE) is the designation of patients who display symptoms that are typical for SLE, but with insufficient criteria to fulfill the diagnosis. Unfortunately, predictive biomarkers for SLE development are lacking. Increased IFN-type I production is an important factor in the pathogenesis of SLE. Interferon-regulated chemokines therefore could possibly be useful as biomarkers for disease progression to SLE. Candidate biomarkers IFN-γ induced protein 10 (IP-10) and monocyte chemo attractant protein (MCP-1) have shown to be increased in SLE and to correlate with disease activity.

Objectives: To determine possible candidate biomarkers IFN-γ induced protein 10 (IP-10) and monocyte chemo attractant protein (MCP-1) in patients with iSLE.

Methods: Serum samples were collected of 30 iSLE patients, 29 SLE patients, and 17 ANA-negative patients with histologically proven cutaneous lupus erythematosus (ACLE). Outcomes were compared with 25 age- and gender-matched controls (CTL) and 31 rheumatoid arthritis (RA) patients as disease control group.

Results: IP-10 was significantly increased in SLE and RA patients compared with CTL and ANCLE. IP-10 levels were increased in 23% of iSLE patients. These patients had higher SLE disease activity index (SLEDAI) and more frequently decreased C3 level and joint involvement compared to those with normal IP-10 levels. Regarding MCP-1 levels, no significant differences were found between any of the groups and no correlations with clinical markers was found.

Conclusions: Levels of IP-10, but not MCP-1, might be useful as a predictive biomarker for progression to SLE in patients with iSLE, although future prospective longitudinal analyses are needed to confirm this hypothesis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4016

THU0275 IMPORTANCE OF SERUM TITERS OF ANTIBODIES AGAINST DOMAIN 1 OF B2 GLYCOPROTEIN 1
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1Rheumatology and Clinical Immunology; 2Dermatology, UMCG, Groningen, Netherlands

Objectives: Our aim was to evaluate the prevalence of Anti-D1 B2GPI antibodies in a cohort of Colombian patients with systemic lupus erythematosus (SLE) with and without thrombosis, primary APS and patients with previous history of recurrent miscarriages (RM) without APS criteria.

Methods: In this cross-sectional study we measured Anti-D1 B2GPI antibodies in a group of patients from Rheumatology Department, Coagulation clinic and Recurrent Pregnancy Loss Program at the Reproduction Group at Hospital San Vicente Fundación and Universidad de Antioquia, respectively, at Medellín, Colombia. Anti-D1 B2GPI antibodies were tested using a chemiluminescent immunoassay (QUANTA Flash B2GPI IgG, Inova Diagnostics). Mann-Whitney tests were used to compare data.

Results: One hundred and seventy seven (median age 33.5±12.1 years; 89% women) patients were included. One hundred thirty eight patients had SLE (78%), 27 primary APS (15%) and 13 RM (7%). Fifty five (31%) out of 177 patients had history of thrombosis and 41 (23%) of pregnancy losses. Overall, Anti-D1 B2GPI antibodies were positive (≥20 CU) in 35 (20%) of patients. Anti-D1 B2GPI were positive in 23%, 17% and 0% of patients with primary APS, SLE and RM, respectively. Overall, serum Anti-D1 B2GPI were significantly higher in patients with than without previous thrombosis (149.1±336.1 vs 16.3±61.8 CU, p<0.0001) and in patients (SLE or primary APS) with previous history of pregnancy losses (40.2±123.1 vs 21.0±74.5 CU, p=0.04). Anti-D1 B2GPI were significantly higher in patients with primary APS vs SLE with thrombosis, and in patients with SLE with thrombosis vs SLE without thrombosis (Figure). No clinical associations were found among Anti-D1 B2GPI antibodies and other APS features.

Conclusions: Serum titers of Anti-D1 B2GPI antibodies were more than 9 times and 2 times higher in patients with thrombosis and pregnancy losses, respectively. In addition, serum titers were significantly higher in patients with primary APS than in SLE patients with thrombosis. Whether Anti-D1- B2GPI antibodies titers are useful to differentiate patient with primary and secondary APS requires further analysis.

Acknowledgements: JA Gómez-Puerta was supported by Colciencias (conv. 656 de 2014). Anti-D1 B2GPI antibodies were provided by Inova, Werfen, Colombia

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4879

THU0274 COMBINED APPROACH TO EVALUATE INFLAMMATORY SYMPTOMS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Systemic lupus erythematosus (SLE) is associated with musculoskeletal complaints, fatigue and reduced quality of life. Physical exercise can play a crucial role in the treatment of rheumatic diseases, optimizing both physical and mental health.

Objectives: To characterize physical activity (PA) and its impact on SLE patients. Methods: 65 SLE outpatients (92% female; age 44.2±12.5; 57.5% with SLEDAI score ≤5, 42.5% with SLEDAI score >5) were included in this study. The following questionnaires were utilized: painDETECT, visual analog scale for pain (VAS 0 - 100 mm), short-form health survey (SF - 36, quality of life), the FACT-P, the Rheumatoid Arthritis Health Assessment Questionnaire (RA-HAQ - D1), PA was assessed for every patient using the long form of International Physical Activity Questionnaire (IPAQ - L) and the Metabolic Equivalent of Task (MET) minutes per week (min/wk) (physiological measurement expressing calories of physical activities). The participants were classified in 3 groups according to the PA levels conforming to the guidelines of IPAQ. Physical inactivity was defined as fewer than 150 min/week spent in moderate or vigorous physical activities. Furthermore, the patient reasons “to be not physical active” and their opinion regarding the influence of PA on disease-related symptoms (on a scale of 0–10) were obtained.

Results: 10.6% of SLE patients were physically inactive (525.2±277.3 MET-Min/wk), 31.8% had a moderate physical activity, and 57.6% were physically active. Physical inactivity was associated with higher fatigue (FACT-F, p<0.04) and lower “vitality” (SF-36, p<0.03) scores. Moreover, the subjective impact of fatigue on PA was significantly higher in physically inactive patients compared to physically active patients (the patient’s score: 7.75±1.25 vs. 5.5±0.94, p<0.04). Moderate and severe pain (more than 40 mm VAS) was also associated with physical inactivity (OR 12.38, 95% CI 1.69 to 144.3, p=0.0056). In contrast, HAQ-D1 was not related to levels of PA. Although physical inactivity correlated
with a higher total disease activity score (SLEDAI ≥6) (OR 9.9, 95% CI 2.1 to 49.9, p=0.0068), neither of the single SLEDAI items and organ manifestations including musculoskeletal manifestations was associated with physical inactivity. Interestingly, the study could not detect any statistical difference in organ manifestations and SLEDAI scores between patients with moderate and high PA. Activating the patient's report, with the main SLE-related reasons "not to be physically active" for all three groups were "lupus flare" (35.6%), "fatigue" (26.9%) as well as "joint complaints" (15.7%). The main general barriers for PA were "comorbidity" (35.6%) and "lack of motivation" (26.9%). Furthermore, the subjective impact of "bad weather conditions" on physical activity was significantly greater in physically inactive patients compared with the two other groups (the patient's report: 6.5±2.3 vs. 3.4±0.7, p<0.03).

Conclusions: The main reason for the patients not to be physically active was fatigue and pain. The study also indicates that not only somatic symptoms could decrease the levels of PA in SLE patients. Further research on psychological factors is needed. The study underlines the need for management strategies that specifically target physical activity as a part of a general SLE management program.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5824

THU0278 COMPARISON OF THE 2016 ACR/EULAR AND THE 2002 AECG CLASSIFICATION CRITERIA IN A COHORT OF PATIENTS WITH SUSPECTED PRIMARY SJÖGREN’S SYNDROME

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Background: New consensual classification criteria for primary Sjögren’s syndrome (pSS) have been recently developed and endorsed by ACR and EULAR. They differ substantially from previously used AECG criteria in that they consider systemic involvement (defined as ESSDAI score ≥1) as well as sicca symptoms as entry criteria before applying a weighted score. Evaluation of the concordance and differences between the two sets of criteria in independent patient populations is mandatory to establish how future clinical studies using the new criteria will be comparable to previously published studies. Major salivary gland ultrasonography (SGUS) has demonstrated promising diagnostic performance in previous studies, but was not included in these new classification criteria.

Methods: This cross-sectional study was conducted in the monocentric Brittany cohort (DiAPSS cohort) of patients with suspected pSS (sicca symptoms, parotidomegaly or extraglandular manifestations suggestive of pSS). All patients had standardized clinical examination, basic biology, immunological tests and minor salivary gland biopsy. SGUS in mode B was performed by the same operator. The study underlines the need for management strategies that specifically target physical activity as a part of a general SLE management program.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5824

THU0279 ARE THE PULMONARY INVOLVEMENT IN SYSTEMIC LUPUS EURHEMATOSIS ASSOCIATED WITH A HIGHER PREVALENCE OF COMORBIDITIES?

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Background: Patients with systemic lupus erythematosus have a very high burden of comorbidities. Identification and management of these comorbidities are critical for optimal medical care to this population.

Objectives: To assess the prevalence of comorbidities in SLE patients with pulmonary involvement.

Methods: In a cross-sectional study, patients who fulfilled the SLICC (2012) classification criteria for SLE were recruited from the Rheumatology Department. Data collection included demographics, disease duration, physician-rated indices of disease activity by (SLAM), (by SLICC/ACR DI) and Charlson comorbidity Index. The pulmonary involvement was assessed by chest X-ray, ECG, Doppler and pulmonary functional tests.

Results: The study included 106 patients (97 women, 9 males) with a mean age (±SD) of 41.7±12.6 yrs, mean disease duration of 90.3±87.3 months. The disease activity by SLAM was 11.5±17 points and mean SLICC/ACR DI 1.9±2.4 points (66% of patients had at least 1 point). Pulmonary assessment revealed that 45 (42.5%) patients had different types of pulmonary involvement due to lupus: pleuritis in 21 patients, pneumonia in 1 patient, pulmonary embolism in 4 patients, interstitial lung disease – 15, shrinking lung syndrome – 1 and pulmonary arterial hypertension – 9 patients. The most frequent comorbidities in study group were: arterial hypertension - in 57 (53.7%) cases, from which 33 (57.9%) patients had pulmonary involvement and 24 (42.1%) without, obesity (BMI ≥30 kg/m²) had 29 (27.4%) patients, from which 17 (58.6%) with lung involvement and 12 (41.4%) without, anemia (Hb<110 g/l) had 24 (22.6%) patients, from them 14 (58.3%) with lung disease and 10 (41.7%) patients - without, heart failure (I-II NYHA) had 23 (21.7%) patients, from them 20 (86.9%) were with lung involvement, thyroiditis had 22 (20.8%) and 15 (88.2%) of them were with our pulmonary involvement, diabetes mellitus type II had only 6 (5.7%) patients and half of them had lung disease. Assessing the impact of associated diseases through Charlson comorbidity index, we found that the score for patients diagnosed with damage to the respiratory system was twice as big vs. patients without respiratory impairment from SLE (6.3±2.4 vs. 3.4±1.4 points). Also, Charlson comorbidity score >1 was identified as a risk factor for lung involvement (OR 5.294, 95% CI 2.12-12.91, p<0.01). Evaluation of disease activity by SLAM showed that patients with lung involvement have a higher disease activity vs. patients without (13.9±6.0 vs. 8.9±4.0, p<0.05). On the other hand, association of comorbidities (Charlson comorbidity score >1) was identified as a risk factor for lung lesions.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6776

THU0280 COMPARISON OF CLASSIFICATION CRITERIA FOR SJÖGREN’S SYNDROME FROM 2002 AND 2016 IN AN INCIDENT COHORT DIAGNOSED 2007 TO 2011 FROM STOCKHOLM COUNTY SWEDEN

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Background: The current American-European Consensus Criteria (AECG) from 2002 has been the most widely used and applied all over the world. New classification criteria for Sjögren’s syndrome was published in 2016, designed in collaboration between ACR and EULAR. They are made up of a scoring system in which 4 points are required for classification. The weight score is as follows:• Labial salivary gland biopsy with focal lymphocytic sialadenitis and focus score of >1 focii/4 mm² – 3
• Anti-SSA/Ro positive – 3
• Ocular Staining Score >5 (or van Buijsterveld score >4) in at least 1 eye – 1
• Schirmer’s test >5 mm/5 minutes in at least 1 eye – 1
• Unstimulated whole saliva rate <0.1 ml/min – 1

Objectives: Comparison of classification criteria for Sjögren’s syndrome from 2002 and 2016 in a 5 year cohort of incident patients diagnosed 2007 to 2011 from Karolinska University Hospital, Stockholm County, Sweden.

We wanted to examine the consistency between the different classification criteria.

Methods: We compared all patients diagnosed with primary Sjögren’s syndrome during the years 2007 to 2011 at the Dep. of Rheumatology at Karolinska University Hospital in Stockholm Sweden. Data on the item Ocular Staining Score >5 was not available since it is not included in AECG. The cohort consisted of 199 patients all fulfilling the 2002 AECG. Another eight patients did
not fulfill the criteria but were regarded as possible Sjögren’s syndrome under development by the rheumatologist who investigated them.

Results: 196 of the 199 pSS patients also fulfilled the new criteria from 2016. The three patients who did not only had SSB autoantibodies and no positive biopsy. Of eight patients with suspicion of Sjögren’s syndrome under development, three fulfilled the new criteria.

Conclusions: The classification criteria for Sjögren’s syndrome from 2002 and 2016 are consistent. This study indicates a possibility that the new criteria may be more sensitive early in the disease development, as long as the classification is not based on autoantibody positivity against SSB.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5377

THU0281 LONG-TERM PROGNOSIS AND PREDICTING FACTORS OF CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTI-CENTER COHORT STUDY FROM CSTAR REGISTRY

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Objectives: To investigate the long-term outcomes, both mortality and damage, and related prognostic factors of patients with systemic lupus erythematosus (SLE) in the CSTAR (Chinese SLE Treatment and Research group) registry cohort.

Methods: All of the patients were enrolled from April 2009 to February 2010. They were followed up at clinic and were telephone interviewed at the endpoint. Demographic data, clinical manifestations, activity (SLEDAI-2K), damage scores (SLICC/Damage Index), and medications were collected. Data were censored at the last clinic visit or telephone interview. Survival rates were studied by Kaplan-Meier method, and COX proportional hazard model was adopted to perform the analysis of predicting factors for mortality.

Results: A total of 2104 patients were recruited at baseline, and 1494 patients were successfully followed up. The cumulative 1, 3 and 5-year survival rates from diagnosis were 99.0%, 98.1% and 97.1%. 78 patients died during follow-up, and the main death causes were infection (34.6%), active disease (26.9%), cardiovascular and cerebrovascular events (6.41%) and malignancy (5.13%). At entry, 247 patients presented with irreversible organ damage and it increased to 398 patients at the endpoint. The major accumulated organ damages were cardiovascular and cerebrovascular events (6.41%) and malignancy (5.13%). COX regression showed that male, late onset age (≥50y), onset to diagnosis time ≥1 year, previous organ damage, renal involvement, pulmonary arterial hypertension, nephritic damage and the number of involved organ systems ≥3 predict for higher mortality.

Table 1: Independent predictors of mortality obtained by univariate analysis

<table>
<thead>
<tr>
<th>Univariate analysis</th>
<th>HR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset ≥ 50 years</td>
<td>3.935</td>
<td>2.111-7.334</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Onset to diagnosis ≥ 1 year</td>
<td>1.996</td>
<td>1.251-3.186</td>
<td>0.004</td>
</tr>
<tr>
<td>Gender</td>
<td>2.082</td>
<td>1.119-3.873</td>
<td>0.021</td>
</tr>
<tr>
<td>Baseline organ damage*</td>
<td>2.846</td>
<td>1.757-4.610</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal involvement*</td>
<td>2.434</td>
<td>1.425-4.156</td>
<td>0.001</td>
</tr>
<tr>
<td>Hematologic involvement*</td>
<td>1.605</td>
<td>0.978-2.635</td>
<td>0.061</td>
</tr>
<tr>
<td>Intestinal lung disease*</td>
<td>2.167</td>
<td>0.973-4.823</td>
<td>0.058</td>
</tr>
<tr>
<td>Pulmonary arterial hyperten*</td>
<td>4.126</td>
<td>2.107-8.081</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neurophysiological involvement*</td>
<td>2.290</td>
<td>1.169-4.486</td>
<td>0.016</td>
</tr>
<tr>
<td>Serositis*</td>
<td>2.580</td>
<td>1.605-4.148</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of involved organ systems (1)*</td>
<td>1.793</td>
<td>0.719-4.466</td>
<td>0.210</td>
</tr>
<tr>
<td>No. of involved organ systems (2)*</td>
<td>2.045</td>
<td>0.805-5.195</td>
<td>0.133</td>
</tr>
<tr>
<td>No. of involved organ systems (3)*</td>
<td>5.638</td>
<td>2.339-12.589</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: Long-term survival rates have improved for Chinese SLE patients. Early diagnosis, preventing from emerging systemic organ involvements and organ damage could be the treating target for the management of SLE patients in China.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5791

THU0282 HOMOCYSTEINE: ANY ROLE IN PERIPHERAL VASCULAR DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS?

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Background: Many are the independent risk factors for premature atherosclerosis in general & peripheral vascular disease (PVD) in particular in SLE patients. Plasma homocysteine (Hcy) is known risk factor for atherosclerosis. Atherosclerosis can lead to many cardiovascular diseases as myocardial infarction, stroke and claudication.

Objectives: To compare the occurrence PVD of the lower extremity of SLE patients (pts) with age and sex matched controls and evaluate the role of Hcy level in its occurrence.

Methods: Body mass index (BMI), blood pressure, lipid profile, titers of autoantibodies [ANA, anticardiolipin antibodies ACL (IgM, IgG)], C3, C4, plasma Hcy level were assessed, SLEDAI and (SLICC/ACRDI) were calculated. PVD evaluation was done by measuring Ankle Brachial Index (ABI) with values ≤0.9 considered diagnostic of PVD; in 60 SLE pts and 30 age-matched controls. Patients with previous hypertension, diabetes, other collagenic diseases & smokers were excluded.

Results: Eighty-eight percent of the pts were women. The mean age (SD) was 30.40 (11.46) years & mean disease duration 3.61 (4.92) years. 50 pts were asymptomatic, 5 had mild & 5 had moderate claudications. SLE pts had significant higher total cholesterol (TC), LDL than controls 224.1±57.8 vs 181.1±41.1 mg/dl & 162.7±57.0 vs 119.5±13.4 (<0.001) respectively, higher HCY 11.6±2.1 & 6.4±1.0 μmol/L (<0.001) & lower HDL 47.2±13.1 & 52.6±3.7 mg/dl (<0.004). Low ABI was found in 30% of SLE pts but none of the controls (p<0.001) & was correlated with higher HCY level (p<0.005), TC & LDL (p<0.001 & <0.001), but not TG (p<0.748) or asymptomatic pts, presence of mild or moderate claudications (p=0.468, 1.000, 0.154), still its value negatively correlated with lupus anticoagulant (LA) (p<0.002), ACL IgM (p<0.001), the presence of lupus nephritis (LN) (p<0.001) & SLICC/ACRDI (p=0.017) but not with disease duration (dd) (p=0.535), Anti ds DNA (p=0.364), ACL IgG (p=0.9840), C4 (p=0.168) or SLEDAI (p=0.074). No correlation was found between HCY level and pts’ age, dd, age at diagnosis, BMI, Anti ds DNA, ACL IgG, C4 & SLEDAI (p=0.521, 0.946, 0.502, 0.346, 0.335, 0.325, 0.787). A positive correlation was found between HCY level and LA, ACL IgM, TC, LDL, The presence of LN & SLICC/ACRDI with a p value of 0.025*, <0.001*, <0.001*, 0.003*, 0.001* & negative one with HDL p=0.023*

Conclusions: 83.3% of SLE pts were asymptomatic or had atypical symptoms of PVD, still 30% of the patients had low ABI. ABI can be a more reliable, non-invasive test to assess PVD than the conventional methods of pulse palpation or history of Claudication in SLE pts. Both traditional & nontraditional risk factors of atherosclerosis are important but HCY can play a role, among other factors, as independent risk factor of PVD in SLE patients.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4815
Resilience and Associated Factors Among Women with Systemic Lupus Erythematosus

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Abstract: Resilience is the human capacity to respond positively to adverse situations, enabling individuals to achieve, maintain, or recover health after devastating illness, losses, or other stressful situations. Resilience may be an important factor in health promotion.

Objective: The aim of this study was to evaluate resilience and possible associated factors in patients with systemic lupus erythematosus (SLE).

Methods: In a cross-sectional study, 123 SLE women and 133 age-matched controls were evaluated using the Spanish version of Wagnild and Young’s Resilience Scale (WYRS, 1993). SLE patients underwent a structured interview to collect sociodemographic data, including socioeconomic status measured by the Graffar method. The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms.

Results: The median age and duration of disease of SLE women was 45 (IQR: 34–54) years and 11 (IQR: 8–15) years, respectively. Thirty-three percent had depressive symptoms (CESD > 16). Resilience scores did not differ between patients and controls (median 80 IQR: 75–87 vs.80 IQR: 74–85p<0.38). However, patients with SLE had a higher personal competence factor than controls. Personal competence factor correlated negatively with age and socioeconomic status (R= -0.220, p< 0.05 and R= -0.357, p<0.001) and positively with educational level (R=0.324, p<0.001). Less resilience (lower WYRS scores) correlated with depressed mood (higher CESD scores) (R= -0.537, p<0.001).

Conclusion: Resilience in patients with SLE did not differ from that of controls. Age, socioeconomic status and depressive symptoms correlated with low resilience. Educational level correlated with higher resilience.

References:

Acknowledgements: We would like to thank David Buss for his valuable guidance and advice during this project.

Disclosure of Interest: None declared

Predicting Survival in 6240 Patients with Primary Sjögren Syndrome (Big Data Sjögren Project)


Objective: The aim of this study was to evaluate resilience and possible associated factors in patients with systemic lupus erythematosus (SLE).

Methods: In a cross-sectional study, 123 SLE women and 133 age-matched controls were evaluated using the Spanish version of Wagnild and Young’s Resilience Scale (WYRS, 1993). SLE patients underwent a structured interview to collect sociodemographic data, including socioeconomic status measured by the Graffar method. The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms.

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Conclusion: Resilience in patients with SLE did not differ from that of controls. Age, socioeconomic status and depressive symptoms correlated with low resilience. Educational level correlated with higher resilience.

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Acknowledgements: We would like to thank David Buss for his valuable guidance and advice during this project.

Disclosure of Interest: None declared

Use of Contraceptive Methods in a Single Center Cohort of Systemic Lupus Erythematosus from Argentina

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Background: Systemic Lupus Erythematosus (SLE) may associate with flares, an unfavorable course and the need of teratogenic treatment during pregnancy. Not every contraceptive method (CM) may be used in this patients. There are guidelines for their use according to existing morbidity and SLE activity1. Objectives: Describe the use of CM in a cohort of outpatients with SLE. Methods: Descriptive, observational, cross-sectional study. Patients ≥16 years old with SLE (SLICC 2012) and ≥1 visit during the last year of our database were included. Those with menopause were excluded. We analyzed demographic data; disease duration; antiphospholipid antibodies (aPL) and antiphospholipid syndrome (APS) (Sapporo 2006); socioeconomic status (Graffar scale); disease activity (SELENA-SLEDAI) and accrual damage (SLICC); use of teratogens; Methotrexate (MTX), Mycophenolate (Myc), Cyclophosphamide (CYC), biological drugs (BD), self-reported sexual activity (active/non active) and CM: intrauterine device (IUD), condom (CDm) and hormonal contraceptive pill (CP).

Results: 132/219 were included. Female 91.6%; 30.1 (16–49) years, disease duration: 38.5 (1–324) months; SELENA-SLEDAI 3.5 (0–29); SLICC 0.5 (0–5). Sexual status and use of CM: were available for 120 patients. Sexually active (SA) 73%, female 77%. CM in SA patients: 74%; 5% CP 77% Cdm and 18% IUD. CM in female patients stratified by SLEDAI ≤3 (n=62); 76% SA, 77% of them used CM (3% CP, 83% Cdm, 14% IUD); SLEDAI 3–12 (n=42): 81% SA, 76% used CM (8% CP, 69% Cdm, 23% IUD); SLEDAI >12 (n=60): 60% SA, 67% used CM (100% Cdm). CM in female patients using teratogenic drugs: MTX (n=8): 100% SA, 75% of them used CM (17% CP, 66% Cdm, 17% IUD); MCV (n=20): 80% SA, 88% used CM (71% Cdm, 29% IUD); CYC (n=3): 33% SA, 100% used CM (100% Cdm); Belimumab (n=1): 100% SA, 100% surgical CM (tubectomy).

aPL was evaluated in 96/132 patients. 17/96 had positive aPL and 5/17 fulfilled APS criteria. 2/17 patients had no CM data available, none with APS. 9/17 patients with aPL were female, 55% SA and all of them used Cdm. 3/5 patients with APS were female, all SA, 66% used Cdm.

Conclusions: Condom was the most reported CM. Use of CM was more frequent in the upper social status (GF I-III) respect to the lower (GF IV-V). The proportion of sexually active female patients was similar in those using teratogenic drugs compared with who had not used them. The self-reported sexual status was similar despite of SLEDAI stratification, being similar in patients with low or high disease activity.

We deem necessary education, counseling and evaluation of use of the CM in every visit of patients with SLE.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3922
**THU0286**  
**RECURRENCE OF ARTERIAL AND VENOUS THROMBOSIS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME**

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**Background:** Antiphospholipid syndrome (APS) is the thrombophilia associated with the highest risk of recurrence of both arterial and venous thromboses. (1.2)

In addition to the standard of care (lifelong oral anticoagulation), identification of other risk factors is important to provide better care and to reduce the incidence of rethrombosis.

**Objectives:** To investigate the risk factors associated with recurrence of arterial and venous thromboses in primary APS patients.

**Methods:** A cross-sectional study was performed in a group of 80 outpatients who fulfilled APS classification criteria (Sydney). The patients were regularly seen in our department, and clinical and serological features were collected during visits and by chart review. They were classified as recurrent or not, and these groups were compared. Recurrence was defined as the presence of 2 or more thrombotic events during lifetime. Patients with 1 thrombotic event were classified as "no recurrent". No history of thrombosis was the only exclusion criterion.

**Results:** Of 80 APS patients, thirty-five had arterial thrombosis and 54 had venous thrombosis. Of them, thirty-six had recurrent thromboses (11 arterial and 25 venous).

Demographic and clinical characteristics of the arterial group are shown in Table 1. In a bivariate analysis, recurrent arterial thromboses were associated with hypertension (p=0.016) and positivity to lupus anticoagulant (LA; p=0.033), and recurrent venous thrombosis correlated to obesity (BMI; ≥30 kg/m²; p=0.003). In a multivariate regression analysis, the model of recurrent arterial thromboses was adjusted to age, sex, and variables with p<0.10 in the bivariate analysis (age, hypertension, dyslipidemia, and positivity to lupus anticoagulant). Hypertension (OR 9.02; 95% CI: 1.05–77.5, p=0.045) and age (OR 1.16; 95% CI: 1.01–1.33; p=0.035) increased the risk of relapse of arterial thrombosis.

**Conclusions:**

Table 1. Demographic and clinical characteristics of patients with recurrent and non-recurrent arterial thromboses (N=35)

<table>
<thead>
<tr>
<th>Variable</th>
<th>No recurrent (N=35)</th>
<th>Recurrent (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial recurrence (N=11)</td>
<td>53 (5.7)</td>
<td>185 (200)</td>
</tr>
<tr>
<td>Age</td>
<td>53 (5.7)</td>
<td>185 (200)</td>
</tr>
<tr>
<td>Female gender</td>
<td>5 (7.2)</td>
<td>10 (9.0)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>19 (9.1)</td>
<td>13 (7.2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8 (3.8)</td>
<td>8 (3.8)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (5.7)</td>
<td>1 (5.7)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1 (5.7)</td>
<td>1 (5.7)</td>
</tr>
<tr>
<td>Obesity</td>
<td>6 (11.5)</td>
<td>6 (11.5)</td>
</tr>
<tr>
<td>Premature CVD</td>
<td>3 (7.3)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>Smoking</td>
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<td>2 (3.4)</td>
</tr>
<tr>
<td>No criteria</td>
<td>24 (7.4)</td>
<td>24 (7.4)</td>
</tr>
<tr>
<td>Livedo</td>
<td>4 (36.4)</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
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<td>1 (9.1)</td>
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<tr>
<td>Valvulopathy</td>
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<td>1 (11.5)</td>
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<tr>
<td>Raynaud phenomenon</td>
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<td>4 (30.4)</td>
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<tr>
<td>Migraine</td>
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<td>6 (54.5)</td>
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</table>

**Discrimination of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3974

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**THU0287**

**CENTRAL ARTERY STIFFNESS MEASURED BY THE AUGMENTATION INDEX IS ENHANCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND IS DETERMINED BY THE LEVELS OF IGm-β2-GLYCOPROTEIN AND THE SMALL-DENSE HDL PARTICLES**

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**Background:** Patients affected by Systemic Lupus Erythematosus (SLE) show an increase in cardiovascular mortality and morbidity. The accelerated atherosclerosis observed in patients with SLE cannot be entirely explained by the traditional cardiovascular risk factors. Patients with SLE show increased subclinical atherosclerosis determined by an increased carotid arterial thickness, endothelial dysfunction and central arterial stiffness. Analysis of lipoproteins by magnetic nuclear resonance (MNR) provide information of those lipoproteins associated with subclinical atherosclerosis in SLE.

**Objectives:** To investigate the metabolic and immunological factors associated with the presence of central arterial stiffness determined by the Augmentation Index (AIx) as well as the detailed analysis of the lipid profile performed by magnetic nuclear resonance (MNR).

**Methods:** Descriptive cross-sectional study of 69 women with SLE compared with a control group of 34 age matched healthy women. On the same day of the study, blood extraction, physical examination and augmentation index (AIx) obtained by Peripheral Arterial Tonometry were performed. The carotid intima-media thickness (IMTc) was also performed on the same day of the study to correlate the arterial stiffness with another subclinical atherosclerosis marker. Analysis of lipoprotein populations by NMR (Liposacle,Bioster Teslab) were performed.

**Results:** Patients with SLE showed significant increased arterial stiffness respect the control group (20.30 (21.54%) vs 10.84 (11.51%), p=0.0021) The values of AIx were well correlated with Framingham risk score (r=0.486, P<0.001) as well as the IMTc (r=0.456, P<0.001). The classic cardiovascular risk factors associated with the AIx were the SBP levels (r=0.456, P<0.001) and age (r=0.456, P<0.001). Patients under antimalarial drugs showed significant decreased AIx (11.74 (11.28) vs 24.97 (20.7), P=0.024). Immunological variables associated with AIx included levels of C4 (r=0.259; P=0.046) and positivity to lupus anticoagulant (LA; r=0.284, P=0.284). As for the lipoprotein populations, AI values correlated with ApoB plasma levels, remnant particles, the number of large, medium and small VLDL particles, the number of small LDL particles and the number of small-dense HDL. In the multivariate analysis we found that age (r=0.377 (0.117–0.636), P=0.005) and IgM-β2-GLP levels (r=0.303 (0.026–0.580), P=0.033) and the small-dense HDL particles (r=1.483 (0.605–3.232), P=0.001).

**Conclusions:** SLE patients showed increased central arterial stiffness respect healthy population. Patients treated with antimalarial drugs show lower arterial stiffness. In multivariate analyses variables that predicted levels of AIx were age, levels of IgM-β2-glycoprotein and the number of small-dense HDL particles.

**Discrimination of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6981

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**THU0288**

**COMPARISON OF THE CLINICAL, SEROLOGICAL, AND PROGNOSTIC DIFFERENCES AMONG JUVENILE-, ADULT-, AND LATE-ONSET LUPUS NEPHRITIS IN KOREAN PATIENTS: A CASE-CONTROL STUDY**

S.-S. Lee 1, J.-H. Kang, J.-E. Kim, K.-E. Lee, D.-J. Park, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic Of

**Objectives:** SLE patients present with different clinical and serological manifestations according to the age at disease onset. However, it is not known whether there is an association between disease onset age and the clinical presentation of lupus nephritis (LN). Therefore, we investigated whether LN patients could be distinguished based on the time of disease onset and, if so, whether the groups differ in their clinical, laboratory features and long-term prognosis in ethnically homogeneous Korean patients.

**Methods:** We enrolled 117 SLE patients with available clinical data at the time of renal biopsy for LN from the lupus cohort at Chonnam National University Hospital. We divided the LN patients according to the age at LN diagnosis into three groups [juvenile-onset LN (JLN), diagnosed at ≤18 years; adult-onset LN (ALN), diagnosed at 18–50 years; and late-onset LN (LLN), diagnosed at >50 years] and compared the baseline demographic, clinical, histological, and relevant laboratory findings. We also compared the treatment and long-term prognosis of LN according to those three groups.

**Results:** Of the 114 LN patients, 20 (17.5%), 84 (71.8%), and 13 (11.1%) had JLN, ALN, and LLN, respectively. LLN patients were less educated than ALN and JLN patients (p=0.001). Hypertension and diabetes mellitus at the onset of LN were more common in JLN patients compared to the age at LN diagnosis into three groups [juvenile-onset LN (JLN), diagnosed at ≤18 years; adult-onset LN (ALN), diagnosed at 18–50 years; and late-onset LN (LLN), diagnosed at >50 years] and compared the baseline demographic, clinical, histological, and relevant laboratory findings. We also compared the treatment and long-term prognosis of LN according to those three groups.

**Conclusions:** The age at disease onset of LN was more common in LLN patients than in JLN and ALN patients (p=0.001). Hypertension and diabetes mellitus at the onset of LN were more common in JLN patients compared to the age at LN diagnosis into three groups [juvenile-onset LN (JLN), diagnosed at ≤18 years; adult-onset LN (ALN), diagnosed at 18–50 years; and late-onset LN (LLN), diagnosed at >50 years] and compared the baseline demographic, clinical, histological, and relevant laboratory findings. We also compared the treatment and long-term prognosis of LN according to those three groups.

**Discrimination of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2385
THU0289  B-CELL ACTivating FACtor genE EXPRESSION IN URINARY SAMPLE AND REnal BIOPSY FOR MONITORING DISEASE ACTIVITY IN LUPUS NEPHRITIS

S. Retamozo 1,2, L. Mas 3, M.J. Haye Salinas 4, V. Sauir 4, F. Caeiro 4, A. Diller 5, J. De La Fuente 4, M. Angelina 7, N.R. Benzaquen 4, J.P. Pirola 4, A. Alvarillos 4, T. Alvarellos 3, 1 Rheumatology, Hospital Privado Universitario de Córdoba; 2 INICSA, CONICET; 3 Molecular Biology; 4 Rheumatology; 5 Pathology; 6 Nephrology, Hospital Privado Universitario de Córdoba; 7 Nephrology, Hospital Raul A. Ferryera, Cordoba, Argentina

Objectives: To evaluate BLyS as biomarker in disease activity in urinary sample and renal biopsy from patients with LN.

Methods: Retrospective study. Between June 2009 and October 2013, 32 patients with SLE and LN fulfilling SLE classification criteria of ACR 1997 were included. The renal biopsies were evaluated according to the ISN/RPS classification system. The gene expression levels of BLyS were quantified using Quantitative Real Time PCR (QPCR). The relative quantification method was used for analysis, where Ct was normalized to an endogenous control j2Microglobulin (j2M) (ΔCt BLyS).

The data expressed as ΔCt was inversely proportional to gene expression level. The value of BLyS is expressed as median (M) and interquartile range (IQR) for filing a non-normal distribution.

Results: 26 (81.3%) patients were female with a mean age at diagnosis of 26.9±13 years and 31.9±29 years at the time of biopsy. The SLEDAI at the time of biopsy was 10.5 (IQR 0–15.7) and SLICC ≤ 1 in 32 (32.5%), hypertensive nephropathy in 13/31 (41.9%) and positive DNA in 1/29 (37.9%) patients. Biopsies from patients with proteinuria ≥0.5 and renal failure (RF) (n=23, 71.9%), proteinuria isolated (n=14, 43.8%), LN remission. The value of the BLyS gene expression in renal biopsy was 8.09 (IQR 7.37–9.16) and BLyS in urinary sample was 0.65 (IQR 0.62–7.76).

Conclusions: BLyS detection in urinary samples could be a potential biomarker for predicting lupus nephritis activity. Our data confirm that the BLyS as urinary biomarker is present in patients with active renal disease especially in patients with proliferative glomerulonephritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4523

THU0290  CLINICAL BACKGROUND FACTORS RELATED TO SILENT OSTEONECROSIS OF THE FEMORAL HEAD UPON INITIATION OF STEROID THERAPY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

T. Kuroda 1, N. Tanabe 2, H. Sato 1, T. Nakatsu 1, Y. Wada 1, M. Nakano 2, T. Nanta 1, 1 Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences; 2 Department of Health and Nutrition, Faculty of Human Life Studies, University of Niigata Prefecture; 3 Department of Medical Technology, School of Health Sciences, Faculty of Medicine, Niigata University, Niigata, Japan

Background: Osteonecrosis of the femoral head (ONF) occurs frequently (3–40%) in patients who receive corticosteroid therapy for SLE. M. H. Houman. Systemic lupus erythematosus (SLE) is more frequent in women and seems to be more severe in men.

Objectives: The aim was to study gender influence on clinical, biological and immunological features of SLE.

Methods: It’s a retrospective study conducted in an internal medicine department. Patients with systemic lupus erythematosus (ACR revised criteria) were included. Data were recorded and compared using SPSS. Variables with a p<0.05 were considered to be statistically significant.

Results: A total of 246 SLE patients were included: 224 female and 19 male (sex ratio F:M was 11.78). Mean ages at disease onset and at SLE diagnosis were comparable for men and women respectively 35.6±14.31 vs 32.7±13.36 years and 35±14.3 vs 34.5±13.6 years.

SLE diagnosis was made earlier in men with an average delay (from first sign of the disease to diagnosis) of 6.1 months vs 21.4 months (p<0.02). Clinically, photosensitivity was significantly more frequent in women (81.4% vs 58.8%; p=0.03). Women complained from alopecia more frequently than men but the difference was not statistically significant (35.1% vs 14.3%; p=0.09). Arthritis were two times more frequent in women (50.7% vs 25%; p=0.04). Lupus nephritis as well as lupus pancreatitis were significantly more frequent in men, respectively 66.7% vs 41.6% (p=0.039) and 11.1% vs 1.4% (p=0.047). There were no differences regarding to gender in neurological involvement and seritis. No significant differences were observed between men and women concerning hematological disorders. Anti-DNA, anti-Sm, anti-RNP, anti-SSA, anti-SSB, anti-cardiolipin and anti-B2G1P1 antibodies frequencies were similar in both genders.

Conclusions: SLE diagnosis was made earlier in men than women, this could be explained by more severe disease in men [1]. However this hypothesis has been highly controversial [2]. Cutaneous and joint manifestations seem to be more frequent in women whereas serious manifestations like lupus nephritis and neurological involvements were more frequent in men [3–4]. In our study, only lupus nephritis and pancreatitis were more frequent in men.

References:

Abstract THU0289 – Table 1. BLyS gene expression in urinary sample and renal biopsy according to clinical and histological findings

<table>
<thead>
<tr>
<th>Variables</th>
<th>ΔCt BLyS Urinary</th>
<th>p</th>
<th>ΔCt BLyS Biopsy</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>SLEDAI ≤0</td>
<td>7.52 (6.59–11.19)</td>
<td>0.04</td>
<td>8.03 (6.50–10.20)</td>
<td>0.04</td>
</tr>
<tr>
<td>SLICC ≤0</td>
<td>7.52 (6.59–11.19)</td>
<td>0.04</td>
<td>8.03 (6.50–10.20)</td>
<td>0.04</td>
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<tr>
<td>MDRD ≥60</td>
<td>7.67 (6.016–12/5)</td>
<td>0.04</td>
<td>8.03 (6.95–8.95)</td>
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<td>Proteinuria &gt;0.5</td>
<td>7.52 (6.59–11.19)</td>
<td>0.04</td>
<td>8.03 (6.50–10.20)</td>
<td>0.04</td>
</tr>
<tr>
<td>Without tubular atrophy in Bi/Bi</td>
<td>7.83 (6.43–6.17)</td>
<td>0.03</td>
<td>8.16 (6.44–8.52)</td>
<td>0.03</td>
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</table>

THU0291  GENDER INFLUENCE ON CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL ASPECTS OF SYSTEMIC LUPUS ERYTHEMATOSUS

T. Ben Salem, M. Tougourti, I. Naceur, I. Ben Ghorbel, M. Lamloum, M.H. Houman. Internal Medicine, Rabta university hospital, Tunis, Tunisia

Background: Systemic lupus erythematosus (SLE) is more frequent in women but seems to be more severe in men.

Objectives: The aim was to study gender influence on clinical, biological and immunological features of SLE.

Methods: It’s a retrospective study conducted in an internal medicine department. Patients with systemic lupus erythematosus (ACR revised criteria) were included. Data were recorded and compared using SPSS. Variables with a p<0.05 were considered to be statistically significant.

Results: A total of 246 SLE patients were included: 224 female and 19 male (sex ratio F:M was 11.78). Mean ages at disease onset and at SLE diagnosis were comparable for men and women respectively 35.6±14.31 vs 32.7±13.36 years and 35±14.3 vs 34.5±13.6 years.

SLE diagnosis was made earlier in men with an average delay (from first sign of the disease to diagnosis) of 6.1 months vs 21.4 months (p<0.02). Clinically, photosensitivity was significantly more frequent in women (81.4% vs 58.8%; p=0.03). Women complained from alopecia more frequently than men but the difference was not statistically significant (35.1% vs 14.3%; p=0.09). Arthritis were two times more frequent in women (50.7% vs 25%; p=0.04). Lupus nephritis as well as lupus pancreatitis were significantly more frequent in men, respectively 66.7% vs 41.6% (p=0.039) and 11.1% vs 1.4% (p=0.047). There were no differences regarding to gender in neurological involvement and seritis. No significant differences were observed between men and women concerning hematological disorders. Anti-DNA, anti-Sm, anti-RNP, anti-SSA, anti-SSB, anti-cardiolipin and anti-B2G1P1 antibodies frequencies were similar in both genders.

Conclusions: SLE diagnosis was made earlier in men than women, this could be explained by more severe disease in men [1]. However this hypothesis has been highly controversial [2]. Cutaneous and joint manifestations seem to be more frequent in women whereas serious manifestations like lupus nephritis and neurological involvements were more frequent in men [3–4]. In our study, only lupus nephritis and pancreatitis were more frequent in men.

References:
V. Milic, G. Radunovic, N. Damjanov. Institute of Rheumatology, Belgrade, Serbia

Objectives: To analyze ultrasoundographic (US) changes of salivary glands (SG) in patients with primary Sjogren’s syndrome (pSS) and assessment of their accuracy for diagnosis pSS.

Methods: This study included 205 pSS patients (mean age 53.9±11.5, disease duration 5.6 years) and 87 healthy controls (mean age 52.3±14.7). All pSS patients fulfilled the AECG diagnostic criteria. The disease activity was measured by EULAR SS disease activity index (ESSDAI). Parotid and submandibular glands on both sides were assessed for size, parenchymal echogenicity and inhomogeneity, posterior glandular border and presence of intraglandular lymph nodes. Intensity of echogenicity of the salivary glands was graded according to the De Vita scoring system [0] homogenous glands; [1] mild inhomogeneous - isolated hypoechoic areas; [2] evident inhomogeneous - scattered hypoechoic areas, and/or multiple punctate or linear densities; [3] grossly inhomogeneous – large hypoechoic areas, and/or to linear densities, and/or for multiple cysts. The global SGUS score (0–6) was the sum of the scores of each pair of salivary glands. Statistical analysis was performed by SPSS v16. Data were compared using Hest, χ² test and Mann-Whitney U test. The optimal cut-off value for SGUS score was calculated as the area under the receiver operating characteristic curve (AUC-ROC).

Results: Xerorhaphalitis and xerostomia were presented in 185/205 (90.2%) and 186/205 (91.2%), respectively. According to ESSDAI, the majority of pSS patients 88/205 (43%) had moderate disease activity. Seventy-eight percent of pSS patients were anti-SSA antibody positive, 44% anti-SSB/La antibody positive. Biopsy of LSG was positive in 140/172 (81.4%) pSS patients. US abnormalities were established in 197 (96%) pSS patients and in 16 (18%) controls (p<0.0001). Pathological sizes of salivary glands were more frequently in pSS patients than controls, 111 (54.2%) vs. 3 (3.4%) patients, respectively (p<0.0001). The echogenicity of the salivary glands was pathological changes in 142 (69.3%) pSS patients and in only 5 (5.7%) control group (p<0.0001). The pathological glandular border was frequently in pSS patients than control group, 48 (23.4%) vs. 2 (2.3%), p<0.0001. No differences were detected between the two groups of patients for enlarged intraglandular lymph nodes. Most of pSS patients had pathological inhomogeneity, 197/205 (96.1%) vs. 16/85 (18.4%) in control group (p<0.0001). The median SGUS was significantly higher in pSS patients in comparison with control group [median (range) 4 (0–6) vs. 0 (0–2), p<0.0001]. Forty-five percent of pSS patients had SGUS score 4. The SGUS cut-off ≥2 showed specificity 95.4%, and sensitivity 93.3%. Diagnostic accuracy of the parenchymal inhomogeneity was very good (AUC-ROC 0.89), followed by the glandular echogenicity (AUC-ROC 0.81), the glandular size (AUC ROC 0.75), the posterior border (AUC ROC 0.60), and the presence of intraglandular lymph nodules (AUC ROC 0.49), respectively.

Conclusions: Our findings confirm that most of established pSS patients had pathological SG US features. Among US parameters, parenchymal inhomogeneity was the most discriminant feature for diagnosis of SS. There is the growing evidence that ultrasound should be considered as the useful method for evaluation of salivary glands in pSS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2323

THU0292

DIAGNOSTIC ACCURACY OF ULTRASOUND AND ULTRASONOGRAPHIC FEATURES OF SALIVARY GLANDS IN PATIENTS WITH PRIMARY SJOGREN’S SYNDROME

V. Milic, G. Radunovic, N. Damjanov. Institute of Rheumatology, Belgrade, Serbia

Objectives: To analyze ultrasoundographic (US) changes of salivary glands (SG) in patients with primary Sjogren’s syndrome (pSS) and assessment of their accuracy for diagnosis pSS.

Methods: This study included 205 pSS patients (mean age 53.9±11.5, disease duration 5.6 years) and 87 healthy controls (mean age 52.3±14.7). All pSS patients fulfilled the AECG diagnostic criteria. The disease activity was measured by EULAR SS disease activity index (ESSDAI). Parotid and submandibular glands on both sides were assessed for size, parenchymal echogenicity and inhomogeneity, posterior glandular border and presence of intraglandular lymph nodes. Intensity of echogenicity of the salivary glands was graded according to the De Vita scoring system [0] homogenous glands; [1] mild inhomogeneous - isolated hypoechoic areas; [2] evident inhomogeneous - scattered hypoechoic areas, and/or multiple punctate or linear densities; [3] grossly inhomogeneous – large hypoechoic areas, and/or to linear densities, and/or for multiple cysts. The global SGUS score (0–6) was the sum of the scores of each pair of salivary glands. Statistical analysis was performed by SPSS v16. Data were compared using Hest, χ² test and Mann-Whitney U test. The optimal cut-off value for SGUS score was calculated as the area under the receiver operating characteristic curve (AUC-ROC).

Results: Xerorhaphalitis and xerostomia were presented in 185/205 (90.2%) and 186/205 (91.2%), respectively. According to ESSDAI, the majority of pSS patients 88/205 (43%) had moderate disease activity. Seventy-eight percent of pSS patients were anti-SSA antibody positive, 44% anti-SSB/La antibody positive. Biopsy of LSG was positive in 140/172 (81.4%) pSS patients. US abnormalities were established in 197 (96%) pSS patients and in 16 (18%) controls (p<0.0001). Pathological sizes of salivary glands were more frequently in pSS patients than controls, 111 (54.2%) vs. 3 (3.4%) patients, respectively (p<0.0001). The echogenicity of the salivary glands was pathological changes in 142 (69.3%) pSS patients and in only 5 (5.7%) control group (p<0.0001). The pathological glandular border was frequently in pSS patients than control group, 48 (23.4%) vs. 2 (2.3%), p<0.0001. No differences were detected between the two groups of patients for enlarged intraglandular lymph nodes. Most of pSS patients had pathological inhomogeneity, 197/205 (96.1%) vs. 16/85 (18.4%) in control group (p<0.0001). The median SGUS was significantly higher in pSS patients in comparison with control group [median (range) 4 (0–6) vs. 0 (0–2), p<0.0001]. Forty-five percent of pSS patients had SGUS score 4. The SGUS cut-off ≥2 showed specificity 95.4%, and sensitivity 93.3%. Diagnostic accuracy of the parenchymal inhomogeneity was very good (AUC-ROC 0.89), followed by the glandular echogenicity (AUC-ROC 0.81), the glandular size (AUC ROC 0.75), the posterior border (AUC ROC 0.60), and the presence of intraglandular lymph nodules (AUC ROC 0.49), respectively.

Conclusions: Our findings confirm that most of established pSS patients had pathological SG US features. Among US parameters, parenchymal inhomogeneity was the most discriminant feature for diagnosis of SS. There is the growing evidence that ultrasound should be considered as the useful method for evaluation of salivary glands in pSS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2323
OBJECTIVES: In the present study, volumes of the hippocampus were examined to identify the responsible lesions for neurobehavioral changes in CPNB, and patterns of atrophy in the hippocampus and brainstem were compared between patients with CPNB and AD.

METHODS: The subjects were 32 patients, including 13 with CPNB (11 males and 2 females, age 51.2±12.1 years old [mean ± SD]), 13 with Behçet’s disease without NB (non-NB) (10 males and 3 females, age 54.4±11.4 years old), and 6 with AD (5 males and 1 female, age 78.8±7.5 years old). All patients with BD satisfied the international classification criteria for BD. CPNB was defined as intractable, slowly progressive neurobehavioral changes and/or cerebellar ataxia accompanied by persistent elevation of interleukin-6 (IL-6) >20 pg/mL in cerebrospinal fluid on two different occasions at an interval of at least 2 weeks. All patients with AD satisfied Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria. Brain magnetic resonance imaging (MRI) was obtained from each subject. The areas of the brainstem, genu and posterior corpus callosum were measured by T1-weighted imaging using image analysis software (Image J ver.1.45; NIH, USA). Severity of gray matter loss in the hippocampal region and whole brain were investigated using Voxel-Based Specific Regional Analysis System for Alzheimer’s Disease (VS-RAD) software (Ensay Co., Ltd) to determine the degrees of hippocampal region atrophy (Z score) and whole-brain atrophy (WBAI). Thus, the 1/Z score is positively correlated with the hippocampus volume. The ratio of the degree of brainstem atrophy to that of hippocampal atrophy was evaluated by the brainstem area value divided by the 1/Z score (BAI/H score) in each patient.

RESULTS: The brainstem area was significantly decreased in CPNB (61.8±58.7 mm² [mean ± SD]) compared with that in AD (66.1±54.6 mm² and non-NB (66.1±55.0 mm²) (Figure A). VS-RAD analysis showed that Z score was significantly increased in CPNB (1.46±0.70) and AD (3.31±1.21) compared with that in non-NB (0.77±0.40) (Figure B). Of note, the BAI/H score, reflecting the brainstem/hippocampus volume ratio, was much lower in CPNB than in AD (663.5±311.8 vs 2018±687.6, p=0.01) (Figure C).

CONCLUSIONS: These results indicate that the hippocampus, in addition to the brainstem, is a common target lesion in CPNB, and this accounts for the progressive neurobehavioral dysfunction in this disease. Moreover, the data emphasize that brainstem atrophy is disproportionately greater than hippocampal atrophy in CPNB, in contrast to AD.

Disclosure of Interest: None declared


THU0295 CLINICAL FEATURES OF TAKAYASU’S ARTERITIS FROM AN INCEPTION COHORT: EARLY DISEASE IS CHARACTERIZED BY “SYSTEMIC INFLAMMATION”

F. Alibaz-Oner on behalf of Turkish Takayasu Arteritis Study Group. Rheumatology, Marmara University, School of Medicine, Istanbul, Turkey

Background: There is only retrospective and very limited data for the long term prognosis of Takayasu’s Arteritis (TAK), a rare large-vessel vasculitis. In this study, we aimed to present the preliminary results of a Takayasu Inception Cohort settled for long term, prospective follow-up of only newly-diagnosed patients with TAK.

Methods: Patients fulfilling the American College of Rheumatology 1990 criteria for TAK and diagnosed in the last 12 months were included to the study. Patients’ data were recorded in an electronic database of an international “Takayasu’s Arteritis Registry” requiring annual visits and at least annual visits is compared with an historical Turkish cohort previously published (Başçakırgil et al., 2009).

Results: The study included 128 patients (age: 38.9±13.1 years, F/M: 112/16) with TAK from 15 tertiary Rheumatology centers in Turkey. The mean symptom duration of patients was 5.2 years at diagnosis. According to the angiographic classification, 59.2% of the study group had type I and only 17.2% had type V disease. When we compared our results to our retrospective cohort (previously published by Turkish Takayasu Arteritis Study Group), constitutional symptoms (72.2% vs 66%) and limb claudication (62.3% vs 48%) were observed to be more frequent, whereas paresthesia (35.6% vs 88%) was less in the inception cohort (55%). Only in the initial phase of TAK, mucocutaneous symptoms also seem to be a feature of newly-diagnosed disease (28.4% vs 8.8%). Regarding comorbidities at diagnosis, the rate of dyslipidemia was 22%, diabetes mellitus 6%, smoking 28.5% and obesity (BMI<30) 15.8% among TAK patients. All patients were given oral corticosteroid (CS) therapy (0.5–1 mg/kg) at diagnosis. Only the patients (7.8%) also having CS pulses. In addition to CSs, 55 patients (43%) were given methotrexate, 14 patients (11%) azathioprine and 5 (4%) cyclophosphamide at disease-onset.

Conclusions: Our results suggest that, in an inception cohort, signs and symptoms of “systemic inflammation” is more prominent in newly-diagnosed TAK patients, whereas vascular extent and damage accumulates during the disease course. The long term follow-up of our inception cohort will better show the actual course and predictors of prognosis in TAK.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3856

THU0296 THE ROLE OF ULTRASOUND IN THE MANAGEMENT OF GIANT CELL ARTERITIS (GCA) IN ROUTINE CLINICAL PRACTICE

S. Monti 1, 2, A. Floris 3, C. Ponte 3, S. Vaggers 2, W.A. Schmidt 3, A.P. Diamantopoulos 3, C. Pereira 3, R. Luqmani 1 1. Rheumatology, University of Pavia, Pavia, Italy; 2IRCCS Policlinico San Matteo Foundation, Pavia, Italy; 3Policlinico Umberto I, University of Rome, Rome, Italy

Background: The role of ultrasound (US) in the management of giant cell arteritis (GCA) in routine clinical care of patients with GCA is still debated.

Objectives: To develop a protocol using CS and explore its value in the routine care of patients with GCA.

METHODS: We developed a structured scanning protocol for CS of temporal and axillary arteries (total of 8 anatomical sites scanned per patient) based on previously published methods. We tested the protocol on consecutive patients referred to a single rheumatology centre, with suspected or established GCA, between July 2014 and September 2016. We defined a positive scan by the presence of halo in at least one branch of a temporal artery (TA) or an axillary artery (AX). We report data from the first 293 consecutively scanned cases.

RESULTS: We assessed 293 patients (mean age 72±10, female/male 196/97), of whom 118 had clinically confirmed GCA. Amongst new referrals with confirmed diagnosis of GCA, 44% had a positive scan; two patients with a positive scan did not have GCA. 82% of newly-diagnosed patients showed exclusive TA involvement, 25% concomitant AX, and 4% exclusive AX involvement. High-dose glucocorticoid therapy had already been started in 78% of these patients for an average of 17±33 days. Amongst this group, the sensitivity of US was 46% (95% IC 37%–55%), specificity 98% (95% CI 93%–99.8%), positive predictive value 99.8% (98%–99.6%), and negative predictive value 60% (95% IC 52%–68%). During the period of observation, the rate of temporal artery biopsies (TAB) decreased significantly from 42% to 25% (p=0.002). During follow up, CS was positive in 21% of 89 routine scans in asymptomatic individuals, compared to 58% in patients with confirmed clinical flares (45% of whom had negative inflammatory markers). Over time, the number of halos per patient reduced; only new or flaring patients showed a halo in >4 sites. Halo size at the TA did not change significantly (average thickness 0.6±1.1 mm), however, the size of AX artery halos significantly reduced from first referral (1.6±0.4 mm) to follow up (1.4±0.2 mm) to follow up (1.4±0.2 mm), p=0.01) during subsequent flares (1.4±0.2, p=0.02).

Conclusions: We have developed and tested a standardised methodology for CS evaluation of GCA. CS provides a high positive predictive value for a diagnosis of GCA in unselected patients from routine clinical practice, although prior high dose glucocorticoid therapy is likely to reduce its sensitivity. CS allows for a significant reduction of TAB. We explored the role of CS to detect disease flares and demonstrated a significant reduction in the extent of abnormalities, and of the size of halo of the AX arteries during follow up or flares. These findings could have a significant impact on the management of patients with suspected and confirmed GCA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4063
A NOVEL ULTRASOUND SCORING SYSTEM FOR GIANT CELL ARTERITIS

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Background: Colour duplex sonography (CDS) can be used for giant cell arteritis (GCA) to detect inflammatory oedema of the vascular wall, known as “halo”. A standardized, quantitative score to grade the intensity and extension of vascular involvement detected by CDS has not yet been developed.

Objectives: To develop and test different scoring models of CDS findings in patients with new onset GCA, and to correlate the models with final diagnosis, histologic findings, and outcome.

Methods: We selected patients with a positive CDS and a confirmed diagnosis of GCA from the Temporal Artery Biopsy vs Ultrasound in Diagnosis of GCA (TABUL) study (1). We designed CDS models combining different ultrasonographic information based on available evidence, or hypothesized clinical relevance of size, anatomical distribution, and extent of halos, summing up to a final numeric score.

Results: We included 135 GCA patients (male/female: 43/92), age 73.3±8. Forty four patients (32%) had a positive CDS, but not a final diagnosis of GCA. We designed 8 different CDS models (Figure 1). Models 1, 4, 6, and 7 were significantly associated with a confirmed diagnosis of GCA (Table 2). Model 7 better discriminated patients with GCA from non-GCA: area under the curve (AUC): 0.844 (0.766–0.923). All, except models 5 and 8, correlated with a temporal artery biopsy (TAB) result diagnostic for GCA. Most models correlated with histologic findings involving the media or transmural infiltrate, but not with small vessel or adventitial involvement. None of the models correlated with permanent ischaemic sequelae, however, the low number of events might have limited their significance.

Conclusions: The CDS findings that better correlate with a diagnosis of GCA, and TAB findings are: the number of positive sites, the size of the halo (maximum, transmural) and TAB findings are: the number of positive sites, the size of the halo (maximum, transmural) involving detected by CDS has not yet been developed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4069

Table 2. Correlation of the different models with clinical and histologic variables

<table>
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<th>Model</th>
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<th>Model 1</th>
<th>Model 2</th>
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| CRP < 6.1mg/L, type 4 disease and DEI.Tak ≥ 9 predicted sustained inactive disease with an AUC of 70.2 (63.3–77.2, p<0.001). Initial steroid dosage of 0.5mg/kg/day was similar to 1mg/kg/day in terms of response or relapse. Overall, there were only 15 (5.9%) patients who never responded to treatment. There were 2 fatalities. At the last visit, 176 (70.5%) had stable disease. Damage progression (delta TADS) was lower in patients with sustained inactive disease than the rest, p<0.001. Conclusions: Medical management arrested disease activity, damage progression and mortality in our cohort. Low baseline CRP and DEI.Tak scores and type 4 disease independently predicted sustained inactive disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4258

LONG TERM OUTCOME OF PATIENTS WITH TAKAYASU ARTERITIS: A SINGLE CENTRE STUDY

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Background: Takayasu Arteritis (TA), a large vessel vasculitis is characterised by a variable clinical course and outcome that differs across populations. Most studies are limited by small sample size.

Objectives: (i) To study treatment outcome in our TA patients with a follow up of ≥12 months (ii) Construct a prediction model for subset of patients with sustained inactive disease.

Methods: Consecutive patients with TA attending our clinics between 1998 and April 2016 were recruited. Details of baseline demographics, clinical profile, angiography, disease extent using DETak, laboratory parameters and TADS (Takayasu arteritis damage score) were recorded. At each follow up visit, disease activity was assessed by Indian Takayasu Activity score (ITAS-2010) and imaging, while damage was assessed by TADS for patients who followed up for ≥12 months (retrospectively for 179 and prospectively for 72 patients). Treatment response was classified as complete response (CR), partial response and no-response. Sustained inactive disease was defined as maintenance of CR throughout the follow up with steroid dose reduced to ≤5mg/day. Relapse was defined as return of active disease after CR. Statistical analysis was performed using SPSS-16. Intergroup comparisons were performed by nonparametric test. Logistic regression was used for determining independent associations. Optimal cut off values were determined using receiver operating curve and prediction model was constructed. Efficacy of medications was compared by Cox proportional hazards model.

Results: Baseline details were noted for 503 patients: mean age at onset of 25.6±11.1 years, disease duration 12 (6–48) months, diagnostic delay 6 (3–24) months and 77.9% were females.

Among 251 patients with follow up of at least 12 months, 95.2% received steroids along with II line immunosuppressant (mycophenolate in 63.7%). Tolcizumab was given induction or rescue therapy to 44 patients. Revascularisation procedures were performed in 71.7%. Complete (ITAS 2010 = 0, CRP <6mg/L, angioiwe not-progression) and partial response was achieved in 176 patients (70.1%) and 42 (16.7%) respectively within 6 months. During a median follow up of 42 (1Q: 24–81) months, 116 (46.2%) maintained complete response till their last follow up with cumulative relapse free survival of 83%, 70% and 55% at 1, 2 and 3 years respectively. A model including baseline CRP<6.1mg/L, type 4 disease and DEI.Tak <9 predicted sustained inactive disease with an AUC of 70.2 (63.3–77.2, p<0.001). Initial steroid dosage of 0.5mg/kg/day was similar to 1mg/kg/day in terms of response or relapse. Overall, there were only 15 (5.9%) patients who never responded to treatment. There were 2 fatalities. At the last visit, 176 (70.5%) had stable disease. Damage progression (delta TADS) was lower in patients with sustained inactive disease than the rest, p<0.001.

Conclusions: Medical management arrested disease activity, damage progression and mortality in our cohort. Low baseline CRP and DEI.Tak scores and type 4 disease independently predicted sustained inactive disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4258

UNDERSTANDING THE HETEROGENEITY OF LARGE-VESSSEL VASCULITIDES

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Background: Adult large-vessel vasculitides (LVV) are rare conditions, currently classified as two different diseases, Takayasu arteritis (TA) and giant cell arteritis (GCA). Despite being biologically and pathophysiologically different, the two are scarce at best. Arterial involvement, despite being the central disease feature, has been poorly addressed by research. We have developed two novel, imaging-based scores (the arteritis stenosis score [ASS] and arteritis dilation score [ADS]). ASS and ADS define stenotic and aneurysmal disease in a
core-set of 17 arteries and respectively represent the sum of stenosis and dilation scores in individual arteries

Objectives: To use ASS, ADS and the stenosis and dilation scores of individual arteries to describe a cohort of LVV patients and identify heterogeneity between patients.

Methods: The ASS, ADS and individual artery scores have been derived from 110 LVV (81 TA, 29 GCA) patients. Model-based clustering optimising the Bayesian Information Criterion and principal component analysis were performed.

Results: Arterial involvement was shown to be differed in GCA and TA. TA has higher ASS than GCA (median, IQR: 20, 11–29 Vs 5, 0–11; p < 0.001) and lower ADS (0, 0–5 Vs 6, 0–13; p = 0.019). The scatterplot of ASS and ADS revealed incomplete overlap of arterial involvement in GCA and TA. No differences were seen in TA with disease onset before or after 40 yrs. Age at onset, ASS and ADS did not correlate in TA, suggesting stenotic and aneuryismal arterial remodelling are independent. In GCA, ASS and ADS were negatively correlated ($p = 0.041; p = 0.031$) and ADS correlated with age at onset ($p = 0.383; p = 0.040$), suggesting the existence of a biologic “switch” between arterial stenosis and dilation, regulated by age at onset.

We accounted for geographical distribution of lesions by evaluating the scores of individual arteries with correspondence analysis. Arterial involvement was symmetric with tripolar segregation: stenosis in the supra-aortic branches, stenosis in the aorto-abdominal district and arterial dilation (Fig 1A). When patients exhibited the first two components, three different clusters were recognized (Fig 1B), with different ASS, ADS and damage as assessed by the TA damage score ($p < 0.001$ for all tests). 27/29 (93%) of GCA patients were included in cluster 1. Of interest, density graphs showed (i) a different distribution of arterial involvement in GCA and TA (Fig 1C-D), and (ii) potential for identification of novel disease subsets (2 in GCA and 3 in TA). A comparable distribution was seen in TA with onset before or after 40 yrs (Fig 1E). Lastly, when patients with disease onset after 50 yrs (11 TA, 28 GCA) were studied, a trimodal distribution was observed, suggesting discrete phenotypes of arterial involvement exist, rather than a continuum (Fig 1F).

Conclusions: Arterial involvement differs in TA and GCA, although some overlap exists. Elderly TA is similar to juvenile TA, while a potential biologic “switch”, yet to be identified, regulating the final outcome of arterial remodelling and influenced by ageing, is present in GCA. Three main patterns of arterial involvement appear to exist. LVVs represent the composition of different discrete subsets rather than a phenotypic continuum.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5386

THU0300 CENTRAL NERVOUS SYSTEM INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS (WEGENER) IN A LARGE SERIES OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIDES (AAV).REVAS STUDY-GEAS-SEMI


Background: GPA is a necrotizing systemic vasculitis that usually involves ENT, lungs and kidneys. Neurological manifestations appear in 25–50% of patients, usually involving peripheral nervous system. CNS involvement, has been reported in only 7–11% of cases

Objectives: to describe the clinical features and outcome of patients with GPA and CNS involvement in a large series of patients with AAV

Methods: multicenter retrospective-longitudinal study that encompassed patients diagnosed with AAV between Jan 1995 and Nov 2014 in 21 Centres from Spain (REVAS Study). Statistical analysis was performed using SPS vs20 package

Results: 455 patients (188 GPA, 167 MPA and 100 EGPA) were included. Mean age at diagnosis was 55.7±17.2y. ANCA were positive in 86.8% of cases (55.8% C-ANCA, 51% P-ANCA). Median time to diagnosis was 4 weeks (IQR 10). Median follow-up time was 80 months (IQR 105). Neurological involvement was documented in 156 (34.5%) patients, but only 33 (7.3%) presented CNS involvement at disease onset. From those patients, 20 (60.6%) had GPA. Mean age at diagnosis of patients with GPA and CNS involvement was 51.±16.7y. ANCA were positive in all cases (15 C-ANCA-PR3, 5 P-ANCA-MPO). Headache was the main neurological symptom (60%) followed by sensory (45%) and motor impairment (35%). MRI and/or ango-CT scan were performed in all cases. Cerebral ischaemic lesions were observed in 10 patients, and granulomatous lesions in 5, including pachymeningitis (n=6), spinal cord pachymeningitis (n=2) and isolated granulomatous lesions (n=1). Lumbar puncture was performed in 8 (40%) patients and revealed CSF abnormalities in 70. Diagnosis was confirmed by meningeal biopsy (n=2), ENT biopsies (n=5) and renal biopsy (n=2) in patients with CNS granulomatous lesions, and by renal, pulmonary or peripheral nerve biopsy in patients with CNS ischaemic lesions. Headache was predominant in patients with granulomatous lesions, while sensory and motor impairment were predominant in patients with ischaemic lesions. Mean BVAS at disease onset was 29.±9.7, significantly higher than in GPA total cohort (18.±9.2). Renal involvement was more common in patients with ischaemic lesions than in those with granulomatous lesions (80% vs. 40%, p<0.001), and ENT involvement in patients with granulomatous forms (70% vs. 50%, p<0.005). Most patients (70%) received oral CF for induction therapy. Two patients received rituximab. For maintenance therapy, 25% of patients received AZA, 20% MMF and the remaining CF. 70% of patients received TM-SX. During follow-up, 58.8% and 40% of patients developed bacterial and opportunistic infections, respectively. Infections were related to oral CF therapy (p<0.029). Long-term neurological sequelae were noted in patients with ischaemic lesions (40%) and spinal cord pachymeningitis (100%)

Conclusions: Patients with GPA and CNS involvement have more severe disease at presentation and more treatment-related side effects than patients without CNS involvement. Long-term neurological sequelae are more frequent in patients with ischaemic lesions and spinal cord pachymeningitis

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2520
SAFETY FOLLOWING INITIATION OF RITUXIMAB IN GRANULOMATOUS WITH POLYANGIITIS (GPA) OR MICROSCOPIC POLYANGIITIS (MPA): INTERIM ANALYSIS OF THE RITUXIMAB IN ANCA-ASSOCIATED VASCULITIS REGISTRY (RAVER)

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Background: Therapy-related serious adverse events (SAEs) are important causes of morbidity in patients with GPA or MPA. Long-term safety data of rituximab in GPA/MPA are limited.

Objectives: To characterize safety events in an observational registry of patients with GPA/MPA initiating rituximab.

Methods: This interim analysis of RaVeR, an ongoing open-label real-world study of adult patients with GPA or MPA initiating rituximab (dose/frequency determined by investigator), was conducted when 50% of patient-years (PY) were collected (July 2015–October 2016). Safety events included serious infections (SI), infusion-related reactions (IRR), serious cardiac events, malignancies, and other serious events. Crude incidence rates (IR) and 95% CI were calculated. Trial registration number: NCT01613599

Results: 97 patients (202 PY) received rituximab, of whom 70% received rituximab retreatment. Median follow-up was 2.4 years. Overall, 91% of patients were ANCA-positive and 78% had GPA. 17 patients (17.5%) had a history of plasmapheresis or dialysis; 20 (20.6%) were receiving rituximab plus cyclophosphamide at baseline. 13 patients had 20 SIs (9.13/100 PYs [95% CI: 5.58–14.10]). 9 patients (9.3%) experienced 13 serious cardiovascular (CV) events (5.93/100 PYs [95% CI: 3.16–10.15]), 12 of which were reported as unrelated to rituximab. Of the 13 CV events, 9 were atrial arrhythmias and most patients had a history of renal or CV disease history. There were no serious IRRs or SAEs within 24 hours of rituximab infusion. There were 6 deaths (2.74/100 PYs [95% CI: 1.01–5.86]); causes of death included septic shock, intestinal lung disease, congestive heart failure, cardio-respiratory arrest and 2 deaths of unknown etiology. The severe disease flare rate was 5.94/100 PYs (95% CI: 3.16–10.15). Among patients who received rituximab retreatment, the IRs of SAEs (26.1/100 PYs) and SIs (7.29/100 PYs) were not increased compared with the overall cohort.

Conclusions: In this interim analysis of patients with GPA/MPA treated with rituximab, SAEs were not increased compared with comparable cohorts of patients with renal involvement. Safety events did not increase with rituximab retreatment. These results are consistent with the known safety profile of rituximab and provide preliminary long-term, practice-level safety data for rituximab in GPA/MPA.

Acknowledgements: This study was funded by F. Hoffmann-La Roche, Ltd. Disclosure of Interest: J. Niles: None declared, N. Allen Grant/research support from: Genentech, Inc., J. Block: None declared, C. Koening Grant/research support from: VA Merit, C. Langford: None declared, A. Abril: None declared, A. Lee: None declared, P. Merkel: None declared, L. Mertz: None declared, P. Monach Grant/research support from: Genentech, Inc., Bristol-Myers Squibb, GlaxoSmithClinne, Speakers bureau: Medscape, L. Moreland Grant/research support from: Genentech, Inc., Bristol-Myers Squibb, Consultant for: Pfizer; Boehringer Ingelheim, P. Nachman: None declared, T. Peikert: None declared, R. Spiera: None declared, D. Wallace: None declared, F. Erblang Employee of: F. Hoffmann-La Roche, Ltd.; M. Cascino Employee of: Genentech, Inc., P. Dumuche Shareholder of: pm Statistical Consulting Services, Ltd., V. Malik Employee of: F. Hoffmann-La Roche, Ltd.; P. Brunetta Employee of: Genentech, Inc.


HISTOLOGY FINDINGS IN GIANT CELL ARTERITIS (GCA) AND THEIR RELATIONSHIP WITH THE ULTRASOUND RESULTS: ANALYSIS OF DATA FROM THE TABUL STUDY (TEMPORAL ARTERY BIOPSY VS ULTRASOUND IN DIAGNOSIS OF GIANT CELL ARTERITIS)

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Background: Although temporal artery biopsy (TAB) has been the gold standard for diagnosis of GCA, ultrasound has superior sensitivity but lower specificity. Occasionally, histological evidence of inflammation is restricted to the vasa vasorum, which is difficult to assess with TABs, and both, which could limit the diagnostic sensitivity of ultrasound for GCA. Moreover, false positive ultrasound results have been described in patients with arteriosclerosis on histology.

Objectives: To compare histologic findings with ultrasound results from patients with suspected GCA included in the TABUL study (a multinational study to assess the relative performance of ultrasound and TAB for diagnosing GCA).

Methods: All patients with newly suspected GCA underwent an ultrasound of both temporal and axillary arteries, followed by a TAB, within 7 days of confirming glucocorticoid therapy. TAB pathological diagnoses were analysed and the different histological features were compared with the ultrasound results using Chi-square or Fisher exact tests.

Results: Results for TAB and ultrasound were available in 388 patients (69% with a final clinician’s diagnosis of GCA). An artery was definitely obtained in 363 (94%) TABs; the pathological diagnosis was GCA in 104 (29%) cases, arteriosclerosis in 35 (10%), normal in 203 (56%) and other conditions in 21 (6%). All TABs compatible with GCA also had a final clinician’s diagnosis of GCA (73% with positive ultrasound). Table 1 shows that ultrasound positivity occurred more frequently in patients where the media was the predominant site of inflammation compared with the ultrasound result was positive in 9 (26%) cases where TAB was consistent with arteriosclerosis, 8 (89%) of whom had a final clinician’s diagnosis of GCA. The ultrasound was positive in 64 (32%) cases where TAB was normal, 52 (81%) of whom had a final clinician’s diagnosis of GCA.

Conclusions: Amongst patients with suspected GCA, ultrasound is more likely to be positive when histological inflammation is predominantly present in the intima-media. No significant correlation between histologic findings and negative ultrasound results was found, but the small number of cases with predominant vasa vasorum infiltrates in our cohort limited this analysis. There was only one false positive ultrasound in patients with arteriosclerosis on TAB.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3544

CLINICAL FEATURES AND PROGNOSIS OF ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT AT DIAGNOSIS


Background: Kidneys are major organs targeted by antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Clinical manifestations, laboratory data, and prognosis of AAV with renal involvement at diagnosis are not elucidated.

Disclosures of Interest: None declared

Objectives: We compared clinical features of AAV with renal involvement with patients without renal involvement.

Methods: We conducted an observational study of 104 patients with AAV (12 esophageal granulomatosis with polyangiitis, 23 granulomatosis with polyangiitis (GPA), 68 microscopic polyangiitis, 3 renal limited vasculitis) between in 2008 to 2016 in Nagasaki University Hospital. Using medical records, we analyzed the patients' baseline variables, laboratory data, clinical symptoms, and therapeutic outcomes after treatments including episodes of relapses, initiation of dialysis, and death. Renal involvement was defined as the state with estimated glomerular filtration rate > 60 mL/min/1.73 m² or microscopic hematuria (2+ or greater) which were not caused by renal diseases except for AAV.

Results: Sixty-nine patients had renal involvement. Patients with renal involvement had higher median age at diagnosis than patients without renal involvement group (75 years vs. 66 years, p < 0.001). Patients with renal involvement included fewer GPA patients compared to other AAV types. Patients with renal involvement had lower hemoglobin levels (10.3 g/dL vs. 12.3 g/dL) and lower platelet levels (23.7x10⁴/μL vs. 28.7x10⁴/μL), Patients with renal involvement had higher erythrocyte sedimentation rate (78 mm/h vs. 20 mm/h), MPO-ANCA titers (16 U/mL vs. 58 U/mL) and urine protein levels (0.81 g/gCr vs. 0.15 g/gCr). Patients with renal involvement had lower C3 levels, but CH50 and C4 levels did not differ between in two groups. There were no differences in treatments including doses of prednisolone and use of mycophenolate pulse and cyclophosphamide between in two groups. Multivariable regression analysis revealed that age at diagnosis is the most significant explanatory variable to renal involvement. Nineteen percent of patients with renal involvement had initiation of dialysis. Multivariable analysis demonstrated estimated glomerular filtration rate at diagnosis is the most significant explanatory variable to initiations of dialysis (p = 0.010). Receiver operating characteristic curve showed the cutoff level of estimated glomerular filtration rate 37mL/min/1.73 m² was predictive of mortality. Renal involvement was defined as the state with estimated glomerular filtration rate > 60 mL/min/1.73 m² or microscopic hematuria (2+ or greater) which were not caused by renal diseases except for AAV.

Conclusions: Our study confirms the high mortality rate among vasculitides patients and mainly among those requiring admission to ICU. SOFA score and pre-admission treatment with rituximab have been found to be predictive of mortality.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4431

THU0305

EPIDEMOLOGY OF ANCA-ASSOCIATED VASCUITIS IN NORTHERN NORWAY

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Background: The ANCA-associated vasculitides (AAV) have increased in prevalence since the 1980s, with granulomatosis with polyangiitis (GPA) being most prevalent in Caucasian population in circumpolar areas. This was also shown in a study on GPA in northern Norway between 1984 and 1998, which further showed an increasing incidence [1].

Objectives: The present study aimed to investigate the subsequent 15-year period in the same region, now including all the AAVs.

Methods: The study area has 11 hospitals, no private specialist in rheumatology or nephrology, and an adult population of 371 928. We retrospectively searched all hospital databases, using ICD-10 codes potentially compatible with AAV. Patients diagnosed with AAV from 1999 through 2013 according to the European Medicines Agency (EMEA) algorithm, and for GPA also the subgroup fulfilling the American College of Rheumatology (ACR) 1990 criteria, were included. For prevalence data, patients residing in the area, but with AAV diagnosis prior to 1999, were included too.

Results: Using the EMEA algorithm, 90 incident cases were classified as GPA, 39 as microscopic polyangiitis (MPA) and 14 as eosinophilic granulomatosis with polyangiitis (EGPA). Within the GPA group, 78 patients also met the ACR criteria. The results for incidence and prevalence are given in Table 1:

<table>
<thead>
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<th>Annual incidence/million</th>
<th>Point prevalence at 31. Dec</th>
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<td>16.7</td>
</tr>
<tr>
<td>EMEA GPA</td>
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<td>EMEA MPA</td>
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</tr>
<tr>
<td>EMEA EGPA</td>
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<td>2.7</td>
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</tbody>
</table>

Conclusions: The GPA incidence and prevalence in this study are the highest reported. Though the incidence has stabilized, prevalence is still increasing, albeit at a decelerating rate (Graph 1). Moreover, the total AAV prevalence doubled in the last 10 years, exceeding previous estimates. Incidence of MPA and EGPA are both within the range found elsewhere. But the GPA incidence appears to be rising reminiscent of GPA before the turn of the century.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4158
null
Methotrexate (MTX), in clinical practice. Other factors associated were also investigated.

Methods: An inception cohort of GCA was assessed in the outpatient clinic at Hospital Clínico San Carlos, including patients from the date of diagnosis (Jan-1991 until Sept-2013), and followed-up until Sept-2014. Main outcome: relapse. A subjective improvement, patient has again symptoms or signs of GCA with high ESR and the need to increase corticosteroids at least 10mg. The independent variable was exposure to MTX over time. Covariates: Sociodemographic, clinical, and treatment. Incidence rates of relapses (IR) per 100 patient-years with their 95% confidence intervals (CI) were estimated using survival techniques. Time of exposure comprised the period from diagnosis until last of follow-up, main outcome, exposure to MTX or the end of the study. MTX influence on IR was analyzed by multivariable Cox models.

Results: 168 patients were included (675 patient-years). 80% of them were females and mean age at diagnosis was 76.7±7 years. 85% of the patients were on MTX, with mean dose of 10 mg/week. 31% of patients had relapses with an IR of 12 [9.6–14.9]. The median number of relapses was 1 [1–2], with a median lag time of 1.6 [0.6–6.3] years. In the multivariate analysis, exposure to MTX had less risk of relapse than those who never on MTX (p<0.05). Other variables included in the final model were: visual alterations, constitutional symptoms or malaise at clinical presentation of GCA.

Conclusions: The use of MTX seems to decrease the risk of recurrences. We also found other factors influencing on flares.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6118

THU0310 FREQUENCY OF RELAPSES AND TREATMENT DISCONTINUATION DURING LONG-TERM FOLLOW-UP OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: There are limited data regarding the long term outcomes of patients with giant cell arteritis (GCA) in the modern therapeutic era.

Objectives: To evaluate relapse, treatment discontinuation and complication rates in GCA patients during long term follow-up. Methods: A retrospective systematic chart review of GCA patients who were followed in an Academic Rheumatology Unit between 2002 to 2016 was performed. Demographic, clinical, laboratory and treatment data were collected and analyzed.

Results: 53 GCA patients were included in the study. 62% (n=33) are women with a mean age at diagnosis of 73±6.8 years and median duration of symptoms of 1.3 months. 41 patients (77%) had biopsy proven GCA while in 5 patients, clinical diagnosis was made. The most common symptoms were headache (60%), fever (51%), scalp tenderness (45%), jaw claudication (39%), visual disturbances (23%), polymyalgia rheumatica symptoms (9%) and vision loss (6%). Regarding laboratory data at baseline, the mean Hb and CRP were 101±32 g/dl and 381.000±134.000, respectively. All patients were initially treated with tapering steroids. Among different variables, only male sex was associated with earlier treatment discontinuation.

Conclusions: This study focuses on follow-up GCA patients with a longer duration of disease with a significant number of patients (n=28, 53%) among these 67% were laboratory and 56% clinical. To evaluate relapse, treatment discontinuation and complication rates in GCA patients during long term follow-up.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6541

THU0311 FECAL MICROBIOTA IN BEHÇET’S SYNDROME PATIENTS WITH MUCOCUTANEOUS AND UVEITIS INVOLVEMENT

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Background: Inflammatory immunity has a major role in the pathogenesis of Behçet’s syndrome. The gut microbiome is a stable component of the immune system. It plays an important role in the formation of the immune system in the early life and in the continuation of immune homeostasis through the life. Dysbiosis, imbalance in the gut microbiota, can lead to many serious metabolic and inflammatory pathologies.

Objectives: We aimed to investigate the gut microbiota structure in Behçet’s syndrome patients with mucocutaneous and uveitis involvement only.

Methods: 6 patients with Behçet’s syndrome with uveitis, 12 patients with familial Mediterranean fever (FMF) and 9 patients with Crohn’s disease (CD) and 10 healthy controls were included. Patients, positive and healthy controls were excluded if they had one of the following combined diseases/situations: a) gastrointestinal surgical history (e.g. bariatric surgery, gastroctomy or colectomy), b) antibiotic or probiotics use in the last 3 months, c) specific dietary restriction, d) malignancy, e) additional autoimmune disease or inflammatory bowel disease.

Conclusions: Fecal microbiota of patients with Behçet’s syndrome and of positive control groups (FMF and CD) differed significantly from that of healthy controls. In a subgroup of patients with Behçet’s disease with uveitis and mucocutaneous involvement only, firmicutes species seem to be the dominant bacterial flora.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6515

THU0312 PERFORMANCE CHARACTERISTICS AND PREDICTORS OF TEMPORAL ARTERY ULTRASOUND AND BIOPSY FOR THE DIAGNOSIS OF GIANT CELL ARTERITIS IN A REAL WORLD POPULATION: A PROSPECTIVE COHORT STUDY

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Background: The diagnosis of giant cell arteritis (GCA) remains a clinical one. Temporal artery (TA) ultrasound (US) has been proposed as a new diagnostic tool in GCA.

Objectives: To assess the performance characteristics of TA US and biopsy in routine clinical practice.

Methods: All patients presenting with suspected GCA to our institutions are recruited to a prospective registry. Patients who had both a TA US and biopsy performed at the time of presentation were included in the current study. US was performed by 2 radiologists. The performance characteristics of both tests were compared to physician diagnosis at six months following presentation. Predictive factors for positive US and biopsy were explored in univariate and multivariable logistic regression analyses.

Results: 132 patients were included, 123 (76%) with GCA. Mean (SD) duration of glucocorticoids was 6.6 days (19.4) at the time of TA US and 6.2 days (8.4) at the time of TA biopsy. US had a sensitivity of 52.8% (95% CI 43.7, 61.9) and specificity of 71.8% (95% CI 54.8, 84.5). There were 11 false positive US results; 5 with migraine, 2 other vasculitides, 2 local infections, 2 malignancies. Biopsy

THU0313 DISCONTINUATION DURING LONG-TERM FOLLOW-UP OF PATIENTS WITH GIANT CELL ARTERITIS

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had a sensitivity of 48.8% (95% CI 39.7, 57.9) and specificity of 97.4% (95% CI 84.9, 99.9). A hypothetical sequential strategy of US followed by biopsy in the case of negative US had a sensitivity of 78.9% (95% CI 70.1, 85.5) and specificity of 71.8% (95% CI 54.9, 84.5), equivalent to a simultaneous testing strategy. Time on glucocorticoids did not significantly impact the results of US or biopsy. The only factor independently predictive of a positive US was male sex (OR 5.53, 95% CI 2.72 to 11.22, p < 0.001). The only factor independently predictive of a positive biopsy was jaw claudication (OR 2.40, 95% CI 1.11, 5.21, p = 0.027).

Table 1. Performance Characteristics of Ultrasound, Biopsy, and Combination Strategies

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>PLR</th>
<th>NLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound alone</td>
<td>52.8</td>
<td>71.8</td>
<td>85.6</td>
<td>32.6</td>
<td>1.87</td>
<td>0.66</td>
</tr>
<tr>
<td>Biopsy alone</td>
<td>48.8</td>
<td>97.4</td>
<td>98.0</td>
<td>37.6</td>
<td>19.02</td>
<td>0.53</td>
</tr>
<tr>
<td>Sequential (Biopsy only if US positive)</td>
<td>22.8</td>
<td>97.4</td>
<td>96.6</td>
<td>28.6</td>
<td>8.88</td>
<td>0.79</td>
</tr>
<tr>
<td>Sequential (Biopsy only if ultrasound negative)</td>
<td>78.9</td>
<td>71.8</td>
<td>89.8</td>
<td>51.9</td>
<td>2.80</td>
<td>0.29</td>
</tr>
<tr>
<td>Simultaneous</td>
<td>78.9</td>
<td>71.8</td>
<td>89.8</td>
<td>51.9</td>
<td>2.80</td>
<td>0.29</td>
</tr>
<tr>
<td>Procedure, glucocorticoid duration</td>
<td>52.8</td>
<td>71.8</td>
<td>85.6</td>
<td>32.6</td>
<td>1.87</td>
<td>0.66</td>
</tr>
<tr>
<td>Ultrasound, 0 days, n=80</td>
<td>51.9</td>
<td>76.9</td>
<td>82.4</td>
<td>43.5</td>
<td>2.25</td>
<td>0.63</td>
</tr>
<tr>
<td>Ultrasound, &gt; 0 ≤ 3 days, n=27</td>
<td>46.2</td>
<td>100</td>
<td>100</td>
<td>6.0</td>
<td>Infinity</td>
<td>0.54</td>
</tr>
<tr>
<td>Ultrasound, &gt; 3 ≤ 7 days, n=25</td>
<td>60.0</td>
<td>40.0</td>
<td>80.0</td>
<td>20.0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Ultrasound, &gt; 7 ≤ 14 days, n=18</td>
<td>64.3</td>
<td>50.0</td>
<td>81.8</td>
<td>28.6</td>
<td>1.29</td>
<td>0.71</td>
</tr>
<tr>
<td>Ultrasound, &gt; 14 days, n=12</td>
<td>44.4</td>
<td>100</td>
<td>100</td>
<td>37.5</td>
<td>Infinity</td>
<td>0.56</td>
</tr>
<tr>
<td>Biopsy, all, n=162</td>
<td>48.8</td>
<td>97.4</td>
<td>98.0</td>
<td>37.6</td>
<td>19.02</td>
<td>0.53</td>
</tr>
<tr>
<td>Biopsy, 0 days, n=53</td>
<td>46.9</td>
<td>100</td>
<td>100</td>
<td>53.5</td>
<td>Infinity</td>
<td>0.53</td>
</tr>
<tr>
<td>Biopsy, &gt; 0 ≤ 3 days, n=24</td>
<td>66.7</td>
<td>83.3</td>
<td>92.3</td>
<td>45.0</td>
<td>4.00</td>
<td>0.40</td>
</tr>
<tr>
<td>Biopsy, &gt; 3 ≤ 7 days, n=38</td>
<td>47.1</td>
<td>100</td>
<td>100</td>
<td>18.2</td>
<td>Infinity</td>
<td>0.53</td>
</tr>
<tr>
<td>Biopsy, &gt; 7 ≤ 14 days, n=29</td>
<td>47.8</td>
<td>100</td>
<td>100</td>
<td>33.3</td>
<td>Infinity</td>
<td>0.52</td>
</tr>
<tr>
<td>Biopsy, &gt; 14 days, n=18</td>
<td>37.5</td>
<td>100</td>
<td>100</td>
<td>17.0</td>
<td>Infinity</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Conclusions: TA US is a useful tool in the diagnosis of GCA; however false positive tests occur in 7% and thorough clinical assessment remains crucial. Prior glucocorticoid treatment has no clear impact on results.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4629

THU0313 INFERIOR AND SUPERIOR VENA CAVA THROMBOSIS IN BEHÇET'S DISEASE. MOROCCAN EXPERIENCE

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Background: Behçet's disease (BD) is a systemic disorder with a vascular tropism where the vessels might be affected. Venous thrombosis is the most common vascular complication. Among its locations, vena cava thrombosis (VCT) is rare but can be life-threatening.

Objectives: To quantify the frequency of VCT and analyse epidemiological, clinical and therapeutic modalities.

Methods: A retrospective study was conducted in the internal medicine department of the University Hospital IbnRochd of Casablanca, over a period of thirty-five years between 1980 and 2016.

Results: Among the 1618 cases of Behçet's disease, all diagnosed in our service and meeting the diagnosis criteria as defined by the international study group (ISG) for Behçet's disease, 52 patients who fulfilled the ACR criteria were included in the study.

Conclusions: Vena cava thrombosis in the context of Behçet's disease is a very serious pathology threatening the patient's vital and functional prognosis. Preventive measures, early diagnosis and effective treatment are the keys to a successful management of such complications' risks.

Disclosure of Interest: None declared


THU0314 RADIOLOGIC ACTIVITY IS THE MAJOR DETERMINANT FOR PHYSICIANS WHILE DECIDING ACTIVE DISEASE IN TAKAYASU ARTERITIS

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Background: There are no valid follow-up parameters in the assessment of disease activity in Takayasu arteritis (TA).

Objectives: To investigate the impact of incorporation of vascular imaging into ITAS in the assessment of disease activity in TA.

Methods: 52 patients who fulfilled the ACR criteria were included in the study. PGA, Kerr et al.'s criteria and ITAS2010/ITAS-A scores were evaluated in all patients in serial visits. All the patients were followed using 3–6 monthly B-mode/Doppler ultrasonography (USG) and 6–12 monthly magnetic resonance angiography (MRA).

Radiological activity (Rad) was defined based on the presence of any of the 3 parameters including new vessel involvement by any technique (5 points), increase in vessel wall thickness on USG (3 points) and vessel wall edema on MRA (3 points). Then we incorporated these scores with ITAS-A to obtain a composite disease activity index (ITAS2010-A-Rad) (Table 1). Active disease was defined as ITAS-A-Rad >4 points.

Results: Total 410 visits of 52 TA patients (mean age 50.7 yrs, 92.3% mean follow-up duration 6.4±2.9 yrs) were evaluated. Radiological assessment was done in 359 visits (by USG in 271 and by MRA in 190). Patients were categorized as having active disease in 194 visits (47.4%) according to Physician’s global assessment of disease activity (PGA) and 72 visits (17.5%) according to Kerr et al. criteria. The agreement between them was fair (κ: 0.29). Radiological activity was determined in 105 out of 359 visits (29.2%). The total agreement between radiological activity and Kerr at al. criteria was 83% (κ=0.52). There were 43 visits with new vessel involvement by any radiologic technique; all visits included patients with active disease based on both PGA and Kerr et al. criteria (Table 2). The ITAS-A-Rad was significantly correlated with all the other activity parameters including ITAS2010, ITAS-A, and APRs.

There were 43 visits with new vessel involvement by any radiologic technique; all visits included patients with active disease based on both PGA and Kerr et al. criteria (Table 2). The ITAS-A-Rad was significantly correlated with all the other activity parameters including ITAS2010, ITAS-A, and APRs.

Conclusions: Vena cava thrombosis in the context of Behçet's disease is a very serious pathology threatening the patient's vital and functional prognosis. Preventive measures, early diagnosis and effective treatment are the keys to a successful management of such complications' risks.

Disclosure of Interest: None declared


Table 1. The definition of ITAS-A-Rad Score

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory APR</th>
<th>ESR 0 for ESR</th>
<th>CRP 0 for CRP: ≤ 20</th>
<th>B-mode Doppler USG</th>
<th>Progression on vessel wall thickness 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0 for ESR ≤ 20</td>
<td>1 for 21–39</td>
<td>2 for 40–59</td>
<td>3 for 60 mm/h</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>0–3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiology</td>
<td>Radiological activity</td>
<td>New vessel involvement with any radiological method</td>
<td>5</td>
<td>3 for –20 mg/L</td>
<td></td>
</tr>
<tr>
<td>MRA</td>
<td>Presence of vessel wall edema</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total ITAS-A-Rad Score: 4–4 Activity.

Figures 1. Change in ITAS-A-Rad scores in serial visits

Table 2. Agreement of angiography and radiography scores in serial visits

<table>
<thead>
<tr>
<th>ITAS-A Rad score</th>
<th>Angiography scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.76 (95% CI 0.60–0.90)</td>
</tr>
<tr>
<td>2</td>
<td>0.68 (95% CI 0.50–0.86)</td>
</tr>
<tr>
<td>3</td>
<td>0.59 (95% CI 0.41–0.77)</td>
</tr>
<tr>
<td>4</td>
<td>0.64 (95% CI 0.47–0.81)</td>
</tr>
</tbody>
</table>
CENTRAL NERVOUS SYSTEM INVOLVEMENT IN PATIENTS WITH TAKAYASU ARTERITIS WITH GRANULOMATOSIS WITH POLYANGIITIS: A SINGLE CENTER EXPERIENCE

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Disclosure of Interest:
None declared

Background: Peripheral nerve involvement is relatively frequently encountered in patients with granulomatosis with polyangitis (GPA). Central nervous system (CNS) manifestations are reported to occur in about 10% of GPA patients.

Objectives: We aimed to estimate the prevalence of CNS involvement in Greek patients with GPA, describe the related clinical characteristics, and identify possible predicting factors for its occurrence. We also compared the clinical picture and long term outcomes of GPA patients with and without CNS involvement.

Methods: We retrospectively reviewed the medical charts of all patients with ANCA-associated and biopsy proven small vessel vasculitis (AAV), diagnosed in our hospital between 1995-2015, who had CNS involvement. Demographics, serological and clinical features, at the time of AAV diagnosis, of CNS involvement and during the follow-up time, were recorded. Comorbidities, associated treatments, and outcome indicators (including relapse rate and treatment-related adverse events), were performed between GPA patients with and without CNS involvement.

Results: 77 patients with GPA were identified in our AAV registry. Of these, nine (11.7%) developed CNS manifestations, either at clinical presentation (33.3%) or during the follow-up (66.7%). At the time of CNS involvement, all patients were characterized by increased acute phase reactants and all but one patients had vasculitic manifestations in several other organs/systems and increased titers of ANCA. CNS symptomatology included: sensor and/or sensorimotor symptoms (33.3%), seizures (33.3%) delirium and/or hearing loss (33.3%), hemiparesis (22.2%), diplopia (11.1%) and cerebellar symptoms (11.1%). Findings of MRI were: cerebral ischemic lesions (55.6%), focal dural thickening with enhancement (22.2%), orbital mass formation (11.1%) and mastoiditis causing facial nerve palsy bilaterally (11.1%). Patients with CNS involvement, compared to those without, at initial AAV disease, experienced vasculitic manifestations of the ENT system more frequently (77.8% versus 25.4%, p=0.004) and they had a lower overall disease activity, as assessed by the BVAS score, while during the course of the overall disease experienced lung vasculitis less frequently (44.6% vs 78.4%, p=0.02). Comparisons between GPA patients with and without CNS manifestations did not reveal any differences in long-term outcomes including relapse rate/100 person-months, (95% CI [1.812 (0.920–2.229) Vs 1.033 (0.757–1.378), respectively] p=0.171), survival (Mantel-Cox test, p=0.244) and treatment-related adverse events.

Conclusions: CNS involvement was recorded in 11.7% of our GPA patients, either during the initial phase or as a late disease sequela. ENT involvement and low BVAS score at disease onset were more common in GPA patients with CNS manifestations. Based on our results, CNS involvement did not affect the long term outcomes of GPA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6574

THU0315 | EPIDEMIOLOGY OF TAKAYASU ARTERITIS IN NORTHERN ITALY

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Background: Takayasu arteritis (TA) is a large vessel vasculitis of unknown etiology, predominantly affecting the aorta and/or its major branches and occurring before the age of 40 years. TA has been described worldwide with an annual incidence in Europe ranging from 0.4 to 1.3 /1.000.000. Tak is more common in female. In the largest study from Japan, the female to male ratio was eight to one. In a recent Swedish epidemiologic study no male were identified. There are no epidemiologic studies regarding Takayasu arteritis in Italian population.

Objectives: To investigate the epidemiology of Takayasu arteritis in a Northern Italy area.

Methods: All patients with incident TA diagnosed between 1997 and 2015 living in the Reggio Emilia area were identified by capture and re-capture checking at computerized discharge diagnosis codes (ICD10) and at outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital and by examining the Reggio Emilia district database for rare diseases. The Reggio Emilia population is predominantly of Caucasian origin (92.5%) with a yearly increase in general population of 0.5% from 438.588 inhabitants in 1997 to 533.827 in 2015.

Results: There were 5 women satisfying ACR 1990 criteria for TA diagnosis during the 18 years study period. The overall age and sex-adjusted 18 years incidence per 100,000 persons aged <40 years was 2.2. (95% CI:0.71 to 5.09). The overall age-and sex-adjusted 20 years incidence per 100,000 women aged <40 years was 4.5. (95% CI:1.46 to 10.48). Median age at disease onset was 29 years and at diagnosis was 39 years. The prevalence of TA in the general population on December 31 2015 was 0.9 (95% CI: 0.31 to 2.19) while in female population aged <40 years was 4.4. (95% CI 1.47 to 10.54). All patients are still alive on December 31, 2015.

Conclusions: As observed in other epidemiological studies, Tak is a rare disease also in Northern Italy with a large prevalence of female.

Disclosure of Interest: None declared


THU0317 | CARDIOVASCULAR RISK FACTORS AND COMORBID DISEASES IN TAKAYASU ARTERITIS

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Objectives: The medical charts of all patients with ANCA-associated and biopsy proven small vessel vasculitis (AAV), diagnosed in our hospital between 1995–2015, were retrospectively reviewed and GPA patients with CNS involvement were identified. Demographics, serological and clinical features, at the time of AAV diagnosis, of CNS involvement and during the follow-up time, were recorded. Comorbidities, associated treatments, and outcome indicators (including relapse rate and treatment-related adverse events), were performed between GPA patients with and without CNS involvement.

Methods: We studied 88 (77F/11M) consecutive TA patients and 71 (66F/5M) SLE patients between May and November 2016. In addition, age and gender matched, 96 (80F/16M) healthy controls were included. Study participants were interviewed with the help of a standardized questionnaire that assess the presence or absence of traditional atherosclerotic risk factors and several comorbid conditions according to the Charlson comorbidity index. Additionally, Framingham coronary heart disease risk score was calculated. In this study we looked at the frequency of traditional atherosclerotic risk factors and comorbidity conditions among patients with TA and suitable diseased and healthy controls.

Results: Smoking was more frequent among the healthy controls, whereas hypertension and family history of cardiovascular diseases were more common among TA patients. Patients with SLE were found to have less hyperlipidemia. The Framingham risk scores did not differ among the groups. Pericardial/pleural and renal diseases were more frequently observed in SLE patients, whereas cardiovascular diseases and chronic lung diseases were more common in TA patients. Inflammation bowel diseases were only observed in TA patients.

Conclusions: Traditional atherosclerotic risk factors are not increased in TA. Comorbidities in these patients are mainly due to the complications of vascular involvement. The frequency of inflammatory bowel diseases and inflammatory upper/lower back pain is substantially high and deserves further research. Moreover, the increased incidence of cardiovascular and rheumatic diseases among the first-degree relatives of TA patients suggest that genetic mechanisms may play role in TA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5477

THU0316 | EPIDEMIOLOGY OF TAKAYASU ARTERITIS IN NORTHERN ITALY

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Background: Takayasu arteritis (TA) is a large vessel vasculitis of unknown etiology, predominantly affecting the aorta and/or its major branches and occurring before the age of 40 years. TA has been described worldwide with an annual incidence in Europe ranging from 0.4 to 1.3 /1.000.000. TA is more common in female. In the largest study from Japan, the female to male ratio was eight to one. In a recent Swedish epidemiologic study no male were identified. There are no epidemiologic studies regarding Takayasu arteritis in Italian population.

Objectives: To investigate the epidemiology of Takayasu arteritis in a Northern Italy area.

Methods: All patients with incident TA diagnosed between 1997 and 2015 living in the Reggio Emilia area were identified by capture and re-capture checking at computerized discharge diagnosis codes (ICD10) and at outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital and by examining the Reggio Emilia district database for rare diseases. The Reggio Emilia population is predominantly of Caucasian origin (92.5%) with a yearly increase in general population of 0.5% from 438.588 inhabitants in 1997 to 533.827 in 2015.

Results: There were 5 women satisfying ACR 1990 criteria for TA diagnosis during the 18 years study period. The overall age and sex-adjusted 18 years incidence per 100,000 persons aged <40 years was 2.2. (95% CI:0.71 to 5.09). The overall age-and sex-adjusted 20 years incidence per 100,000 women aged <40 years was 4.5. (95% CI:1.46 to 10.48). Median age at disease onset was 29 years and at diagnosis was 39 years. The prevalence of TA in the general population on December 31 2015 was 0.9 (95% CI: 0.31 to 2.19) while in female population aged <40 years was 4.4. (95% CI 1.47 to 10.54). All patients are still alive on December 31, 2015.

Conclusions: As observed in other epidemiological studies, TA is a rare disease also in Northern Italy with a large prevalence of female.

Disclosure of Interest: None declared

CORONARY ARTERY DISEASE IN PATIENTS WITH BEHÇET’S DISEASE: A RETROSPECTIVE, SINGLE CENTER STUDY

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Background: Behçet’s disease (BD) is a chronic inflammatory disease affecting various size of arteries and veins. Coronary artery disease (CAD), a life-threatening condition, is rarely reported in patients BD.

Objectives: To investigate the clinical characteristics of BD patients complicated with CAD, and to elucidate the potential risk factors of CAD in BD patients.

Methods: We retrospectively reviewed all the medical records of patients who were admitted to our institute from 2001 to 2016. CAD was defined as at least one coronary artery stenosis (≥50%) (or) occlusion of coronary arteries confirmed by angiography or contrast-enhanced computer tomography. BD patients with CAD and age- and gender-matched BD patients without CAD (at 1:3 ratio) were enrolled. Demographic, clinical and laboratory data were systemically collected, analyzed and compared between two groups.

Results: In total, 19 patients, including 17 male and 2 female, were complicated with CAD. The mean onset age of BD was 34 and the mean duration from the onset of BD to the diagnosis of CAD was 4.1 year. Angina pectoris (8/19) and acute myocardial infarction (8/19) were the most common CAD symptoms, arrhythmia was presented in one patient, and three patient remained asymptomatic. Coronary artery aneurysm, stenosis and occlusion were presented in 9, 13 and 3 patients, respectively. Smoking (7/19) was frequently observed, while hypertension (3/16), diabetes mellitus (2/19), obesity (1/19) and alcohol consumption (1/19) were rarely present. Additionally, seven arterial and two veins in BD patients with CAD presented with active BD disease symptoms and elevated inflammatory markers, which implicated aberrant vascular inflammation was the key mechanism of CAD in BD patients. CRP, but not traditional CAD risk factors, was the risk factor of CAD in BD patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5991

MR ANGIOGRAPHY FOR EVALUATION OF VASCULAR INFLAMMATION IN ELDERLY PATIENTS WITH LARGE VESSEL VASCLITUSS

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Objectives: The aim of the study was to evaluate the feasibility of MR angiography (MRA) for evaluation of vascular inflammation in elderly patients with large vessel vasculititss.

Methods: 16 patients with established on PET with 18F-FDG large vessel vasculitits (14 female and 2 male, average age 66 years) were enrolled in our study. 14 patients had giant cell arteritis (just only 3 biopsy-proven cases), 2 patients with isolated aortitis of thorax aorta and 2 cases of PMR-associated arteritis. The average duration of any disease was 8 months. All patients underwent MRA with or without contrast enhancement of aorta and its branches at 1.5T Philips scanner (Avanto, Maastricht, The Netherlands). All patients had repeated MRA at 6 and 12 months. All images were studied by one specialist. We evaluated the role of mural oedema as a sign of activity of vasculitis. The results of MR-angiography were compared with clinical and laboratory data, ultrasound and PET/CT results.

Results: A total of 42 MRA were obtained in 16 patients. Significant mural oedema of thorax aorta or large arteries was shown by imaging in 20 of 42 cases (48.0%) and correlated with clinical and laboratory signs of vasculitits activity. Progressive arterial stenosis detected by ultrasound and increased uptake of 18F-FDG on PET, 12 patients with high degree of inflammation on MRA were steroid-naïve. In 22 cases (52%), MRA had showed mild or moderate oedema of the arteries’ wall. Low-moderate activity of vascular inflammation in our patients was associated with moderate or high of immunosuppressive therapy (mean ± SD). However, gradual reduction in the intensity of immunosuppression in 4 patients with mild mural oedema was associated with development of relapse of large vessel vasculitis. Notably, contrast enhancement did not improve significantly edema imaging.

Disclosures: Visualization of artery wall oedema by MRA may be a useful approach to detect persisting inflammation elderly patients with large vessel vasculitits.

Disclosure of Interest: None declared

THU0321 ALTERATIONS IN THE PERIPHERAL B CELL COMPARTMENT IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGITIS (CHURG-STRAUSS SYNDROME)

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) belongs to the group of ANCA associated vasculitides. While the combination of asthmatic symptoms and vasculitits characterizes the disease clinically, eosinophilia and increased serum IgE concentrations are serologic hallmarks. The role of B lymphocytes in EGPA has not been defined so far, but therapeutic response to rituximab in EGPA points towards a role of B-cells in the pathogenesis of EGPA.

Objectives: To characterize the peripheral B cell compartment in patients with EGPA, to analyze the in vivo potential of B lymphocytes to class-switch to IgE, and to assess in vitro the differentiation of naïve B cells to IgE-secreting plasmablasts.

Methods: 25 laboratory works were included as ANCA-positive EGPA patients. PBMCs were stimulated with CD40L and IL-21 and IL-4 in enriched Iscoves’ medium with fluorescent-labeled monoclonal antibodies against: CD27, CD20, CD38, IgD, IgG, IgA, IgM, and peripheral CD19 B-cell count. B cell populations (naïve, marginal zone, class-switched B cells and plasmablasts) were analyzed by staining PBMCs with fluorescent-labeled monoclonal antibodies against: CD27, CD20, CD38, CD21, and BAF-F. For in vitro differentiation assays magnetically isolated B lymphocytes from EGPA patients and aged matched healthy controls were stimulated with CD40L and IL-21 and IL-4 in enriched Iscoves’ medium supplemented with 10% FCS, 1 μg/mL insulin, 2.5 μg/mL apo-transferrin, 1% nonessential amino acids, 2 mmol/L glutamine, and 1 μg/mL reduced glutathione. Starting the cultures with equal number of B cells, the absolute number of plasmablasts, and IgE class switched cells after 9 days was determined by counting the events in the CD20mphCD38mph and the IgG4CD19mph gate by flow cytometry. IgE secretion in the supernatant was measured by ELISA.

Results: 18 patients (8 females, median age 59 years) with EGPA diagnosed according to ACR and CHC-criteria were included into the study. 22% of patients were ANCA-positive. Immunosuppressive therapy was azathioprine in 11 patients, methotrexate in 3 patients, and leflunomide or mycophenolate in one patient each and two patients received no immunosuppressive treatment. 7 patients had a history of a prior cyclophosphamide therapy. Median lymphocyte count was
normal (1.2×10⁴/μl; normal range 1.1 to 3.2×10⁴/μl) but peripheral B cell numbers were markedly diminished (37/μl normal range: 100 – 500/μl). While the percentage of naïve B cells (53%) and marginal zone like cells (10.5%) were within normal range, the percentage of class-switched memory B cells was high (28.2%). To assess the in vitro class switch capacity to IgE the number of IgE class-switched cells was determined by counting the events in the IgA/D/IgE gate. The percentage of IgE-classed switched was 6.8% (range: 0.3%-34%) and not statistically different from healthy controls.

Conclusions: In the EGPA-patients we report we observed markedly diminished B-cells despite of normal lymphocyte counts. Within the B cell compartment, there was a shift toward late B cell maturation stages. In vitro B-cell development to IgE-classed switched was not increased in EGPA-patients pointing towards a non-B cell intrinsic mechanism.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6507

THU0322

DESCRIPTIVE STUDY OF ASIAN INDIAN PATIENTS WITH RHEUMATOID VASCLITIS IN RETROSPECTIVE: A SINGLE, TERTIARY CARE CENTRE EXPERIENCE

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Background: Rheumatoid vasculitis (RV) is a severe extra-articular manifestation of rheumatoid arthritis (RA), with high morbidity and mortality reported in literature

Objectives: To describe the Asian Indian perspective on RV patients, their clinico-laboratory features and their outcome along with the factors affecting them

Methods: A retrospective review of cases with documented RV in our tertiary care centre was carried out. The visit during 1993-2014 was selected for those satisfying Scott & Bacon criteria for RV

Probable RV was defined as patients not satisfying Scott & Bacon criteria, but were managed like RV after exclusion of alternate diagnosis. Birmingham Vasculitis activity score (BVAS) version 3.0 was used for monitoring activity of RV

Results: 63 patients of RV were identified, with a study period prevalence of 0.7%, in our RA cohort. 33 (52.4%) patients were female. Mean age of patients was 50.7±11.5 years with median duration of RA being 6 years. Involvement of Peripheral Nerve System (PNS) was the commonest manifestation of RV in 52/63 (82.5%) patients followed by skin in 34/63 (53.9%) patients. Rheumatoid Nodule was seen in 14/ 63 (22.2%) patients. Percentage of current and ex-smokers combined,was same as rheumatoid nodule prevalence, 52 (82.5%) patients had biopsy evidence of vasculitis. 28/51 (55.8%) patients were started on mycophenolate, 13/51 (25.5%) patients on cyclophosphamide, 8/51 (15.7%) patients on azathioprine, 4/51 (7.8%) patients on Methotrexate as immunosuppressive (IS) agent along with mean dose of 46.0±23mg/kg/day) prednisolone. Additionally, Rituximab & IVIg were used in 2 patients each respectively. 3 months after initiation of immunosuppression 26/50 (52%) patients on follow-up were in remission and 39/47 (82.9%) patients attained remission at 6 months. Mean time to achieve remission was 151.1±86.3 days. All IS agents were equally effective in inducing remission at 3 and 6 months and showed statistically similar BVAS reduction at 3 and 6 months from baseline (t test & chi-square test). 7 (11.2%) patients were lost to follow up during 1993-2014 year cumulative follow up. Multiple regression analysis showed that at baseline presence of PNS involvement, eosinophilia, thrombocytosis, higher BVAS score and above of eye involvement and higher hemoglobin % at baseline were predictors for remission, at 3 months (p<0.05). 4/50 (8%) patients had relapse of vasculitic symptoms. 2 and 5 year survival rates were 96.2% and 83.9% respectively

Conclusions: Our cohort of Asian Indian RV was comparatively younger with lesser RA duration, less percentage of ever-smokers, lesser rheumatoid nodule prevalence, higher PNS involvement with better survival/mortality rates compared to published literature. All IS agents showed equal rates of BVAS remission & BVAS reduction at 3 and 6 months of treatment

References:
[1] Scott DG, Bacon PA. Intravenous cyclophosphamide plus methylprednisolone BVAS reduction at 3 and 6 months of treatment to published literature. All IS agents showed equal rates of BVAS remission & lesser RA duration, less percentage of ever-smokers, lesser rheumatoid nodule prevalence determined by counting the events in the IgA/D/IgE gate. The percentage of IgE-classed switched was 6.8% (range: 0.3%-34%) and not statistically different from healthy controls.

Conclusions: In the EGPA-patients we report we observed markedly diminished B-cells despite of normal lymphocyte counts. Within the B cell compartment, there was a shift toward late B cell maturation stages. In vitro B-cell development to IgE-classed switched was not increased in EGPA-patients pointing towards a non-B cell intrinsic mechanism.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6507

THU0324

NEUTROPHILS IN GIANT CELL ARTERITIS: MONITORING DISEASE PROGRESSION DURING THERAPY TAPERING

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Background: Giant Cell Arteritis (GCA) represents a medical emergency due to risk of permanent vision loss and/or cerebrovascular insults. Polymyalgia rheumatic (PMR) frequently coexists with GCA1. No diagnostic or prognostic markers are yet known for GCA and predicting relapses during steroid therapy tapering is difficult. Biomarkers, such as serum amyloid A (SAA) and interleukin-6 (IL-6) provide added value for monitoring inflammation and a recent investigational study indicated the potential use of neutrophils and their surface markers in GCA pathogenesis2.

Objectives: To determine the percentage of neutrophils, T and B cells, and the mean fluorescence intensity (MFI) of L-selectin (CD62L) and Integrin αM (CD11b) on CD16+ neutrophils in peripheral blood of newly diagnosed, untreated GCA and PMR patients vs. healthy controls (time 0) and at GCA follow-up (7, 30 and 90 days after therapy)

Methods: Flow cytometry of stained, lysed and fixed whole blood was performed in 10 GCA patients (6 followed longitudinally), 7 PMR patients and 5 healthy controls (7-colour immunophenotyping kit, Miltenyi). Levels of SAA and IL-6 were measured in sera of GCA patients (n=6) using nephelometry and ELISA, respectively.

Results: Percentage of neutrophils was significantly higher at time 0 in GCA and PMR patients compared to healthy controls. Expression of both CD62L and CD11b on CD16+ neutrophils was also higher in GCA and PMR patients, as compared to healthy controls. Longitudinally, GCA patients showed an initial decrease in percentage of neutrophils, at day 7 in comparison with time 0, increasing on days 30 and 90, while both T (CD4+) and B cells exhibited a significant elevation in % at day 7, with a decline at days 30 and 90. The MFI of neutrophil CD62L steadily decreased from day 0 (85.80±45.45) to day 7 (71.99±29.93) and day 30 (57.61±42.17), while showing a substantial increase on day 90 (85.40±60.33), CD11b expression diminished initially and remained reduced on day 90. Levels of SAA and IL-6 declined sharply from day 0 to 7 (>10-fold drop) and day 30, with gradual elevation of both on day 90.

Conclusions: Neutrophil CD62L may represent a good surface marker for monitoring disease progression following glucocorticoid tapering. SAA and IL-6 exhibit a sharp decrease at early time points, increasing at day 90. In the future, a larger, longer study of neutrophils and their CD62L expression could support clinicians in their decision when and how to re-evaluate therapy in GCA patients

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3283
RELATIONSHIP OF THE INITIAL SYMPTOMS TO THE DIAGNOSIS DELAY AND POOR PROGNOSIS IN PATIENTS WITH TAKAYASU ARTERITIS

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Background: Clinical courses of Takayasu arteritis are of great variety. Its non-specific initial symptoms can cause the delay in diagnosis and lead to poor prognosis. However, the symptoms of very early phase of Takayasu arteritis and their effects on diagnosis delay and prognosis are unclear.

Objective: To clarify the characteristics of initial symptoms of Takayasu arteritis, the delay in diagnosis, and its relationship with prognosis.

Methods: The consecutive patients with Takayasu arteritis with analysable information in our hospital were enrolled. Initial symptoms, laboratory findings before diagnosis, the duration from symptom onset to diagnosis, and prognosis were investigated. Initial symptoms were divided into 7 groups; cranial symptoms (dizziness, syncope, headache, neck pain, hemi-paralysis, and jaw claudication), visual symptoms (vision loss and visual field loss), extremities symptoms (claudication of extremities, coldness of limbs, bilateral difference in blood pressure, and limb numbness), cardiaco/aortic symptoms (dyspnea on exertion, palpitation, and chest compression), hypertension, general illness (fever, fatigue, body weight loss, and arthralgia), and abnormal medical examinations (heart murmur, bruit on any extremities, and abnormal chest X-ray). Poor outcome was defined as a cardiovascular surgery or death.

Results: A total of 98 patients were enrolled with the median observation period of 12.1 years (range, 1 month to 59 years). Eighty-seven (88.7%) patients had poor outcomes. The initial symptoms before diagnosis were cranial symptoms in 25.5%, visual symptoms in 5%, extremities symptoms in 26%, cardiaco/aortic symptoms in 7%, hypertension in 9%, general illness in 26%, and abnormal medical examinations (heart murmur, bruit on any extremities, and abnormal chest X-ray). The duration from symptom onset to diagnosis was 792, 52, 567, 752, 1318, 293 and 1014 days (p=0.10), respectively; the rate of poor outcome was 29.6 vs 38.9 years, p=0.026, and resulted in poor outcome more frequently than those with (42.6 vs 22.6%, p=0.058).

Conclusions: The initial symptoms of Takayasu arteritis before diagnosis varied widely, and majority of them were non-specific. Lacking inflammatory signs were related with delayed diagnosis and poor prognosis.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3577

THU0326 ASSOCIATION BETWEEN THE TC-HDL RATIO AND DISEASE ACTIVITY IN PATIENTS WITH TAKAYASU ARTERITIS

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Background: Accelerated atherosclerosis has become the main cause of morbidity in patients with autoimmune diseases such as RA and SLE [1]. The Cholesterol/High-density Lipoprotein Cholesterol (TC-HDL-C) ratio is a high discriminatory power index for coronary heart disease. A high TC-HDL-C ratio has been extensively used as a predictor of CVDs [2]. EU-Mark Task Force recommended that the TC-HDL-C ratio should be regarded as an important prognostic indicator for future cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) [3]. However, the relationship between the TC-HDL-C ratio and disease activity of Takayasu arteritis (TAK) is unclear.

Objectives: To investigate changes in the TC-HDL-C ratio and to evaluate the relationship between the TC-HDL-C ratio and disease activity of TAK.

Methods: A retrospective study of 103 patients with TAK and 73 healthy controls was performed. We compared the triglyceride (TG), TC, low-density lipoprotein cholesterol (LDL-C), HDL-C and TC-HDL-C ratio between patients and healthy controls, and we analyzed correlations between the lipid parameters and indexes

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4818
of TAK activity. A ROC curve was used to determine the predictive value of TC/HDL-C ratio in patients group.

Results: The TG level was higher in patients with TAK than in the controls (p=0.000). The TC, LDL-C, and HDL-C levels were significantly lower in patients with TAK than in the controls (p=0.000, p=0.000, and p=0.000, respectively). The HDL-C level was significantly higher in the active TAK group than in the inactive TAK group (p=0.005). The TC/HDL-C ratio was significantly increased in patients with disease activity (p=0.001), and it exhibited a positive relationship with the high-sensitivity C-reactive protein level (r=0.234, p=0.003) and Kerr score (r=0.219, p=0.031). In addition, the TC/HDL-C ratio of 3.698 was determined as a predictive cut-off value of TAK (sensitivity 61.0%, specificity 78.6%, area under the curve=0.743) (Figure 1).

Conclusions: For the first time, we showed that serum levels of TC, LDL-C, and HDL-C were significantly lower in patients with TAK, and the TC/HDL-C ratio has a positive relationship with the disease activity of TAK, suggesting that the TC/HDL-C ratio may be a potential indicator for monitoring the disease activity of patients with TAK.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1564

THU0328 PRECURSORS OF SEVERE DAMAGE IN ANCA-ASSOCIATED VASCULITIS: DATA FROM A MONOCENTRIC INCIDENCE COHORT

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Background: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are multi-systemic diseases associated with anti-neutrophil cytoplasmatic antibodies (ANCA). Patients develop severe and irreversible damage, even in early stages of the disease, but data about prognostic factors are limited.

Objectives: To assess items and predictors of severe damage in a monocentric cohort of ANCA-associated vasculitis (AAV) patients, classified as GPA or MPA.

Methods: Clinical and serological data of patients, followed-up in a daily practice setting, were retrospectively revised. Severe damage, defined as a Vascular Damage Index (VDI) 3 5, was assessed after 12 months and at last examination (LE). The number of flare/year at LE was significantly higher in patients with disease activity (p=0.001), and it exhibited a positive relationship with the high-sensitivity C-reactive protein level (r=0.234, p=0.003) and Kerr score (r=0.219, p=0.031). In addition, the TC/HDL-C ratio of 3.698 was determined as a predictive cut-off value of TAK (sensitivity 61.0%, specificity 78.6%, area under the curve=0.743) (Figure 1).

Conclusions: For the first time, we showed that serum levels of TC, LDL-C, and HDL-C were significantly lower in patients with TAK, and the TC/HDL-C ratio has a positive relationship with the disease activity of TAK, suggesting that the TC/HDL-C ratio may be a potential indicator for monitoring the disease activity of patients with TAK.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1564

THU0329 BUDD-CHIARI SYNDROME IN BEHÇET’S DISEASE: A RETROSPECTIVE MULTICENTER STUDY

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Background: The aim of this study was to determine the demographic, clinical,
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**Background:** Takayasu's arteritis (TA) is a rare large-vascular vasculitis characterized by the persistent involvement of the vessel walls. The role of innate immune cells in TA is poorly understood. Biomarkers to be used for assessment of TA activity and clinical outcome are missing. A trivial model of myeloperoxidase (MPO) distribution (simultaneous occurrence of neutrophils with complete depletion, reduced and normal content of the enzyme) is detectable in the very early phase of acute myocardial infarction and has been associated with a burst of neutrophil interaction with activated platelets.

**Objectives:** Here, we aimed at characterizing the phenotype of neutrophils and platelets in patients TA and correlating these biological findings with clinical data.

**Methods:** Neutrophil MPO expression has been studied in 93 subjects, including 20 age-matched controls and 73 patients with systemic vasculitis. Interestingly, 25 patients with chronic stable atherosclerosis (CSA), eight patients with giant cell arteritis (GCA), five patients with granulomatosis with polyangiitis (GPA), four patients with eosinophilic GPA (EGPA) and ten patients with polymyalgia rheumatica (PMR). Blood samples were collected and processed as described.

**Results:** High neutrophil MPO content, platelet P-selectin and High-Mobility Group I (HMGB1) in platelet microparticles (PDMP) release were assessed by flow cytometry.

**Conclusions:** Neutrophils and platelets are significantly activated in TA. Paroxysmal neutrophil activation, leading to complete MPO depletion, is a common feature and predict ischemic events and as such the clinical disease outcome.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6068
led to the myocardial infarction, and death. Pathological manifestation of cardiac involvement in PAN included the left ventricular hypertrophy due to renovascular arterial hypertension in 26 cases (70.3%). In addition, interstitial myocarditis was observed in 4 cases (10.8%).

**Conclusions:** Our data suggest that cardiac involvement is common in polyarteritis nodosa (81.1%), and coronary vasculitis affecting medium and small-sized arteries with wide range of acute and chronic changes can be the life-threatening condition.

**Disclosure of Interest:** None declared


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**THU0334**

**EVALUATION OF SUBCLINICAL VASCULAR DAMAGE IN PATIENTS WITH POLYMYALGIA RHEUMATICA: A CROSS-SECTIONAL STUDY USING AN INTEGRATED, NON-INVASIVE APPROACH OF COLOR DOPPLER ULTRASOUND AND CARDIO-ANKLE VASCULAR INDEX (CAVI) MEASUREMENT OF ARTERIAL STIFFNESS**

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**Background:** The association of chronic inflammatory rheumatic disorders with an increased risk of vascular disease, especially cardiovascular and cerebrovascular disease, is a consolidated matter, but data on polymyalgia rheumatica (PMR) are still inconsistent.

**Objectives:** The aim of our cross-sectional study was to investigate the presence of vascular damage in patients with PMR by analyzing subclinical vascular disease through validated, non-invasive cardiovascular damage markers.

**Methods:** We enrolled patients with PMR diagnosed according to the EULAR classification criteria and, as controls, patients with major cardiovascular risk factors (MVCVR) including hypertension, diabetes, hypercholesterolemia, cigarette smoking, and obesity. In all of them we performed color Doppler ultrasound to evaluate the common and peripheral main arteries, followed by ankle-brachial index (ABI) and carotid artery stenosis (APAD); we also assessed the ankle-brachial vascular index (CAVI) to measure arterial stiffness.

**Results:** Forty-eight patients with PMR and 56 with MVCVR were included. Demographic parameters were balanced between groups. A significant increase of IMT (1.03±0.23 vs 0.89±0.20; p=0.02), CAVI (8.59±1.23 vs 7.59±0.93; p=0.001) and APAD values (22.0±4.86 vs 19.1±4.65; p=0.03) was found in PMR patients with respect to MVCVR controls. No differences were reported with regards to the prevalence of carotid artery stenosis or ABI values between the two groups. No significant correlation between disease duration or duration of glucocorticoid treatment and IMT or CAVI values was found in PMR patients. Results of bivariate analysis showed a significant correlation between IMT and CAVI in both PMR and MVCVR patients (r²=0.845 and 0.556, respectively; p<0.001).

**Conclusions:** Our study adds new information on cardiovascular risk in PMR patients, showing an increase in subclinical cardiovascular lesions and paving the way for further studies to define the utility and modality of cardiovascular screening for primary prevention in these patients.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4831

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**THU0333**

**ACETYLCHOLINESTERASE IS HIGHLY EXPRESSED IN THE INFLAMED VESSEL WALL OF PATIENTS WITH GIANT CELL ARTERITIS**

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**Background:** The temporal artery biopsy (TAB) remains the gold standard in the diagnosis of giant cell arteritis (GCA) and is part of the ACR Classification criteria for GCA. However, TABs are false-negative in 10–60% of cases [1]. Cellular studies have shown that activated immune cells upregulate the acetylcholinesterase (ACHE) expression [2]. If ACHE is upregulated in the active GCA vessel wall, it may potentially improve the TAB as a diagnostic tool.

**Objectives:** To investigate the in-situ expression of acetylcholinesterase (ACHE) in the vessel wall of patients with biopsy-positive GCA and compare to non-GCA patients.

**Methods:** In this histological case-control study, TABs from a total of 24 TAB-positive GCA and 44 TAB-negative non-GCA patients (21 patients with a final diagnosis of PMR, 23 patients with other diagnosis) were retrospectively selected from TABs performed between January 2012 and December 2015. A total of 295 TABs were assed for inclusion. Only positive TABs showing clear tranvilral inflammation in the vessel wall were included. Patients treated with ~7 days of prednisolone prior to the TAB were excluded. Clinical data were obtained from electronic patient records to confirm or dismiss clinical diagnosis. TAB-HE-stains were reviewed by a pathologist with expertise in vasculitis. Immunohistochemical methods were used to determine the ACHE expression. The histological inflammation and ACHE

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5074
expression were assessed and graded on 0–4 scale, blinded to histological and clinical data. Solitary AChE staining of the media was not included in the assessment.

Results: 24 positive and 44 negative TABs, with corresponding clinical positive and negative GCA diagnosis, were included in this study. We found that 10/24 positive TABs showed high AChE expression (grade 2) and 14/24 showed moderate AChE expression (grade 1). No AChE expression was observed outside the media in negative TABs from non-GCA patients (i.e. grade 0). The AChE expression was in 79% agreement with the degree of histological inflammation with a kappa value of 0.58. Prednisolone treatment for up to 7 days did not suppress the AChE expression. Neither the AChE expression, nor the histological inflammation showed correlation to any clinical or biochemical findings.

Conclusions: Our study shows that high to moderate AChE expression was observed in all 24 biopsies from TAB-positive GCA patients and that the AChE expression was in good agreement with the histological inflammation. No non-specific AChE expression was observed outside the media in any of the 44 TABs from TAB-negative non-GCA patients. This indicates that AChE could play a significant role in the inflammatory process in GCA and may be a potential biomarker in inflammatory diseases such as GCA.

References:
[2] Fujii, T., et al., Expression of acetylcholine in lymphocytes and modulation of specific AChE expression was observed outside the media in any of the 44 TABs from TAB-negative non-GCA patients. This indicates that AChE could play a significant role in the inflammatory process in GCA and may be a potential biomarker in inflammatory diseases such as GCA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4935

THU0337 CLASSIFICATION OF ANTINEUTROPHILIC CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS AND CLINICAL IMPACT AND OUTCOME

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Background: Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitides (AAV) have overlapping manifestations. Classifications based on clinical criteria or ANCA specificity have emerged to individualize homogenized group of patients in terms of clinical forms and outcomes.

Objectives: The aim of our study was to retrospectively re-evaluate the clinical impact and outcome of our monocentric AAV patients' cohort, according to classifications based on clinical criteria and/or ANCA specificity.

Methods: A retrospective monocentric study carried out in Caen university hospital led to identify proteinase-3 (PR3) or myeloperoxidase (MPO)-ANCA AAV patients (via an ELISA technique), respectively from March 1997 to June 2016, and from September 2011 to June 2016. Patients with eosinophilic granulomatosis with polyangiitis were excluded. AAV were classified between granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), and GPA vs MPA (p < 0.001) and GPA vs MPA (p < 0.005). As expected, ear-nose throat involvement were significantly higher in PR3-ANCA vs MPO-ANCA, and GPA vs MPA (p < 0.001). Survival was significantly higher in
anti-MPO GPA but relapse-free survival was lower, compared to anti-MPO MPA (p=0.038 and p=0.015, respectively). Without difference in treatments. Relapse-free survival was lower in GPA, compared to MPA (p<0.001). Among GPA patients, there was significantly more deaths in PR3 than MPO patients (p=0.02), but without significant difference between ANCA types for all other considered criteria, including survival (p=0.08).

Conclusions: The clinicopathological classification appeared as the strongest criteria for distinguishing homogeneous forms and prognosis of AAV. Besides their diagnostic value, ANCA may not exhibit further great interest, especially in GPA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2274

THU0338 CLINICAL PRESENTATION AND OUTCOMES OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: ANCA-NEGATIVE VS ANCA-POSITIVE

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Objectives: The aim of the prospective study was to compare clinical presentation at diagnosis and long-term outcomes of eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA) patients according to antineutrophil cytoplasmic antibody (ANCA) status.

Methods: EGPA was classified according to the Revised CHCC Nomenclature and ACR1990 criteria. Activity of vasculitis was evaluated using BVAS. A minor relapse was defined as an increase in at least one new or worse minor item and no major BVAS item. A major relapse was an increase in at least one major BVAS item.

Results: We followed 93 patients with EGPA for a mean±SD of 6.3±5.6 years. Their mean±SD age was 46.6±13.8 years, and 96.8% patients had a history of asthma. The most common EGPA manifestations at diagnosis included ENT manifestations (88.2%), fever (78.5%), peripheral neuropathy (73.1%), lung involvement (59.1%) and skin lesions (49.5%). Thirty seven of 93 patients (39.8%) were ANCA-positive. These patients had significantly more frequent myalgia and mononeuritis multiplex, than the ANCA-negative patients. The difference in occurrence of kidney disease between the two groups did not reach statistical significance. However, all three patients with rapidly progressive kidney failure were ANCA-positive. BVAS at diagnosis and VDI at the end of the follow-up were significantly higher for ANCA-positive patients. The follow up duration was 587.7 patient-years. The incidence of all vasculitis relapses was 14 per 100 patient-years and 3.7 per 100 patient-years, respectively. The 3- and 5-year relapse-free survival rate was 65.4% (95% CI 54.6–76.2) and 43.1% (95% CI 30.4–55.7), respectively. The frequency of vasculitis relapses was 2.1 per 100 patient-years in the ANCA-positive group versus 1.9 per 100 patient-years in the ANCA-negative group (P=0.4).

Table 1. Main clinical characteristics at diagnosis of the 71 patients with EGPA, according to ANCA status

<table>
<thead>
<tr>
<th>Manifestations</th>
<th>ANCA-negative (n=37)</th>
<th>ANCA-positive (n=34)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>30 (81.1)</td>
<td>25 (73.5)</td>
<td>0.57</td>
</tr>
<tr>
<td>Myalgia</td>
<td>22 (59.5)</td>
<td>10 (29.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>ENT</td>
<td>33 (89.2)</td>
<td>30 (88.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Lung</td>
<td>24 (64.9)</td>
<td>19 (55.9)</td>
<td>0.47</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>24 (64.9)</td>
<td>15 (44.1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>30 (81.1)</td>
<td>21 (61.8)</td>
<td>0.17</td>
</tr>
<tr>
<td>Mononeuritis multiplex</td>
<td>17 (45.9)</td>
<td>6 (17.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>13 (35.1)</td>
<td>10 (29.4)</td>
<td>0.62</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>4 (10.8)</td>
<td>4 (11.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>Renal</td>
<td>11 (29.7)</td>
<td>5 (14.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>BVAS at diagnosis</td>
<td>15.6±6.44</td>
<td>12.6±5.52</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>VDI at the end of the follow-up</td>
<td>2.4±3.57</td>
<td>1.7±1.16</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Conclusions: The characteristics of EGPA patients differ according to their ANCA status. Although clinical outcomes were similar in both groups, EGPA is characterized by relapsing course of disease. The minor vasculitis relapses predominated in the structure of relapses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5259

THU0339 FECAL CALPROTECTIN LEVELS AS AN INDICATOR OF ACTIVE DISEASE IN BEHÇET’S SYNDROME PATIENTS WITH GASTROINTESTINAL INVOLVEMENT: A CONTROLLED STUDY

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Background: Elevated fecal calprotectin (FC) levels indicate activity in Crohn’s disease (CD) and ulcerative colitis and are used as non-invasive biomarkers in these diseases. Gastrointestinal involvement of Behçet’s syndrome (GIBS) shows clinical and endoscopic similarities to CD. A previous study suggested that FC may help to diagnose GIBS patients (1), but we are not aware of any studies addressing its role in identifying disease activity in such patients.

Objectives: To determine whether FC helps to distinguish active GIBS patients from those in remission.

Methods: We collected fecal and serum specimens before colonoscopy from 39 GIBS patients who agreed to participate (Table). Twenty-six patients were asymptomatic whereas 13 had abdominal pain and/or diarrhea. We also filled disease activity index for intestinal Behçet’s disease (DAIBD) and Crohn’s disease activity index (CDAI) in each patient. Active gastrointestinal (GI) involvement was defined as having ulcers on colonoscopy. We included 22 active and 25 inactive CD patients as controls. We used 150 μg/L as the cut-off for a positive FC level. None of the patients were receiving NSAIDs that could increase FC levels.

Results: Among the 39 GIBS patients, 14 had active ulcers on colonoscopy (8/13 symptomatic and 6/26 of asymptomatic). FC level was >150 μg/L in 12/14 active GIBS patients and in 6/25 patients in GI remission (OR: 19, 95% CI: 3 to 110). The median FC and CRP levels were higher among active GIBS patients whereas serum calprotectin levels were not different (Table). Among CD patients, 16/25 active patients and 3/22 patients in remission had a FC level >150 μg/L (OR: 11, 95% CI: 11 to 49). There was a high correlation between FC and CDAI scores (r=0.64, p<0.001) and a very high correlation between FC and DAIBD scores (r=0.71, p<0.001), while FC was not correlated with serum calprotectin and CRP levels. Among the 6 GIBS patients who had high FC levels despite being in remission for GI involvement, 2 had active mucocutaneous lesions, 1 had concomitant macrophage activation syndrome (MAS), 1 had polylymphocytosis with trisomy 8 and 2 were started high dose corticosteroids. Repeat FC levels could be obtained in 3 of these patients, after the resolution of MAS and mucocutaneous lesions, and were <150 in all 3.

Table 1. Demographic, clinical and laboratory features of active GIBS patients and in GIBS patients who are in remission.

<table>
<thead>
<tr>
<th>Active GIBS</th>
<th>GIBS in remission</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, M/F</td>
<td>5/9</td>
<td>10/15</td>
</tr>
<tr>
<td>Mean±SD age, years</td>
<td>47.5±7.2</td>
<td>40±11</td>
</tr>
<tr>
<td>Median (IQR) FC, μg/L</td>
<td>301 (176-957)</td>
<td>30 (30-134)</td>
</tr>
<tr>
<td>FC ≥150 μg/L, n (%)</td>
<td>12 (86)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Median (IQR) serum calprotectin, ng/mL</td>
<td>98 (39-128)</td>
<td>69 (54-101)</td>
</tr>
<tr>
<td>Median (IQR) serum CRP, mg/dL</td>
<td>2 (1-5)</td>
<td>3 (2-15)</td>
</tr>
<tr>
<td>Median (IQR) DAIBD scores</td>
<td>52 (4-189)</td>
<td>30 (9-92)</td>
</tr>
<tr>
<td>Median (IQR) DAIBD scores</td>
<td>40 (4-81)</td>
<td>20 (4-37)</td>
</tr>
</tbody>
</table>

Conclusions: FC seems to be a useful non-invasive tool for identifying active GI involvement in GIBS patients. Whether the presence of other BS manifestations can cause false positive results in GIBS patients in remission remains to be studied. On the other hand, serum calprotectin levels do not seem to be useful in identifying active disease in GIBS patients.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6124
ADRENAL INSUFFICIENCY DURING GLUCOCORTICOID TREATMENT IN PATIENTS WITH POLYMYALGIA REUMATICA OR GIANT CELL ARTERITIS

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Background: Adrenal insufficiency secondary to long-term systemic glucocorticoid treatment is a well-recognized problem. However, the extent and prevalence of this phenomenon has not been thoroughly explored.

Objectives: To investigate the prevalence of adrenal insufficiency in patients with polymyalgia reumatica (PMR) and giant cell arteritis (GCA) during treatment with low-dose methylprednisolone (10 mg/day) and to correlate the adrenal response to a 250 microgram Synachten® test.

Methods: Outpatients were examined when prednisolone doses were between 2.5 and 10 mg/day for >6 months. Adrenal function was evaluated after a 48-hour pause of prednisolone, using a 250 μg Synachten® (ACTH) test where plasma cortisol levels were measured at baseline and 30 minutes after Synachten injection. Adrenal insufficiency was defined as plasma cortisol <420 nmol/l after 30 minutes according to the validated Roche Elecsys®Cortisol II assay. Accumulated doses of prednisolone for the individual patients were calculated. A multiple regression analysis was used to test for an association between the plasma cortisol after 30 minutes and the accumulated dose of prednisolone.

Results: Forty-eight patients (35 women) completed the Synachten® test. Seven (14.6%) patients exhibited adrenal insufficiency. Median age was 74 years (Range: 52–99 years). Median accumulated dose was 3,402 mg (Range: 820–21,200 mg). Median plasma cortisol after 30 minutes was 562 nmol/l (Range: 92–989 nmol/l). In patients with adrenal insufficiency, median plasma cortisol was 122 nmol/l (Range: 56–275 nmol/l) at baseline and 207 (Range: 92–420 nmol/l) after 30 minutes. In patients without adrenal insufficiency, median plasma cortisol was 359 (Range: 97–1104 nmol/l) at baseline and 584 nmol/l (Range: 429–989 nmol/l) after 30 minutes. Accumulated doses of prednisolone did not differ in patients with and without adrenal insufficiency (p=0.49). Plasma cortisol after 30 minutes was not associated with accumulated dose of prednisolone (estimate: −0.01, 95% CI: −0.02 to 0.05, p=0.66) when adjusting for sex and age.

Conclusions: Iatrogenic adrenal insufficiency was prevalent among patients with PMR or GCA treated with low dose prednisolone. Adrenal function was not affected in AAV patients. Secondary aims were to correlate the FLT3 ligand serum concentrations with clinical and laboratory parameters. The elevation more likely reflects the therapeutic regimen and history than disease activity as we could show that patients with more intensive treatment including both CYC and AZA show higher FLT3 ligand serum levels when compared to patients with less intense therapy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6823

FLT3 LIGAND CONCENTRATIONS ARE ELEVATED IN ANCA-ASSOCIATED VASCULITIDES (AAV) AND ARE INFLUENCED BY IMMUNOSUPPRESSIVE THERAPY

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Background: The cytokine Flt3 ligand is an important co-factor for early hematopoiesis by mainly driving the development of lymphoid and early B-cell precursors. In the periphery functions of Flt3 are more pleiotropic involving the regulation of differential T cells, dendritic cells as well as peripheral B-cells. Besides its well-known roles in hematological disorders and as an indicator of bone marrow (BM) output capacity, the possible involvement of Flt3 ligand in autoimmune disorders was only discovered recently.

Objectives: Our primary aim was to analyze if FLT3 ligand serum concentrations are influenced in AAV patients. Secondary aims were to correlate the FLT3 ligand serum concentrations with clinical and laboratory parameters. And, since FLT3 ligand concentrations are elevated in different states of bone marrow failure, we are affected in AAV patients. Secondary aims were to correlate the FLT3 ligand concentrations are elevated in different states of bone marrow failure, we

Methods: We performed a cross sectional study using a sandwich ELISA to determine FLT3 ligand concentrations in the serum of 98 well-characterized AAV patients (69 GPA, 20 MPA and 9 EGPA) and 144 healthy controls (HC). Statistical evaluation was done using Mann-Whitney or unpaired, two-tailed Student’s t-test. Results: In patients with AAV, FLT3 ligand concentrations were significantly elevated (207 pg/ml +/- 116.2 in AAV versus 142.5 pg/ml +/- 65.98 in HC; p<0.0001). Disease specific analysis revealed significantly elevated FLT3 ligand concentrations in GPA (217.6 pg/ml +/- 123; p<0.0001), but no significant differences for MPA and EGPA when compared to HC. FLT3 ligand concentrations did not correlate to serological or clinical markers of disease activity, however, overall disease activity was low in the studied cohort. To assess the influences of treatment regimen on FLT3 ligand concentrations, we focused our analysis on treatment histories of cyclophosphamide (CYC) and azathioprine (AZA) and grouped the patient cohort according to the cumulative CYC dose (< or >5g and/or duration of AZA therapy (< or >6 months). AZA and CYC naïve patients (n=10) showed FLT3 concentrations comparable to HC (121 pg/ml +/- 42.3), but in patients with low dose CYC and short term AZA therapy FLT3 concentrations were significantly higher (176.6 pg/ml +/- 51.6), both compared to treatment naïve patients and HC (p=0.0095 vs. AAZ/CYC naïve, p=0.0105 vs HC). Intensified treatment was associated with even further increased concentrations of FLT 3 ligand with highest concentrations found in patients treated with >5g CYC cumulative dose or AZA treatment for >6 months (263.4 pg/ml +/- 172.6; p=0.0024 vs. AAZ/CYC naïve, p<0.0001 vs HC).

Conclusions: FLT3 ligand concentrations are elevated in patients with AAV, especially in patients with GPA. The elevation more likely reflects the therapeutic regimen and history than disease activity as we could show that patients with more intensive treatment including both CYC and AZA show higher FLT3 ligand serum levels when compared to patients with less intense therapy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6349

UTILIZING “REAL LIFE” DATA IN ORDER TO EVALUATE THE ASSOCIATION BETWEEN GIANT CELL ARTERITIS AND AUTOIMMUNE THYROID DISEASE

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Background: In 1977, How et al.1 described the case of a simultaneous presentation of giant cell arteritis (GCA) and hypothyroidism. In the following decades, numerous studies have attempted to determine whether a significant association exists between GCA and autoimmune thyroid dysfunction, with conflicting results2–6.

Objectives: To evaluate whether a genuine association exists between GCA and autoimmune thyroid disease.

Methods: Utilizing the medical database of Clalit Health Services, we compared the proportion of autoimmune thyroid disease between patients with GCA and age- and gender-matched controls in a cross-sectional study. Univariate analysis was performed using Chi-square and student t-test and a multivariate analysis was performed using a logistic regression model.

Results: 5,663 GCA patients and 23,308 age- and gender-matched controls were
included in the study. The proportion of hypothyroidism amongst GCA patients was increased in comparison with controls (18.2% vs. 6.91%, respectively, \( p < 0.001 \)), as was hyperthyroidism (2.56% and 1.19% respectively, \( p < 0.001 \)). After controlling for confounders, GCA demonstrated a robust independent association with hypothyroidism on multivariate logistic regression (OR 2.097, 95% CI 1.187-4.188, Table 1). In contrast, when a similar model was performed in order to assess the nature of the association between GCA and hyperthyroidism, it was found to be non-significant, with an OR of 1.097.

Table 1. Multivariate logistic regression of covariates associated with hypothyroidism.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR</th>
<th>CI</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.03</td>
<td>1.02–1.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>3.32</td>
<td>2.93–3.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>1.02</td>
<td>1.01–1.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SES: Medium vs. Low</td>
<td>1.42</td>
<td>1.29–1.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SES: High vs. Low</td>
<td>1.63</td>
<td>1.45–1.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCA</td>
<td>1.30</td>
<td>1.12–1.42</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BMI: Body Mass Index, kg/m²; SES: Socioeconomic status, GCA: Giant Cell Arteritis.

Conclusions: GCA patients have a higher proportion of hypothyroidism in comparison with matched controls. A significant association between GCA and hyperthyroidism was not found. Physicians treating GCA patients should consider screening for thyroid dysfunction on a regular basis.

References:

Disclosure of Interest: None declared

THU0343 | THE EFFECT OF ADAлиммабУМ ON CLINICAL MANIFESTATIONS AND PRO-INFLAMMATORY CYTOKINES MИЛІЄУ IN PATIENTS WITH BЕHЕТС’S DІЗІАС

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Background: Behet’s disease is a multisystemic chronic relapsing inflammatory disease, classified among the vasculitides. The etiology of Behet’s disease is unknown. Several cytokines, among them TNF-\( \gamma \), are involved in the pathogenesis of the disease.

Objectives: We aimed to assess efficacy and safety of Adalimumab (ADA) in patients with active Behet’s arthritis not responding to one or more DMARDS and to assess the impact of treatment on the cytokine milieu.

Methods: Eligible patients (pts) with active Behet’s arthritis were enrolled in a 24 weeks single center prospective open-label study. Pts who relapsed within 12 weeks following ADA discontinuation could enter a 3 year extension study. The efficacy was assessed by 68 tender and 66 swollen joint count, patient visual analogue scale (VAS) for pain, physician overall disease activity VAS, health assessment questionnaire (HAQ), Behet’s Disease Current Activity Form (BDCAF), C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). TNF-\( \gamma \), IL-1\( \beta \), IL-6, INF-\( \gamma \), IL-10 and IL-17A were evaluated at baseline, after 24 and 48 weeks of treatment, by ProcartaPlex Human High Sensitivity – Immunoassay kit. Trough ADA serum level and no antibodies improved after providing ADA weekly.

Results: Tender joints were increased in comparison with controls (18.2% vs. 6.91%, respectively, \( p < 0.001 \)). The disease relapsed in 9/10 pts, within 4–6 weeks following ADA interruption, 7 pts with low ADA trough levels and no antibodies improved after providing ADA weekly. The disease relapsed in 9/10 pts, within 4–6 weeks following ADA interruption, 7 pts enrolled into the extension study.

Conclusions: ADA treatment was well tolerated and achieved a significant improvement in arthritis and mucocutaneous manifestations and lowered IL-6 serum concentration in all study pts but only 40% reported significant pain reduction. A subset of pts with insufficient improvement in joint tenderness and generalized pain may require comprehensive pain management besides anti-inflammatory therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4939

THU0344 | A RHEUMATOLOGY LED PATHWAY FOR THE INITIAL MANAGEMENT OF GCA IMPROVES DIAGNOSTIC OUTCOMES COMPARED TO THE GENERALIST

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Background: Giant Cell Arteritis (GCA) is a medical emergency requiring prompt and appropriate management to prevent complications. The British Society of Rheumatology (BSR) has set out guidelines on the appropriate management of suspected GCA targeting both primary and secondary-care physicians. Hospitals increasingly using care-pathways to facilitate appropriate initial management of GCA by non-rheumatologists. Evidence is limited, however, on the impact of such interventions on patient care.

Objectives: To evaluate the impact of designing a GCA care-pathway for non-rheumatologists (acute and general physicians) on patient care in terms of: (i) duration from referral to temporal artery biopsy (TAB) and rheumatology review; (ii) glucocorticoid therapy burden; and (iii) proportion of referrals with a final diagnosis of GCA.

Methods: We performed a retrospective study of all patients diagnosed with GCA between 3 periods: prior to introducing a GCA pathway (2007–2009), rheumatology led GCA pathway (2010–2012), and non-rheumatology led GCA pathway (2012–2016). We identified patients from a TAB database and collected general demographic data, initiation of glucocorticoid therapy, referral for TAB and rheumatology clinic, date of TAB and clinic review, biopsy findings, and final diagnosis.

Results: Table 1 summarises the main findings. After introducing the rheumatology-led pathway (2010–2012), rate of referrals for TAB per month declined to 0.78, the proportion of patients having a TAB within 14 days of referral reached 100%, and the proportion of patients with a positive biopsy increased to 30% suggesting appropriate use of the pathway and an improvement in care. However introducing a non-rheumatology led GCA pathway (2012–2016), led to increased referral numbers. The proportion of TAB within 14 days decreased, and the proportion with a positive biopsy declined (17%).

Table 1. A statistically significant improvement was observed in swollen joint count, physician VAS and BDCAF and in IL-6 levels, but not in tender joint count or HAQ. Resolution of oral and urogenital ulcers was achieved in all pts. Significant reduction of pain was reported by 40% of pts. No relapse of uveitis or other disease manifestations occurred during the study. The reduction in IL-6 levels correlated with the physician VAS and BDCAF but not with HAQ. No correlation was found between change in IL-10 level and VAS pain. The levels of INF-\( \gamma \), IL-17A, TNF-\( \alpha \) were undetectable in all pts. IL-1\( \beta \) was elevated in 1 patient only. ADA serum trough levels were in the therapeutic range in 7/10 pts. One patient developed high antidrug antibodies titer and ADA serum trough level of 0 with a concomitant increase in VAS pain and IL-6 concentration. Another patient with low ADA trough levels and no antibodies improved after providing ADA weekly. The disease relapsed in 9/10 pts, within 4–6 weeks following ADA interruption, 7 pts enrolled into the extension study.

Abstract THU0344 – Table 1
Before GCA Pathway | Rheumatology Led GCA Pathway (1st Cycle) | Non-Rheumatology Led GCA Pathway (2nd Cycle)

<table>
<thead>
<tr>
<th>Dates</th>
<th>Study Design</th>
<th>Source of Data</th>
<th>Number of Patients Biopsied</th>
<th>Number of Months</th>
<th>Days of referral to TAB</th>
<th>Proportion with TAB within 14 days</th>
<th>Proportion with a positive biopsy for GCA</th>
<th>Mean Age (years)</th>
<th>Gender Ratio (M:F)</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-2010 (Jan 07–Sep 09)</td>
<td>Retrospective</td>
<td>Histology database, electronic records</td>
<td>54</td>
<td>27</td>
<td>5 (0–56)</td>
<td>87%</td>
<td>36%</td>
<td>73</td>
<td>18:36 (F 66.7%)</td>
<td>GCA Pathway introduced</td>
</tr>
<tr>
<td>2010 to 2012 (Jan 10–Mar 12)</td>
<td>Retrospective</td>
<td>Histology database, electronic records</td>
<td>21</td>
<td>27</td>
<td>5 (0–13)</td>
<td>100%</td>
<td>30%</td>
<td>73</td>
<td>4:17 (F 60.9%)</td>
<td>Pathway continued</td>
</tr>
<tr>
<td>2016 (Nov 12–June 16)</td>
<td>Retrospective</td>
<td>Histology database, electronic records</td>
<td>129</td>
<td>66.2%</td>
<td>2.93</td>
<td>17%</td>
<td>Pathway review</td>
<td>48:81 (F 62.7%)</td>
<td>Pathway review</td>
<td></td>
</tr>
</tbody>
</table>
The non-rheumatology led GCA pathway was associated with higher glucocorticoid burden. In this cohort, 23/35 (41.1%) patients who were found not to have GCA received more than 21 days of high dose steroids (40-60mg Prednisolone) whilst awaiting rheumatology review. 4 patients whose final diagnosis was not GCA received high dose steroids for more than 30 days (max 109 days).

Conclusions: 1. Availability of a rheumatology-led GCA pathway leads to improved care for patients with suspected GCA
2. Easy access for referral of patients with headache as assessed by the non-specialist can lead to over-use of the pathway and inappropriate referrals
3. Non-rheumatology-led GCA pathway can lead to a high glucocorticoid burden, especially in an elderly demographic with other comorbidities

Disclosure of Interest: None declared


THURSDAY, 15 JUNE 2017

Spondyloarthritis - treatment

THU0345


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Background: Tumour necrosis factor inhibitors (TNFi) have revolutionized treatment of axial spondyloarthritis (axSpA). The five different available TNFi have not been compared directly, and whether effectiveness differs between agents is unknown. In Norway national authorities consider the different TNFi equivalent, and since 2009 the least expensive drug following an annual national tender has been the drug-of-choice in the publicly funded healthcare system. This has lead to variations across different years in drug use where choice of TNFi has been predominantly based on national price policy and not clinical characteristics.

Objectives: Comparing response to TNFi during the first year of treatment of axSpA in biologics-naïve patients over years with highly varying uptake of different TNFi.

Methods: We included the 981 biologics-naïve patients with axSpA from the NOR-DMARD register who started their first TNFi from 2009 through 2015. The preferred drugs in national recommendations were: 2009 adalimumab, 2010 golimumab, 2011 etanercept, 2012 etanercept, 2013 golimumab, 2014 certolizumab, 2015 certolizumab/biosimilar infliximab (CT-P13). We compared the estimated change in Ankylosing Spondylitis Disease Activity Score (ASDAS) between treatment years at 3, 6 and 12 months after treatment start using a mixed model with subject-specific random intercept, adjusting for baseline disease activity, age, sex and treatment centre.

Results: Demographics, drug uptake and baseline characteristics for each year 2009–2015 are listed in table 1. The preferred drug was started in 57–91% of patients. There was a trend towards lower ASDAS and disease duration over time. There were no differences in treatment effectiveness between the years, regardless of the substantial differences in type of TNFi used (figure).

Conclusions: Real-life data do not show differences in response to TNFi despite large annual variation in type of TNFi prescribed, indicating similar effectiveness of the available TNFi in patients with axSpA. This supports the practice of selecting drug based on cost and feasibility of use, as is the current practice in Norway. Further adoption of this principle can provide access to TNFi treatment to more patients, as it reduces costs and healthcare resources are limited.


Table 1. Demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>Age (years), mean (SD)</th>
<th>ASDAS, mean (SD)</th>
<th>Certolizumab</th>
<th>Etanercept</th>
<th>Infliximab</th>
<th>Biosimilin infliximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>110</td>
<td>42.3 (11.2)</td>
<td>3.26 (0.84)</td>
<td>0.0%</td>
<td>7.3%</td>
<td>1.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>2010</td>
<td>104</td>
<td>40.3 (11.5)</td>
<td>3.20 (0.92)</td>
<td>0.0%</td>
<td>8.7%</td>
<td>3.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>2011</td>
<td>200</td>
<td>41.7 (13.0)</td>
<td>3.10 (0.94)</td>
<td>29.8%</td>
<td>11.0%</td>
<td>22.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>2012</td>
<td>200</td>
<td>40.0 (12.0)</td>
<td>2.96 (1.01)</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>2013</td>
<td>148</td>
<td>40.9 (12.7)</td>
<td>3.02 (0.87)</td>
<td>14.5%</td>
<td>4.0%</td>
<td>12.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>2014</td>
<td>192</td>
<td>41.6 (11.8)</td>
<td>2.87 (0.89)</td>
<td>24.3%</td>
<td>7.9%</td>
<td>5.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>2015</td>
<td>103</td>
<td>41.6 (12.3)</td>
<td>2.71 (1.01)</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

p-values for between-year differences.

DOI: 10.1136/annrheumdis-2017-eular.1261

THU0346

CONCOMITANT FIBROMYALGIA IN AXIAL SPONDYLOARTHRITIS HAS A NEGATIVE IMPACT ON TNF ALPHA BLOCKERS TREATMENT EFFECT IN REAL LIFE


Background: Coexisting fibromyalgia (FM) in axial spondyloarthritis (axSpA) can represent therapeutic challenges, particularly when evaluating the treatment effect of biologics (i.e. TNF alpha blockers (TNFB)). Indeed, since FM patients often report high levels of pain and disability there is the risk of classifying such patients as refractory to TNFb (i.e. as not reaching a significant improvement in disease activity).

Objectives: To evaluate the impact of concomitant FM on the TNFb treatment effect in axSpA.

Methods: Design: Prospective observational national study with 2 visits 3 months apart (baseline and 12 weeks after TNFb initiation) (Predict-Spa study ClinicalTrials.gov: NCT03309088). Patients: axSpA patients (diagnosis according to treating rheumatologist) initiating a TNFb. Data collection: the FIRST questionnaire (Fibromyalgia Rapid Screen Test) which screens for FM, patients and disease characteristics and effectiveness measures (e.g. ASAS response components). Statistical analysis: FM positive screening was defined by a FIRST score ≥5/6; the primary efficacy outcome was the ASAS 40. Non-responder imputation and baseline observation carried forward imputation (for binary and continuous outcome variables, respectively) was performed. Impact of FM on the TNFb treatment effect was evaluated by multivariable logistic regression, with ASAS 40 as the dependent variable and FM as the independent variable; were also included in the model other factors previously reported in the literature as associated with treatment efficacy (i.e. X-ray and MRI sacroiliitis, abnormal CRP (<-3mg/L), HLA B-27, smoking status, previous TNFb exposure, age>40 and male gender).

Results: Among the 527 patients enrolled in the study, 508 patients were analysed. Mean age was 41.4 ± (11.6), 237 (46.7%) were women, with a 6.1±8.5 mean disease duration. Among them, 192 (37.8%) were screened as FM by the FIRST questionnaire. Overall efficacy of the TNFb was good (ASAS40, 201/508 (39.6%)) though 50 patients (9.8%) patients discontinued the TNFb before the follow-up visit and were considered as non-responders. Patients with FM presented less frequently an ASAS 40 response (87/192 (45.3%) vs 171/316 (54.1%), for the FM vs non-FM groups according to the FIRST definition. Presence of FM was independently associated with poorer ASAS40 response (adjusted odds ratio, OR = 0.5 [95% CI 0.3 – 0.8]) while X-ray sacroiliitis (1.8 [1.2 – 2.8]), abnormal CRP (1.6 [1.0 - 2.4]) and absence of previous exposure to TNFb (1.7 [1.1 – 2.6]) were found to be associated with an ASAS40 response.

Conclusions: This study 1) confirms the “conventional” predisposing factors of TNFb treatment response such as X-ray sacroiliitis, abnormal CRP and absence of previous exposure to TNFb; and 2) suggests that concomitant FM influences treatment response. FM deserves to be screened in axSpA, in particular in case of a decision to initiate a TNFb therapy.

References:


**THU0347 IMPACT OF OBESITY ON THE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS IN AXIAL SPONDYLOARTHRITIS**


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**Methodology:** Children with a new diagnosis of early axSpA (≤ 18 yrs) were included if they fulfilled the ASAS criteria for axSpA, started a first TNFi after recruitment and had available BMI data as well as a baseline and follow-up visit at wk16.

**Results:** In comparison to normal weight and overweight patients, obese individuals were significantly older, had a longer symptom duration and higher BASFI and BASMI levels, while ASDAS levels were comparable between the 3 groups (Table 1). Data to calculate the ASAS40 response was available in 496 patients (7%). It was reached by 44%, 35% and 28% of patients with normal weight, overweight and obesity, respectively. (p=0.02; Table 2). A significantly lower odds ratio (OR) for achieving ASAS40 response was found in adjusted analyses in obese patients vs patients with normal BMI (OR 0.35, 95% confidence interval (CI) 0.11–0.73, p=0.01). Comparable results were found for the other outcomes assessed. The adjusted predicted ASAS40 OR in overweight vs normal weight patients was 0.69, 95 CI 0.38–1.24, p=0.22.

**Table 1. Baseline characteristics at start TNFi**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N (%)</th>
<th>BMI category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>632</td>
<td>54</td>
</tr>
<tr>
<td>Age, years</td>
<td>632</td>
<td>37.0 (11.2)</td>
</tr>
<tr>
<td>Symptom duration, years</td>
<td>627</td>
<td>11.8 (10.1)</td>
</tr>
<tr>
<td>HLA-B27 positive, %</td>
<td>579</td>
<td>77</td>
</tr>
<tr>
<td>BASDAI</td>
<td>552</td>
<td>5.3 (2.0)</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>520</td>
<td>3.4 (0.9)</td>
</tr>
<tr>
<td>Elevated CRP, %</td>
<td>587</td>
<td>55</td>
</tr>
<tr>
<td>BASFI</td>
<td>558</td>
<td>3.6 (2.4)</td>
</tr>
<tr>
<td>BASMI</td>
<td>541</td>
<td>2.0 (2.0)</td>
</tr>
<tr>
<td>CRP</td>
<td>587</td>
<td>3.6 (2.4)</td>
</tr>
</tbody>
</table>

**Table 2. Unadjusted response rates after 1 year of treatment with a first TNFi inhibitor**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N (%)</th>
<th>BMI category</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS40</td>
<td>496</td>
<td>45</td>
</tr>
<tr>
<td>ASDAS improvement ≥1</td>
<td>425</td>
<td>26</td>
</tr>
<tr>
<td>ASDAS improvement ≥2</td>
<td>472</td>
<td>30</td>
</tr>
</tbody>
</table>

**Conclusions:** IV GLM 2mg/kg was efficacious in reducing the signs and symptoms of AS compared with PBO. GLM was well-tolerated through wk28; the safety profile was consistent with other anti-TNFs, including SC GLM.
However, anti-drug antibodies (ADA) may be responsible for decreased efficacy. Methotrexate reduces adalimumab immunogenicity in rheumatoid arthritis (1). **Objectives:** The aim of the study was to evaluate the effect of methotrexate on ADA detection in SpA patients receiving adalimumab. **Methods:** One hundred and ten SpA patients eligible for adalimumab 40 mg S/C every other Wednesday were randomized on a 1:1 ratio to receive MTX 10 mg S/C every week or 2 weeks prior (V0) adalimumab (MTX+), or adalimumab alone (MTX-). ADA detection and adalimumab concentration were assessed 4 weeks (V2), 8 weeks (V3), 12 weeks (V4) and 26 weeks (V5) after starting adalimumab (V1). The main outcome was the percentage of positive patients for ADA detection at V5 or last visit. **Results:** Patients’ characteristics (sex, previous TNF inhibitors, disease duration, HLA B27, BMI, BML) were comparable between the two groups. One hundred and seven patients were analyzed, 55 in the MTX+ group versus 52 in the MTX- group. ADA were detected at V5, in 39/107 (36.4%) patients; 13/52 (25%) in the MTX+ group versus 26/55 (47.3%) in the MTX- group (p=0.03). Adalimumab concentrations were statistically higher in the MTX+ group as compared with the MTX- group at V2, V3, V4 and V5 (Figure 1). There was no difference in terms of adverse events and efficacy between the two groups. **Conclusions:** MTX reduces immunogenicity and ameliorates pharmacokinetics of adalimumab in SpA patients. The clinical impact of this combination requires longer period studies. **References:**


**THU0351 ADALIMUMAB TAPERING WITH COMBINED METHOTREXATE CAN BE EFFECTIVE AS MAINTENANCE THERAPY IN SPA-RELATED UVEITIS**

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**Background:** Anti-TNF agents have deeply improved the therapeutic efficacy of spondyloarthritides (SpA)-related uveitis [1]. Despite the benefits of anti-TNF drugs, patients need to stay on treatment for a long time. There has been a clear medical need to consider the long-term safety and increased drug costs. Unanswered question for physicians is whether TNF blockers can be reduced or even stopped in SpA-related uveitis, or how can it be reduced in patients have achieved remission or LDA. The current study aimed to investigate the effectiveness and safety of adalimumab tapering strategy in SpA-related uveitis.

**Objectives:** The aim of this study was to evaluate the effectiveness of tapering of adalimumab combined with MTX in patients with spondyloarthritides (SpA)-related uveitis.

**Methods:** We performed a retrospective analysis. SpA patients with uveitis admitted to a south China hospital were enrolled. Demographic information, clinical characteristics, laboratory findings, intraocular inflammation, visual acuity, and macular thickness were documented every 3 to 6 months. **Results:** In 32 cases of SpA-related uveitis who achieved clinical remission for at least 6 months after receiving a standard dose of adalimumab in combination of MTX, adalimumab was tapered and MTX was continued. Dosing interval of adalimumab was spaced by 30% every 3 months up to complete stop. Twenty-six cases without MTX were analyzed for comparison. No significant difference of demographic characteristics and BASDAI, CRP, ESR was found between the two groups at the baseline. During the first 12 months of adalimumab tapering, tapering of MTX and BASDAI remains stable in both groups. Recurrent uveitis was found in the group with combined MTX. In the group without combined MTX, 2 patients (2/6, 7.7%) presented increased anterior chamber inflammation and visual acuity. At the end of 24 months, mean BASDAI, CRP and ESR remained low in both groups. Two cases (2/32, 6.3%) in the group of combined MTX were documented increased BASDAI higher than 4, but no recurrent uveitis was observed. Altogether 5 cases (5/32, 15.6%) in the group of combined MTX had recurrent uveitis, in which 4 cases (4/5, 80%) initiated adalimumab tapering at 6 months’ remission. In comparison, 8 cases (8/26, 30.8%, p<0.001) in the group without combined MTX had recurrent uveitis, in which 6 cases initiated highly relevant for these patients with chronic NSAIDs use and increased CV risk (1).

**Objectives:** The objective of this study was to determine the relationship between NSAIDs use and the occurrence of CV events, including myocardial infarction (MI) and stroke, in patients with SpA.

**Results:** In this is an ancillary study of the observational, cross-sectional, multicenter, international ASAS-COMOSPA study. The inclusion criteria were: age >18 years and SpA diagnosis. In order to overcome prescription bias when comparing patients who ever received/did not receive NSAIDs, a propensity score (PS) to predict NSAIDs intake was calculated. Patients who had never received NSAIDs were matched to patients who ever received an NSAID according to the PS. In this matched population, the probability for a patient to present a CV event was estimated by logistic regression. Furthermore, in the global population of the study, factors associated with the occurrence of CV event were explored by logistic univariate analysis, here including the NSAIDs score (2) for the last three months, age and gender, and using the PS as an adjustment variable. **Results:** Of the 3984 patients enrolled in the study, data on CV event occurrence was available for 3961 patients. Among them, 3548 patients received NSAIDs (89.6%) and 376 had never received NSAIDs (10.4%). Patients who had never received NSAIDs had more often inflammatory bowel disease (9.9% vs 5.3%), and a less severe disease (% of bamboo patients: 2.0% vs 7.6%). Among the 756 matched patients, 29 (3.8%) patients reported a CV event (21 MI, 13 strokes and 5 MIs+stroke). The number of patients with CV event was not significantly different between the two groups, ever and never NSAIDs exposure respectively (16 (2.1%) vs 13 (1.7%), OR =1.86 [0.94–3.69]). No difference was observed between the two groups for MI and stroke compared separately (12 (1.6%) vs 9 (1.2%), OR =2.96 [0.41–21.03] and 8 (1.1%) vs 5 (0.7%), OR =0.926 [0.288–3.21] respectively). In the second model, where PS was used as a covariate, the occurrence of overall CV event was independent of age (OR =2.7 [2.3–3.2]) and male sex (OR =1.9 [1.2–3.0]), but not with the NSAIDs score (OR =1.0 [0.9–1.1]). **Conclusions:** The use of NSAIDs does not seem to be as associated with the occurrence of CV event in patients with SpA, however it cannot be excluded that the study is underpowered. Further prospective studies are needed to confirm these results.

**References:**


**DOI:** 10.1136/annrheumdis-2017-eular.2665
adalimumab tapering at 6 months’ remission and 2 cases initiated adalimumab tapering at 9–12 months’ remission. No patients had recurrent uveitis at 12 months’ remission or longer in both groups. Adalimumab plus MTX were well tolerated in patients experiencing increases and decreases in structural lesion scores over 2 yrs.

Conclusions: Pts who received tofacitinib who had AS experienced clinically meaningful reductions in axial MRI inflammation. Pts achieving MIC for MRI inflammation had increased clinical response rates.

References:

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMC and funded by Pfizer Inc.

Disclosure of Interest: W. P. Maksymowych Grant/research support from: AbbVie, Pfizer Inc, Sanofi, UCB; Consultant for: AbbVie, Amgen, Elen Lilly, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, UCB; D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi; Grant/research support from: AbbVie, Pfizer Inc, Roche, UCB, UCB, UCB, UCB, UCB; R. Pedersen Consultant for: AbbVie, Amgen, Elen Lilly, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, UCB; X. Baraliakos Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer Inc, Roche, MSD, UCB; A. Deodhar Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer Inc, UC; M. Dougados Grant/research support from: Abbott, AbbVie, Amgen, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer Inc, Roche, Schering-Plough, UCB; Employee of: Imaging Rheumati; UCB, V. Branco Consultant for: AbbVie, Amgen, Elen Lilly, Janssen, Novartis, Pfizer Inc, Sanofi, UCB.

Figure 1. Cumulative Probability of Change in MRI SIJ Erosion, BL to Week 104.

Table 1. Relationship between Wk 12 clinical response rates and achievement of MIC

| Table 1. Relationship between Wk 12 clinical response rates and achievement of MIC |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| MIAAS20 | MIAAS40 | MIAAS MI | MIAAS ID |
| ASAS20 | n (%) | n (%) | n (%) | n (%) |
| Placbo | SIJ (MIC) (3) | 3/40 (7.5) | 1/4 (25.0) | 0/4 | 0/4 |
| ASAS40 | 14/20 (70.0) | 6/8 (75.0) | 3/8 (37.5) | 3/8 (37.5) |
| MIAAS MI | 3/40 (7.5) | 2/4 (50.0) | 2/4 (50.0) | 2/4 (50.0) |
| MIAAS ID | 14/20 (70.0) | 7/8 (87.5) | 2/8 (25.0) | 2/8 (25.0) |

**THU0352**

TOSTATINIB TREATMENT IS ASSOCIATED WITH ATTAINMENT OF THE MINIMALLY IMPORTANT REDUCTION IN AXIAL MRI INFLAMMATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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1 University of Alberta, Edmonton, AB, Canada; 2Leiden University Medical Center, Leiden, Netherlands; 3RheumaZentrum Rutheger, Herne, Germany; 4Oregon Health & Science University, Portland, OR, United States; 5Queensland University of Technology, Brisbane, Australia; 6Pfizer Inc, Cambridge, MA; 7Pfizer Inc, Collegeville, PA

**Objectives:** To assess whether MIC in SIJ and spine can discriminate between tofacitinib and placebo (PBO) in patients with ankylosing spondylitis (AS) and if the clinical response is consistent with global change scores.

**Methods:** In this 16-week (wk) Phase 2, double-blind, dose-ranging study (NCT01786668), 207 adult pts meeting modified New York AS criteria were randomised 1:1:1 to PBO or tofacitinib 2, 5 or 10 mg twice daily (BID) for 12 wks. Clinical endpoints included in this post-hoc analysis were: Assessment of SpondyloArthritis International Society 20% improvement (ASAS20) and ASAS40, 40% improvement (ASAS40) response rates, AS disease activity score major improvement (ASDAS MI; change ≥ 5 from baseline), ASDAS inactive disease (ASDAS ID; < 1.3), Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI) and back pain. Pts (%) achieving MIC in SIJ, spine and both SIJ and spine, in tofacitinib and PBO groups, were summarised based on observed data, and pooled tofacitinib (5 and 10 mg BID) vs PBO data were compared using Fisher’s exact test. Concordance between achieving MIC and Wk 12 clinical responses was assessed. Wk 12 clinical responses were compared between pts achieving MIC in SIJ and spine.

**Results:** MRI data for 164 pts were evaluated. Baseline demographics were generally well balanced between treatment groups and typical of AS populations. Tofacitinib 2, 5 and 10 mg BID improved mean (range) SPARC scores vs PBO (SIJ: -2.2 (-22.0, 10.5), -3.5 (-34.5, 11.0), -3.6 (-29.0, 0.5) vs 0.0, 0.0, 0.0; spine: -2.3 (-34.5, 20.5), -2.5 (-38.5, 8.0), -2.7 (-32.5, 7.5) vs -0.8 (-8.0, 14.0). Approximately 3 times more pts achieved MIC in SIJ or spine in the pooled tofacitinib group vs PBO (SIJ: 34.1% ≥ 11.8%, p < 0.05; spine: 38.6% ≥ 11.8%, p < 0.01). Achieving MIC in SIJ and spine correlated with clinical response. In pts of the pooled ASAS20, ASAS40 and ASDAS MI responses were more likely in pts achieving MIC in SIJ or spine (Table) vs not achieving MIC. Compared with not achieving MIC, pts on tofacitinib achieving MIC in SIJ had larger improvements in BASDAI, BASFI and back pain.

**Conclusions:** Pts who received tofacitinib who had AS experienced clinically meaningful reductions in axial MRI inflammation. Pts achieving MIC for MRI inflammation had increased clinical response rates.

References:

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2507

**THU0353**

CHANGE IN MRI STRUCTURAL LESIONS IN THE SACROILIAC JOINT AFTER TWO YEARS OF ETANERCEPT THERAPY IN NON-RADIOGRAPHIC AXIAL SPONDYLARTHROPATHY

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1University of Alberta, Edmonton, Canada; 2Paris Descartes University, Hôpital Cochin, Paris, France; 3Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands; 4Université Paris Est Cretel, Creteil, France; 5Leiden University Medical Center, Leiden, Netherlands; 6Pfizer, Collegeville, United States; 7Pfizer, Paris, France; 8InVentiv Health, Princeton, United States

**Background:** Demonstrating a structural effect of TNF inhibitors in axial SpA is not straightforward and the results are conflicting among the available studies. We aimed to evaluate the impact of ETN on imaging outcomes in a 2-year follow-up using the SpA MRI Scoring System (SSS). For each group, differences were calculated between percentages of patients experiencing increases and decreases in structural lesion scores over 2 yrs.

**Objectives:** To compare 2 yrs of structural lesion changes on T1W MRI in the sacroiliac joints (SIJ) of pts receiving etanercept (ETN) in a clinical trial to similar pts not receiving biologics in a cohort study.

**Methods:** Pts had recent onset non-radiographic (nr)-axSpA fulfilling ASAS criteria. Study group: pts receiving ETN 50 mg once weekly for 2 yrs in EMBARK (NCT01258738). Control group: pts in a longitudinal cohort study not receiving biologics for 2 yrs (DESIIR, NCT01648907). Outcome measure: change in structural lesions of erosion, backfill, fat metaplasia, and ankylosis. MRI images were read by 3 experienced readers unaware of image chronology and pt group, using the SpondyloArthritis Research Consortium of Canada SIJ Structural Score (SSS). For each group, differences were calculated between percentages of patients experiencing increases and decreases in structural lesion scores over 2 yrs.

**Results:** Pts had recent onset non-radiographic (nr)-axSpA fulfilling ASAS criteria. Study group: pts receiving ETN 50 mg once weekly for 2 yrs in EMBARK (NCT01258738). Control group: pts in a longitudinal cohort study not receiving biologics for 2 yrs (DESIIR, NCT01648907). Outcome measure: change in structural lesions of erosion, backfill, fat metaplasia, and ankylosis. MRI images were read by 3 experienced readers unaware of image chronology and pt group, using the SpondyloArthritis Research Consortium of Canada SIJ Structural Score (SSS). For each group, differences were calculated between percentages of patients experiencing increases and decreases in structural lesion scores over 2 yrs.

**Conclusion:** Pts achieving MIC, pts on tofacitinib achieving MIC in SIJ had larger improvements in BASDAI, BASFI and back pain.

**Shareholder of:** Pfizer Inc; Employee of: Pfizer Inc; K. Kanik; Pfizer Inc; Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2447
Explorative analyses in the NOR-SWITCH study showed similar efficacy, drug levels and safety in SpA patients switched to CT-P13 as those on continuous INX. The study was not powered to show non-inferiority within each diagnosis.

References:

Disclosure of Interest:
[1] Maksymowych WP, Grant/research support from: Pfizer, Roche-Chugai, MSD, Consul-

Cases THU0354

DISEASE WORSENING AND SAFETY IN PATIENTS SWITCHING FROM ORIGINATOR INFlixIMAB TO BIOSIMILAR INFlixIMAB (CT-P13) IN THE RANDOMIZED NOR-SWITCH STUDY: EXPLORATIVE ANALYSIS IN SPA PATIENTS

G.L. Goll1, I.C. Olsen1, N. Bolstad2, K.K. Jørgensen3, M. Lorentzen4, C. Merk5, J. Jahnsen3, E.A. Haavardsholm1, T.K. Kvien1 on behalf of the NOR-SWITCH-STUDY: EXPLORATIVE ANALYSIS IN SPA PATIENTS

Background: The NOR-SWITCH study is a 52-week randomized, double-blind, non-inferiority, phase IV switch trial in patients with Crohn’s disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and plaque psoriasis (Ps) on stable treatment with originator infliximab (Remicade®), INX, funded by the Norwegian government. Previously, primary analyses of the pooled indications have been published1.

Objectives: To investigate efficacy, safety and immunogenicity in SpA patients treated with continuous INX vs patients switched to CT-P13 (biosimilar infliximab, Remsima®) in the NOR-SWITCH study (explorative analyses).

Methods: Patients were randomized 1:1 to continued INX or switch to CT-P13. Serum drug levels were analysed by automated in-house assay. The primary endpoint was disease worsening according to disease-specific composite measures and/or consensus between investigator/patient. Exploratory subgroup analyses examined disease worsening and safety in SpA. The primary endpoint was analysed by logistic regression, adjusted for diagnosis and disease duration.

Results: Demographics, occurrence of disease worsening, change in disease measures and treatment-emergent adverse events (TEAE) were similar (Table), as were serum drug levels for INX and CT-P13 (Figure).

Conclusions: Explorative analyses in the NOR-SWITCH study showed similar efficacy, drug levels and safety in SpA patients switched to CT-P13 as those on continuous INX. The study was not powered to show non-inferiority within each diagnosis.

References:

Disclosure of Interest: G. Goll Consultant for: AbbVie, Boehringer Ingelheim, University Hospital, Lørenskog; 4 Dermatology, Oslo University Hospital, Oslo;

University Hospital, Trondheim, Norway;

2 Dermatology, St Olav University Hospital, Trondheim, Norway

INX

CT-P13

Baseline

Week 8

Week 16

Week 24

Week 32

Week 52

Disease worsening

53 (26.2%)

61 (29.6%)

-12.7±3.9

95% CI of group difference after 52 weeks

Data are n (%), mean (SD) or median (25–75 percentiles). 95% CI. 95% confidence interval of the adjusted treatment difference. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index. ASDAS, Ankylosing Spondylitis Disease Activity Score. FAS, Full Analysis Set. PPS, Per Protocol Set. TEAE, treatment emergent adverse events.
Objectives: To investigate changes in width of hyaline cartilage of hip joints in patients with AS under treatment with sulfasalazine and adalimumab during 12 month.

Methods: The 53 patients with AS (42 male, 9 female, average age is 37.6 years old, duration of disease is 14–152 month) were included into study. All patients were treated by NSAIDs and sulfasalazine (2 g per day) at least 3 month before study. In treatment of 27 patients (1st group) was added adalimumab (40 mg subcutaneously every 2 weeks), other 26 patients (2nd group) were left on previous treatment regime. Patients were observed during 12 months of treatment including measurements of pain visual analog scale (VAS) in hip movement, maximal distance between ankle, pelvic, X-ray and sonography of hip joints by 10–18 MHz probe. BASRI-Hips index was applied for radiographic estimation of structural damage of hip joints [3]. During sonography width of hip joint capsule and hyaline cartilage were measured. The Mann-Whitney-U test was used for comparison of changes in clinical and sonographic data between two groups of patients.

Results: After 12 month treatment period in patients of 1st group in comparison with patients of 2nd group more significant decrease of pain VAS during hip movement (on 27.3 [18.8; 32.5] mm vs 4.7 [0.5; 9.6] mm, p =<0.01), increase of maximal distance between ankle (on 124.3 [92.2;145.6] mm vs 3.5 [1.2; 6.5] mm, p =<0.05) and decrease of joint capsule width (on 2.4 [1.0; 3.6] mm vs 0.4 [0.1; 1.1] mm, p =<0.05) had been determined. In patients of 1st group width of hyaline cartilage had been increased on 0.15 [0.4; 0.22] mm, while in patients of 2nd group width of hyaline cartilage had been decreased on 0.8 [0.0; 1.4] mm (p =<0.05). These cartilage changes were accompanied by decrease of mean BASRI-Hips index on 1 point in 2nd group and absence of changes of BASRI-Hips index in 1st group. The correlation between changes in width of hip hyaline cartilage and pain VAS during movement in hip joints (∼r=0.52 [0.38; 0.61]) and maximal distance between ankle (∼r=0.47 [0.32; 0.60]) had been revealed.

Conclusions: Treatment with adalimumab leads to decrease of clinical and sonographic signs of coxitis and improvement of hyaline cartilage structure. The increase of width of hip hyaline cartilage correlates with clinical effect of treatment of coxitis in patients with AS. More prolonged observation is needed for analysis of correlation between changes in hyaline cartilage structure and radiographic progression of hip joints damage in AS.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1672
to the application of the EMA recommendation (interaction p value=0.140). In the 59 pts not treated in accordance with the EMA recommendation, the treatment effect in the sub-groups of pts without (vs with) concomitant FM was 38% vs 40% respectively, p=0.891. In the 449 pts treated in accordance with the EMA recommendation, the treatment effect in the sub-groups of pts without (vs with) concomitant FM was 50% vs 46%, p=0.042.

Conclusions: This study suggests that 1/ French rheumatologists are applying the EMA recommendation in daily practice 2/ these recommendations result in a better outcome in terms of short term symptomatic treatment effect. In this study, concomitant FM was not more frequently observed in patients without (vs with) objective sign of structural damage on inflammation and the impact of a concomitant FM was not more pronounced (or even lower) in pts without (vs with) objective sign of structural damage or inflammation.


Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4718

THU0358 ROSUVASTATIN IMPROVES NITRIC OXIDE AND ENDOTHELIAL FUNCTION AND SUPPRESSES INFLAMMATORY DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS

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Background: Nitric oxide (NO) regulates the synthesis of several inflammatory mediators, functions of inflammatory cells in the inflamed joint and plays a central role in the regulation of blood vessel tone 1. Therefore, NO inhibitors represent important therapeutic advancement in the management of inflammatory diseases. Rosuvastatin improves NO and endothelial dysfunction in patients with heart failure but its effect on NO has not yet been tested in Ankylosing Spondylitis (AS) patients.

Objectives: To investigate the effect of rosuvastatin on nitrite levels (NO surrogate) and its relationship with endothelial function and inflammatory measures in AS.

Methods: 40 consecutive patients (20 in Rosuvastatin (10 mg/day) and 20 in placebo arm) meeting the modified New York criteria for AS, with active disease despite treatment with conventional synthetic DMARDs were recruited. Serum nitrite estimation was carried out by Griess reaction. Flow-mediated dilatation (FMD) was assessed using AngioDefender. Inflammatory measures included BASDAI, BASFI, ESR and CRP. Pre-inflammatory cytokines (TNF-α, IL-6 and IL-1) were measured at baseline and after 24 weeks.

Results: After 24 weeks, significant improvement in serum nitrite was observed in rosuvastatin group (5.27±0.26 to 4.11±0.19, p<0.01) compared with placebo (5.47±0.26 to 5.36±0.23, p=0.33). At 24 weeks; FMD, TNF-α, and IL-6 improved significantly in rosuvastatin group compared with placebo. At 24 weeks, ESR, CRP, BASDAI and BASFI significantly improved in rosuvastatin group compared with placebo. After treatment with rosuvastatin, nitrite correlated inversely with FMD (r=-0.47, p=0.03) (Fig.1A) and positively with TNF-α (r=0.64, p=0.01) (Fig.1B), CRP (r=0.52, p=0.01) (Fig.1C) and LDL (r=0.54, p=0.01) (Fig.1D).

Conclusions: Rosuvastatin reduced serum nitrite concentration and improved endothelial dysfunction in AS patients. Rosuvastatin lowers the proinflammatory cytokines, especially IL-6 and TNF-α, which downregulates CRP production and thus the production of NO. Rosuvastatin also favorably improved the lipid levels in AS patients. Rosuvastatin exerts anti-inflammatory, immunomodulatory and vasculoprotective effect in ankylosing spondylitis through both cholesterol dependent and cholesterol independent pathways.

THU0359 SECUKINUMAB DEMONSTRATES CONSISTENT SAFETY OVER LONG-TERM EXPOSURE (UP TO 3 YEARS) IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: POOLED ANALYSIS OF THREE PHASE 3 TRIALS

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Background: Safety data for secukinumab in the treatment of ankylosing spondylitis (AS) have been reported from three Phase 3 studies: MEASURE 1 (NCT01358175)1, MEASURE 2 (NCT01649375)2 and MEASURE 3 (NCT02009816).2 Objectives: To report long-term (up to 3 years) pooled safety and tolerability data for secukinumab in AS (data cut-off: 25 June 2016).

Methods: Overall, 371, 219 and 226 patients with active AS were randomised in MEASURE 1, MEASURE 2 and MEASURE 3, respectively. Study design, efficacy and safety results of these studies have been published earlier.2 Secukinumab doses differed in the studies and included intravenous 10 mg/kg or subcutaneous (75–300mg) multi-dose loading, followed by subcutaneous (i.e., maintenance dosing (75, 150, or 300mg). Data collected up to the last patient performing the Wk 156 visit in MEASURE 1, the Wk 104 visit in MEASURE 2, and the Wk 52 visit in MEASURE 3 were pooled at the patient level. Exposure-adjusted incidence rates were calculated to account for differences in treatment exposure and analyses included all patients who received ≥1 dose of secukinumab 150 or 300mg.

Results: A total of 510 patients were included in the analysis (968.9 patient-years of exposure). The exposure-adjusted AE and SAE rates with secukinumab across the entire safety period were 159.2 and 5.4 per 100 patient-years, respectively. Nasopharyngitis, diaphoresis and headache were the most frequently reported AEs. The incidences of Candida infections, serious infections, inflammatory bowel disease, major adverse cardiac events, neutropenia and uveitis were low and consistent with previous reports over shorter exposure periods.2 (Table). No cases of suicidal ideation or depression were reported.

Table 1. Summary of pooled safety across 3 AS studies (Entire safety period)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>All Secukinumab Doses (N=510)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total exposure, patient-years</td>
<td>968.9</td>
</tr>
<tr>
<td>Minimum–maximum exposure (days)</td>
<td>0–1530</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>0-8</td>
</tr>
<tr>
<td>AEs by EIR: AE per 100 Patient-years (95% CI)</td>
<td>0-8</td>
</tr>
<tr>
<td>Any AE</td>
<td>159.2 (144.4, 175.1)</td>
</tr>
<tr>
<td>Any SAE</td>
<td>5.4 (4.9, 7.1)</td>
</tr>
<tr>
<td>Frequent AEsa</td>
<td>13.6 (11.2, 15.6)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6.4 (4.9, 8.3)</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>6.7 (5.1, 8.7)</td>
</tr>
<tr>
<td>Migraine</td>
<td>4.3 (3.1, 5.9)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>0-8</td>
</tr>
<tr>
<td>AEs of special interest</td>
<td>0-8</td>
</tr>
<tr>
<td>Candida infections</td>
<td>0.8 (0.4, 1.6)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>0.7 (0.3, 1.5)</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>0.4 (0.1, 1.1)</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>0.2 (0.0, 0.7)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>0.2 (0.0, 0.7)</td>
</tr>
<tr>
<td>MACE</td>
<td>0.4 (0.1, 1.1)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1.2 (0.6, 2.1)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>1.6 (0.9, 2.6)</td>
</tr>
</tbody>
</table>

aAEs that occurred in Any secukinumab group with an IR >4.0 during the entire safety period. AE, adverse event; CI, confidence interval; EIR, exposure adjusted incidence rate per 100 patient-years; MACE, major adverse cardiac events; N, number of patients in the analysis; n, number of patients with event; SAE, serious adverse event.

Conclusions: This longer-term safety assessment of secukinumab in the treatment of AS was consistent with previous reports and did not identify any new safety signals.


Disclosure of Interest: A. Deodhar Grant/research support from: AbbVie, Amgen,
Improvments in sleep problems and pain in patients with active ankylosing spondylitis treated with intravenous golimumab: 28-week results of the phase III GO-ALIVE trial

A. Deodhar, J.D. Revillée, E.K. Chan, S. Peterson, N. Li, E. Hsiu, L. Kim, K.H. Lo, D.D. Harrison, C. Han, T. Fox, Shareholder of: Novartis, Employee of: Novartis, T. Fox

Objectives: To investigate the effect of intravenously administered (IV) Golimumab (per modified New York criteria) and BASDAI in patients with active Ankylosing Spondylitis (AS).

Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Pts (aged >18 years) had a diagnosis of definite AS (per modified New York criteria) and BASDAI >4, total back pain visual analogue scale (VAS) >40 mm, CRP >0.3 mg/dL. At baseline, 208 pts were randomized to IV golimumab 2mg/kg (N=105) at Wks 0, 4, and every 8 wks or placebo (N=103) at Wks 0, 4, and 12, with crossover to IV golimumab at Wk 16 and through Wk 52. Sleep problems were assessed using the Medical Outcomes Study Sleep Scale (MOS-SS). An increase in score also used to generate the composite Sleep Problems Index. An increase in score through Wk 52. Sleep problems were assessed using the Medical Outcomes Study Sleep Scale (MOS-SS). An increase in score also used to generate the composite Sleep Problems Index.

Results: Mean changes in MOS-SS Sleep Index and 6 subscales are presented through Wk 52. Sleep problems were assessed using the Medical Outcomes Study Sleep Scale (MOS-SS). An increase in score also used to generate the composite Sleep Problems Index. An increase in score also used to generate the composite Sleep Problems Index. An increase in score also used to generate the composite Sleep Problems Index. An increase in score also used to generate the composite Sleep Problems Index.

Conclusions: Adult pts with active AS treated with IV golimumab showed improvements in sleep problems, total back pain, and night back pain. Night back pain improvement was associated with improvement in sleep problems.


DOI: 10.1136/annrheumdis-2017-eular.4894

PRESCRIPTION PATTERNS OF BIOLOGICAL DISEASE MODIFYING DRUGS AND BIOSIMILARS IN ANKYLOSING SPONDYLITIS – A COLLABORATION BETWEEN BIOLOGICAL REGISTERS IN THE FIVE NORDIC COUNTRIES


Objectives: To explore the prescription patterns of old (TNF-inhibitors) and newer bDMARDs (secukinumab, ustekinumab) including bsDMARDs (SB4, CT-P13) over time in AS in the Nordic countries in order to illustrate the potential of a common Nordic collaboration.

Methods: Data regarding the numbers of AS patients (pts) (ICD10 code M45) who initiated bDMARD treatment (irrespective of treatment course number) during the period 2011–2016 were collected from the Nordic rheumatologic biological registries Sbgr (Sweden), Nor-DMARD (6 Norwegian treatment centres), DANBIO (Denmark), ROB-FIN (Finland, 2011–2015) and ICEBIO (Iceland).

Results: In total, 6,610 bDMARD treatment initiations were identified (Sweden 3654, Norway 1078, Denmark 782, Finland 789, Iceland 307). The prescription patterns of bDMARDs changed substantially over time. In 2016, the number of pts initiating a bsDMARDs exceeded those starting an originator bDMARD (figure). Few patients were treated with ustekinumab (Denmark <10 pts, Finland <10, Sweden 26) and secukinumab (Denmark <10 pts, Sweden 57).

Figure: The 5 Nordic countries, total number of AS patients initiating bDMARD per year

Conclusions: The use of bsDMARDs in AS is rapidly increasing. The use of drugs with new modes of action is still low, which illustrates the need for collaboration across countries to provide real life data with sufficient power for new innovative therapies in the future. The Nordic rheumatologic registries represent a unique resource for these efforts.
opportunity to study effectiveness and safety of bDMARDs, including bsDMARDs in AS.

**Acknowledgements:** Partly funded by a grant from NordForsk

**Disclosure of Interest:** B. Glintborg Grant/research support from: abbvie, K. Chatzidionysiou: None declared, J. Asklipidou Grant/research support from: AbbVie, Eli Lilly, Janssen, Merck, Roche, UCB, Samsung, K. Aaltomaa Speakers bureau: AbbVie, BMS, Janssen, MSD, Pfizer, Roche, UCB, E. Kristianslund: None declared, B. Gudjonsson Grant/research support from: Actavis, Celgene, MSD, Pfizer, D. Nordström Speakers bureau: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB, M. Helland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, Speakers bureau: BMS, MSD, UCB, Janssen Pharmaceuticals, L. E. Kristensen Speakers bureau: AbbVie, Pfizer, Biogen, Agen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen pharmaceuticals, T. Jørgensen Speakers bureau: AbbVie, Roche, Novartis, UCB, Biogen, K. E. Korneski: None declared, G. Gronndal: None declared, S. Ernstman: None declared, J. Joensuu Grant/research support from: Pfizer, T. Kvien Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, E. Lie Speakers bureau: AbbVie, Celgene, Hospira, Pfizer, K. Fagerl: None declared, A. J. Girson: None declared, H. Jonsson: None declared, L. Jacobsson Consultant for: Abbvie, Celgene, MSD, Novartis, UCB

**DOI:** 10.1136/annrheumdis-2017-eular.1891

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**THU0362 EFFECT OF BIOTECHNOLOGICAL DRUGS ON EXTRA-ARTICULAR MANIFESTATIONS OF ANKYLOSING SPONDYLITIS: SYSTEMATIC REVIEW**

A.L.R. Pinto, 1 C.V. Pessoa

**Conclusions:**

- Certolizumab pegol 0,0 0,9
- Golimumab No results No results
- Etanercept 1,1 0,7
- Infliximab No results No results

**Uveitis Randomized Controlled Trials**

<table>
<thead>
<tr>
<th>Drug</th>
<th>% patients with events under therapy</th>
<th>% patients with events under placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>2.9</td>
<td>8.6</td>
</tr>
<tr>
<td>Etanercept</td>
<td>1.1</td>
<td>3.5</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>No results</td>
<td>No results</td>
</tr>
<tr>
<td>Golimumab</td>
<td>No results</td>
<td>No results</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>0.9</td>
<td>2.8</td>
</tr>
</tbody>
</table>

**Table 1. Percentage of patients with events of uveitis on Randomized Controlled Trials**

**Methods:** To analyze evidence on efficacy of anti-TNF drugs approved for AS treatment in UV, IBD and dactylitis as associated with.

**Objective:** To analyze evidence on efficacy of anti-TNF drugs approved for AS treatment in UV, IBD and dactylitis associated with.

**Results:** Fifty studies were included (seventeen RCTs, six meta-analyses and twenty seven observational studies). From the RCT we extracted the results presented in Table 1 for uveitis and in Table 2 for IBD. None reported results for dactylitis. Of the meta-analyses included, only one presents results. These one shows that the incidence of uveitis is lower in patients taking etanercept than placebo (incidence of 8.6 and 19.3 per 100 patients per year, respectively; p value =0.03). In OS comparing different drugs, in one the risk of developing uveitis (UV), inflammatory bowel disease (IBD) and dactylitis is scarce.

**Background:** Treatment with biotechnological agents (infliximab, etanercept, adalimumab, golimumab and certolizumab pegol) in ankylosing spondylitis is effective. However, evidence regarding the potential efficacy of these anti-TNF drugs in the extra-articular manifestations of ankylosing spondylitis, namely in uveitis (UV), inflammatory bowel disease (IBD) and dactylitis is scarce.

**Objective:** To analyze evidence on efficacy of anti-TNF drugs approved for AS treatment in UV, IBD and dactylitis associated with.

**Methods:** A systematic literature review was performed using the PubMed and Cochrane Library databases. Randomized controlled trials (RCT), meta-analyses and observational studies (OS) reporting efficacy of anti-TNF agents in extra-articular manifestations of AS were included.

**Results:** Results: Fifty studies were included (seventeen RCTs, six meta-analyses and twenty seven observational studies). From the RCT we extracted the results presented in Table 1 for uveitis and in Table 2 for IBD. None reported results for dactylitis. Of the meta-analyses included, only one presents results. These one shows that the incidence of uveitis is lower in patients taking etanercept than placebo (incidence of 8.6 and 19.3 per 100 patients per year, respectively; p value =0.03). In OS comparing different drugs, in one the risk of developing uveitis (UV), inflammatory bowel disease (IBD) and dactylitis is scarce.

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IMMUNOGENICITY OF ANTI-TNF DRUGS AND CLINICAL RESPONSE IN PATIENTS WITH SPONDYLOARTHROPATHIES

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Background: Antidrug antibodies (ADAB) seem to be associated with a loss of response in immune-mediated inflammatory diseases (1) and in psoriatic arthritis (2). Objectives: To assess the effect of ADAB on clinical response in patients with spondyloarthritis (SpA) treated with anti-TNF drugs. Methods: We conducted a systematic literature review of controlled trials and observational studies looking at the effect of ADAB on response to anti-TNF drugs (Adalimumab (ADL), Certolizumab (CTZ), Etanercept (ETA), Golimumab (GOL) and Infliximab (INF)) in patients with axial or peripheral SpA. Databases analysed were PubMed, the Cochrane library, and ACR/EULAR meeting abstracts, until January 2017. A meta-analysis was performed using the inverse variance approach and statistical heterogeneity was assessed with the Cochran Q-test. Results: The study included 503 patients with axSpA treated with ADL (172[34.2%] women, mean age [±SD] 40.5 [±13.2] years, mean disease duration 9.7 [±14.7] years), receiving a total of 675 lines of treatment ([I-line n=503, II-line n=118, III-line n=54]) with a TNFα antagonist ([IFX, 173 infliximab [IFX], 173 adalimumab [ADL], 89 golimumab [GOL], 141 etanrect [ETNI]). At the time of TNFI introduction, 28.6% patients claimed at least one EAM (IBD 11.3%, uveitis 10.9%, and PsO 8.8%). The baseline presence of at least one EAM was associated with a more frequent prescription of an anti-TNF monoclonal antibody rather than etanercept (34.1% versus 21.9%, respectively, p=0.005). In detail, EAMs were found in 41.6, 39.9, 29.8, and 21.9% patients treated with GOL, ADA, IFX, or ETN, respectively. The prevalence of IBD was significantly higher (p=0.004) in patients treated with ADA (12.7%), IFX (14.3%), or GOL (11.2%) compared with ETN (4.9%). Uveitis was numerically more frequent in GOL (20.2%) and ADA (13.5%) rather than IFX (9.5%) and ETN (9.9%) groups. Finally, PsO was similarly high in patients treated with ADA (10.9%) and GOL (10.1%), and numerically lower in the ETN (7.1%) and IFX (5.9%) groups. Conclusions: In our cohort of axSpA patients treated with TNFis, EAMs were highly heterogeneous. The presence of extra-articular involvement has been carefully taken into account when a TNF was required to better control the disease. In particular, IBD and uveitis drove more frequently the choice toward an anti-TNF monoclonal antibody instead of the receptor. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.7379

GASTROINTESTINAL INFECTIONS IN PATIENTS WITH SPONDYLOARTHROPATHIES TREATED WITH ANTI-TNF DRUGS: RESULTS OF GISEA REGISTER

1Department of Rheumatology, Gaetano Pini Institute, 2Rheumatology Institute of Lucania (IRel) - Rheumatology Department of Matera; Potenza; 3UOC Reumatologia, Dipartimento di Medicina, AOUI, Verona; 4Department of Clinical Sciences and Community Health, Division of Rheumatology, University of Milan and Gaetano Pini Institute, Milan, Italy

Background: Extra-articular manifestations (EAMs), such as uveitis, inflammatory bowel diseases (IBD) and psoriasis (PsO), frequently complicate the disease course of patients with axial spondyloarthritis (axSpA), although prevalence data on this regard are still controversial. The occurrence of EAMs might also contribute to the decision of introducing a biologic therapy and even influence the choice between the available TNF inhibitors (TNFIs). Objectives: The aim of this study was to retrospectively evaluate the prevalence of IBD, uveitis, PsO, and IBD, uveitis and PsO in patients treated with TNFis, investigating how these influences the choice of treatment. Methods: Clinical data from axSpA patients treated with a TNFi between 2003 and May 2016 where obtained from a multicentre registry. Prevalence of EAMs (uveitis, IBD and PsO) was calculated at the time of TNFi prescription, evaluating the distribution according to drug subgroup. Results: The study included 503 patients with axSpA (172[34.2%] women, mean age [±SD] 40.5 [±13.2] years, mean disease duration 9.7 [±14.7] years), receiving a total of 675 lines of treatment ([I-line n=503, II-line n=118, III-line n=54]) with a TNFα antagonist ([IFX, 173 infliximab [IFX], 173 adalimumab [ADL], 89 golimumab [GOL], 141 etanrect [ETNI]). At the time of TNFI introduction, 28.6% patients claimed at least one EAM (IBD 11.3%, uveitis 10.9%, and PsO 8.8%). The baseline presence of at least one EAM was associated with a more frequent prescription of an anti-TNF monoclonal antibody rather than etanercept (34.1% versus 21.9%, respectively, p=0.005). In detail, EAMs were found in 41.6, 39.9, 29.8, and 21.9% patients treated with GOL, ADA, IFX, or ETN, respectively. The prevalence of IBD was significantly higher (p=0.004) in patients treated with ADA (12.7%), IFX (14.3%), or GOL (11.2%) compared with ETN (4.9%). Uveitis was numerically more frequent in GOL (20.2%) and ADA (13.5%) rather than IFX (9.5%) and ETN (9.9%) groups. Finally, PsO was similarly high in patients treated with ADA (10.9%) and GOL (10.1%), and numerically lower in the ETN (7.1%) and IFX (5.9%) groups. Conclusions: In our cohort of axSpA patients treated with TNFis, EAMs were highly heterogeneous. The presence of extra-articular involvement has been carefully taken into account when a TNF was required to better control the disease. In particular, IBD and uveitis drove more frequently the choice toward an anti-TNF monoclonal antibody instead of the receptor. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5726

DO EXTRA-ARTICULAR MANIFESTATIONS AFFECT THE CHOICE OF BIOLOGIC THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS? A MULTICENTRE REAL-LIFE ANALYSIS

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Background: Extra-articular manifestations (EAMs), such as uveitis, inflammatory bowel diseases (IBD) and psoriasis (PsO), frequently complicate the disease course of patients with axial spondyloarthritis (axSpA), although prevalence data on this regard are still controversial. The occurrence of EAMs might also contribute to the decision of introducing a biologic therapy and even influence the choice between the available TNF inhibitors (TNFIs). Objectives: The aim of this study was to retrospectively evaluate the prevalence of IBD, uveitis, PsO, and IBD, uveitis and PsO in patients treated with TNFis, investigating how these influences the choice of treatment. Methods: Clinical data from axSpA patients treated with a TNFi between 2003 and May 2016 where obtained from a multicentre registry. Prevalence of EAMs (uveitis, IBD and PsO) was calculated at the time of TNFi prescription, evaluating the distribution according to drug subgroup. Results: The study included 503 patients with axSpA (172[34.2%] women, mean age [±SD] 40.5 [±13.2] years, mean disease duration 9.7 [±14.7] years), receiving a total of 675 lines of treatment ([I-line n=503, II-line n=118, III-line n=54]) with a TNFα antagonist ([IFX, 173 infliximab [IFX], 173 adalimumab [ADL], 89 golimumab [GOL], 141 etanrect [ETNI]). At the time of TNFI introduction, 28.6% patients claimed at least one EAM (IBD 11.3%, uveitis 10.9%, and PsO 8.8%). The baseline presence of at least one EAM was associated with a more frequent prescription of an anti-TNF monoclonal antibody rather than etanercept (34.1% versus 21.9%, respectively, p=0.005). In detail, EAMs were found in 41.6, 39.9, 29.8, and 21.9% patients treated with GOL, ADA, IFX, or ETN, respectively. The prevalence of IBD was significantly higher (p=0.004) in patients treated with ADA (12.7%), IFX (14.3%), or GOL (11.2%) compared with ETN (4.9%). Uveitis was numerically more frequent in GOL (20.2%) and ADA (13.5%) rather than IFX (9.5%) and ETN (9.9%) groups. Finally, PsO was similarly high in patients treated with ADA (10.9%) and GOL (10.1%), and numerically lower in the ETN (7.1%) and IFX (5.9%) groups. Conclusions: In our cohort of axSpA patients treated with TNFis, EAMs were highly heterogeneous. The presence of extra-articular involvement has been carefully taken into account when a TNF was required to better control the disease. In particular, IBD and uveitis drove more frequently the choice toward an anti-TNF monoclonal antibody instead of the receptor. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5779
Furthermore, univariate models showed that age (p=0.738), disease duration (p=0.090), previous DMARDs (p=0.616), and HAO (p=0.674) and BASFI (scores p=0.850) were not statistically significant predictors of gastrointestinal infections.

Conclusions: The incidence rate of gastrointestinal infections in SpA patients treated with anti-TNF drugs is not increased. Being female and having comorbidities are predictive factors of gastrointestinal infections.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5936

**THU0368**

**THE INFLUENCES OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON SERUM VEGF AND BMP-2 LEVELS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS**

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Background: VEGF has been found abnormal in patients with SpA and related to disease activity [1, 2]. BMP-2 has a function of promoting the osteothesis formation, and may be involved in the integration process of AS spine [3, 4]. VEGF and BMP-2 interact with each other, participating in the formation of osteoblast [5]. COX-2 works together with the expressions of BMP2 and VEGF is an important factor of heterotopic ossification [6].

Objectives: To investigate the serum levels of VEGF and BMP-2 in axSpA treated with different anti-TNF drugs and their possible relationship with disease activity.

Methods: 120 patients with axSpA were randomized administered with imrecoxib or celecoxib respectively for 3 months. Serum VEGF and BMP-2 were detected. ESR, CRP, BASDAI, BASFI and SPARC were measured.

Results: A statistically significant change was found in ESR, BASDAI, patients global assessment of disease activity, Schober test and intermalleolar distance (r=0.628, 0.542, 0.238, 0.299, 0.353, 0.369, 0.373, 0.359, -0.274, P <0.05). And the BMP-2 levels were correlated with CRP and lumbar side flexion (r=0.213, -0.190, P <0.05). Serum VEGF levels were significantly increased in HLA-B27-positive patients than in HLA-B27-negative ones (P <0.05).

Conclusions: NSAIDs can not only improve symptoms and function, but also reduce saccroilitis possibly by affecting the levels of VEGF and BMP-2. Imrecoxib and celecoxib have the same efficacy. The response to treatment was correlated with the expression of HLA-B27.

References:


Secukinumab 150mg provides sustained improvements in the signs and symptoms of active ankylosing spondylitis with high retention rate: 3-year results from Phase III trial, measure 2


Background: Secukinumab improved signs and symptoms of ankylosing spondylitis (AS) over 2 years in the MEASURE 2 study (NCT01649376).1,2

Objectives: To report the efficacy and safety of secukinumab over 3 years from the MEASURE 2 study.

Methods: 219 patients (pts) with active AS were randomised to subcutaneous secukinumab 150mg (72 pts), 75mg (73 pts) or placebo (PBO, 74 pts). At Week (Wk) 16, PBO treated pts were re-randomised 1:1 to secukinumab 150mg or 75mg, irrespective of clinical response. Pts initially randomised to secukinumab and those who switched from PBO to secukinumab at Wk 16 were included in the analysis (secukinumab 150mg, N=106 and secukinumab 75mg, N=105).

Outcome measures were ASAS20 and ASAS40 at Wk 156, ASAS-6/5/6, BASDAI, ASDAS CRP, ASDAS-CRP Inactive Disease, ASDAS-CRP partial remission, ASAS partial remission.

Results: 156 Wks (n=156) achieved ASAS 20, 18 (60%) ASAS 40, 12 (40%) of patients with marked ASAS 5/6 responses, and 72.4% (76/105) for 75mg. Higher discontinuation rates for 75mg were in part due to lack of efficacy or patient/guardian decision. Efficacy reported as observed. Safety analyses included all pts who received ≥1 dose of secukinumab.

Conclusions: Secukinumab 150mg provided sustained improvement in the signs & symptoms along with physical functions with >80% retention rate through 3 years in pts with AS. Safety profile remained favourable and was consistent with previous reports.1,2

References:

ASAS, Assessment of Spondyloarthritis International Society criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high sensitivity C-reactive protein; n, number of responders; N, number of pts in the treatment group with evaluation TD: 36.9±3.9 (87) 28.4±14.4 (94) p <0.0001.

Table 1. Summary of Efficacy Results at Wks 52 and 156

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wk</th>
<th>Secukinumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20, % responders</td>
<td>52</td>
<td>74.2 (69/93)</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>70.1 (61/87)</td>
</tr>
<tr>
<td>ASAS40, % responders</td>
<td>52</td>
<td>57.0 (53/93)</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>60.9 (53/87)</td>
</tr>
<tr>
<td>ASDAS-CRP Inactive Disease, % pts</td>
<td>52</td>
<td>19.4 (18/93)</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>25.6 (22/87)</td>
</tr>
<tr>
<td>ASAS 5/6, % responders</td>
<td>52</td>
<td>61.3 (57/93)</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>58.6 (51/87)</td>
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<tr>
<td>sSD (N)</td>
<td>52</td>
<td>-3.2±2.3 (93)</td>
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<td></td>
<td>156</td>
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</tr>
<tr>
<td>tSD (N)</td>
<td>52</td>
<td>-7.6±7.9 (94)</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>6.4±7.3 (85)</td>
</tr>
<tr>
<td>ASAS partial remission, % pts</td>
<td>52</td>
<td>24.7 (29/93)</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>32.2 (28/87)</td>
</tr>
</tbody>
</table>

ASAS40, % responders (n/N) 52 57.0 (53/93) 43.2 (38/90) 156 60.9 (53/87) 38.2 (29/76)

ASAS5/6, % responders (n/N) 52 61.3 (57/93) 49.4 (44/90) 156 58.6 (51/87) 40.8 (34/85)

ASAS partial remission, % pts (n/N) 52 24.7 (29/93) 18.0 (10/69) 156 32.2 (28/87) 11.8 (9/76)

THU0369

Increased interleukin-17a concentration remains high in patients with ankylosing spondylitis treated with tumour necrosis alpha inhibitors within the year

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Background: Ankylosing spondylitis (AS) is associated with changes in the serum cytokines concentrations. During the treatment cytokines profile could change in different manner.

Objectives: The aim of the study was to evaluate the changes in concentration of interleukin-17A (IL-17A) in patients with AS, treated with tumour necrosis factor alpha inhibitors (anti-TNFα) during the year.

Methods: 30 patients with AS, fulfilled m. New-Y ork criteria, with BASDAI ≤4.0 and NSAIDs non-responders were involved in the study. Mean age of AS patients at baseline was 36.3±9.19 years (M ± SD), the duration of AS was 11.4±9.6 years, 22 (73.3%) of patients – male. 20 healthy volunteers were involved as controls (mean age 40.1±7.7 years, male - 12 (60%). All AS patients were treated during the year with Remicade (infliximab, MSD®) - 5 mg/kg at the recommended scheme. BASDAI, ASDAS CRP indices were calculated. C-RP, TNFα and IL-17A levels were measured before the treatment with anti-TNFα (baseline) and 52±2 weeks after the baseline. Number of patients achieved ASAS 20, ASAS 40 responses, and ASAS partial remission was evaluated. The statistics was performed with SPSS17.

Results: Baseline concentrations of TNFα and IL-17A in AS patients were higher than in healthy subjects (28.4±14.4 and 2.4±2.1, respectively, p <0.000). Significant reduction of AS activity, but not of IL-17A serum concentration was marked at week 52, Table 1. 24 (80%) achieved ASAS 20, 18 (60%) – ASAS 40, 12 (40%) of patients with...
AS achieved ASAS partial remission. IL-17A was lower in patients who achieved remission compared to those who achieved the remission.

**Disclosures:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3321

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**THU0372**  
**EFFECT OF TNFI VERSUS NSAID ON SPINAL RADIOGRAPHIC PROGRESSION OVER 4 YEARS IN EARLY ANKYLOSING SPONDYLITIS: RESULTS FROM TWO OBSERVATIONAL COHORTS IN SOUTH KOREA

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1Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul; 2Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Gyeonggi-do, Korea, Republic Of

**Background:** It is uncertain whether early suppression of inflammation by tumor necrosis factor inhibitor (TNFI) leads to a decreased radiographic progression in axial spondyloarthritis (axSpA).

**Objectives:** To compare the radiographic progression over 4 years in patients with early ankylosing spondylitis (AS) using TNFI versus nonsteroidal antiinflammatory drug (NSAID)

**Methods:** A total of 215 patients with early AS (symptom duration<10 years) were included based on the availability of radiographs at baseline and 2- and/or 4-years of follow up. Among them, 135 patients with TNFI were from SNUH-biologics cohort (TNFi group) and other 80 patients with NSAID were from control cohort in Seoul National University Bundang Hospital (NSAID group). Radiographic progression was assessed by two blinded readers using modified Stokes AS Spinal Score (mSASSS). Linear mixed model was applied to compare the radiographic progression between the two groups after adjustment for clinical factors. We also performed a sensitivity analysis after the propensity score matching in which age, smoking status, baseline CRP and baseline mSASSS were included as covariates.

**Results:** Patients in the TNFI group showed higher baseline BASDAI (6.7 vs. 3.1) and CRP (2.2 vs. 1.1mg/dL) as compared with those in the NSAID group. There were no differences between the two groups regarding age, gender, HLA-B27, smoking status and baseline radiographic damage. Overall, radiographic progression rate (95% CI) during the observation was 0.72 (0.57–0.87) unit/year. TNFI group showed significantly slower progression than NSAID group (β=0.33 unit/year, p<0.042). This result was consistent after adjusting for age, smoking status, baseline CRP and presence of baseline syndesmophytes (β=0.50 unit/year, p<0.001) (Table). In the subgroup analysis of patients without baseline syndesmophytes, TNFI group showed no radiographic progression over time whereas NSAID group did not (0.03 [-0.22–0.27] vs. 0.45 [0.20–0.71] unit/year). These results were not changed when the same analysis was performed in the post-matched population (78 TNFi group vs. 78 NSAID group).

**Conclusions:** In patients with early AS, TNFI led to a decreased radiographic progression as compared with NSAID treatment. This result suggests that early and durable suppression of inflammation using TNFI can have beneficial effect on the radiographic outcome of AS.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3321

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**Table 1. Radiographic progression over time in early AS patients using NSAID vs. TNFi**

<table>
<thead>
<tr>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
<th>p value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression coefficient (95% CI)</td>
<td>Regression coefficient (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age&lt;40</td>
<td>0.82 (0.48–1.16)</td>
<td>&lt;0.001</td>
<td>0.27 (0.07–0.61)</td>
</tr>
<tr>
<td>Ever-smoker</td>
<td>0.31 (-0.01–0.62)</td>
<td>0.056</td>
<td>0.03 (0.20–0.37)</td>
</tr>
<tr>
<td>Baseline CRP (mg/dL)</td>
<td>0.12 (0.05–0.19)</td>
<td>0.001</td>
<td>0.10 (0.04–0.16)</td>
</tr>
<tr>
<td>Baseline syndesmophytes</td>
<td>1.30 (1.00–1.62)</td>
<td>&lt;0.001</td>
<td>1.14 (0.80–1.48)</td>
</tr>
<tr>
<td>Group</td>
<td>0.33 (-0.05–0.61)</td>
<td>0.042</td>
<td>0.50 (-0.79–2.02)</td>
</tr>
<tr>
<td>NSAID group</td>
<td>0.93 (0.68–1.18)</td>
<td>&lt;0.001</td>
<td>0.45 (0.18–0.71)</td>
</tr>
<tr>
<td>TNFI group</td>
<td>0.60 (0.40–0.79)</td>
<td>&lt;0.001</td>
<td>0.06 (0.31–0.19)</td>
</tr>
</tbody>
</table>

*Regression coefficient indicates the progression of mSASSS over one year. Gender, HLA-B27, baseline BASDAI and time-averaged NSAID index were not included because they did not show a significant (p<0.1) interaction with time in the univariate analysis.

**Conclusions:** In patients with early AS, TNFI led to a decreased radiographic progression as compared with NSAID treatment. This result suggests that early and durable suppression of inflammation using TNFI can have beneficial effect on the radiographic outcome of AS.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3321
THU0373 USE OF CORTICOSTEROID HIP JOINT INJECTIONS IN Spondyloarthritis Patients under TNF Alpha Inhibitors

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Background: The hip disease is a serious complication of spondyloarthritis (SpA), engaging the functional prognosis of patients. TNF alpha inhibitors are a breakthrough for the treatment of SpA and the management of this complication.

Objectives: To assess the efficacy of TNF alpha inhibitors on hip involvement in SpA by evaluating the use of intra-articular corticosteroid infiltrations.

Methods: Observational cohort study that included 94 SpA patients with hip disease (ASAS2009). Two groups were studied. Group 1 (G1): patients under anti-TNF alpha therapy and Group 2 (G2): TNF alpha inhibitors naïve patients. Clinical (BASDAI, BASFI, hip (pain/mobility), index of severity for osteoarthritis for the hip (ISH)), biological (CRP) data were assessed and the use of corticosteroid hip joint infiltration was compared. Evaluations were performed and compared between the 2 groups at baseline (T0), two years (T2) and Tn (greater than or equal to 3 years). The correlation study was made by Pearson test. A correlation was considered statistically significant if p < 0.05.

Results: Group 1 and 2 included 48 and 46 patients respectively. The socio demographic and clinical characteristics of the disease were comparable between the two groups. Significant and radiological assessment of the two groups of patients were comparable at T0. Group 1 had however a more active disease and a greater functional impairment. NSAIDs were prescribed in 40% of patients in G1 and 86% in G2 (p < 0.0001). DMARDs were prescribed in 20 patients in G1 and in 22 patients in G2 (p < 0.06). In G1 patients received infliximab, adalimumab and etanercept in 48%, 15% and 37% of cases respectively. Four patients of G1 and three of G2 patients received intra-articular corticosteroid infiltration in the year prior to the initial assessment (p = 0.7). Assessment at T2 showed a greater improvement in clinical and biological parameters of the disease in group 1 than in group 2 (p2-T0) significantly lower in group 1 for the BASDAI (p < 0.0001), the BASFI (p < 0.0001) and the ISH (p = 0.017). The number of painful hip was significantly lower in group 1 (p < 0.0001). The evaluation at Tn showed a sustained clinical and biological efficacy of TNF alpha inhibitors in Group 1. The use of corticosteroid injections was significantly higher in group 2. Table 1 summarizes the assessment of different parameters at T2 and Tn.

Conclusions: Hip involvement is a marker of severity of spondyloarthritis. Anti-TNF alpha treatment is effective on hip disease. It reduces the use of intra-articular injections of corticosteroids.

Disclosure of Interest: None declared


THU0374 LONG-TERM EFFECTS OF TNF-ALPHA INHIBITORS ON BONE MINERAL DENSITY AND THE INCIDENCE OF VERTEBRAL FRACTURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) is not only characterized by pathological bone formation leading to ankylosis but also by bone loss which may lead to vertebral fractures (VFx). TNF-alpha inhibitors (TNFi) have proven to be effective in blocking the inflammation process. A few studies also showed an increase of bone mineral density (BMD) in AS patients treated with TNFi but the incidence of VFx after two years of treatment was increased.

Objectives: To evaluate the long-term effect of TNFi on BMD and the incidence of VFx in patients with AS.

Methods: Consecutive TNFi naive patients diagnosed with AS according to the Modified New York criteria were included. Patients were recruited from the VUMc and the Amsterdam outpatient clinic Reade and were treated with TNFi for 4 years. BMD at hip and lumbar spine (LS) were measured at baseline, after 2 and 4 years. T-scores were categorized as “normal BMD”, “osteopenia” and “osteoporosis”, based on the WHO osteoporosis criteria.3 The incidence of VFx was determined by two observers using the Genant method.6

Results: In total, 70 AS patients with complete datasets (67.1% male) were included. The mean age was 41.6 years and the disease duration (time since diagnosis) was 9.8 years. At baseline 42% of the patients had a decreased BMD of the hip and 34% of the spine, of whom 19 patients (27%) had both a decreased hip BMD as well as a decreased lumbar BMD. The BMD of spine and hip improved after 2 and 4 years of TNFi treatment (Table 1). In 7 patients (10%), 8 VFx were observed both at baseline and after 2 years. After 4 years of TNFi-treatment 11 VFx were observed in 9 patients.

Conclusions: After 4 years, 2 out of 9 patients with ≥1 VFx had a decreased BMD at hip and lumbar spine whereas the other 7 patients had a normal BMD. The majority of VFx was localized in the mid or lower thoracic spine.

Table 1. BMD measurement in spine and hip of 70 AS patients treated with TNFi

Abstract THU0374 – Table 1. Comparison of Clinical and biological variations between the 2groups at T2 and Tn

THU0375 CHARACTERISTICS ASSOCIATED WITH IMPROVEMENTS IN SPARCC SIJ AND ASDAS SCORES IN PATIENTS WITH NON-RADIODIGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH ETANERCEPT

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Background: The EMBARK trial of etanercept (ETN) (NCT01258738) has demonstrated the long-term efficacy of ETN in patients with non-radiographic axial spondyloarthritis (nr-axSpA) and shown correlations between decreased inflammation and clinical outcomes.2

Objectives: To determine which baseline (BL) characteristics are associated with clinical improvements after 48 weeks of treatment with ETN in patients with nr-axSpA.

Methods: This post hoc analysis was performed on data from patients with nr-axSpA enrolled in the 92-week open-label phase of the EMBARK trial. The primary analysis population was the EMBARK modified intent-to-treat (mITT) population (patients who had ≥1 dose of ETN, had ≥1 on-therapy evaluation, and met the Assessment in Ankylosing Spondylitis classification criteria for axSpA). Patients’ SpondyloArthritis Research Consortium of Canada (SPARCC) sacroiliac joint (SIJ) scores and Ankylosing Spondylitis Disease Activity Scores (ASDAS) were recorded, and patients were divided into 4 quadrants (Q1–4) based on the minimally important change (MIC) for each instrument (SPARCC SIJ change from Baseline above [≥2]; ASDAS cTB <1; 1). Patients in Q1 achieved MIC in SPARCC SIJ but did not achieve MIC in ASDAS. Q2 did not achieve MIC in SPARCC SIJ and did not achieve MIC in ASDAS. Q3 did not achieve MIC in SPARCC SIJ but achieved MIC in ASDAS. Q4 achieved MIC in SPARCC SIJ and achieved MIC in ASDAS. Missing data were imputed using last observation carried forward. P-values were obtained using the Chi-squared test (categorical variables) and the Kruskal-Wallis test (continuous variables) in order to compare BL characteristics across improvement status. Multivariable
multinominal logistic regression modelling was used to calculate which BL characteristics were associated with clinical improvements when adjusted for all other BL characteristics.

Results: At screening, male patients had significantly higher median SPARCC SIJ scores compared with female patients (4.83 [range 0.0–48.0] vs 1.5 [0.0–32.0], P < 0.0001). Male patients comprised 59.1% of 194 patients included in either SPARCC SIJ scores, ASDAS or both (Q1/3, Figure). There was a statistically significant difference in the number of male versus female patients who achieved MIC in both scores (Q4), compared with patients who achieved MIC in only one or neither (Q1–3, Figure) (P < 0.0001). However, multinominal logistic regression modelling showed that age (P=0.0358), BL ASDAS (P=0.0001), and screening SPARCC Spine (P=0.0358) and SPARCC SIJ (P=0.0001) scores, not gender, were significantly associated with achievement of MIC in both SPARCC SIJ and ASDAS at wk48 for the total population (after adjustment for the effects of other variables).

Figure: Numbers of Patients who Did or Did Not Achieve MIC in SPARCC SIJ Score (≥2.5 cU/mL) or ASDAS (≥1.1 cU/mL).

Conclusions: Although BL summaries showed a significant difference in gender across quadrants, the BL SPARCC SIJ score was strongly correlated with gender (male patients had more inflammation). When both were included in a multivariable model, gender was non-significant. Only age, BL ASDAS, and screening SPARCC SIJ and Spine scores were associated with MIC after 48 weeks of etanercept treatment.

References:


DOI: 10.1136/annrheumdis-2017-eular.1873

THU0376 REAL-WORLD USE OF SECUKINUMAB WITH AND WITHOUT A LOADING REGIMEN AMONG PATIENTS WITH ANKYLING SPONDYLITIS IN THE UNITED STATES: PATIENT PROFILE AND DOSING

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Background: Secukinumab is a fully human anti-interleukin-17 monoclonal antibody for the treatment of patients with moderate to severe plaque psoriasis, psoriatic arthritis and ankylosing spondylitis (AS), and may be administered with or without a loading regimen of 150 mg at weeks 0, 1, 2, 3 and 4 followed by maintenance dosing every 4 weeks. The dosing pattern of secukinumab in a real-world setting of patients with AS has not been evaluated in clinical practice in the United States.

Methods: Retrospective data from the Symphony Health Solutions Lx commercial claims database were used to identify AS patients who had ≥1 secukinumab treatment between January 15, 2016 and June 30, 2016. Patients eligible for inclusion were ≥18 years of age who had the diagnosis of AS and ≥1 pharmacy or medical claim in the 12 months prior to their first secukinumab treatment (index date). Patient demographics and secukinumab dosage were examined at the index date. Clinical characteristics, comorbidities and treatment history in the 12 months prior to the index date were identified and presented by use versus no use of a loading regimen of secukinumab.

Results: A total of 152 patients who initiated secukinumab were included in this study; the mean (SD) age of included patients was 45.3 (11.1) years and 53.9% were female. Of the 152 patients, 119 patients (78.3%) received a loading regimen and 33 (21.7%) did not. Patient demographics, clinical characteristics and treatment history were not significantly different between the two cohorts (Table 1). The majority of patients (65.5%) with loading initiated secukinumab with the 150-mg dose, whereas the majority of patients (60.6%) without loading initiated with the 300-mg dose. More than half of the patients in each cohort received a biologic therapy during the 12-month baseline period (loading, 65.5%; no loading, 51.5%). Other prior treatments included oral corticosteroids (30.3% for both), conventional synthetic disease-modifying antirheumatic drugs (DMARDs) (loading, 31.9%; no loading, 21.2%) and targeted synthetic DMARDs (loading, 4.2%; no loading, 12.1%). The prevalence of comorbidities was similar between the two cohorts, with the most prevalent comorbidities being hypertension (19.1%), rheumatoid arthritis (19.1%) and other skin diseases (18.4%).

Table 1. Demographics, clinical characteristics and treatment history of patients with AS treated with secukinumab with or without a loading dose of 150 mg

<table>
<thead>
<tr>
<th>Age, mean (SD) (years)</th>
<th>45.3 (11.1)</th>
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<tbody>
<tr>
<td>Treatment history, N (%)</td>
<td>35 (22.9)</td>
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<tr>
<td>Loading, 150 mg, N (%)</td>
<td>85 (55.7)</td>
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<tr>
<td>No loading, 300 mg, N (%)</td>
<td>80 (51.8)</td>
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<td>Treatment regimen, N (%)</td>
<td>33 (21.7)</td>
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<tr>
<td>Loading, 150 mg, N (%)</td>
<td>88 (57.9)</td>
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<tr>
<td>No loading, 300 mg, N (%)</td>
<td>64 (41.9)</td>
</tr>
</tbody>
</table>

Conclusions: In this retrospective, administrative claims-based study, the majority of patients with AS who received secukinumab treatment with a loading regimen. Although only the 150-mg dose of secukinumab is approved for the treatment of AS, almost 40% of patients received the 300-mg dose, indicating a need to better understand patient and treatment characteristics for secukinumab in patients with AS. The results of this study provide early insights into real-world use of secukinumab with and without a loading regimen in patients with AS in the United States.

Acknowledgements: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

Disclosure of Interest: K. Oelke Consultant for: Novartis, Speakers bureau: AbbVie, AbbVie, Pfizer, G. Chun Employee of: Pfizer


DOI: 10.1136/annrheumdis-2017-eular.1543

THU0377 LOW DOSE IL-2 THERAPY CAN RECOVERY TH17/TREG CELL BALANCE IN PATIENTS WITH SPONDYLOARTHRITIS THROUGH INCREASING REGULATORY T CELLS NUMBERS

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Background: The imbalance in the number of Th17 and Treg cells is suggested to be associated with the pathogenesis of SpA. Recent studies have shown that interleukin-23 (IL-23) and Th17 play a crucial role in the pathogenesis of SpA. However the status of CD4+CD25+Foxp3+T cells which exert immunoregulatory functions are remains to investigate.
Objectives: To explore the status of the immunologic balance between Th17 cells and Treg cells in patients with SPA, and to assess the effect of low dose IL-2 on the peripheral CD4+ T cells.

Methods: Two hundred and two patients, who met the Assessment of Spondyloarthritis International Society (ASAS) criteria were enrolled and given conventional therapy, including Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), biological agents, Sulfasalazine, glucocorticoid. Eighty seven patients were not only given conventional therapy, but also injected subcutaneously low dose IL-2 (50 WIU/day for 5 days). Clinical and laboratory indicators were compared before and after IL-2 treatment. The CD4+ T cells in peripheral blood were measured by multicolor flow cytometry. A side effects were observed in the course of therapy.

Results: The absolute number and ratio of CD4+CD25+Foxp3+ regulatory T cells in peripheral blood of patients with SPA was significantly decreased compared with the healthy control group, (25.13 (18.76,37.37) vs. 33.06 (22.87,42.33), P<0.001); Th17/Treg (0.29 (0.18, 0.49) vs. 0.20 (0.15, 0.34), P=0.001). The absolute number of Treg cells increased more than 3-times (22.70 (14.47, 30.10) vs.67.87 (48.21, 105.82), p<0.001) after 5 days of low dose IL-2 treatment. Th17/Treg was significantly higher (0.32 (0.18, 0.57) vs. 0.20 (0.15, 0.34), P<0.001) before treatment compared with healthy controls.

Conclusions: The decrease of CD4+ CD25+ Foxp3+ T cells might play a key role in the pathogenesis of SPA. Low dose IL-2 therapy can restore and maintain the balance of Th17 and Treg cells by increasing Treg cells numbers specificity. The therapy is safe. More attention should be paid on the long term benefits of low-dose IL-2 therapy in the further research.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6529

THU0378 IMPACT OF THE ADALIMUMAB PATIENT SUPPORT PROGRAM ON CLINICAL OUTCOMES IN ANKYLOSING SPONDYLITIS: RESULTS FROM THE COMpanIY STUDY

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Background: Adalimumab (ADA) is a TNF-α inhibitor indicated for various inflammatory autoimmune diseases including ankylosing spondylitis (AS). Patients receiving ADA in Canada are eligible to enroll in the AbbVie Care patient support program (PSP) which provides them with personalized services including ongoing monitoring of disease state as determined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score and received prior NSAID(s) at baseline (BL) were categorized by BL: (1) time since diagnosis (< 2 years), (2) age (< 35 years vs 35–45 years vs ≥ 45 years), and (3) number of prior NSAIDs (≤ 2 vs >2) and (4) at the time of the follow-up BASDAI assessment was compared in patients with received CCC and patients without CCC. Robust Poisson regression was used to estimate the adjusted relative risk (RR) of controlled disease. Analyses were adjusted for patient age group, sex, region, prior biologic use, days lapsed between last follow-up visits, and baseline disease control status category.

Results: A total of 249 patients met eligibility criteria and 123 (49%) of these had received CCC. Of the 249 patients, 184 (74%) had controlled disease (BASDAI ≤ 4) at the follow-up assessment, 98 (80%) in the CCC group and 86 (68%) in the no CCC group. In the multivariable regression analysis, there was an increased likelihood of achieving controlled disease in the CCC group relative to the group without CCC (RR = 1.23, 95% confidence interval: 1.06–1.42; p-value = 0.0055).

Conclusions: AS patients receiving tailored services through the ADL PSP in the form of care coach calls have an increased likelihood of achieving controlled disease within 6 to 18 months. These results may help refine interventions aiming at improving clinical outcomes in AS patients.

Acknowledgements: Project management support for this study was provided by Jennifer Glass from QuintilesIMS. Analytical support was provided by Marc Duclos from QuintilesIMS. This support was funded by AbbVie.


THU0379 IMPACT OF TIME SINCE DIAGNOSIS, AGE, AND NUMBER OF PRIOR NSAIDS ON ANKYLosing Spondylitis: EFFECTS OF ADALIMUMAB 52-WEEK CLINICAL RESPONSE TO ADALIMUMAB IN PATIENTS WITH ANKYLosing SPONDYLITIS

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Objective: The objective of this analysis was to examine the impact of time since diagnosis, age, and number of prior NSAIDs as surrogates for disease duration on clinical outcomes in AS pts from ATLAS trial treated with ADA for 52 wks.

Methods: ATLAS3,4 was a phase 3 randomized double-blind placebo (PBO)-controlled trial evaluating the safety and efficacy of originator ADA in pts with active AS who failed NSAID therapy. In this post hoc analysis, pts who received at least one dose of ADA during the PBO-controlled period or open label extension and received prior NSAID(s) at baseline (BL) were categorized by BL: (1) time since diagnosis (< 2 years vs ≥ 2 years), (2) age (<35 years vs 35–45 years vs ≥45 years), and (3) number of prior NSAIDs (≤ 2 vs >2). The effect of time since diagnosis, age, and number of prior NSAIDs on AS outcome measures following 52 wks of ADA treatment was examined.

Results: At wk 52, 274 pts had received at least one dose of ADA and had at least one prior NSAID at BL. A majority of pts were ≥ 5 y since AS diagnosis (188 [68.6%]), <5 y of age (163 [59.5%]), HLA-B27+ [213 [77.7%]], and had <2 prior NSAIDs (158 [57.7%]). Pts with shorter time since diagnosis were generally younger (late thirties). Across all subcategories, ~70% of pts were male. The BL disease activity measures were numerically similar across most categories. Following 52 wks of ADA treatment, the proportions of pts achieving ASAS20 and ASAS40 responses were numerically higher and mean decreases in BASDAI and BASFI scores from BL larger in subcategories with shorter time since diagnosis, younger age, and fewer prior NSAIDs (Table). There were significant differences in ASAS40, BASDAI, and BASFI scores between time since diagnosis (<2 vs ≥ 2 and < 5 vs ≥ 5) and age (<35 vs ≥ 45) subcategories.

Conclusions: Following 52 wks of ADA treatment, shorter time since diagnosis and younger age were associated with greater clinical improvements and improvements in disease activity and functionality. Although younger age (<35 vs ≥ 45) had significant positive impact on the clinical outcomes similar to wk 12 results, shorter time since diagnosis (<2 vs ≥ 2 and < 5 vs ≥ 5) was also associated with better 52-wk clinical outcomes. These results suggest that early effective therapeutic intervention may improve long-term clinical outcomes in AS pts.

References:
RESULTS OF A REAL LIFE DOSE-REDUCTION STRATEGY
CERTOLIZUMAB PEGOL IS EFFECTIVE IN UVEITIS

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<th>ESR (mm/1°h)</th>
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<tr>
<td>BASFI (0-10)</td>
<td>4±2.7</td>
<td>2.8±2.9</td>
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<tr>
<td>BASDAI (0–10)</td>
<td>4.2±2.6</td>
<td>2.1±2.2</td>
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<td>Gender (%)</td>
<td>Male/Female</td>
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**Background:**
Published reports suggest that patients with Spondyloarthritis (SpA) in remission under treatment with TNFalpha inhibitors (TNFi) could obtain the best benefit at lower dose of the drug. **Objectives:**
To evaluate effectiveness of a strategy of dose reduction of TNFi in SpA patients in clinical remission and to explore baseline characteristics predictive of maintenance of the response. **Methods:**
Retrospective observational study, including patients with SpA meeting ASAS criteria treated with TNFi following a dose optimization protocol (lower doses or longer intervals than approved), from 2008 to 2015. Criteria for optimization was patients with BASDAI≤2 and/or C reactive protein level (CRP)<5 mg/L for at least 6 months. Patients who relapsed (BASDAI>2 and/or CRP>5 mg/L) returned to standard dose. Clinical/analytical parameters and drug’s survival time until relapse were recorded. SPSSv.17 software was used for contrast means. Survival Kaplan-Meyer curves was analysed. **Results:**
148 SpA patients treated with TNFi, 32/149 patients (21.5%) included in optimization protocol. 27 patients (84.3%) with increased interval between doses, remaining with reduced dosifiction. Table 1 shows baseline characteristics of patients on optimization group (means/SD or proportion). 18/32 patients (56.2%, C39.01–73.4) maintained clinical remission with optimized dose at 36.5 months (median). Table 2 shows activity parameters of both relapsed and maintained response patients. There were either baseline differences or at optimization time between patients who maintained remission and not, but relapsed patients showed higher CRP at optimization time, without statistically significant differences. 72.2% (13/18) of patients on sutained remission were on intermediate uveitis. Mean disease duration was 151±117.1 months (range 6–27), 9 patients are still on CZP treatment. Ten eyes showed improvement of visual acuity (41.7%), 10 remained stable and 2 worsened. During the follow-up no serious adverse events were reported. Four cases withdrew CZP treatment: 2 due to worsening of articular symptoms but without any uveitis events; 1 due to macular edema and 1 due to uveitis activity. One patient switched to infliximab, one to golimumab, and 2 required switch to tocilizumab. In all 13 patients except 2, CZP achieved a good control of SpA activity.

**Conclusions:**
CZP demonstrated effectiveness in patients with uveitis-associated to SpA refractory to previous TNFi treatment. **References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4245

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**RESULTS OF A REAL LIFE DOSE-REDUCTION STRATEGY**

**CERTOLIZUMAB PEGOL IS EFFECTIVE IN UVEITIS ASSOCIATED TO SPONDYLOARTHROPATHY REFRINGATORY TO OTHER TUMOUR NECROSIS FACTOR INHIBITORS**


**Background:**
Uveitis is one of the most common extra-articular manifestations of patients with spondyloarthritis (SpA). In severe cases, uveitis may require the use of biological therapy, primarily tumor necrosis factors inhibitors (TNFi), being infliximab the currently used infliximab and adalimumab. However, another TNFi such as certolizumab pegol (CZP), with indication for SpA patients, could be an effective option in cases of inefficacy or adverse events to other TNFi, as we have previously reported 1.

**Objectives:**
Our objective is to analyze the effectiveness and the safety profile of CZP in patients with refractory SpA-associated-uveitis.

**Methods:**
Observational, multicentric, retrospective study. We selected all patients with a diagnosis of SpA (including ankylosing spondylitis (AS), psoriatic arthropitis (PsA), non-radiographic axial SpA (nr-axSpA) and SpA associated to inflammatory bowel disease (IBD-SpA)) who had refractory uveitis (confirmed by an Ophthalmologist) as main extra-articular manifestation, and who received CZP for at least 6 months. Variables analyzed: age, sex, diagnosis, type of uveitis, duration since the first uveitis episode and number of eyes affected; previous treatment (NSAID, disease-modifying anti-rheumatic drugs (DMARDs), immunosuppressive or biological therapy); outcome, and time to follow-up.

**Results:**
Twenty-four eyes of 13 patients (10 men); age 49.5±11.7 (range 29–71 years) were included in the study. Diagnosis were: seven AS, four PsA, one nr-axSpA, and one IBD-SpA. Type of uveitis: 9 anterior, 3 panuveitis, and 1 intermediate uveitis. Mean disease duration was 151±117.1 months (range 5–420). 84.6% patients had previously received biological therapy (46.1% ≥2 biological agents). 61.5% received CZP in monotherapy and 5 patients received concomitant treatment: 4 methotrexate and 1 azathioprine. In all cases CZP was started due to inefficacy to previous treatment except for 2 cases whose primary reason was the occurrence of adverse events (one injection site reaction and one development of relapsing polychondritis). After a follow-up of 13.1±6.6 months (range 6–27), 9 patients are still on CZP treatment. Ten eyes showed improvement of visual acuity (41.7%), 10 remained stable and 2 worsened. During the follow-up no serious adverse events were reported. Four cases withdrew CZP treatment: 2 due to worsening of articular symptoms but without any uveitis events; 1 due to macular edema and 1 due to uveitis activity. One patient switch to infliximab, one to golimumab, and 2 required switch to tocilizumab. In all 13 patients except 2, CZP achieved a good control of SpA activity.

**Conclusions:**
CZP demonstrated effectiveness in patients with uveitis-associated to SpA refractory to previous TNFi treatment.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2633
INCIDENCE OF UVEITIS IN NON-STEROIDAL

Acceptable treatment with etanercept compared with the other treatments.

Disclosure of Interest: None declared.

Disclosure of Interest: None declared.


Conclusions: This analysis confirms the slow rate of radiographic SIJ progression over 2 yrs in nr-axSpA. The observed data suggest a lower rate of progression with ETN than without a TNF inhibitor.


THU0384 THE EFFECT AND SAFETY OF YISAIPU (YISAIPU) IN THE TREATMENT OF PATIENTS WITH NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN CHINA

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease, which includes AS and nr-axSpA. Anti-TNF-α agents, such as Yisaipu (Yisaipu) are frequently used in nr-axSpA patients in China, but the related data is limited.

Objectives: The aim of this research is to assess the efficacy and safety of Yisaipu in the treatment of patients with nr-axSpA in China.

Methods: The inclusion of study population consisted of 150 patients who met the ASAS criteria for axial SpA but not the modified New York radiographic criteria for AS, had a score of ≥4 on the BASDAI or a score of ≥2.1 on the ASDAS-CRP and had been treated unsuccessfully with ≥1 NSAIDs for 4-week. Patients were assigned to receive Yisaipu (made in China) 50 mg/week and contin- 

**Abstract THU0382** – Table 1. Observed Radiographic Changes from BL to Week 104

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Cohort</th>
<th>Improved X-ray (%)</th>
<th>Worsened X-ray (%)</th>
<th>Mean Difference*</th>
<th>Mean differences (Control – ETN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mNY criteria</td>
<td>Control</td>
<td>3/193 (1.6)</td>
<td>6/193 (3.1)</td>
<td>1.6% (1.5, 4.6)</td>
<td>3.4% (0.7, 7.5)†</td>
</tr>
<tr>
<td></td>
<td>ETN</td>
<td>4/161 (2.5)</td>
<td>1/161 (0.6)</td>
<td>-1.9% (-4.6, 0.9)</td>
<td>4.7% (0.5, 9.9)†</td>
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<tr>
<td>Δ ≥ 1 grade in ≥ 1 SIJ</td>
<td>Control</td>
<td>2/193 (10.9)</td>
<td>36/193 (18.7)</td>
<td>7.8% (0.1, 15.4)</td>
<td>9.6% (0.9, 20.2)†</td>
</tr>
<tr>
<td></td>
<td>ETN</td>
<td>18/161 (11.5)</td>
<td>41/161 (25.8)</td>
<td>-19% (9.1, 54.8)</td>
<td>18.2% (5.6, 30.9)‡</td>
</tr>
<tr>
<td>Δ ≥ 1 grade in ≥ 1 SIJ, Δ from 0 to 1 and 0 to 1 considered no Δ</td>
<td>Control</td>
<td>16/193 (8.3)</td>
<td>29/193 (15.0)</td>
<td>6.7% (-0.1, 13.5)</td>
<td>7.4% (2.1, 16.8)‡</td>
</tr>
<tr>
<td></td>
<td>ETN</td>
<td>15/161 (9.3)</td>
<td>14/161 (8.7)</td>
<td>-0.6% (7.2, 6.0)</td>
<td>16.4% (5.1, 27.8)‡</td>
</tr>
</tbody>
</table>

Based on 2 of 3 readers assigning same category; otherwise considered no change. Some patients started with lowest possible score and could not improve. Δ, change. Percent pts with worsening – percent pts with improvement. 1One-way ANOVA. 2Adjusted for covariates listed in Methods. 3P=0.005.
primary efficacy end point was the improvement of ASDAS-CRP. Secondary end points included ASAS 20, ASAS 40, ASAS 5/6, ASAS partial remission and BASDAI. Safety was evaluated during scheduled visits.

**Results:** 123 patients with active nr-axSpA were enrolled between April 19, 2014, and July 10, 2015. The mean age of the 123 nr-axSpA patients was 25.3±5.9 years. The ASDAS-CRP and BASDAI decrease from 2.7±0.9 to 0.7±0.4, from 4.5±1.0 to 0.9±0.8, respectively between weeks 0 and 24. The patients achieved the ASDAS-CRP<2.1 was 96.7%. ASDAS-CRP major and important improvement were achieved by 41.4%, 79.8%, respectively at weeks 24. ASAS 20, ASAS 40, ASAS5/6 and ASAS partial remission were achieved by 75.0%, 54.8%, 65.4% and 35.2%, respectively at week 24. Yisaipu-treatment was associated with statistically significant improvements in all parameters, including BASFI, BASMI, PGH, PSA, EL, CRP concentrations. Most adverse events in the open-label phase were mild or moderate in severity.

**Conclusions:** Yisaipu was effective and well-tolerated during the 24-week study period and was associated with a significant improvement in the signs and symptoms of active nr-axSpA.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3846
THU0387 THE CLINICAL IMPORTANCE OF THE THYROID NOODULES DURING TUMOR NECROSIS FACTOR-ALPHA INHIBITOR THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: TNF is a pivotal regulator of inflammation and the cytokine system. Besides this, there is no doubt that TNF has a major role in cancer biology. TNF has a dual defensive and offensive role in carcinogenesis (1). TNF-blocking treatment has led to improvements in the management of inflammatory diseases. Even though their efficacy as anti-inflammatory drugs is well-proven, there are some concerns about the adverse effects of anti-TNF therapy (2). Basic research suggests that the evaluation of infections and malignancy as major adverse effects should be performed effectively (3). However, some studies conducted so far have dubious notions that anti-TNF therapy increases the risk of cancer (3,4). Objectives: Objective of the study was to determine the clinical importance of the thyroid nodules in patients with axial spondylarthropathy (axSpA) rests with the need to exclude thyroid malignancy. The aim of this study is to assess the risk of thyroid malignancy in axSpA patients receiving anti-TNF therapy.

Methods: From September 2015 until December 2015, 70 patients diagnosed with axSpA according to ASAS criteria, were included in the research. Forty of the patients had received anti-TNF therapy, and 30 of the patients were anti-TNF naive. A clinician from the Physical Medicine and Rehabilitation clinic performed ultrasonography on all patients to screen for thyroid nodule(s). If thyroid ultrasonography revealed an abnormal finding, the patient was referred to a radiologist.

Results: The mean (SD) age was 38±9.87 years; % 75.7 of the patients were male. None of the demographic differences between the groups were statistically significant. Fifteen of the forty patients that received anti-TNF therapy and eleven of the thirty anti-TNF naive patients had thyroid nodule(s). Four patients from the anti-TNF group underwent fine needle aspiration biopsy, and two of them were diagnosed with papillary thyroid carcinoma. None of the nodules in anti-TNF naive patients required biopsy. When compared to the normal population, the standardized incidence ratio (SIR) was found to be increased in both male (SIR: 2.03% 95 CI: 1.9 to 18) and female (SIR: 2.7% 95 CI: 2.6 to 24) cases.

Conclusions: We see a mild increase in thyroid malignancies in axSpA patients that received anti-TNF therapy. Consequently, the thyroid gland should also be taken into consideration while screening for malignancy before anti-TNF therapy.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1530

THU0388 EFFICACY AND SAFETY OF ADALIMUMAB IN PATIENTS WITH NON-RADILOGIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE 28-WEEK OPEN-LABEL PERIOD OF THE ABILITY-3 STUDY

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Background: Adalimumab (ADA) significantly improved clinical response at wk 12 vs placebo in patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA) in the ABILITY-1 study. The subsequent, ongoing ABILITY-3 study is assessing continuation vs withdrawal of ADA in nr-axSpA pts who respond to ADA.

Objectives: Evaluate the efficacy and safety of ADA during the open-label lead-in period of ABILITY-3.

Methods: ABILITY-3 has a 28-wk lead-in open-label ADA (40 mg every other wk) period; pts who achieve sustained remission (Ankylosing Spondylitis Disease Activity Score inactive disease [ASDAS-ID] at wk 16, 20, 24 and 28) are randomized to double-blind placebo (withdrawal) or ADA (continuation) for 40 wks (longing). From wk 20–28, pts who did not achieve ASDAS-ID were discontinued. Adult pts with nr-axSpA (fulfilling Assessment of SpondyloArthritis International Society [ASAS] criteria but not modified New York criteria) with objective evidence of inflammation in the sacroiliac joints or spine on MRI or elevated hs-CRP at screening; active disease at baseline (defined by ASDAS ≥ 2.1; BASDAI ≥ 4, and total back pain score ≥ 4); and inadequate response to ≥ 2 NSAIDs were eligible.

Results: Of 673 pts enrolled, 51% were women and mean BASDAI was 7.0±1.4 (Table). At wk 28, 305 (45%) pts were randomized (ASDAS-ID: 33% at wk 12, 44% sustained at wk 28; nonresponder imputation) and 368 (55%) pts achieved sustained remission (not achieving sustained remission, n=300 [45%]; other reasons, n=68 [10%]). In observed analysis, 59%, 35%, and 22% of pts achieved ASAS40, ASDAS-ID, and ASAS partial remission, respectively, at wk 12, similar to wk 12 data from ABILITY-1 pts with objective inflammation at baseline. The proportions of pts achieving ASAS20, ASAS40, ASDAS-ID, ASDAS CII, and ASDAS M1 increased, and mean BASDAI and back pain scores decreased over time (observed analysis; Figure). Adverse events (AEs) were reported by 468 pts (70%), most commonly nasopharyngitis (n=121 [18%]), upper respiratory tract infection (n=81 [12%]), and headache (n=56 [8%]); serious AEs occurred in 19 (3%) pts.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Mean ± SD (n=673)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>White, n (%)</td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td>Symptom duration, y</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
</tr>
<tr>
<td>TJC</td>
</tr>
<tr>
<td>SJC</td>
</tr>
<tr>
<td>MASES</td>
</tr>
<tr>
<td>PGA-disease activity</td>
</tr>
<tr>
<td>Patient-pain</td>
</tr>
<tr>
<td>BASDAI</td>
</tr>
<tr>
<td>ASDAS</td>
</tr>
<tr>
<td>hs-CRP</td>
</tr>
<tr>
<td>BASFI</td>
</tr>
<tr>
<td>HAQ-S</td>
</tr>
</tbody>
</table>

Acknowledgements: AbbVie funded the study and approved the abstract for submission. Medical writing support was provided by Maria Hovenden, PhD, of Complete Publication Solutions, LLC (North Wales, PA) and was funded by AbbVie.

Disclosure of Interest: R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, Consultant.

Conclusions: Baseline disease activity was higher in ABILITY-3 pts than reported in prior trials. After 28 wks of open-label ADA therapy, disease activity improved and sustained remission was achieved in 44% of pts. Efficacy and safety in this nr-axSpA population were consistent with findings from ABILITY-1.
IS THERE ANY ROLE OF IMMUNOGENICITY ON THE RESIDUAL RESPONSE TO THE ANTI-TUMOR NECROSIS FACTOR ALPHA THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: THE FIRST RESULTS OF A PROSPECTIVE COHORT STUDY


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Background: Although anti-tumour necrosis factor agents (anti-TNFs) are very effective in most patients with ankylosing spondylitis (AS) significant proportion of patients quit the treatment due to non-response or adverse events. The development of anti-drug antibodies (ADAs) and low serum drug levels might have a mechanistic role in loss of efficacy of or the development of adverse events in patients treated with anti-TNFs. There is limited data regarding the immunogenicity of anti-TNFs in patients with AS.

Objectives: Therefore the aim of this study was to evaluate the relationship between the formation of ADAs, serum through drug levels and clinical response to anti-TNFs in patients with AS.

Methods: In total 350 AS patients with a new anti-TNF agent prescription in the last two weeks period were planned to include this multi-center prospective observational cohort study. Herein we are presenting the data of first 102 patients who had >3 months follow-up. Clinical data and serum samples were collected at baseline and at every three months of treatment. Serum drug levels and ADAs were measured by ELISA in one center to avoid inter-assay variability.

Results: 102 biologic naïve AS patients (75 [74%] male, mean ±SD age; 37.2±10.7 years) who started anti-TNF agents (14 infliximab [13.7%], 27 adalimumab [26.5%], 33 etanercept [32.4%] and 28 golimumab [27.5%]) were included in the present analysis. In comparison to baseline values BASDAI, ASDAS- CRP and CRP values were significantly decreased in third months of follow-up (P <0.001) (table). At 12 weeks of follow-up 9 patients (9%; 2 on infliximab and 7 adalimumab) had ADAs and 20 (20%; 10 on adalimumab, 4 infliximab, 4 golimumab and 2 etanercept) had no detectable drug levels. The presence of ADAs were significantly correlated with serum drug levels (P <0.001). Up to 12 months of follow-up none of patients treated etanercept developed ADAs. Third month BASDAI and ASDAS-CRP values were significantly higher in patients with ADAs (BASDAI values were 5.2±1.4 vs 3.0±1.8; P <0.001 and ASDAS-CRP values were 3.1±1.0 vs 1.9±1.1; P <0.001) (figure) and patients with no detectable drug levels BASDAI values were 4.1±1.8 vs 2.9±1.8; P=0.012 and ASDAS-CRP values were 2.7±1.3 vs 1.9±1.0; P=0.015).

Conclusions: ADAs against anti-TNF agents might develop as early as 12 weeks of treatment. Our results confirm that ADA development may hinder the anticipated response to anti-TNF agents in patients with AS.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6119

THU0389 | EFFECT OF REHABILITATION ON THE CHEST EXPANSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis that leads to pain, stiffness, progressive spinal deformity, and spinal fusion, limitation of the spine, rib cage motion and severe functional impairment. Pulmonary function is altered in AS owing mainly to the limited chest expansion.

Objectives: The purpose of this study was to investigate the effect of rehabilitation on the limited chest expansion measured by respiratory index and relationship between duration of the rehabilitation and age, disease onset, disease duration and respiratory index in patients with AS during physical treatment and rehabilitation.

Methods: The study was designed as a retrospective study that included 47 consecutive AS patients (33 male and 14 female), average age of 52.5±11.58 years that were hospitalized and treated in rehabilitation center. Average duration of the rehabilitation was 17.7±5.92 days. Respiratory index was measured for all AS patients at the beginning and at the end of rehabilitation with a centimeter ribbon. Student’s t-test and Pearson’s test of correlation were used for statistically analysis.

Results: Average disease duration was 13.35±8.74 years, disease onset was at 39.64±12.87 years. Respiratory index was 1.98±1.34 cm at beginning of rehabilitation and 3.01±1.75 cm at the end of rehabilitation. The difference was statistically significant (t=8.025, p <0.001). Pearson’s test of correlation was shown statistically significant correlation between value of respiratory index at beginning and at the end of rehabilitation (r=0.872, p <0.001). Duration of the rehabilitation (hospital days) statistically significant correlate with value of respiratory index at beginning rehabilitation (r=−0.289, p <0.05), but not with age, disease duration and disease onset (p >0.05).

Conclusions: The physical therapy and rehabilitation has led to the improvement the respiratory index in patients with AS, which confirms its effectiveness. The value of respiratory index at beginning rehabilitation is associated with duration of the rehabilitation. Significant limitation in respiratory index indicates longer hospital stay. These results could be having importance in planning of rehabilitation of patients with AS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3729

THU0391 | FEMALE GENDER IS ASSOCIATED WITH A POORER RESPONSE TO TNF INHIBITORS IN ANKYLOSING SPONDYLITIS

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Background: Limited data are available on the influence of gender and lifestyle factors, such as smoking, alcohol consumption and Body Mass Index (BMI) on disease activity and response to TNF inhibitors in ankylosing spondylitis (AS).

Objectives: This study aimed to determine whether these factors influence age at diagnosis, disease activity and response to TNF inhibitors.

Methods: In a prospective study, clinical data (age, gender, C-reactive protein, Ankylosing Spondylitis Disease Activity Score (BASDAI), Bath Ankylosing Spondylitis Disease Activity Score (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI), smoking, alcohol consumption and BMI) were collected in AS patients from an observational cohort, who started or switched treatment with TNFI. Data were collected at baseline and after 6, 12 and 24 months. Independent t-tests and linear regression analyses were performed to assess the influence of gender and lifestyle factors on age at diagnosis and disease activity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2669
Results: In total, 312 consecutive AS patients, 34% female, were included with a mean follow-up of 18.9 months. Most patients (72%) 55% showed significant improvement after start of TNFi of whom 86 patients (28%) had a clinically important (ASDAS decrease -1.1) and 86 (26.9%) a major clinical improvement (ASDAS decrease -2.2). BMI was significantly correlated with age at diagnosis (p=0.016; 95% CI: 0.07(-0.65)); an increase of BMI with three points delayed the AS diagnosis with one year. At baseline, smoking and gender were not correlated with the ASDAS, but BASDAI and BASMI were both inversely related to BMI. Male gender was significantly associated with a higher chance at clinical response (improvement of the BASDAI with 50% or a 2 point decrease) to TNFi (p=0.041). At one year follow-up the clinical improvement of males versus females was respectively 62% vs. 43% and at two year follow-up 59% vs. 46%. Males also showed a significantly higher ASDAS improvement after one year of follow-up compared to females (p=0.015).

Conclusions: Significantly less females had a clinical response compared to males after one and two years of TNFi treatment. A higher BMI not only prolonged the time to AS diagnosis up to one year, but also negatively influenced the BASDAI and BASMI scores. Female gender and high body weight should be taken into consideration when the efficacy of TNFi is assessed, by stratifying for these factors in the analysis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1290

THU0039

DO WE REALLY NEED DMARDS ADDITION TO ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH TUMOR NECROSIS FACTOR ALPHA INHIBITORS?

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Background: The management of systemic inflammatory diseases, such as Rheumatoid arthritis (RA) and Ankylosing spondylitis (AS) has been revolutionized with the introduction of tumor necrosis factor alpha inhibitors (TNF-I). Significant reduction in disease activity and achievement of remission resulted in halting of joint damage and improved quality of life. Unfortunately, approximately 15–30% of patients fail to reach desirable improvement or lose drug effectiveness with time. It may be explained by immunogenicity and production of human anti chimeric antibodies (HACA). Presence of HACA against TNF-I have been associated with low levels of the drug and lose of therapeutic response. The prevalence of HACA in RA is estimated between 20–40%, and in AS between 25–64%. The difference in the pathogenesis of RA and AS as well as diverse approach in using disease modifying anti-rheumatic drugs (DMARDs) may influence HACA production and TNF-I levels in these conditions.

Objectives: To compare the incidence of HACA and infliximab, Etanercept, Adalimumab levels in patients with RA and AS with respect to concomitant DMARDs.

Methods: Patients with RA and AS data treated with TNF-I for at least 3 months in whom tests for HACA and infliximab, Etanercept, Adalimumab levels were available were extracted from patients’ files. Data included: demographics, concomitant treatment, and disease activity scores (BASDAI for AS and DAS-28 for RA). Serum for assessment of drugs level (ELISA) and HACA (ADAb;Promonitor, Bridging, ELISA) was obtained before the next drug administration. Univariate comparison was done using Student t test for the continuous variables and Chi square test for the categorical variables (P <0.05 was considered significant).

Results: Data on 53 patients with AS (mean age 47.9±11.9 years, 41.5%, 5% female) and 29 patients with RA (mean age 54.8±6.1 years, 75, 9% female) were available: 22 RA patients were treated with Methotrexate and 7 with other DMARDs; no one AS patient was treated with concomitant DMARDs. High level of HACA was found in 22.6% AS patients and in 34.5% RA patients (p=0.05); 86.8% patients with AS reached therapeutic level of drug compared to 69% RA patients (p=0.027). Drugs levels were similar in AS and RA patients (Table). Low

THU0392

SECUKINUMAB PROVIDES SUSTAINED REDUCTION IN FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS THROUGH 3 YEARS: LONG-TERM RESULTS OF TWO RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED PHASE 3 STUDIES

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Background: In patients (pts) with ankylosing spondylitis (AS), fatigue is a common symptom affecting health-related quality of life (HRQoL) and social functioning. Secukinumab (SEC), a fully human anti-IL-17A mAb, rapidly improved signs and symptoms, physical functioning, and HRQoL in pts with AS.1,2

Objectives: To assess the long-term effects of SEC on fatigue in TNF inhibitor (TNF-I) naïve and TNF inhibitor inadequate responder/intolerant (TNF-IR) AS pts in MEASURE 1 and MEASURE 2.

Methods: 371 and 219 pts were randomized to SEC or placebo (PBO) in MEASURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and MEASURE 2 (150 or 75 mg SC), respectively. At Week (Wk) 16, non-responder PBO pts were re-randomized to SEC 150 or 75 mg SC (in MEASURE 1) or SEC 300 mg SC (in MEASURE 2). PBO pts achieving ASAS20 response at Wk 16 were switched to SEC at Wk 24. Fatigue was measured at baseline (BL) and Wks 4, 8, 12, 16, 24, 52, 104 and 156 using FACIT-F, which assesses fatigue in the previous 7 days using 13 questions graded on a 0–4 scale (higher scores=less fatigue). An increase from BL in FACIT-F score of ≥4 points (based on MCID) was used to define “response”. Approximately 69% of pts were TNF- naive and 31% were TNF-IR across both trials. Analyses were based on the full analysis set and subgroups stratified by prior TNF therapy. Correlations between BL characteristics and improvements in fatigue were investigated using a logistical regression model. Only data from the approved dose (SEC 150 mg) are presented.

Results: FACIT-F was 24.5–25.6 and 22.6–24.3 at BL across groups in MEASURE 1 and 2, respectively. Improvements in FACIT-F with SEC at Wk 16 were sustained through Wk 156 in MEASURE 1 and Wk 104 in MEASURE 2 (Table). Rapid and sustained fatigue response were also seen in subgroups stratified by prior TNF use. In the overall population, LS mean changes (+SEM) from BL in FACIT-F scores were significantly greater with SEC vs PBO at Wk 16 in both MEASURE 1 (7.60±0.99 vs 3.34±1.05, P=0.002) and MEASURE 2 (8.10±1.09 vs 3.27±1.09, P=0.018); reductions in fatigue were sustained throughout the entire follow up in both trials (MEASURE 1 Wk 156: 9.81±0.95; MEASURE 2 Wk 104: 9.27±1.13). Similar results were reported in both TNF- naïve and TNF-IR pts. Correlational analyses based on pooled data from both trials did not identify any BL factors that
consistently predicted improvement in fatigue activity at Wks 16, 52, and 104. A one-unit increase in BL BASDAI score (i.e. worsening) was a significant factor for achieving FACIT-F response at Wk 104 (P<0.02).

Conclusions: SEC provided sustained improvements in fatigue for up to 156 wks in both TNF-naive and TNF-IR pts with AS. Fatigue response was generally highest for TNF-naive pts.

References:

Disclosure of Interest: M. Eberhardt Employee of: Novartis, Consultant for: AbbVie, BMS, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Lilly, Pfizer, Roche, AbbVie, BMS, Biogen, Boehringer-Ingelheim, Celgene, Chugai, Eli Lilly, Eire, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Sanofi, USV.

Background: The 2016 AASAS guidelines recommend the use of a 50% improvement in BASDAI score (BASDAI 50) as a threshold for discontinuing biologics. However, this will result in suboptimal management of disease in a substantial proportion of pts. 

Objectives: To evaluate the impact of switching to BASDAI 28 (BASDAI 28) from BASDAI 50 in pts with AS and to assess the impact on treatment satisfaction, comorbidities, and drug-related treatment costs.

Methods: 2000 patients with AS were enrolled in a phase IV, non-interventional, real-life, observational study across 14 countries. A total of 2400 patients were assessed for eligibility, and 2000 were included, with a baseline mean BASDAI score of 5.0 (±2.2). AS patients enrolled in this trial had a high disease activity and comorbidities in patients with active PsA or AS in daily practice treated with secukinumab in Germany.

Results: Patients were reassessed at 0, 3, 6, 12, and 24 months. The proportion of pts with an elevated CRP was highest in gr.2 at BL. Proportion males n (%) 117 (68.0%), 21 (65.6%), 27 (73.0%), 27 (73.0%), 28 (69.0%). Mean age ± SD (range) 52.8 (3.3–660.0), 18.3±17.8 (1.0–60.6), 19.7±52.7 (0.3–660.0), 11.8 (±2.6).

Conclusions: The baseline characteristics of the population are comparable with those in previous studies. Secukinumab was well tolerated, and the efficacy of secukinumab in this real-world setting is consistent with the results of previous randomized, controlled, clinical trials.

Disclosure of Interest: J. Braun Consultant for: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Eire, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Sanofi, USV. J. Braun Grant/research support from: Eli Lilly, Janssen, Lilly, Merck, Novartis, Pfizer, Sanofi, USV.

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THU0396

References:

Disclosure of Interest: M. Eberhardt Employee of: Novartis, Consultant for: AbbVie, BMS, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Lilly, Pfizer, Roche, AbbVie, BMS, Biogen, Boehringer-Ingelheim, Celgene, Chugai, Eli Lilly, Eire, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Sanofi, USV.

Background: The 2016 AASAS guidelines recommend the use of a 50% improvement in BASDAI score (BASDAI 50) as a threshold for discontinuing biologics. However, this will result in suboptimal management of disease in a substantial proportion of pts. 

Objectives: To evaluate the impact of switching to BASDAI 28 (BASDAI 28) from BASDAI 50 in pts with AS and to assess the impact on treatment satisfaction, comorbidities, and drug-related treatment costs.

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Results: Patients were reassessed at 0, 3, 6, 12, and 24 months. The proportion of pts with an elevated CRP was highest in gr.2 at BL. Proportion males n (%) 117 (68.0%), 21 (65.6%), 27 (73.0%), 27 (73.0%), 28 (69.0%). Mean age ± SD (range) 52.8 (3.3–660.0), 18.3±17.8 (1.0–60.6), 19.7±52.7 (0.3–660.0), 11.8 (±2.6).

Conclusions: The baseline characteristics of the population are comparable with those in previous studies. Secukinumab was well tolerated, and the efficacy of secukinumab in this real-world setting is consistent with the results of previous randomized, controlled, clinical trials.

Disclosure of Interest: J. Braun Consultant for: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly and Company, Lilly, Pfizer, Roche, AbbVie, BMS, Biogen, Boehringer-Ingelheim, Celgene, Chugai, Eli Lilly, Eire, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Sanofi, USV. J. Braun Grant/research support from: Eli Lilly, Janssen, Lilly, Merck, Novartis, Pfizer, Sanofi, USV.

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other studies in the phase III program of secukinumab\(^2\). Major difference is represented by the high number of biological-experienced patients and comorbidities. Potential differences between these real world results and previously obtained phase III results will have to be discussed to assess their impact on patients.

**References:**


**Disclosure of Interest:**

K. Gratacos\(^3\), J. Gratacós\(^3\), E. de Miguel\(^1\), A. Balsa\(^1\), P. Diaz del Campo\(^2\), J. Gratacos\(^3\), Hospital la Paz, IdiPaz; 2 Spanish Society of Rheumatology, Madrid; 3Hospital Parc Taulí, Sabadell, Spain

**Background:**

bDMARDs (TNF or IL-17 inhibitors) have been shown to be efficacious in patients with axial spondyloarthritis (axSpA). However, approximately 30–50% of patients who receive a first bDMARD do not respond well. Current practice in these patients is switching to another bDMARD but the scientific evidence for this attitude is sparse.

**Objectives:**

To evaluate the efficacy of switching bDMARDs in patients with axSpA.

**Methods:**

A systematic literature review until February 2016 was performed using Medline, EMBASE and Cochrane databases. Furthermore, abstracts from the previous EULAR and ACR meetings were reviewed. The research question was formulated according to the PICO(s) method: Population (axSpA patients); Intervention (bDMARD); Outcome (clinical response); and Setting (longitudinal studies with follow-up ≤12 weeks of follow up including data from ≥50 patients).

Data was extracted using a form developed for this specific purpose. The quality of the studies was assessed based on CEBM Oxford. Clinical response in patients who switched to a second bDMARD was determined and compared with the one achieved after receiving the first bDMARD (a TNF) in all cases. Results are shown as median (range) and relative frequencies (%).

**Results:**

In total, 7 studies out of 1506 retrieved citations were included. All studies included patients with ankylosing spondylitis (AS). The study design was prospective observational (n=3), retrospective observational (n=2), open-label trial (n=1) and post-hoc analysis from two RCTs (n=1). The level of evidence for all the studies was 4. In these studies, a total of 4678 patients received a first bDMARD and 1198 patients switched to a second bDMARD (a TNF in all cases except in 51 patients that switched to secukinumab). Baseline characteristics of patients included in the studies were:

- 41 (38–44) years old, 67% (64–74) males, 78% (74–89) HLA-B27+ and BASDAI before switching 6.1±1.5.
- Mean change from baseline\(^4\) −3.3±2.4 (0.017) −3.1±0.2 −2.9±0.2

**Conclusions:**

In patients with AS who do not respond to a first TNF, switching to another bDMARD (either a TNF or secukinumab) is efficacious in a considerable number of patients (30–50%). However, the clinical response after receiving a second bDMARD is logical in those in pts with active AS over ≥3 yrs. Secukinumab was well tolerated with a favorable safety profile consistent with that reported previously.

**References:**

Disclosure of Interest: X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCBS, Werfen, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCBS, Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCBS, Werfen, A. Kivitz Consultant for: AbbVie, Pfizer, Genentech, UCB, Celgene, Sponsors bureau; Celgene, Pfizer, Genentech, A. Deodhar Grant/research support from: Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant for: Eli Lilly, Janssen, Novartis, Pfizer, UCB, J. Braun Grant/research support from: AbbVie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EUBEWE Pharma, Medac, MSD (Scherwing-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, UCB, Speakers bureau: AbbVie (Abbott), Amgen, BMS, Boehringer, Celltrion, Celltrion, Centocor, Chugai, EUBEWE Pharma, Medac, MSD (Scherwing-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, UCB, J. Wei Grant/research support from: BMS, Janssen, Pfizer, Sanofi-Aventis, Novartis, Consultant for: Pfizer, Celgene, Chugai, UCB Pharma, TSH Taiwan, Speakers bureau: AbbVie, BMS, Chugai, Janssen, Pfizer, E. Delicha Employee of: Novartis, Z. Tallochery Shareholder of: Novartis, Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis

THU0398 SECUKINUMAB SUSTAINS INDIVIDUAL CLINICAL RESPONSES OVER TIME IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 2-YEAR RESULTS FROM A PHASE 3 TRIAL, MEASURE 2

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Background: The assessment of achieving, maintaining or improving clinical response to biologics in ankylosing spondylitis (AS) is a part of treat-to-target recommendations aimed at optimising treatment goals.1

Methods: This is a post-hoc analysis of AS pts originally randomised to secukinumab 150mg (approved dose) who completed the 16wk-double blind treatment period, followed by long-term uncontrolled treatment. Shift analyses on ASAS response between Wks 2 and 16 and Wks 16 and 52 or 104 were performed on subgroups of secukinumab 150mg treated pts categorised by their highest ASAS criteria response at the earlier time point (ASAS non-responder [ASAS NR], ASAS20 responder, ASAS40 responder) and evaluating whether this response was improved, sustained, or worsened at the later time point, based on observed analysis.

Results: Overall, 65, 61 and 59 pts treated with secukinumab 150mg had available data to determine ASAS responses for shift analyses from Wk 2 to 16 and Wk 16 to 52 or 104, respectively. At baseline, mean age was 41.9±12.5 years, mean time since diagnosis was 7.0±8.2 years and mean Bath Ankylosing Spondylitis Disease Activity Index score was 6.1±11.5. Approximately half of the ASAS NR pts at Wk 2 or 16 subsequently developed an ASAS 20 or 40 response at the later time point of Wk 16 or 52, respectively. A total of 79% pts improved their response from ASAS20 to ASAS40 at Wk 16 (Wk 2 to 16) and another 44% pts improved their response from ASAS20 to ASAS40 at Wk 16 from Wk 16 to 52. A majority (84%) of ASAS40 responders at Wk 2 or 16 maintained this response at Wk 16 or 52, respectively. Similar trends were observed in responses from Wk 16 to 104 (Figure).

Conclusions: In this post-hoc pt-level analysis, the majority of secukinumab 150mg treated pts maintained or improved their ASAS responses over time, consistent with the sustainability of group-level ASAS responses reported previously.2 In particular, the majority of pts who achieved either an ASAS20 or ASAS40 response at Wk 2 or 16 maintained or improved their response at Wks 16, 52 or 104, respectively.

References:

THU0399 TAPERING THERAPY OF TNF-INHIBITOR FOR MRI CHANGES IN SPONDYLOARTHRITIS

Y. Song, Y. Cui, X. Zhang, H. Zeng, Y. Zeng. Guangdong General Hospital, Guangzhou, China

Background: TNF-inhibitors could significantly improve disease activity of SpA patients, however, there is still no answer to the effect of prolonged the interval of TNF-inhibitors on MRI changes.

Objectives: The aim of the study was to investigate whether prolonged the interval of TNF-inhibitor injection could maintain SpA at low disease activity and improve imaging changes of sacroiliac joint.

Methods: A total of 98 SpA patients were included and 67 of them received TNF-i with or without conventional DMARDs. TNF-i included Etanercept, Infliximab and Adalimumab. The full dosage treatment was defined as patients received Etanercept 50 mg per week, Infliximab 4 mg/kg at 0, 2, 6 week and Adalimumab 40 mg every two weeks. The dose of Etanercept was gradually reduced to 50 mg every two weeks, 50 mg every three weeks and then 50 mg per month. The infusion of Infliximab was reduced to every 8 weeks, every 12 weeks and then every 16 weeks. The interval of Adalimumab injection was changed from 3 weeks to 4 weeks and then to two months. After full dose treatment in the first 3 months, patients who administrated TNF-i were evaluated every 3–6 months. According to laboratory tests including ESR, CRP and IgA levels, BASDAI, BASFI, ASDAS results and sacroiliac joint SPARCC scores, the interval of TNF-i treatment was gradually prolonged. Fat metaplasia, bone erosion, sclerosis and ankylosis changes on MRI were compared between baseline, 4–6 months and 1–2 years.

Results: After 3 months of treatment, inflammatory indexes, BASDI, BASFI, ASDAS results and sacroiliac joint SPARCC scores, the interval of TNF-i treatment was gradually prolonged. Fat metaplasia, bone erosion, sclerosis and ankylosis changes on MRI were compared between baseline, 4–6 months and 1–2 years.

Conclusions: In this study, we have demonstrated that increasing the interval of TNF-inhibitors was associated with the maintenance of disease activity and MRI changes in SpA patients. Further research is needed to evaluate if this observation can be confirmed in additional studies.

References:

Disclosure of Interest: X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCBS, Werfen, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCBS, Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, Consultant: for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCBS, Werfen, A. Kivitz Consultant for: AbbVie, Pfizer, Genentech, UCB, Celgene, Sponsors bureau; Celgene, Pfizer, Genentech, A. Deodhar Shareholder of: Novartis, Employee of: Novartis, Z. Tallochery Shareholder of: Novartis, Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, C. Gailezz Shareholder of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.1196

Table 1. ESR, CRP and IgA changes before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>15 months</th>
<th>18 months</th>
<th>24 months</th>
</tr>
</thead>
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<tr>
<td>ESR (mmh)</td>
<td>8.35</td>
<td>2.35</td>
<td>2.35</td>
<td>2.35</td>
<td>2.35</td>
<td>2.35</td>
<td>2.35</td>
<td>2.35</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>10.54</td>
<td>10.54</td>
<td>10.54</td>
<td>10.54</td>
<td>10.54</td>
<td>10.54</td>
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<td>10.54</td>
</tr>
<tr>
<td>IgA (mg/L)</td>
<td>2.96</td>
<td>2.96</td>
<td>2.96</td>
<td>2.96</td>
<td>2.96</td>
<td>2.96</td>
<td>2.96</td>
<td>2.96</td>
</tr>
</tbody>
</table>

P<0.05, **P<0.01.
group. The SPARCC scores in TNF-i group also decreased significantly (Figure 1, P<0.01). There was no significant progression in fat metaplasia, bone erosions, sclerosis and ankylosis during the follow-up period (P<0.05). Even though the inflammatory indexes and clinical evaluation of non-TNF-i group did not improved remarkably, SPARCC score were significantly reduced at 4–6 months and 1–2 years follow up at baseline (P<0.05).

Conclusions: TNF-i could reduce clinical and imaging inflammatory degree. Prolonged the interval of TNF-i treatment could maintain low disease activity and improve bone marrow edema, whereas fat metaplasia, bone erosion, sclerosis and ankylosis were not exacerbated.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4775

**THU0400**  RISK FACTORS OF SAGITTAL TRANSLATION AFTER PEDICLE SUBTRACTION OSTEOTOMY ON ANKYLOSING SPONDYLITIS

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Background: Few studies on sagittal translation and its risk factors after pedicle subtraction osteotomy (PSO) in ankylosing spondylitis (AS) patients have been conducted. There is also no study on overall evaluation of radiologic parameters as the candidate of its risk factor.

Objectives: The aim of this study was to report the cases of sagittal translation which developed after PSO in AS patients with kyphotic deformity and to analyze its risk factors.

Methods: The subjects of this study were 53 AS patients (58 cases) who underwent PSO to correct their kyphotic deformity between March 2006 and August 2016. The 53 subjects consisted of 45 males and 8 females. Their mean age was 39.3 ±12.7 years (range: 23–67). After osteotomy, the patient was examined for the presence of sagittal translation in the correction site through intraoperative radiograph. The low modified Stoke AS spine score (mSASSS) was measured before the surgery. The vertebral parameters such as lumbar lordosis angle, thoracic kyphotic angle, and sagittal vertical axis, and the pelvic parameters such as pelvic incidence, pelvic tilt, and sacral slope were also measured before and after the surgery.

The subjects were grouped according to the presence and absence of sagittal translation, and their radiologic parameters were compared. In addition, the correlation between sagittal translation and each parameter was analyzed. Complications that developed during and after the surgery were also analyzed.

Results: Sagittal translation developed in 18 subjects (34%) or 19 cases (35%) (p<0.001). The mean lumbar lordosis angle and the mean sagittal vertical axis of both the sagittal translation (ST) group and the non-sagittal translation (Non-ST) group were successfully corrected (p=0.000, respectively). A significant difference in preoperative mean sacral slope was observed between the groups (p=0.045). The ST group showed a significantly higher mSASSS (48±12.07) than the Non-ST group (36±18.62) (p<0.002). In the multivariate regression analysis, sagittal translation was positively correlated with mSASSS (odds ratio 1.34, P=0.002) and the preoperative sacral slope (odds ratio 1.46, P=0.0009), and negatively correlated with the difference between preoperative and postoperative thoracic kyphotic angle (odds ratio 0.68, P=0.01). Both groups showed no finding of permanent neurologic complication after the surgery.

Conclusions: The incidence of sagittal translation after pedicle subtraction osteotomy was closely related with the severity of ankylosis in AS patients. Therefore, when pedicle subtraction osteotomy is performed for AS patients with severe ankylosis and high sacral slope, it is required that surgeon considers sagittal translation which could induce neurologic complication.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4941

**THU0402** ULTRASONOGRAPHY AND DUAL-ENERGY CT (DECT) DO NOT PROVIDE THE SAME QUANTIFICATION OF URATE DEPOSITION IN GOUT: RESULTS FROM A CROSS-SECTIONAL STUDY


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Background: Gout is due to monosodium urate (MSU) deposition in joints and soft tissues. Ultrasonography (US) and dual-energy CT (DECT) have been shown to be effective in identifying MSU deposits. Both techniques can examine topi size. DECT is effective to identify soft-tissue MSU deposits and US can show joint deposition with the double contour (DC) sign. It is unknown if these two techniques provide the same quantification of the extent of urate deposition on a given joint.

Objectives: The main objective of this study is to compare the tophus size measured by US and by DECT. The secondary objective is to evaluate the correlation between the prevalence of the US DC sign and the global volume of urate deposits measured by DECT.

Methods: This prospective cross-sectional study included patients fulfilling the 2015 ACR/EULAR criteria for gout. Patients underwent US and DECT examinations of their knees and feet. The largest US tophi was selected as the index tophus. US examination of the DC sign was performed on the femoro-patellar joints, talo-crural joints and 1st metatarsophalangeal joints. Total volume of urate deposits of knees and feet was measured by DECT. The primary endpoint was the intra-class correlation coefficient (ICC) of the volume of the index tophus measured by US and DECT [CI 95%].

Results: A total of 64 patients were included in the study, of which 35 patients presented with at least one US tophus. Patients were in average 64.2 ± 13.9 years old. 84.4% were male, had an average ACR/EULAR score of 13 ± 6.25, and disease duration was 12 ± 14.7 years. Overall, 44 patients (88.8%) were currently taking urate lowering therapy and 22 patients (34.4%) had clinical tophi. Out of the 35 US selected largest tophi, 6 tophi were not seen in DECT. Of the tophi identified with both techniques, 10 were localized in the feet and 8 in the knees. The ICC of the tophus volume assessment by US and DECT was 0.45 [0.12–0.69]. The average volume of the largest US tophi was 2.7 ± 6.5 cm³ and 1.5 ± 3.3 cm³ when measured by DECT. If the index tophus was localized in the knee, the ICC was 0.36 [0.0–0.82] and was 0.68 [0.37–0.86] if the tophus was in the
the foot. The Spearman correlation coefficient between the DECT urate volume and the number of joints with a positive DC sign was 0.15.

**Conclusions:** US and DECT do not provide the same assessment of tophus size. The correlation is improved when considering tophi localized in the feet. The number of joints with positive DC sign does not correlate to the volume of tophus deposition in the soft tissues measured by DECT.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-earl.4118

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**THU0403**

URATE-LOWERING TREATMENT AND RISK OF INCIDENT UROLITHIASIS IN PEOPLE WITH GOUT: A NESTED CASE-CONTROL STUDY

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**Background:** A higher risk of uric lithiasis has been reported in gout patients. However, whether urate-lowering treatments, including both xanthine oxidase inhibitors and uricosuric agents, are beneficial to reduce the risk or uric lithiasis in gout patients has not been examined.

**Objectives:** To investigate the independent associations between urate-lowering treatment (ULT) and the risk of uricolithiasis in incident gout patients.

**Methods:** We conducted a nested case-control study based on the Taiwan National Health Insurance Research Database (NHIRD), which was used to identify 473,858 newly diagnosed gout patients from the period from January 1, 2000 through December 31, 2004. All these patients were followed until December 31, 2013. We considered patients who first diagnose uricolithiasis after the date of entry cohort (gout onset) as cases and the diagnostic date was defined as index date. Each case was matched up to five eligible controls whose follow-up period included the case’s index date by sex, birth of year and gout diagnosis year. And the index date of case was assigned to the matched controls. Odds ratios (ORs) and 95% confidence interval (CI) of uricolithiasis associated with cumulative defined daily dose (cDDD) of xanthine oxidase inhibitor and uricosuric agents were modeled using multivariable logistic regression.

**Results:** Gout patients with incident uricolithiasis (n=32,654) occurring after the initial diagnosis of gout aged 20–79 were age- and sex-matched 1:5 to 163,270 gout patients without uricolithiasis. After adjusting for age, sex, urbanization status, income, occupation, and pertinent drugs and comorbidities, the OR of uric lithiasis associated with use of ULT among gout patients were 1.04 (95% CI 1.00 to 1.07) for those with 28–90 cDDD, 0.95 (95% confidence interval 0.91–0.99) for 91–365 cDDD and 0.77 (95% confidence interval 0.73–0.82) for >365 cDDD, compared with those with a cDDD <28. The OR (95% CI) for uricolithiasis associated with xanthine oxidase inhibitor use was 0.94 (0.89–0.99) for 28–90 cDDD, 0.90 (0.84–0.97) for 91–365 cDDD and 0.73 (0.63–0.83) for >365 cDDD. For uricosuric agents, the OR (95% CI) for uricolithiasis among those with 28–91, 91–365 and <365 cDDD were 1.04 (1.01, 1.08), 0.94 (0.90–0.98) and 0.78 (0.73–0.84), respectively.

**Conclusions:** Higher ULT consumption was associated with a lower risk of uric lithiasis. Xanthine oxidase inhibitors associated with reduced uricolithiasis risk consistently across the range of consumption studied but for uricosuric agents inadequate cumulative dose results in a higher risk despite the risk reduced gradually with a higher cumulative dose.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-earl.3452

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**THU0404**

SELF-REPORTED SEVERITY OF GOUT IN A PRIMARY CARE SETTING AND ASSOCIATED FACTORS – RESULTS FROM A GOUT SURVEY IN PRIMARY CARE


**Background:** Patients with gout are usually seen in primary care. There are numerous reports regarding severity of gout in cohort studies and patients seen in more specialized care, less is known about the spectrum of severity of the disease in primary care.

**Objectives:** To describe the pattern of self-reported disease severity of gout and predictors thereof in a primary care setting.

**Methods:** All patients above 18 with an ICD10-diagnosis of gout at a health care visit in primary care (Jan 2015 through Aug 2016) were identified from primary care (Jan 2015 through Aug 2016) were identified from primary care. All patients above 18 with an ICD10-diagnosis of gout at a health care visit in primary care (Jan 2015 through Aug 2016) were identified from primary care. All patients above 18 with an ICD10-diagnosis of gout at a health care visit in primary care (Jan 2015 through Aug 2016) were identified from primary care. All patients above 18 with an ICD10-diagnosis of gout at a health care visit in primary care (Jan 2015 through Aug 2016) were identified from primary care.

**Results:** Over 40% of patients with gout in a primary care setting rated their disease as moderate or severe. The validity of the patients rating was supported by other covariates reflecting disease severity. The observations that women and those with hyperlipidemia reported a more severe disease needs to be further explored.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-earl.2913

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**THU0405**

KILLING TWO BIRDS WITH ONE STONE? THE DASH DIET AND THE RISK OF GOUT: 26-YEAR FOLLOW-UP OF A PROSPECTIVE COHORT

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**Background:** The Dietary Approaches to Stop Hypertension (DASH) diet, which reduces blood pressure and is recommended in cardiovascular disease (CVD) (1,2), has also been found to lower serum uric acid (SUA) levels, particularly among those with hyperuricemia (3). Thus, the DASH diet may be particularly useful in gout care by reducing both SUA and CVD risk, especially among patients with hypertension which affects 74% of gout patients (4), thereby “killing two birds with one stone”. However, corresponding data for the risk of gout are not available. In contrast, a Western dietary pattern may increase the risk of gout.

**Objectives:** To prospectively examine the relation between the DASH and Western dietary patterns and the risk of gout among men.

**Methods:** Using the Health Professionals Follow-Up Study, we prospectively examined the relation between the DASH and Western diets and incident gout in 44,444 male participants with no history of gout at baseline. Using validated food frequency questionnaires, each participant was assigned a DASH score (higher intake of fruits, vegetables, nuts, legumes, low-fat dairy products, and whole grains, and low intake of sodium, sweetened beverages, and red and processed meats) and a Western pattern score (reflecting higher intake of red and processed meats, French fries, refined grains, sweets, and desserts). We identified incident cases of gout meeting the preliminary ACR survey criteria for gout, adjusting for potential confounders including age, total energy intake, body mass index (BMI), diuretic use, history of hypertension, history of renal failure, and intake of alcohol and coffee. We conducted stratified analyses to evaluate whether the association between the DASH and Western patterns scores and the risk of gout differed by other variables, including BMI, alcohol use, and hypertension status.

**Results:** During 26 years of follow-up, we documented 1,731 confirmed cases of incident gout. A higher DASH score was associated with a lower risk for gout (multivariable relative risk [RR] for extreme quintiles, 0.68 [95% confidence interval, 0.57 to 0.80]; P for trend <.001) (Table 1). In contrast, a higher Western pattern score was associated with an increased risk for gout (multivariable RR for extreme quintiles, 1.42 [95% confidence interval, 1.16 to 1.74]; P for trend <.005) (Table 1). These associations persisted regardless of BMI, alcohol use, and hypertension status, and there was no significant interaction between these variables (all P for interaction >.17).

**Table 1. Characteristics of gout patients stratified by disease severity and logistic regression models**

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Mild*</th>
<th>Moderate*</th>
<th>Severe*</th>
<th>Univariable analyses**</th>
<th>Multivariable analyses***</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI-lowest quintile</td>
<td>0.87</td>
<td>0.94</td>
<td>0.81</td>
<td>0.87 (0.85–0.90)</td>
<td>0.87 (0.84–0.90)</td>
<td>0.26</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI-lowest quintile</td>
<td>0.77</td>
<td>0.94</td>
<td>0.80</td>
<td>0.77 (0.74–0.81)</td>
<td>0.77 (0.73–0.81)</td>
<td>0.03</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*The response rate was 54%. Response rates were significantly lower in women overall and in men under the age of 50. Covariates that were significantly associated with more severe self-reported severity of gout in the bivariate logistic regression models (Table 1) were: female sex, hyperlipidemia, higher number of previous attacks, attack during last month, HAQ. In the multivariate analysis objective measures of gout severity such as more than ten previous attacks and attack during last month were strongly associated with the patients grading of severity, in addition to presence of hyperuricemia (Table 1).

**Conclusions:** Over 40% of patients with gout in a primary care setting rated their disease as moderate or severe. The validity of the patients rating was supported by other covariates reflecting disease severity. The observations that women and those with hyperlipidemia reported a more severe disease needs to be further explored.
Conclusions: The DASH dietary pattern is associated with a lower risk of gout, suggesting that its urate-lowering effect among hyperuricemic individuals translates to a lower risk of gout. Conversely, the Western dietary pattern is associated with a higher risk of gout. The DASH diet may provide an attractive preventive dietary approach for the risk of gout, particularly given the high level of cardiovascular comorbidities among this patient population.


Acknowledgements: This research was supported by NIH grant R01AR65944.

Disclosure of Interest: None declared.


THU0406 SERUM URIC ACID LOWERING TREATMENT APPEARS UNNECESSARY DURING HEMODIALYSIS

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1 Departamento de Medicina Clínica, Universidad Miguel Hernández; 2 Sección de Reumatología; 3 Servicio de Análisis Clínicos, Hospital General Universitario de Alicante; 4 Unidad de Nefrología, Hospital Vithas Perpetuo Socorro; 5 Emeritus Professor, Universidad Miguel Hernández, Alicante, Spain.

Background: Gout patients often suffer from renal disease, some ultimately developing end-stage renal disease (ESRD) and requiring hemodialysis (HD) replacement therapy. Though some reports suggested that tophi disappear after HD, urate-lowering agents are frequently continued, often based on persistent high SUA levels before HD. Also, the impact of SUA levels in the survival of patients on hemodialysis (HD) is under discussion.

Objectives: To assess the SUA reduction achieved under HD and analyze the kinetics of SUA in a week of intermittent HD.

Methods: SUA levels were determined before and after HD sessions in consecutive 96 patients with end-stage renal disease (ESRD), and compared through paired samples. Student’s t test. Variables related to HD were analyzed whether associated with SUA reductions >80% using Student’s t test or ANOVA. Also, a kinetics study on selected 10 patients with hyperuricemia (SUA before HD) <6.8 mg/dL throughout intermittent HD sessions in a week period was performed; differences in SUA levels were analyzed by repeated measures ANOVA.

Results: Patients were mean aged 66.5 years (SD±13.8), 62 males (64.6%). Mean time on HD replacement was 7.1 years (±7.2). Before starting HD, 43.0% had hyperuricemia and 21.6% reported gout. Sixteen (16.4%) continued on urate-lowering agents after HD. Mean SUA levels before and after HD session was 5.2mg/dL (±1.0) and 1.0mg/dL (±2.4), respectively. Mean SUA reduction following HD was 80.2% (95% CI 78.4–82.0); 51 patients (56.7%) showed SUA reduction ≥80%. HD-related variables Kt/V<1.3 (p=0.006) and blood efflux <400mL/min (p=0.004) significantly associated with achieving SUA reduction >80%. Figure shows the SUA kinetics study: SUA significantly reduced all over the period and persisted below hyperuricemia threshold (p=0.015).

Conclusions: Under HD replacement therapy SUA levels effectively reduced and persisted below saturation point, suggesting that urate-lowering therapy appears unnecessary for patients with gout and ESRD.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2392

THU0407 HIGH GOUT CLASSIFICATION SCORE IS ASSOCIATED WITH ULTRASOUND FINDINGS IN PATIENTS WITH CRYSTAL-PROVEN GOUT

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Background: The recent ACR/EULAR classification (1) classify gout in patients with at least 8 out of maximum 23 points, but presence of monosodium urate crystals in a symptomatic joint/tophus alone is sufficient for gout classification without need for further scoring. It is not known how in crystal-proven patients with increased serum urate (sUA) the whole range of classification points distribute.

Objectives: To determine the distribution along the spectrum of ACR/EULAR criteria in crystal-proven patients with insufficiently treated sUA levels, and if disease factors in gout are associated with high classification scores.

Methods: Baseline data from a prospective observational study were used from patients with crystal-proven gout who presented after a recent gout flare. Included patients had at baseline insufficiently treated sUA level (>360 μmol/L [>6 mg/dl]). Demographic, clinical data and sUA levels were collected from September 2015 to December 2016 in one rheumatology department. Ultrasound of joints was assessed with one total score for double contour sign, tophus, and aggregates in several joints and tendons/entheses. The score for ACR/EULAR criteria for gout was calculated.

Results: 89 patients were included, with baseline mean (SD) age 56.0 (14.8) years, 92% males, 88% Caucasians, disease duration 7.9 (7.3) years, presence of palpable tophi 19%, ultrasound score 19.9 (13.8), serum urate 486 (90) μmol/L, creatinine 78 (18) mg/dl, creatinine clearance 78 (18) ml/min, ESR 14 (14) mmh, body mass index 29.4 (4.9) kg/m², comorbidity score [SCQ] 3.5 (3.2), and physical function [HAQ] 0.3 (0.5). All patients satisfied clearly the scoring arm of the classification criteria with a median (range) 19 (11 – 23) of 23 possible points (Figure 1). Patients with a median and higher score above the median (>19 points) vs. lower score reported more gout flares during the last 12 months (p=0.001), had longer disease duration (9.2 vs. 6.2 yrs, p=0.05), and a higher ultrasound score (23.9 vs. 14.9, p=0.001). The groups with high and low scores were similar for age, gender, ethnicity, level of education, BMI, physical function, comorbidity score, sUA level and kidney function.


Disclosure of Interest: T. Uhlig: None declared, L. F. Karolussen: None declared, E. A. Haavardsholm: None declared, T. K. Kvien Consultant for: Fees for speaking and/or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, H. B. Hammer. None declared.

DOI: 10.1136/annrheumdis-2017-eular.2196

THU0408 GOUT IS AN IMPORTANT PREDICTOR OF WORK DISABILITY IN BOTH MEN AND WOMEN

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1 Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg; 2 Centre for Clinical Research Dalarna, Falun, Sweden.

Background: Gout is the most common form of inflammatory arthritis with a prevalence of 1.5% in our area in the age group 50–59 years (1). Gout has a
substantial association with several comorbidities. Studies on the impact of gout on work disability on a population level are scarce.

**Objectives:** The primary objective of the study was to investigate if gout was a predictor of work absenteeism exceeding 90 days in a calendar year, controlling for comorbidities and socioeconomic status in men and women separately. Another aim of the study was to explore if urate lowering therapy (ULT) attenuated the risk of work disability for gout cases.

**Methods:** Gout cases were defined in the population based health care database (VEGA) of the Western Swedish Health Care Region (WSHCR) by having a first diagnosis of gout in the years 2003–2009 by ICD-10 codes (M10 and M14.0) in VEGA. Cases were included if their age at the time of diagnosis of gout was ≥82 years. Five controls for each case, matched for age, sex and place of residence were chosen from the census register by Statistics Sweden. Individuals with any work disability in the year before the index year were excluded from analysis. Data on predefined comorbidities registered previous to the index year was collected from VEGA by ICD-10 codes. Data on prescribed medications was collected from the national prescription database. Data on educational level, income and number of days per calendar year with sick-leave and disability pension was provided by Statistics Sweden. Conditional logistic regression taking into account the 1-to-5 matched design of the study was performed in individuals without work disability in the year before the index date for the outcome of ≥25% (≥90 days) work disability in the year after the index year. Possible predictors of work disability for gout cases were analyzed using logistic regression.

**Results:** 3068 incident gout cases (females N=1,654 (18%) of working age without prior work disability were matched to 15,077 population controls. After matching, 3258 controls with prior work disability were excluded leaving 11,819 controls for analysis. Of the women with gout, 69 (12.5%) became ≥25% work disabled in the year after the index-year as opposed to 117 (6.1%) of the female controls, p<0.0001. 163 men with gout (6.6%) became ≥25% disabled vs. 377 (3.8%) of male controls, p<0.0001. After adjusting for comorbidities and educational level gout increased the risk of work disability to a similar extent for men (OR 1.4, 95% CI 1.2–1.8) and women (OR 1.9, 95% CI 1.4–2.6). Cardiovacular and renal comorbidity as well as alcoholism, female sex and low educational level (less than 12 years) were important predictors of work disability in gout patients whereas receiving ULT during the time period being studied did not attenuate the risk (OR 0.8, 95% CI 0.5–1.1).

**Conclusions:** Gout is a significant independent predictor of work disability in both men and women. ULT did not attenuate the risk of work disability early after diagnosis for gout cases in this study, possibly explained by under-prescribing and sub-optimal dosage as previously shown in our region (1).

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4022

**THU0409 NOT JUST A SWOLLEN BIG TOE: INCREASING ALL-CAUSE HOSPITALIZATIONS IN PATIENTS WITH GOUT IN THE UNITED STATES: 1993–2014**

G. Singh 1, A. Mithal 2, A. Mithal 3

**Background:** Gout is a disorder of uric acid metabolism and often presents as acute severe joint pain. However, several recent studies have highlighted systemic complications of associated hyperuricemia in patients with gout, including possible increased risk of renal and cardiovascular comorbidities.

**Objectives:** To study all-cause hospitalizations in patients with gout in the United States (US) from 1993 to 2014.

**Methods:** The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary or secondary diagnosis of gout, and compared them to total all-cause US hospitalizations during the same period. US population estimates and projections for the resident US population were obtained from the US Census Bureau.

**Results:** There were 789.8 million all-cause hospitalizations in 6.4 billion person-years of observation from 1993 to 2014 (123.4 hospitalizations per 1,000 person-years). During this time-period, 9,741,598 hospitalizations occurred in patients with gout (152.2 per 100,000 person-years). All-cause US hospitalizations increased from 33.7 million in 1993 to 35.4 million in 2014, an increase of 4.8% over 22 years (Figure, dotted blue line). All-cause hospitalizations in gout patients have increased from 167,441 in 1993 (64.2 per 100,000 person-year) to 854,475 in 2014 (267.9 per 100,000 person-years, a dramatic increase of over 410% (p<0.0001, Figure solid red line). In 2014, hospitalizations in gout patients accounted for over 4.6 million hospital days at a total national cost of over US $42.6 billion.

**Conclusions:** All-cause hospitalizations in patients with gout in the US have significantly increased by 410% in the last 22 years, almost hundred-fold of the 4.8% increase in US population all-cause hospitalization rate in the same time period. This calls for an increase need for identification and management of serious co-morbid conditions in patients with gout.

**Disclosure of Interest:** G. Singh Grant/research support from: Horizon Pharmaceuticals, A. Mithal: None declared, A. Mithal: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5458

**THU0410 GOUT AND THE RISK OF INCIDENT ERECTILE DYSFUNCTION: A BODY MASS INDEX-MATCHED POPULATION-BASED STUDY**

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**Background:** Gout is the most common inflammatory arthritis. Erectile dysfunction is common in the general population; however, evidence regarding erectile dysfunction among gout patients is limited.

**Objectives:** Our purpose was to study whether there was an increased risk of erectile dysfunction among gout patients, as compared with the general population.

**Methods:** We conducted a cohort study using The Health Improvement Network, a large electronic medical record database in the United Kingdom. Up to five individuals without gout were matched to each case of incident gout by age, enrolment time, and body mass index. Multivariate Hazard Ratios for erectile dysfunction were calculated after adjusting for smoking, alcohol consumption, comorbidities and medication use.

**Results:** We identified 2290 new cases of erectile dysfunction among 38,438 patients with gout (mean age 63.6 years) and 8447 cases among 154,332 individuals in the comparison cohort over a 5-year median follow up (11.9 vs. 10.5 per 1000 person-years, respectively). Univariate (age, entry time and body mass index-matched) and multivariate Hazard Ratios for erectile dysfunction among patients with gout were 1.13 (95% CI, 1.08 to 1.19) and 1.15 (95% CI, 1.09 to 1.21), respectively. In our sensitivity analysis, restricting gout cases to those receiving anti-gout treatment (n=31,227) the magnitude of relative risk was stronger than the primary analysis; (multivariate Hazard Ratios =1.29; 95% CI, 1.22 to 1.37).

**Conclusions:** This population-based study suggests an increased risk of erectile dysfunction among gout patients, supporting a possible role for hyperuricemia and inflammation as independent risk factors for erectile dysfunction.

**References:**

**Disclosure of Interest:** N. Schlesinger Grant/research support from: Astra Zeneca, Consultant for: Astra Zeneca, Horizon, Celgene, ProteoThera, Pfizer, N. Lu: None declared, H. Choi Grant/research support from: Astra Zeneca, Consultant for: Takeda, Selecta

**DOI:** 10.1136/annrheumdis-2017-eular.2710
TREATMENT WITH NERIDRONATE IN CHILDREN AND ADULTS WITH OSTEONECROSIS IMPERFECTA: DATA FROM OMERACT, NOT CONTROLLED, THREE-YEAR ITALIAN STUDY

A. Fassio, L. Idalazzi, O. Viapiana, C. Benini, E. Vantaggiato, A. Giolli, M. Rossini, D. Gatti. Rheumatology, Ospedale S. Giovanni Battista, Turin, Italy

Background: Osteonecrosis Imperfecta (OI) is a rare generalized connective tissue disease. Its main features are skeletal fragility and substantial growth delay. Patients with tophaceous gout, improves significantly with allopurinol.

Objectives: To assess the long-term efficacy and safety of the treatment in young adults.

Methods: A cohort of patients with gout (ARA/ACR-EULAR) from the GRESGO cohort; this analysis includes the patients with ≥1 clinical node(s) considered as tophi in the baseline visit. Tophi size had r=0.93 among the 3 evaluations (ITst, ITSc, ITScr) and r=0.3 with ITh. Inter- and intraobserver variability was 0.8 and 0.9 respectively; there was significant improvement (p<0.001) in ITS, sUA, painful, swollen, limited to motion joints, HAQ, EROQOL, VAS pain, VAS health (patient and physician) also improved significantly.

Conclusions: in patients younger than 20 years, while, in patients older than 20 years, BMD significantly increased from baseline only at month 18, 30 and 36 respectively. The mean ultralradial BMC significantly increased from baseline to any time point in patients younger than 20 years, while there were no substantial or statistically significant differences from baseline to any time point in patients aged older than 20 years. The mean of fractures observed in the 3 years of treatment was significantly lower than that observed in the 3 years before the start of treatment in both groups (table 1).

Most of AE were symptoms of an acute phase reaction, which was reported in 47.3% of patients younger than 20 years and in 22.8% of those older than 20 years. Serious adverse events (SAEs) were reported in 19 patients (34.5%) younger than 20 years and in 26 patients (22.8%) aged older than 20 years. None of the reported SAEs in both groups was considered as treatment-related.

Table 1. Results of number of fractures per patient during treatment in the two patient populations

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Conclusions: long-term treatment with i.v.neridronate has positive effects on BMD, BMC, bone turnover markers and fracture risk with a good safety profile in both groups.

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Disclosure of Interest: None declared

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TREATMENT WITH NERIDRONATE IN CHILDREN AND ADULTS WITH OSTEONECROSIS IMPERFECTA: DATA FROM OMERACT, NOT CONTROLLED, THREE-YEAR ITALIAN STUDY

A. Fassio, L. Idalazzi, O. Viapiana, C. Benini, E. Vantaggiato, A. Giolli, M. Rossini, D. Gatti. Rheumatology, Ospedale S. Giovanni Battista, Turin, Italy

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disfunction or BP. Endothelial dysfunction or BP might be associated with changes in sUA when measured longitudinally in individuals, but not when measured cross-sectionally in populations. Larger studies will be needed to confirm these results.

References:

Acknowledgements: National Institute of Arthritis and Musculoskeletal and Skin Diseases P50AR060772, K24AR052631 (to KGS).

Disclosure of Interest: M. Saddehkani: None declared, K. Saag Grant/research support from: AstraZeneca, Crealet, Takeda, Consultant for: Aredea/AstraZeneca, Crealet, Takeda, D. Redden: None declared, O. Al-Ghamdi: None declared, A. Gaffo Grant/research support from: US Government, University, Actelion Pharmaceuticals US, NIH/NHLBI, Merck and Co., Consultant for: Amgen, Bayer, Boehringer Ingelheim, AstraZeneca, Medtronic, GlaxoSmithKline, Forest Labs Inc., D. Feig: None declared, P. Muntrer: None declared, A. Foster: None declared, S. Biggess: None declared, E. Rahm: None declared, P. Li: None declared, D. Redden: None declared, A. Gatto Grant/research support from: Aredea/AstraZeneca, Consultant for: Cymbay, Ardea, Employee of: US Government

DOI: 10.1136/annrheumdis-2017-eular.5313

THU0414 INCIDENCE AND PREDICTORS FOR NEPHROLITHIASIS IN GOUT PATIENTS AND THE GENERAL POPULATION

A.J. Landgren1, L. Jacobsson1, U. Lindström1, T.Z. Sandström1, E. Fjellstedt2, P. Drivelégka1, V. Sigurdardottir1, L. Björkman 1, M. Dehlin 1.

A well-known complication of gout is an increased risk for nephrolithiasis (NL). The incidence rate of NL in the general population varies in different studies between 85 and 170/100 000 person-years, with a peak incidence in the ages 40–49 years. Several medications used in gout patients could affect the risk for NL, including allopurinol, losartan, thiazide- and loop-diuretics. Effect of these medications on risk of NL in gout patients, and the general population, has only scarcely been studied.

Objectives: In this cohort study we investigated: 1) overall incidence of NL in gout and general population (GP) controls 2) risk for first time NL in gout patients vs general population (GP) controls, and 3) predictors for first time NL in both groups separately.

Methods: Gout patients were identified from the regional health care database in western Sweden (VEGA), containing ICD10-codes for all regional Healthcare visits from 2000. Matched (birthyear, sex, county) GP controls were selected from the population register. National registers and VEGA were used to retrieve information on comorbidities, socioeconomic factors and current medications at start of follow-up. The study population had to be above 19 years of age, without NL prior to start of follow-up, and living in the Western Swedish Health Care Region (WSHCR). Follow-up began 2006–01–01, or at the first gout-diagnosis if this occurred later, and ended at death, emigration or 2012–12–31, whichever occurred first. Incidence rates (IR) per 1000 person-years and hazard ratios (HR) were calculated. Possible predictors for NL were based on risk factors presented in the literature.

Results: 29,968 gout patients and 138,678 matched GP controls were included. In gout patients there were 678 NL-events (IR: 6.2 per 1000 ppyrs at risk (95% CI: 5.7–6.6)) and in GP controls 2125 (IR 3.9 per 1000 ppyrs at risk (95% CI 3.7–4.0)). Risk for NL was increased in gout (HR=1.49, 95% CI: 1.35–1.64), and was higher in men compared to women (p<0.0001) in all age groups for gout cases and controls. All comorbidities and medications were more frequent in cases compared to controls (p<0.0001) at start of follow-up. Risk-factors for NL such as kidney disease (KD), obesity, diabetes were 2–4 times more common in gout patients compared to GP controls. Predictor point estimates for NL were similar as kidney disease (KD), obesity, diabetes were 2–4 times more common in gout cases compared to GP controls. In patients with gout, male sex, diabetes mellitus (DM), obesity predicted NL, whereas use of loop diuretics was protective. Overall, the most commonly used CVD drugs did not increase the risk for NL in patients with gout.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2836

THU0415 A STRUCTURED MONITORING PROGRAM FOR DRUG ALLERGY IN PATIENTS NEWLY INITIATED ON ALLOPURINOL

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Background: Allopurinol allergy (drug eruption, severe cutaneous adverse reactions [SCAR] and drug induced hypersensitivity syndrome [DIHS]) develops during the first 2–12 weeks after initiation. SCAR risk factors include Chinese ethnicity, HLA-B*5801 positivity and chronic kidney disease. HLA-B*5801 testing to prevent SCAR has not been shown to be cost-effective in Singapore.

Objectives: To retrospectively study whether a structured monitoring program (SMP) can lead to early diagnosis of allopurinol allergy and prevent development of SCAR/DIHS.

Methods: SMP patients (cases) managed by rheumatologists were compared with controls managed by non-rheumatologists during the study period 1 Jan 2015 to 30 Jun 2016. Cases upon initiation of allopurinol had baseline full blood count (FBC), serum creatinine (Cr), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) measured. If drug eruptions/abnormal laboratory tests developed during monitoring, allopurinol was stopped. The electronic dispensing system and computerized medical records were used for collection of patient demographics, indication for allopurinol use, initiation dose, monitoring intervals, laboratory results and clinical features of drug allergy. This was compared with the control group without an SMP. Chi square tests were used to compare differences in proportions and Mann-Whitney U test for differences in medians. P value ≤0.05 was considered statistically significant.

Results: There were 61 cases and 30 controls with comparable age (p=0.81), ethnicity (~80% Chinese) (p=0.63) and estimated glomerular filtration rate, eGFR (p=0.72). There were significantly more cases with tophaceous gout (41% vs 10%, p=0.003), while more controls tumour lysis syndrome prophylaxis (30% vs 0%, p=0.001). Median (interquartile range, IQR) starting dose of 50 (50) mg was lower among cases versus controls of 100 (200) mg (p<0.001); all cases had baseline and follow-up laboratory tests compared to controls (p<0.001). Cases were followed up at a median (IQR) of 2 (1.1) weeks after initiation then 5 (2.0) weeks after the first visit, whereas controls were reviewed 8 (8.9) weeks after initiation, then 11 (4.6) weeks after the first visit. Two patients in the SMP group with normal eGFR developed maculopapular eruption (MPE), 1 elevated ALT/AST, and 1 both MPE and elevated ALT/AST within the first 14 days of initiation. One control with lymphoma and baseline eGFR 31 ml/min/1.73m² developed DiHS (fever, MPE, elevated ALT/AST less than twice upper limit of normal) 43 days after initiation for tumour lysis prophylaxis. This occurred while on 2-weekly monitoring of FBC, ALT, AST. There were no cases of SCAR in both groups.
Conclusions: SMP facilitates early diagnosis of allopurinol allergy/DiHS which occurred during the first 2–6 weeks after initiation. Whether early cessation of allopurinol prevents development of SCAR, and reduces the need for HLA-B*5801 testing will require a larger prospective study.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5060

THU0416
RAPID TOPHUS RESOLUTION IN CHRONIC REFRACTORY GOUT PATIENTS TREATED WITH PEGLOTICASE

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Background: It has been suggested that the velocity of resolution of tophi in persons with chronic tophaceous gout is related to the serum urate levels. However, few studies have measured serum urate less than 4.0 mg/dL or in nonresponders. Pegloticase is a recombinant uricase conjugated to polyethylene glycol approved in the US for treatment of patients with chronic refractory gout. It profoundly decreases serum uric acid in responders to <1 mg/dL. The results from the pegloticase clinical trials provided the opportunity to determine the impact of persistent and markedly low levels of serum urate on the velocity of tophus resolution.

Objectives: To assess the velocity of tophus resolution in subjects treated with pegloticase for chronic refractory gout.

Methods: This analysis used results from two randomized controlled trials (RCTs) of 6 months duration. 2,3 For tophus measurements, serial standardized digital photographs were analyzed by a blinded reader using computer-assisted quantitative measurement software. Subjects were defined as responders and nonresponders based on maintenance of a serum urate <8 mg/dL during intensive monitoring periods after 3 and 6 months of treatment.

Results: During the 6 months of the RCTs, a total of 952 tophus measurements were analyzed in 87 subjects, including 341 in 30 responders; 361 in 36 nonresponders receiving pegloticase infusions; and 250 in 21 subjects receiving placebo infusions. Mean serum urate levels in these subjects were 10.1, 0.3 and 0.3 mg/dL at baseline, 3 months and 6 months in responders; 10.7, 8.9 and 9.6 mg/dL in nonresponders; and 10.2, 9.8 and 9.7 mg/dL in placebo treated patients, respectively. At baseline, the mean tophus area in responders was 581.6 ± 742.7 mm² (mean ± SD; n=90 toph); in nonresponders it was 676.5 ± 1416.6 mm² (n=93 toph); and in placebo treated subjects it was 672.9 ± 1039.5 mm² (n=68 toph). By regression analysis, the velocity of tophus resolution over the 6 months of treatment was 50.1 mm²/month in responders; 14.0 mm²/month in placebo-treated patients (responders vs placebo treated subjects, p=0.001). In responders, the mean time to total tophus resolution was estimated to be 347 days (11.5 months, with a range of 5.6–36.4 months). During the 6 month treatment period, the area under the curve (AUC) of multiple serum urate measurements in responders was 6,067.9 ± 6,781.6 mg/dL hr compared with 34,647.4 ± 8,586.7 for placebo treated patients, and a correlation coefficient of 0.59 ± 0.58 between the two groups (p=0.01).

Conclusions: Pegloticase treatment causes a rapid resolution of tophi in responders as predicted from the profound and persistent serum urate lowering associated with this therapy.

References:


THU0417
PERIPHERAL NEUROPATHY IN PATIENTS WITH GOUT: ALTERATIONS BEYOND LOCAL DAMAGE

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Background: Peripheral neuropathies (PN), are peripheral nervous system disorders associated to several causes. According to distribution are classified as: Local (mononeuropathy [MNPI]) or Systemic (Multiple mononeuropathy [MNP]). and polyneuropathy (PNP)). PN in gout has been scarcely described. Previous reports only consider MNP of median nerve at the wrist and MNPI of the ulnar nerve at the elbow, due to tophus compression.

Objectives: To describe the frequency and characteristics of PN in patients with gout and its association to gout related variables, co-morbidity and treatment.

Methods: Consecutive patients in GRESGAH, a cohort of 450 gout (ARA/ACG/ACR-EULAR) patients seen for the first time at Rheumatology department and treated according to published guidelines for gout. Variables included: demographic, clinical, biochemical data, HAO and 3 questionnaires for PN (DN4, LANSS and MNSI) previously translated and validated in our country. We perform urate Conduction Studies (NCS) following AAME guidelines (Include:Sensory action potential [sural, ulnar and median nerves], Compound muscle action potential [peroneal, tibial, median and ulnar nerves] and late F-wave [tibial and ulnar nerves]). This protocol was approved by the local IRB and the patients signed an informed consent. Statistical analysis: Student’s t-test, Mann–Whitney U test and X2.

Results: We included 162 gout patients, 98% males, 72% tophaceous gout, 48% severe tophaceous gout (STG), mean age 49±12 years, 14±10 years of disease duration, educational level 8±4 years, BMI 27.9±4.6kg/m². According to questionnaires: 56% DNA, 45% MNSI and 36% LANSS could be classified as PN. Sixty five percent had abnormal NCS: MNP: 52%, most of them (58%) neuropraxis. PNP 35% and 13% MNPI in them, axonal damage was reported in 88%. MNPI localization: Median nerve/carpal tunnel (89%); peroneal nerve/ibidia halluces (14%); ulnar nerve/medial elbow (1%). In responders vs placebo treated patients (p=0.001). In responders, there was a significant correlation between serum uric acid and responders as predicted from the profound and persistent serum urate lowering associated with this therapy.

Conclusions: PN is common among gout patients, PN could be diagnosed by questionnaires (particularly DN4) and NCS in 65%. L-PN (median nerve most of them) and S-PN (STG) 35% of the patients were nonresponders vs placebo treated subjects (p=0.001). In responders, the mean time to total tophus resolution was estimated to be 347 days (11.5 months, with a range of 5.6–36.4 months). During the 6 month treatment period, the area under the curve (AUC) of multiple serum urate measurements in responders was 6,067.9 ± 6,781.6 mg/dL hr compared with 34,647.4 ± 8,586.7 and 42,451.1 ± 6,396.1 mg/dL hr in nonresponders and placebo treated subjects, respectively (p=0.001). In responders, there was a significant correlation between the velocity of tophus resolution and serum urate AUC (p=0.009).

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5060

THU0418
A PROOF-OF-CONCEPT STUDY: TREATING TO THE TARGET WITH URATE LOWERING THERAPY IN REAL-WORLD GOUT PATIENTS

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Background: Gouty arthritis is a common, potentially disabling and increasingly prevalent disease [1]. Last year, the European League Against Rheumatism (EULAR) task force gave gout the updated 2006 recommendations for the management of gout [2,3]. The guideline stresses the application of a targeted approach when initiating urate lowering therapy (ULT) in gout patients for reaching the recommended urate target (sUA) target values. However, data on clinical outcomes of real-world gout patients treated according to this approach are limited.

Objectives: To examine the clinical outcomes achieved in two patient cohorts in which differing targeted ULT treatment approaches were employed, both aiming to reach the EULAR recommended sUA targets.

Methods: We conducted a retrospective chart review study. Gout patients were included that had been treated at the rheumatology departments of two clinical centers in the Netherlands, applying different targeted ULT treatment approaches. Patients in cohort A followed an approach combining two modes of action once allopurinol monotherapy failed to reach the predefined target, whereas patients in cohort B were treated with sequential monotherapy following allopurinol
monotherapy failure. Outcome parameters were defined to reflect the EULAR recommendations concerning ULT [3].

**Results:** A total of 177 patients were included in the study; 99 in cohort A and 78 in cohort B. The majority (N=146, 82.5%) of the included patients from both cohorts were able to meet the predefined sUA target of <360 μmol/L. In addition, more than half (54.10%) of the patients reached the stringent sUA target of <300 μmol/L. The proportion of patients reaching sUA targets did not differ significantly (p=0.51) between the cohorts, with 80.8% (n=80) of the patients in cohort A reaching the primary sUA target, compared to 85.7% (n=66) in cohort B (Figure 1). In total, patients following treatment with first-line allopurinol, second-line monotherapy options or second-line combination therapy, 102/124 (82.3%), 25/31 (80.6%) and 19/21 (90.5%) respectively, reached the primary sUA target.

**Conclusions:** This chart review provides a proof-of-concept of the treat-to-target approach in gout patients when a targeted approach with ULT is applied. Further pragmatic randomized studies to investigate differences between specific treatment regimes in gout patients, together with costs, safety and patient-reported outcome measures are needed.

**References:**

**Disclosuire of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.2885

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**THU0420**

**IMPROVED SURVIVAL OF POST-MYOCARDIAL INFARCTION PATIENTS TREATED WITH ZOFENOPRIL COMBINED WITH XANTHINE OXIDASE INHIBITORS AS COMPARED TO PLACEBO OR OTHER ACE-I**

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**Background:** Oxidative stress is increased in hyperuricemic patients with acute myocardial infarction (AMI). In these patients, use of sulhydrylACE-inhibitors (ACEIs), such as zofenopril or captopril, and xanthine oxidase inhibitors (XOIs), may potentially result in an enhanced antioxidant effect and improved survival. However, the benefit of such combination in post-myocardial infarction has never been verified.

**Objectives:** To test the usefulness of the combination therapy Zofenopril + XOI in improving survival free from MACE in post-AMI patients.

**Methods:** We re-analyzed the data of the four SMILE (Survival of Myocardial Infarction Long-term Evaluation) studies by grouping patients according to the type of ACEIs and the use of XOIs. 165 (31.4%) of the 525 patients were treated with XOIs (79 under zofenopril and 86 under placebo, lisinopril or ramipril), whereas 360 were not (192 zofenopril and 168 placebo or other ACEIs). In these four groups, we separately estimated the 1-year combined risk of major cardiovascular events (MACE, death or hospitalization for cardiovascular causes).

**Results:** MACE occurred in 10.1% of patients receiving zofenopril + XOIs, in 18.6% receiving placebo or other ACEIs + XOIs, in 13.5% receiving zofenopril without XOIs and in 22.0% receiving placebo or other ACEIs, but no XOIs (p=0.034 across groups). Rate of survival free from MACE was significantly larger in patients treated with zofenopril and XOIs than with other ACEIs with no XOIs (hazard ratio: 2.29 (1.06, 4.91), p=0.034). A non-significant trend for superiority of zofenopril + XOIs combination was observed vs. zofenopril alone [1.19 (0.54, 2.64), p=0.669] or vs. placebo or other ACEIs combined with XOIs [1.82 (0.78, 4.26), p=0.169].

**Disclosuire of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.2377

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**THU0419**

**RISK OF TOTAL HIP AND KNEE REPLACEMENT IN GOUT PATIENTS PRIOR TO AND FOLLOWING DIAGNOSIS: A NATIONAL POPULATION STUDY IN TAIWAN**

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**Background:** Total joint replacement (TJR) is a major surgical procedure aiming to replace damaged natural joints with artificial prosthesis to restore function and alleviate pain. Total knee replacement (TKR) and total hip replacement (THR) are major surgical procedures aiming to replace damaged natural joints with artificial prosthesis to restore function and alleviate pain. TJR has been associated with increased risks of cardiovascular disease and death, particularly in men with a history of diabetes mellitus, renal failure, and gout. Whether gout associates with an increased risk of TJR independent of these primary risk factors is controversial, despite tophaceous or chronic deforming gouty arthritis may lead to joint destruction and subsequent TJR.

**Objectives:** We carried out a case control study using the National Health Insurance (NHI) database with full coverage of the general population of Taiwan to investigate the burden of TJR in gout patients at diagnosis compared to matched controls. We further followed incident gout patients and their matched controls after diagnosis to compare their subsequent risk for TJR.

**Methods:** The Taiwan National Health Insurance database was used to identify 74,729 new diagnosis gout patients in 2005. These were matched 1:1 to 74,729 controls by birth year and sex with people who did not have gout diagnosis or urate-lowering treatment prescription. Odds ratios (ORs) of total hip or knee replacement (THR or TJR) at diagnosis and hazards ratios (HRs) after diagnosis were estimated adjusted for gender, age at diagnosis, comorbidities, co-medications, place of residence, income and occupation.

**Results:** Gout was associated with adjusted ORs (95% CI) of 0.87 (0.54 to 1.40), 1.01 (0.57 to 1.79), 0.93 (0.64 to 1.35) for the THR, TKR and TJR at diagnosis, respectively. The incidence rate of THR or TKR in the patients with gout was 1.60 and 1.76 (per 1,000 person-years) which was higher than matched controls (0.99 and 0.98, respectively). Gout was also associated with an adjusted HR (95% CI) of 1.41 (1.19 to 1.68), 1.37 (1.16 to 1.61) and 1.37 (1.22 to 1.56) for developing THR, TKR and TJR.

**Conclusions:** Compared to matched controls people with gout did not have an increased risk of TJR at diagnosis but the risk increased substantially after diagnosis. Whether adequate urate-lowering treatment reduces the risk requires further study.

**References:**

**Disclosuire of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.5012

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**THU0421**

**FEMALE PRIMARY GOUT HAD ITS UNIQUE ULTRASOUND FEATURES**

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**Background:** Primary gout is a metabolic disease occurred in male and post-menopause female in most cases. Though the ultrasound features of gout had been discovered for several years, no reports illuminated whether there would be difference presentations between different genders in the joints.

**Objectives:** We employed ultrasound instead of dual-energy CT to explore more refined pathological manifestation of primary gout in different genders.

**Methods:** All cases were confirmed as gout fulfilling 1997 ACR classification criteria. All cases excluded secondary gout induced by drug, tumor, hypertension, diabetes mellitus, renal failure. Ultrasound was performed during chronic stage of gout but not at acute attack. The process was done by 2 observers blinded to
SEL-212: ENHANCED SERUM URIC ACID CONTROL IN HYPERURICEMIC PATIENTS THROUGH SELECTIVE MITIGATION OF ANTI-DRUG ANTIBODIES AGAINST PEGASITASE

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Objectives: To assess the initial safety and impact on sUA levels and ADA formation of SEL-212, which is designed to be the first non-immunogenic uricase therapy for refractory gout.

Methods: Cohorts of hyperuricemic (sUA ≥ 6 mg/dL) patients consented to a single dose of 0.4 mg/kg pegasitase alone, SVG-R alone (0.03–0.5 mg/kg), or 0.4 mg/kg pegasitase co-administered with SVG-R (0.03–0.3 mg/kg, SEL-212). A total of 124 patients were included in this analysis. Patients were dosed at baseline and at days 1, 14, 21, and 30 days after dosing.

Results: Sixty-three patients were enrolled with a median age of 49.4 years. Mean baseline sUA was 7.4±1.3 mg/dL. Patients dosed with pegasitase alone showed an immediate drop in sUA, which returned to baseline levels by 14–21 days after dosing. Patients treated with SVG-R alone showed no meaningful change in sUA. A 0.5 mg/kg dose of SVG-R showed no detectable ADA at day 30, and all 10 subjects showed a decrease in ADA titers by day 100. Patients treated with SVG-R alone showed no meaningful change in sUA.

Conclusion: SEL-212 was generally well tolerated at effective dose levels. One SAE (grade 2 rash) was observed in the lowest of the three effective dose levels (0.1 mg/kg SVG-R). A second SAE was determined by the investigator to be not related to study drug. All SAEs fully resolved. No SAEs were observed with SEL-212 at the higher effective dose levels (0.15 or 0.3 mg/kg). The maximum tolerated dose was defined as 0.3 mg/kg.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3548
a trained musculoskeletal radiologist. For each DECT, clinical and biochemical characteristics of each patient were collected retrospectively.

**Results:** 22 patients (men 77%), mean age 62.5 years and mean BMI 28.4 kg/m² were included. Mean gout duration was 108 ±114.4 months, mean of last available serum uric acid level was 520 ±193 μmol/L, and 15 patients had at least one clinical tophus. Mean estimated glomerular filtration rate (MDRD formula) was 47.27 ±1 m²/1.73 m². One patient was on hemodialysis and one had received kidney transplant.

A total of 39 DECT has been performed: 28 of peripheral joints and 11 of the spine (9 lumbar, 1 sacroiliac and 1 cervical). Spinal DECT were done in 10 patients to explore recurrent inflammatory pain (n=3 lumbar, 1 cervical and 1 buttock) or mechanical back pain (n=2 lumbar). 4 spinal DECT were performed in asymptomatic patients with extended peripheral tophi. Spinal MSU crystal deposits were disclosed by DECT in 83% (5/6) and 25% (1/4) of symptomatic and asymptomatic patients, respectively. In all painful patients, MSU crystal deposition was considered as a likely explanation of spinal symptoms. Spinal MSU crystal deposits was identified in apophyseal joints (n=5), cervical intervertebral disc (n=1) and yellow or interspinous ligaments (n=4). All involved apophyseal joints were eroded (figure 1). No vertebral bone erosion was observed. Categorification of spinal tophus was observed in 4 patients. DECT identified peripheral deposits in 15/18 (83.3%) patients. In peripheral DECT, bone erosions were observed in 71.4% and joint effusion in 32.1% of DECT positive peripheral joints. MSU crystal deposits were observed in tendons, cartilages or synovial membranes in 82.1% of positive DECT joints and in soft tissues in 64.3% of positive patients. MSU crystal deposits were calcified in 7 cases.

**Conclusions:** MSU crystal deposits at the spine are present in 60% of patients in this retrospective DECT study. DECT can represent a performing imaging procedure for their detection in symptomatic patients. Further studies are needed to assess the clinical utility of DECT of the spine in gout.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.8335

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**THU0426 THE FIRST METATARSOPHALANGEAL JOINT (MTP1) IS NOT THE MAIN LOCALIZATION OF GOUT AT DIAGNOSIS IN SUB-SAHARAN AFRICA**

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**Background:** Numerous data in sub-Saharan Africa suggest that MTP1 is not the hallmark of gout (1–5).

**Objectives:** We carried out this study with the aim to determine the joint most involved at the time of diagnosis of gout in Cameroon.

**Methods:** We performed a cross-sectional study in all outpatients seen at the Rheumatology unit of the Douala General Hospital, Cameroon, between 2004 and 2014. We included patients with diagnosis of gout according to ACR criteria 1997.

The main characteristics of gout at diagnosis were collected, particularly the joints involved. A p <0.05 was significant.

**Results:** At the end of this study, 511 patients (415 men and 96 women) with the diagnosis of gout were included. The mean age was 55.9±10.8 years. Joint pain (n=508, 99.4%) was the leading reason for consultation at the time of diagnosis. The knees (n=390, 62.6%), ankles (n=187, 39.0%), and MTP1 (n=128, 26.7%) were the most affected joints. Table 1 presents the frequency of the joints affected, comparing our results with those of the other African series. There was no difference between MTP1 and others joints location (particularly knees and ankles) according to age, sex, place of residence, duration of disease, uric acid level, and associated comorbidities (p >0.05).

**Conclusions:** MTP1 is not the joint most involved at the time of diagnosis of gout in sub-Saharan Africa. Diagnosis of gout should be considered before any inflammatory knee and ankle pain in patients from sub-Saharan Africa. Genetic studies would provide a better understanding of this feature.

**References:**

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**Table 1. Comparison of the most affected joints of the different African series**

<table>
<thead>
<tr>
<th>Joint</th>
<th>Cameroon</th>
<th>Malawi</th>
<th>Nigeria</th>
<th>Cameroon</th>
<th>Cameroon</th>
</tr>
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<tbody>
<tr>
<td>Number of patients</td>
<td>511</td>
<td>100</td>
<td>146</td>
<td>139</td>
<td>160</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>435/166</td>
<td>45/55</td>
<td>138/32</td>
<td>131/18</td>
<td>159/1</td>
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<tr>
<td>Mean age</td>
<td>55.9±11</td>
<td>57</td>
<td>53.4±11</td>
<td>55.7±10</td>
<td>44</td>
</tr>
<tr>
<td>Joint involved</td>
<td>55.5±11</td>
<td>57</td>
<td>53.4±11</td>
<td>55.7±10</td>
<td>44</td>
</tr>
<tr>
<td>Joints involved</td>
<td>tender</td>
<td>and/or stiffness, n (%)</td>
<td>and/or stiffness, n (%)</td>
<td>and/or stiffness, n (%)</td>
<td>and/or stiffness, n (%)</td>
</tr>
<tr>
<td>Knee</td>
<td>390 (62.6%)</td>
<td>282 (66.3%)</td>
<td>81 (55.5%)</td>
<td>60 (43.2%)</td>
<td>52 (51.2%)</td>
</tr>
<tr>
<td>Ankle</td>
<td>187 (39.0%)</td>
<td>45 (45%)</td>
<td>50 (34.2%)</td>
<td>47 (28.8%)</td>
<td>90 (56.2%)</td>
</tr>
<tr>
<td>Elbow</td>
<td>81 (16.9%)</td>
<td>14 (14.4%)</td>
<td>12 (8.2%)</td>
<td>10 (10.7%)</td>
<td>35 (21.9%)</td>
</tr>
<tr>
<td>Shoulder</td>
<td>49 (10.2%)</td>
<td>6 (6.6%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Other joints</td>
<td>24 (5.0%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Others</td>
<td>30 (6.3%)</td>
<td>1 (1%)</td>
<td>–</td>
<td>13 (9.6%)</td>
<td>9 (5.6%)</td>
</tr>
</tbody>
</table>

*In bold, the joint most involved; †Unspecified fings on joints; ‡PJP & MCP joints.

**Table 1. Comparison of the most affected joints of the different African series**

**THU0426 LONG-TERM ADHERENCE TO URATE-LOWERING THERAPY IN GOUT: DO NOT BLAME THE PATIENTS**

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**Background:** adherence to urate-lowering treatment (ULT) in patients with gout is reported to be lower than 50% in the first year, below 20% at 2-year, and worse than in other chronic conditions such as hypertension, diabetes, or hyperlipidemia.

**Objectives:** to evaluate adherence to ULT both overall and during follow-up, to compare it to the adherence to medications for associated comorbidities, and to explore potential causes for non-adherence to ULT.

**Methods:** transversal study of a nested cohort of patients in a gout clinic in the hospital setting who were scheduled for a follow-up visit during 6 consecutive months in 2016. General data of patients, along with variables related to gout and to comorbidity conditions are systematically retrieved at first visit; prescribed ULT doses, adherence, and serum urate levels were obtained during the follow-up visits. Adherence was retrieved as medication possession rate (MPR) according to pharmacy offices from government electronic databases (including ~98% of the general population). Also, MPRs of drugs prescribed for hypertension, diabetes (only oral), and hyperlipidemia were obtained; if more than one drug prescribed for any of the previous, the best adherence per comorbidity treatment was entered.

Good adherence was considered as MPR> 80 percent of that prescribed, target serum urate (sUA) as <0.36 mmol/L. Patients are educated at first visit and encouraged to be adherent from baseline through follow-up visits.

**Results:** data were available from 209 patients who were scheduled for a follow-up visit during the observation period; 14 (6.7%) patients did not attend the visit. This sample was formed by 90% male, only 55% had received ULT previous to first visit, median age was 65 years at follow-up visit, 47% could be an opportunity for further improvement.

Good adherence was considered as MPR> 80 percent of that prescribed, target serum urate (sUA) as <0.36 mmol/L. Patients are educated at first visit and encouraged to be adherent from baseline through follow-up visits.

**Conclusions:** adherence to ULT measured as MPRs in a cohort of educated comorbidity. Therefore, we cannot blame poor adherence on the patients anymore. Targeting absenteeism could be an opportunity for further improvement.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6799
AMBIENT AIR POLLUTION AND RISK OF ACUTE GOUT FLARES: A TIME-SERIES STUDY

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Background: Air pollution is caused by substances that consist of solid particles, liquid droplets, or gases including carbon monoxide (CO), nitrate (NO), sulfur dioxide (SO2), ozone (O3), lead, toxic product from tobacco smoke and particulate matter (PM). Inhaled air pollutants can induce oxidative stress and this can contribute to trigger or exacerbate systemic inflammation and autoimmunity. The relations of air pollution with rheumatic diseases have been reported, especially in rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis and juvenile idiopathic arthritis. Gout is an inflammatory disease caused by deposition of monosodium urate (MSU) crystals. Acute gout flare is initiated with activation of the NLRP3 inflammasome and release of IL-1β by MSU crystals. PM <10μm in diameter (PM10) exposure has been reported to activate NLRP3 inflammasome in airway epithelial cells. The influence of air pollutants including PM10 to acute gout flares has not yet been known.

Objectives: To investigate the association between air pollution and acute gout flares

Methods: We obtained data from the National Health Insurance Database between 2007 and 2015 in Incheon, Republic of Korea by Health Insurance Review and Assessment (HIRA) service. The HIRA data included age, gender, national health insurance type, diagnosis code based on the International Classification of Diseases version 10 (ICD–10), visit date, procedure code, and prescription code. We studied the subjects of age ≥19 years who visited emergency department (ED) due to acute gout flare between 2008 and 2015. An acute gout flare was defined as an ED visit due to gout (ICD-10, M10) with any prescription of non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, or colchicine. Comorbidities and prescription history were collected. The data of ambient PM10, O3, NOx, CO, and SO2 levels were obtained from the Ministry of Environment data sources. We performed time-series study. The group means with Poisson regression distribution were used to investigate the association between single air pollutant level and acute gout flares. To examine the delayed effect of air pollutant exposure before the ED visit day on acute gout flare, we established cumulative lag models (averaging levels of consecutive days).

Results: The total number of ED visits for acute gout flare from 2008 to 2015 in Incheon was 139,665, including 48.8% of 40–59 year-old men. The ED visits for acute gout attack were most likely to occur in summer (29.1%). Among the ED cases of acute gout flares, 11.0% had a prescription history of allopurinol or flurbiprofen as an ED visit due to gout (ICD-10, M10) with any prescription of non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid, or colchicine. The prevalence of allopurinol and flurbiprofen prescription was higher in the summer. 20% of the ED cases of acute gout flares had multiple comorbidities. Acute gout flares showed more significant association with O3 in the cases with hypertension and use of NSAIDs, colchicine, or statins. PM10 was more significantly associated with acute gout flares in the cases with congestive heart failure.

Conclusions: Ambient air pollution can induce acute gout flares and its influence on acute gout flares may increase according to the comorbidities or medications.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8188

FGF23 IN FIBROUS DYSPLASIA

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Background: Fibrous dysplasia of bone (FD) is an uncommon skeletal disorder, caused by missense mutations of the GNAS1 gene and is characterized by the development of fibro-osseous lesions that replace normal bone. FD can present with a broad spectrum of clinical manifestations, including the development of hypophosphatemic osteomalacia which is due to the production of the phosphaturic hormone fibroblast growth factor 23 (FGF-23) by the dysplastic bone tissue. Nevertheless, the prevalence of this clinical complication is not well known.

Objectives: To analyse the serum levels of FGF-23 in patients with FD and determine their relationship with the extension and activity of the disease, as well as with serum phosphate levels.

Methods: Twelve patients (7F:5M) with FD with a mean age of 50.67±16.4 years (24–79) were included. The clinical reports of the patients were reviewed, with special attention to the extension and activity of the disease, number and location of the affected bones, clinical complications and treatments received. Serum FGF-23 values were recorded in all subjects (determined by Immunotopsics, CA, USA [measuring FGF23 C- terminal], normal value <100 RU/ml), as well as serum phosphate and calcium values, bone turnover markers and their evolution with treatment.

Results: Serum levels of FGF-23 were increased (>130 RU/ml) in 6/12 patients (50%). In patients with and without high FGF-23 levels the number of affected bones (2.2±2 vs. 1.9±1, respectively) and the skeletal locations of FD were similar as was the age in both groups of patients (48.2±14 vs. 53.2±19 years). In addition, FD disease activity and extension were similar in the two groups as were the bone turnover marker values (FAO, PINP and CTx). Strikingly, differences between serum phosphate values were not observed between the two groups (FGF-23 >130: 3.9±0.9 mg/dl vs. FGF-23 <130: 3.5±0.6 mg/dl). Indeed, none of the patients with high FGF-23 levels had low serum phosphate values. Following bisphosphonate (zoledronate) treatment, there were no significant changes in FGF-23 values by "subsequently, an increase of 123% was found in one patient receiving denosumab, although hypophosphatemia was not associated.

Conclusions: Patients with FD frequently present elevated FGF-23 values with no effects on serum phosphate levels, thereby suggesting the presence of an alteration in processing this protein in the dysplastic bone tissue in this disease. The role of denosumab treatment in FD and its repercussion on FGF-23 levels need further study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5261
PHARMACOKINETICS, PHARMACODYNAMICS, AND COMPARATIVE EFFECTIVENESS OF ALLOPURINOL VERSUS VERINURAD (RDEA3170) AND FEBUXOSTAT IN HEALTHY ADULT MALE SUBJECTS

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Background: Verinurad (RDEA3170) is a novel selective uric acid reabsorption inhibitor in clinical development for the treatment of gout and asymptomatic hyperuricemia.

Objectives: This Phase 1, single-blind, multiple dose, drug-drug interaction (DDI) study evaluated the pharmacokinetics (PK), pharmacodynamics, and tolerability of verinurad in combination with febuxostat (FBX) in healthy male volunteers.

Methods: Subjects were randomized to receive once-daily doses of FBX or verinurad or verinurad alone for 7 days, FBX + verinurad or FBX + placebo on days 8–14, and the alternative single agent (FBX or verinurad or placebo) on days 15–21. Subjects received either the combination of verinurad 10 mg + FBX 40 mg or verinurad 2.5 mg + FBX 80 mg. Serial plasma/serum and urine samples were drawn at predetermined time points on Days 7, 14 and 21, and assayed for verinurad, FBX, and uric acid. Baseline samples were drawn on Day –1. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).

Results: Of 23 randomized subjects, 20 completed the study. FBX 40 mg had no apparent effect on the plasma Cmax and AUC for verinurad 10 mg, whereas FBX 80 mg increased the plasma Cmax and AUC for verinurad 2.5 mg by 25% and 33%, respectively. Verinurad had no effect on FBX PK. Renal clearance of verinurad was unchanged by FBX.

The mean maximal reduction in serum uric acid (sUA) was 76% with verinurad 10 mg + FBX 40 mg compared with verinurad 10 mg (56%) or FBX 40 mg (49%) alone (Figure 1A) and was 67% with verinurad 2.5 mg + FBX 80 mg compared with verinurad 2.5 mg (38%) or FBX 80 mg (57%) alone (Figure 1B). Consistent with the mechanism of action (MOA) of verinurad, 24-hr fractional excretion of uric acid (FEUA) increased (2.5 mg: 7.6%; 10 mg: 12.8%) vs baseline (6.5% and 6.0%, respectively). Renal clearance of uric acid (CLUR) increased similarly (2.5 mg: 9.0 mL/min; 10 mg: 12.3 mL/min) vs baseline (8.3 and 7.3 mL/min, respectively).

The increases were maintained for 24 hours with verinurad 10 mg + FBX 40 mg (40%) vs baseline (6.4% and 6.5%; CLUR: 4.91 and 4.96 mL/min, respectively). The alternative single agent (verinurad 10 mg or ALLO 300 mg) on Days 8–14, the alternative single agent (verinurad 10 mg or ALLO 300 mg) on Days 15–21. Colchicine 0.6 mg was taken once daily from day –14. Serial plasma/serum and urine samples were drawn at predetermined time points on Days 7, 14 and 21 and assayed for verinurad, FBX, oxypurinol (OXY), colchicine, and colchicine acid. Baseline samples were drawn on Day –1. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).

Conclusions: No DDI was found with the verinurad 10 mg + FBX 40 mg combination and only a modest one with verinurad 2.5 mg + FBX 80 mg. Both combinations were safe and well tolerated and resulted in greater reduction of sUA than either verinurad or FBX alone. These results support the continued development of this novel approach for the treatment of gout and hyperuricemia.


DOI: 10.1136/annrheumdis-2017-eular.5264

THU0431 COMPARATIVE EFFECTIVENESS OF ALLOPURINOL VERSUS FEBUXOSTAT FOR PREVENTING INCIDENT RENAL DISEASE IN OLDER ADULTS: AN ANALYSIS OF MEDICARE CLAIMS DATA

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Background: Large scale randomized studies are underway to assess whether compared to placebo, each XO-inhibitor, allopurinol or febuxostat, can prevent renal function loss. This evidence is needed and will confirm their nephroprotective potential. However, neither study will answer a key question: Does the renal protective effect of allopurinol differ from that of febuxostat?

Objectives: To assess the comparative effectiveness of allopurinol vs. febuxostat for preventing incident renal disease in elderly.

Methods: In a retrospective study using Medicare claims data, we included patients newly treated with allopurinol or febuxostat (baseline period of 183 days without either medication). We used 1:5 propensity-matched Cox regression analyses to compare the hazard ratio (HR) of incident renal disease with allopurinol use and allopurinol dose vs. febuxostat (reference category).

Sensitivity analyses included multivariable-adjusted regression models.

Results: There were 31,465 new allopurinol or febuxostat treatment episodes in 26,443 patients; 8,570 ended in incident renal disease. Crude rates of incident renal disease per 100,000 person-days were 53 with allopurinol vs. 93 with febuxostat. Crude rates of incident renal disease per 100,000 person-days were lower with higher daily doses: allopurinol < 200 mg, 200–299 mg and >300 mg/day with 65, 48 and 43; and febuxostat 40 mg and 80 mg/day with 93 and 89, respectively.

In propensity-matched analyses, compared to febuxostat use, allopurinol use was associated with lower HR of incident renal disease, 0.61 (95% confidence interval: CI: 0.49, 0.77). Compared to febuxostat 40 mg/day, allopurinol doses <200, 200–299 and >300 mg/day were associated with lower HR of incident renal disease, 0.75 (95% CI: 0.65, 0.86), 0.61 (95% CI: 0.52, 0.73) and 0.48 (95% CI: 0.41, 0.55), respectively. Sensitivity analyses using multivariable-adjusted regression confirmed these findings.

Conclusions: Allopurinol was more effective than febuxostat in preventing incident renal disease in elderly patients. Future studies need to examine the mechanism of this renal benefit of allopurinol.

Disclosure of Interest: J. Singh Grant/research support from: Savient, Takeda, Consultant for: Savient, Takeda, Regeneron, Mez, Iroko, Biobenera, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology. J. Cleveland: None declared

DOI: 10.1136/annrheumdis-2017-eular.6837

THU0432 PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF COMBINATION MULTIPLE DOSE ADMINISTRATION OF VERINURAD (RDEA3170) AND ALLOPURINOL IN ADULT MALE SUBJECTS WITH GOUT

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Background: Verinurad (RDEA3170) is a novel selective uric acid reabsorption inhibitor in clinical development for the treatment of hyperuricemia and gout.

Objectives: This Phase 1, single-blind, multiple dose, drug-drug interaction study evaluated the pharmacokinetics (PK), pharmacodynamics (PD), pharmacokinetic interactions and tolerability of verinurad in combination with allopurinol (ALLO) in adult male subjects with gout.

Methods: Adult males with gout, aged 18–75 years, with serum uric acid (sUA) ≥8 mg/dL were randomized to receive once-daily oral doses of ALLO 300 mg or verinurad 10 mg alone for 7 days, ALLO 300 mg + verinurad 10 mg on Days 8–14, and the alternative single agent (verinurad 10 mg or ALLO 300 mg) on Days 15–21. Colchicine 0.6 mg was taken once daily from day –14. Serial plasma/serum and urine samples were drawn at predetermined time points on Days 7, 14 and 21 and assayed for verinurad, ALLO, oxypurinol (OXY), colchicine, and colchicine acid. Baseline samples were drawn on Day –1. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).

Results: Subjects (N=12) were mostly white (58.3%) with mean (SD) age of 51 (10) years. Following multiple doses, ALLO had no effect on Cmax and AUC of verinurad. ALLO Cmax was increased 33% but AUC was unaltered by verinurad. The Cmax and AUC for OXY, the active metabolite of ALLO, were reduced 32% and 38%, respectively, by verinurad. Colchicine plasma exposures were unaltered by verinurad. ALLO had no effect on urinary excretion of verinurad, whereas urinary excretion of OXY increased 19% by verinurad. The mean maximal decrease in sUA was 65% with verinurad + ALLO compared with verinurad (51%) or ALLO (43%) alone (Figure). Consistent with the mechanism of action (MOA) of verinurad, 24-hr fractional excretion of uric acid (FEUA) and clearance of uric acid (CLUR) were increased in the absence (9.2% and 11.5 mL/min, respectively) of ALLO (20% and 11.5 mL/min, respectively) versus baseline (4.5% and 5.7 mL/min) or ALLO alone (3.7% and 5.0 mL/min). Consistent with its MOA, ALLO decreased the amount of uric acid excreted in 24-hr urine (363 mg) compared with baseline (683 mg), verinurad alone (739 mg) or verinurad + ALLO (522 mg) but had no effect on FEUA or CLUR. No
serious AEs, discontinuations due to AEs, or clinically significant laboratory or ECG abnormalities were noted.

Conclusions: Although a modest drug–drug interaction was found between verinurad and ALLO, the combination was safe and well tolerated at the studied doses and resulted in greater reduction of sUA than either alone. These results support the evaluation of verinurad + ALLO as an alternative once-daily treatment option for hyperuricemia and gout.


DOI: 10.1136/annrheumdis-2017-eular.5308

THU0434 PHARMACODYNAMIC EFFECTS AND SAFETY OF VERINURAD (RDEA3170) IN COMBINATION WITH FEBUXOSTAT VERSUS FEBUXOSTAT ALONE IN ADULTS WITH GOUT: A PHASE 2A, OPEN-LABEL STUDY

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Background: Verinurad (RDEA3170) is a high-affinity, selective URAT1 inhibitor in development for the treatment of gout and asymptomatic hyperuricemia.

Objectives: This Phase 2a, randomized, open-label, multicenter study investigated the multiple-dose pharmacodynamics (PD), pharmacokinetics (PK), and safety of oral verinurad in combination with febuxostat versus febuxostat alone in adults with gout (NCT02246673).

Methods: Patients aged ≥18 and ≤75 years with gout and serum uric acid (sUA) ≥8 mg/dL were randomized to 1 of 5 cohorts to receive febuxostat (40 mg and 80 mg) alone and in combination with verinurad (dose range 2.5 mg to 20 mg; 4 treatment periods per cohort, each treatment period 7 days). Medications were administered once daily ~30 min after breakfast. Colchicine 0.6 mg for gout flare prophylaxis was initiated at approximately Day -14 (start of urate-lowering therapy [ULT] washout) or Day -7 if not on ULT. Serial blood and urine samples were measured at preset intervals on Days -1, 7, 14, 21, and 28 for PD and PK endpoints. Safety assessments included adverse events (AEs) and laboratory, electrocardiograms, and vital sign parameters.

Results: Sixty-four patients were randomized (n=12–14 per cohort). Serum PD data pooled across cohorts demonstrated maximal % decrease in sUA from baseline (Emax) at 8–12 h after dosing. Addition of verinurad to febuxostat decreased sUA in dose-dependent manner (Figure 1). Greater sUA reductions were observed for dose combinations of verinurad ≥5 mg with febuxostat 40 mg versus febuxostat 80 mg alone. The rate of urinary uric acid excretion was reduced by febuxostat alone, but comparable to baseline levels with verinurad combined with febuxostat. Verinurad plasma exposures increased with verinurad dose and were comparable for febuxostat 40 mg and 80 mg doses. No drug-drug interaction on verinurad and febuxostat plasma PK parameters was observed. Verinurad at doses from 2.5 mg to 20 mg was well tolerated, with no serious AEs, withdrawals due to AEs, or renal-related events. The most frequent treatment-emergent AE possibly related to study medication was pain in extremity, in 2 patients receiving verinurad. Laboratory values and vital signs showed no clinically meaningful changes. There were no cases of serum creatinine elevation ≥1.5x baseline.

Conclusions: Verinurad coadministered with febuxostat dose-dependently decreased sUA while maintaining urinary uric acid levels comparable to baseline. All dose combinations of verinurad and febuxostat in this study were generally well tolerated with no serious AEs or renal-related events during combination treatment.


THU0435 PHARMACODYNAMICS, PHARMACOKINETICS, AND SAFETY OF VERINURAD (RDEA3170) IN COMBINATION WITH FEBUXOSTAT VERSUS FEBUXOSTAT ALONE AND VERINURAD ALONE IN JAPANESE ADULTS WITH GOUT OR ASYMPTOMATIC HYPERURICEMIA: A PHASE 2A, OPEN-LABEL STUDY

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Background: Verinurad (RDEA3170) is a high-affinity URAT1 inhibitor in development for the treatment of gout and asymptomatic hyperuricemia.
RESULTS: Seventy-two patients with gout (n=37) or hyperuricemia (n=35) were randomized in this study. Addition of verinurad (2.5 mg to 10 mg) to febuxostat (10 mg, 20 mg, or 40 mg) decreased SUA in dose-dependent manner (Figure). Verinurad coadministered with febuxostat increased the amount of uric acid recovered in urine (Aeur), compared with baseline and the same dose of febuxostat administered alone, yet comparable with benzbromarone. Plasma CrmA and AUC exposures of verinurad and febuxostat exhibited dose proportional increases within the investigated dose range. No clear PK drug-drug interaction of verinurad and febuxostat with each other was observed. Verinurad at doses from 2.5 mg to 15 mg was well tolerated, with no serious AEs or withdrawals due to AEs. One treatment-emergent AE (diarrhea) was considered possibly related to both verinurad and febuxostat. Laboratory values and vital signs indicated no clinically meaningful changes.

CONCLUSIONS: Verinurad coadministered with febuxostat dose-dependently decreased SUA while maintaining Aeur comparable to benzbromarone. All dose combinations of verinurad and febuxostat in this study were generally well tolerated.


DOI: 10.1136/annrheumdis-2017-eular.5391

THU0437 IMPACT OF DIURETICS ON THE URATE LOWERING THERAPY IN PATIENTS WITH GOUT: ANALYSIS OF AN INCEPTION COHORT

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Background: Use of diuretics is a common bystander in patients with gout, and it has been reported to impact response to allopurinol [1,2] and likely lead to treatment failure and refractoriness. However, after the introduction of new urate-lowering therapies (ULT) and treat-to-target strategies, whether this inconvenient effect of diuretics persists has not received critical attention to date.

Objectives: To analyze the impact of the diuretic therapy on the response to ULT in patients with gout.

Methods: Retrospective analysis of an inception cohort in patients with crystal-proven gout (Jan2014-Nov2016). Patients were classified according to the use of diuretics (loop and/or thiazide) at baseline. The primary outcome variables were the reduction of serum uric acid (SUA) levels and the achievement of different objectives of SUA (6, 5, and 4mg/dL); as secondary outcome variable the maximum dose of ULT was registered, as well as other clinical, analytical, and ULT-related data. A comparative analysis was performed according to the use of diuretics, using Student’s t and chi-2 tests. Also, the analysis was stratified according to the ULT used.

Results: The inception cohort included 225 patients with an average age of 66 years (SD 14.1), being 98.2% of them men. The median duration of gout inclusion was 4 years (p25–75 1–10) and 21.3% presented tophi. At baseline, the median (p25–75) SUA and estimated glomerular filtration rate were 8.2 mg/dL (7.2–9.2) and 75.9 mL/min (27.2–88.3), respectively. A total of 98 patients

Outcome variable Diuretic therapy p

<table>
<thead>
<tr>
<th>Whole sample (N=209)</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=117</td>
<td>n=92</td>
<td></td>
</tr>
<tr>
<td>– SUA reduction (mg/dL, mean (SD)</td>
<td>3.2 (2.1)</td>
<td>3.7 (2.5)</td>
</tr>
<tr>
<td>– SUA –6 (%)</td>
<td>80.0%</td>
<td>75.9%</td>
</tr>
<tr>
<td>– SUA –5 (%)</td>
<td>61.0%</td>
<td>50.6%</td>
</tr>
<tr>
<td>– SUA –4 (%)</td>
<td>31.4%</td>
<td>28.9%</td>
</tr>
<tr>
<td>Allopurinol (n=158)</td>
<td>N=92</td>
<td>N=66</td>
</tr>
<tr>
<td>– SUA reduction (mg/dL, mean (SD)</td>
<td>3.1 (1.9)</td>
<td>3.2 (2.0)</td>
</tr>
<tr>
<td>– SUA –6 (%)</td>
<td>80.6%</td>
<td>74.2%</td>
</tr>
<tr>
<td>– SUA –5 (%)</td>
<td>60.2%</td>
<td>43.9%</td>
</tr>
<tr>
<td>– SUA –4 (%)</td>
<td>28.0%</td>
<td>21.2%</td>
</tr>
<tr>
<td>– Maximum dose (mg/day), mean (SD)</td>
<td>316.5 (126.9)</td>
<td>278.6 (121.8)</td>
</tr>
<tr>
<td>Febuxostat (n=33)</td>
<td>N=14</td>
<td>N=19</td>
</tr>
<tr>
<td>– SUA reduction (mg/dL, mean (SD)</td>
<td>3.7 (3.4)</td>
<td>5.4 (4.9)</td>
</tr>
<tr>
<td>– SUA –6 (%)</td>
<td>70.0%</td>
<td>82.4%</td>
</tr>
<tr>
<td>– SUA –5 (%)</td>
<td>70.0%</td>
<td>76.6%</td>
</tr>
<tr>
<td>– SUA –4 (%)</td>
<td>60.0%</td>
<td>58.8%</td>
</tr>
<tr>
<td>– Maximum dose (mg/day, mean (SD)</td>
<td>80.9 (16.3)</td>
<td>80.0 (25.3)</td>
</tr>
</tbody>
</table>

A DNI level of 1.9% was determined as the cut-off value for predicting septic arthritis in the multivariate analysis, DNI was the most powerful independent value for predicting septic arthritis (odds ratio 14.003).

Table 1. Comparison of variables between patients with acute gout attack and those with septic arthritis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with acute gout attack (n=194)</th>
<th>Patients with septic arthritis (n=149)</th>
<th>Total (n=343)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>65.0±15.0</td>
<td>60.9±16.4</td>
<td>63.2±15.8</td>
<td>0.016</td>
</tr>
<tr>
<td>SUA crystals confirmed, n (%)</td>
<td>41 (81.8%)</td>
<td>N/A</td>
<td>81 (23.6%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Positive culture, n (%)</td>
<td>N/A</td>
<td>98 (65.8%)</td>
<td>97 (28.3%)</td>
<td>N/A</td>
</tr>
<tr>
<td>WBC count, mm3</td>
<td>9600±3000.0</td>
<td>11,200±4700.0</td>
<td>10,300±3800.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DNI, %</td>
<td>0.6±0.9</td>
<td>3.3±4.0</td>
<td>1.8±3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>61.7±33.8</td>
<td>78.2±32.5</td>
<td>69.3±34.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP, mg/dL</td>
<td>76.5±68.7</td>
<td>126.6±104.0</td>
<td>98.7±89.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>29.5±21.9</td>
<td>22.7±14.7</td>
<td>26.6±19.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.9±1.1</td>
<td>2.1±1.7</td>
<td>1.6±1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SUA, mg/dL</td>
<td>7.6±2.5</td>
<td>4.4±1.6</td>
<td>6.3±2.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Multivariate analysis of the predictive values for septic arthritis in patients with acute gout attack and those with septic arthritis*
Lack of Predictive Value of the NIAID/FAAN Criteria to Identify Subjects with Evidence of Immune Activation and Post-Hoc Designation of Pegloticase-Treated Subjects as Meeting NIAID/FAAN Anaphylaxis Criteria

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Background: The NIAID/FAAN criteria have been widely applied to identify anaphylaxis despite having only modest specificity.1

Objectives: To evaluate the predictive value of the NIAID/FAAN criteria to identify evidence of immune activation in subjects with chronic refractory gout treated with pegloticase in randomized clinical trials (RCTs) who experienced infusion reactions (IRs), by assessing the capacity of biochemical testing for immunologic activation to confirm the likelihood of anaphylaxis.

Methods: During the RCTs supporting the approval of pegloticase for treatment of chronic refractory gout, subjects remained on therapy despite becoming nonresponders, which reflected the development of anti-drug antibodies (ADA); ~60% of subjects continued to receive pegloticase despite elevated ADA titers and many had IRs. In subjects receiving pegloticase every 2 weeks (q2w), 22/85 (26.5%) had a total of 43 IRs and 34/84 (40.5%) receiving pegloticase every 4 weeks (q4w) had a total of 70 IRs. 21/22 (95.5%) and 29/34 (85.3%) subjects with IRs in the q2w and q4w groups, respectively, were nonresponders. The 113 total IRs were categorized post hoc as to whether they met NIAID/FAAN criteria for anaphylaxis. Six IRs in 6 subjects met criteria, 53 IRs in 33 subjects had only one feature and were designated as “hypersensitivity”, and 54 IRs in 29 subjects had no features and were designated “other”. The clinical courses of these IRs and whether they were associated with elevated tryptase levels as a measure of mast cell degranulation or complement consumption as a measure of immune complex formation were assessed.

Results: Of all 852 infusions in subjects receiving q2w pegloticase, 43 (5.0%) were associated with IRs as were 70 of 830 infusions (9.5%) in subjects receiving q4w pegloticase. Of the 70 IRs associated with q4w administration, 3 (4.3%) met the criteria for anaphylaxis, 31 (44.3%) for hypersensitivity and 36 (51.4%) were other. The respective values for subjects receiving pegloticase q2w were 3/43 (7.0%), 22/43 (51.1%), and 18/43 (41.9%). A total of 14 IRs (12.4%) were associated with elevated tryptase and 31 (27.4%) with decreased complement CH50 levels. Immunologic abnormalities were not significantly different in the 3 groups, with 16.7%, 17.0%, and 7.4% of anaphylaxis, hypersensitivity and other IRs, respectively, having increased tryptase; and 0%, 30.2%, and 27.8%, respectively, having decreased complement. No subjects were classified as experiencing anaphylaxis by investigators, none required hospitalization, and 82 of the 113 IRs were attributed to pegloticase.

Conclusions: Post-hoc designation of pegloticase-treated subjects as meeting NIAID/FAAN criteria for anaphylaxis was not associated with a higher frequency of biochemical evidence of immune activation or a more severe clinical course. In pegloticase-treated subjects, the NIAID/FAAN anaphylaxis criteria did not identify subjects with IRs associated with elevated tryptase and decreased complement CH50 levels.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3905

Table 1. Comparison of variables between early-onset group and control group

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Early-onset group (N=99)</th>
<th>Control group (N=402)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>30±48.2</td>
<td>35.8±13.5</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Female, %</td>
<td>1.0%</td>
<td>12.7%</td>
<td>0.001</td>
</tr>
<tr>
<td>Age of onset, years</td>
<td>24.2±5.8</td>
<td>51.7±13.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of gout, years</td>
<td>6.2±5.8</td>
<td>6.2±5.6</td>
<td>0.953</td>
</tr>
<tr>
<td>Frequency of flare in last year</td>
<td>10.6±2.4</td>
<td>8.9±2.5</td>
<td>0.022</td>
</tr>
<tr>
<td>sUA, mg/dl, &gt;10mg/dl</td>
<td>59.6%</td>
<td>32.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, kg/m², &gt;30kg/m²</td>
<td>5.8±0.0</td>
<td>5.9±0.5</td>
<td>0.981</td>
</tr>
<tr>
<td>Tophi, %</td>
<td>20.2%</td>
<td>26.1%</td>
<td>0.397</td>
</tr>
<tr>
<td>Alcohol avoidance, %</td>
<td>35.4%</td>
<td>34.1%</td>
<td>0.811</td>
</tr>
<tr>
<td>Obesity, %</td>
<td>27.3%</td>
<td>15.5%</td>
<td>0.005</td>
</tr>
<tr>
<td>Dyslipidemia, %</td>
<td>51.5%</td>
<td>54.0%</td>
<td>0.666</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>41.4%</td>
<td>44.0%</td>
<td>0.001</td>
</tr>
<tr>
<td>DM, %</td>
<td>6.1%</td>
<td>24.6%</td>
<td>0.001</td>
</tr>
<tr>
<td>Urolithiasis, %</td>
<td>19.2%</td>
<td>33.6%</td>
<td>0.007</td>
</tr>
<tr>
<td>eGFR, mln/min/1.73m²</td>
<td>84±5.10</td>
<td>62±9.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>sUA, mg/dl</td>
<td>26.1±4.2</td>
<td>24.8±3.9</td>
<td>0.004</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>5.8±0.0</td>
<td>5.9±0.5</td>
<td>0.981</td>
</tr>
</tbody>
</table>
| sUA: serum uric acid; BMI: body mass index; DM: diabetic mellitus; eGFR: estimated glomerular filtration rate; CH50: chronic kidney disease.

Conclusions: Early-onset gout exhibited higher sUA and was associated with obesity but not with hypertension, diabetic mellitus and renal insufficiency. Longer disease duration and lower BMI were associated with tophi in the early-onset gout patients.

Acknowledgements: The present study was supported by Guangdong Natural Science Foundation, China (Grant no. 2011A03010088) to Qian-Hua Li.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6307

Thursday, 15 June 2017

More Obesity and Higher Serum Uric Acid in Early-Onset Gout Patients in South China


Background: Gout incidence increases in a linear fashion with age until 70 years. It was reported that there was a trend of earlier onset gout. Few studies about clinical features of early-onset gout in China are reported.

Objectives: To investigate the characteristics of early-onset gout in south China.

Methods: We conducted a matched cohort study using a population based administrative health database that includes all outpatient visits, hospital admissions, vital statistics, and dispensed medications for all residents in British Columbia, Canada. Gout cases were defined using one ICD-9/10 code (274/M10) from a
physician or hospital visit. To ensure incident gout, we required that all cases have ≥10 years of prior registration without a gout diagnosis. Gout cases were matched 1:1 with controls on age, sex, and cohort entry time. Prior VTE events were excluded after matching. VTE was defined using ICD-9/ICD-10 codes plus use of oral anti-coagulant. We calculated incidence rate ratios (IRR) and age, sex, and entry time matched multivariable hazard ratios (HRs) for the risk of VTE. Sensitivity analyses were conducted to assess for unmeasured confounders (e.g., obesity).

**Results:** Among 105,307 individuals with newly diagnosed gout (61% male, mean age of 55 yrs), we observed 1,212 VTE events (mean follow-up time of 5.3 yrs). The fully adjusted HR was 1.27 (95% CI, 1.18–1.39) (Table 1). Our results remained significant in the sensitivity analyses (OR of 2.0 between gout and unmeasured confounder and a 50% prevalence for obesity). There were 437 incident VTE events within 3 yrs prior to the gout diagnosis. Compared to controls, during the 3rd, 2nd, and 1st yrs before gout diagnosis, the fully adjusted HRs for VTE in patients with imminent gout were 1.51, 1.58, and 1.73. The corresponding HRs in the 1st, 2nd, 3rd, 4th, and 5th yrs after gout diagnosis were 1.54, 1.39, 1.37, and 1.32, respectively.

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Gout Control</th>
<th>No. of VTE events</th>
<th>IRR (95% CI)</th>
<th>Age-, sex-, and entry time adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1yr</td>
<td>105,495</td>
<td>105,526</td>
<td>229</td>
<td>1.99 (1.58, 2.51)</td>
</tr>
<tr>
<td>2yrs</td>
<td>105,307</td>
<td>105,965</td>
<td>390</td>
<td>1.68 (1.31, 2.19)</td>
</tr>
<tr>
<td>3yrs</td>
<td>105,307</td>
<td>105,965</td>
<td>390</td>
<td>1.65 (1.33, 2.08)</td>
</tr>
<tr>
<td>4yrs</td>
<td>105,307</td>
<td>105,965</td>
<td>331</td>
<td>1.65 (1.35, 2.00)</td>
</tr>
<tr>
<td>5yrs</td>
<td>105,307</td>
<td>105,965</td>
<td>277</td>
<td>1.55 (1.23, 1.95)</td>
</tr>
</tbody>
</table>

*Adjusted for Charlson comorbidity index, cancer, alcoholism, hypertension, seizures, trauma, healthcare utilization, NSAIDS, HRT, glucocorticoids and fractures, surgery within 1 year before entry cohort.*

**Conclusions:** Patients with gout have an increased risk of VTE. The risk increases gradually before gout diagnosis, peaks in the year prior to gout diagnosis, and then progressively declines. Our findings suggest that hyperuricemia or gout associated inflammation may be a contributing factor for VTE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4146
HYPERURICEMIA IS ASSOCIATED WITH INCREASED INTEGRATED SAFETY OF LESINURAD, A NOVEL URIC ACID REABSORPTION INHIBITOR FOR THE TREATMENT OF GOUT

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Background: Lesinurad is a selective uric acid reabsorption inhibitor recently approved at 200 mg daily in combination with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid on an XOI (allopurinol or febuxostat) alone.

Objectives: To investigate the safety profile of lesinurad (LESU), we integrated safety data based on: (1) 3 large, pivotal, placebo-controlled, 12-month phase III (core) trials evaluating LESU 200 mg and LESU 400 mg in combination with an XOI, and (2) 2 extension studies, in which LESU-treated patients continued to receive LESU + XOI at the same dose and initially placebo-treated patients were randomized to receive LESU 200 mg or LESU 400 mg in addition to the XOI provided in the preceding core trial.

Methods: Safety data were pooled from the 3 core studies and 2 12-month extension studies using descriptive statistics for patients receiving ≥1 dose of study medication. To adjust for varying treatment durations, treatment-emergent adverse events (TEAEs) are expressed as exposure-adjusted incidence rates (number of subjects with events per 100 person-years [PY]).

Results: In the core studies, adverse event rates were comparable for XOI alone and LESU 200 mg + XOI groups for any TEAEs, serious TEAEs, and TEAEs leading to discontinuation (Table 1). Adverse event rates were higher with LESU 400 mg + XOI. Major adverse cardiovascular event (MACE) rates, which included cardiovascular death, myocardial infarction, or stroke, in the core studies were 0.71 (95% CI 0.15, 2.08), 0.96 (0.26, 2.47), and 1.94 (0.84, 3.82) per 100 PY for XOI alone and LESU 200 mg + XOI groups, respectively.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2714

THU0443 HYPERURICEMIA IS ASSOCIATED WITH INCREASED CORONARY ARTERY CALCIFICATION IN MEN BUT NOT WOMEN

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Background: Hyperuricemia is closely associated to cardiovascular disease although it has not been definitively established whether it is a marker or a causative agent. Serum uric acid (sUa) is strongly linked to the metabolic syndrome, hypertension (HT), dyslipidemia (DL) and higher BMI and higher CRP (hsCRP). CACs, reflecting calcification of coronary arteries, was determined (using computed tomography) in a Swedish cohort of 30 000 men and women aged between 50 and 64 years. A comprehensive pilot study in 1111 individuals was completed in 2012. In this pilot study we have examined the relation between CACs and sUa

Methods: In the SCAPIS pilot study we identified 1106 (552 males) individuals who were screened for traditional CVDRFs such as HT, DL, diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), BMI, high sensitive CRP (hsCRP). CACs, reflecting calcification of coronary arteries, was determined according to Agatston. We measured sUa and related quartiles to CACs with multiple logistic regression analyses adjusting for traditional CVDRFs. CAC was defined positive if ≥1.

Table 1. Baseline characteristics of the study population divided by sex

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male, n=552</th>
<th>Female, n=556</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57.8 (4.5)</td>
<td>57.6 (4.3)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>27.7 (4.0)</td>
<td>26.9 (3.7)</td>
</tr>
<tr>
<td>hsCRP, mean (SD)</td>
<td>2.3 (3.3)</td>
<td>2.4 (3.7)</td>
</tr>
<tr>
<td>CAC positive (%)</td>
<td>305 (55%)</td>
<td>142 (26%)</td>
</tr>
<tr>
<td>Smoking status, never</td>
<td>226 (41%)</td>
<td>249 (45%)</td>
</tr>
<tr>
<td>Smoking status, previous</td>
<td>242 (44%)</td>
<td>222 (40%)</td>
</tr>
<tr>
<td>Smoking status, active</td>
<td>82 (15%)</td>
<td>81 (15%)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>178 (32%)</td>
<td>190 (34%)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>45 (8%)</td>
<td>23 (4%)</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>160 (29%)</td>
<td>128 (23%)</td>
</tr>
</tbody>
</table>

Table 2. Quartiles of sUa and age as predictors for presence of CAC (>0 CACs score) in male and female in multivariate logistic regression analyses adjusted for age, smoking, BMI, DL, HT, hsCRP, EDU and PA

<table>
<thead>
<tr>
<th>sUa, μmol/L</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio, multivariate*, (CI)</td>
<td>p-value</td>
<td>Odds ratio, multivariate*, (CI)</td>
</tr>
<tr>
<td>31–305, Ref</td>
<td>143–229, Ref</td>
<td>0.01</td>
</tr>
<tr>
<td>306–350</td>
<td>2.1 (1.2–3.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>351–404</td>
<td>1.8 (1.3–3.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>405–665</td>
<td>2.1 (1–3.8)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

3Departments of Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå, Sweden

Objectives: Examine the association between sUa and CAC in men and women separately.

Methods: In the SCAPIS pilot study we identified 1106 (552 males) individuals who were screened for traditional CVDRFs such as HT, DL, diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), BMI, high sensitive CRP (hsCRP). CACs, reflecting calcification of coronary arteries, was determined according to Agatston. We measured sUa and related quartiles to CACs with multiple logistic regression analyses adjusting for traditional CVDRFs. CAC was defined positive if ≥1.

Results: Age, BMI, smoking status, hsCRP, HT and DL showed no differences between sex while presence of CAC and diabetes was twice as common in men (Table 1). The three upper quartiles of sUa, (≥306 μmol/L), all significantly (p<0.05) predicted presence of CACs in men even adjusting for HT, DL, DM, smoking, PA, EDU, BMI, hsCRP and age in multivariate logistic regression, but not in women (Table 2).

Conclusions: Higher levels of sUa is associated with presence of CACs in men but not in women. This may merely reflect the earlier onset of atherosclerosis in men or possibly suggest biological differences in the effect of sUa on calcification of coronary arteries between sexes.


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4177
alone, LESU 200 mg + XOI, and LESU 400 mg + XOI, respectively. Renal-related TEAE rates in the core studies were 5.6, 7.3, and 15.4 per 100 PY, respectively. Longer exposure in the core + extension studies did not result in increases in any TEAEs, serious TEAEs, or TEAEs leading to discontinuation (Table 2). MACE rates were low in the core + extension studies, at 1.05 (95% CI 0.50, 1.39) and 1.48 (0.81–2.48) in the LESU 200 mg + XOI and LESU 400 mg + XOI groups, respectively. Renal events in the core + extension studies were lower in the LESU 200 mg + XOI than LESU 400 mg + XOI group at 8.6 and 14.6, respectively.

Conclusions: Lesinurad at the approved dose of 200 mg once daily demonstrated a consistent, acceptable safety profile. There were no new safety concerns in the core + extension studies.

Acknowledgements: This study was funded by Ardea Biosciences/AstraZeneca. None declared.

Methods: The Skåne Healthcare Register includes information on all health care visits with given ICD10-coded diagnoses for all citizens in the region (total population 1.3 million). SHR was searched for all adult (≥18 years) residents in Skåne region in year 2014, who between 1980 and 2014 had received at least one diagnosis of non-gout crystal arthropathy (ICD-10 code M11.0-M11.9) by any physician. The crude point prevalence at December 31st 2014 and the cumulative incidence in the calendar year 2014 were calculated. In addition, we examined the 2014 age- sex- standardized point prevalence and cumulative incidence of non-gout crystal arthropathy according to occupation (white collar blue collar with high or low skilled occupations), income (low/middle/high) and level of education (primary school/high school/university).

Results: The crude 2014 point prevalence and 2014 cumulative incidence of non-gout crystal arthropathy were 0.23% (0.22% - 0.24%) and 21.5 (18.6–24.3) cases per 100 000 persons at risk, respectively. Compared to women, men had numerically but not significantly higher prevalence (0.26% vs 0.20%) and incidence (24.6 vs 18.5 per 100 000 persons). This pattern remained regardless of age. The mean (SD) age of a person with prevalent non-gout crystal arthropathy was 71.5 (14.4) years. Both prevalence and incidence increased with increasing age and were highest in individuals ≥85 years (prevalence 1.4%), but decreased with years of education. Persons with middle income and blue collar high skilled occupation (e.g. skilled agricultural, forestry and fishery workers and craft and related trades workers) had the highest point prevalence and incidence of non-gout crystal arthropathy (figure).

Table 1. Univariate model analyses of predictors of positive DECT results

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (reference: male gender)</td>
<td>0.48 (0.24–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>Body Mass Index (per kg/m²)</td>
<td>1.03 (0.96–1.11)</td>
<td>0.36</td>
</tr>
<tr>
<td>Cardiovascular disease yes/no</td>
<td>2.72 (1.36–5.42)</td>
<td>0.04</td>
</tr>
<tr>
<td>Diabetes mellitus yes/no</td>
<td>3.69 (1.26–10.71)</td>
<td>0.01</td>
</tr>
<tr>
<td>Urate lowering therapy use at the moment of DECT yes/no</td>
<td>2.6 (1.15–6.28)</td>
<td>0.02</td>
</tr>
<tr>
<td>Disease duration years</td>
<td>1.01 (1.005–1.02)</td>
<td>0.01</td>
</tr>
<tr>
<td>Frequency of attacks per year</td>
<td>1.2 (1.08–1.33)</td>
<td>0.01</td>
</tr>
<tr>
<td>Uric acid levels between flares (per μmol/L)</td>
<td>1.004 (1.001–1.007)</td>
<td>0.008</td>
</tr>
<tr>
<td>Creatinine clearance (per ml/min)</td>
<td>0.95 (0.90–0.99)</td>
<td>0.01</td>
</tr>
<tr>
<td>Joint involvement at the moment of DECT: MTP-1 other joints</td>
<td>1.69 (1.05–3.37)</td>
<td>0.1</td>
</tr>
<tr>
<td>Past first metatarsophalangeal (MTP1) joint involvement yes/no</td>
<td>3.37 (1.69–6.72)</td>
<td>0.01</td>
</tr>
<tr>
<td>MSU crystals at microscopy yes/no</td>
<td>1.62 (1.22–2.17)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: Although considerably less prevalent than gout in southern Sweden non-gout crystal arthropathy affects about 0.2% of the adult population, i.e. a similar prevalence as for psoriatic arthritis in the same region. The prevalence increases with age and is highest among individuals aged 85 years or higher. There is a socioeconomic gradient with more affected individuals among people with lower level of education, middle income, and more manual work.


Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3089
CO-MORBID GOUT IS ASSOCIATED WITH INCREASED CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH TYPE 2 DIABETES, BUT NOT CARDIOVASCULAR EVENTS OR MORTALITY

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Background: Gout is an inflammatory arthropathy characterised by elevated serum uric acid levels. In Australia, gout has a prevalence of 1.7 - 4%. This increased to 10% in a community based Australian patients with type 2 diabetes, although elevated serum uric acid did not predict cardiovascular (CV) or all-cause mortality. To date, the long-term outcomes of patients with diabetes and comorbid gout being followed up in the hospital out-patient setting have not been studied.

Objectives: To compare cardiovascular risk factors and long-term outcomes and mortality in patients with type 2 diabetes according to the presence or absence of gout.

Methods: 1,405 patients with type 2 diabetes were prospectively recruited from the outpatient setting at Austin Hospital. Baseline cardiovascular risk factors and comorbidities were identified. Patients were classified as having gout if they gave a history of gout or were taking medication for the treatment of gout. For statistical analysis, patients with diabetes (Group 1) were compared to those with diabetes and gout (Group 2).

Cardiovascular events and long-term CV mortality were assessed over a 10 year period.

Results: There were 1,329 patients with diabetes (Group 1, 95%) and 76 with diabetes and gout (Group 2, 5%). Patients with gout were older (68±11 vs. 64±12y, p<0.004), more likely to be male (80% vs. 59%, p=0.201). Results

- Serum uric acid levels in both groups. Comparison of results from baseline and after 6 months

- PGA (P=0.009), TJC and SJC (P=0.003), and SF-36 Bodily Pain (P<0.0001) for patients without clinically apparent tophat at baseline indicated significant improvements in serum UA (P<0.0001), flares (P<0.0001), PGA (P<0.0001), TJC and SJC (both P<0.0001), HAQ-DI (P<0.0001), and SF-36 Bodily Pain (P<0.0001).

Conclusions: These results indicate that chronic refractory gout patients may present with or without clinically apparent tophi. Tophaceous patients are distinguished by more tender and swollen joints, greater disability, and greater arthritis severity, but otherwise are similar to nontophaceous patients. Both groups had significant clinical benefit over 6 months of treatment with pegloticase.

References:

EVIDENCE BASED DEVELOPMENT OF CRITERIA FOR COMPLETE RESPONSE IN PATIENTS WITH CHRONIC REFRACTORY GOUT

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Background: Preliminary criteria for remission in gout patients have recently been proposed. These include serum urate, acute flares, tophus, pain and patient global assessment. These preliminary criteria were based on consensus exercises and have not yet been tested in a large clinical trial database of chronic gout patients. Because of the availability of clinical results from subjects with chronic refractory gout treated with pegloticase (8 mg every 2 weeks), a mammalian recombinant uricase conjugated to polyethylene glycol that is approved in the US for treatment of adult patients with chronic gout refractory to oral urate lowering therapy, the utility of these proposed criteria could be assessed.

Objectives: To test the utility of the preliminary criteria to discern a complete response (CR) in subjects with chronic refractory gout treated with pegloticase (8 mg every 2 weeks).

Methods: Data from two randomized clinical trials (RCT) evaluating the impact of pegloticase therapy in subjects with chronic refractory gout were examined. Of this group of subjects, 42% had persistently lowered serum urate and 58% did not meet the urate-lowering endpoint of this RCT. Initially, individual patient data was reviewed to establish the frequency with which subjects, who were responders to pegloticase, met the proposed remission criteria. Mixed modeling was therefore employed on data from these subjects to determine the components of the model that best correlated with time of maximum benefit.

Results: Of 34 pegloticase responders, 25 (73.5%) met the published criteria of remission. However, pain assessment was often an outlier; data obtained by visual analogue scale and Medical Outcomes Study Short Form-36 questionnaire often differed. Mixed modeling was therefore employed on data from the subjects meeting criteria for remission to determine the components that best correlated with time to maximum benefit.

Other clinical outcome measures assessed in the clinical trial were also analyzed. Besides serum urate levels, the mixed model also included components of response that best correlated with time of maximum benefit included assessment of tophus (analyzed photographically), number of swollen joints, number of tender joints and patient global assessment. Using these criteria, 25 of the responders (73.5%) and 29.4% of the entire pegloticase-treated population met criteria for a CR. The median time to reach a CR was 252 days (range: 126-896 days). Of interest, when a decrease in serum urate was omitted, 6 (12.2%) of the pegloticase nonresponders also met criteria for a CR. Patients receiving placebo did not achieve the composite outcome measure considered as CR.

Conclusions: These results have defined criteria for achieving CR in individuals with chronic refractory gout treated with pegloticase and suggest that most individuals who persistently lowered their serum urate levels while on pegloticase reached criteria for CR in a median of 8.4 months. This composite CR definition can serve as an evidence-based target aiding the design and endpoints of future clinical trials.

References:

CHARACTERIZATION OF PATIENTS WITH CHRONIC REFRACTORY GOUT WHO DO AND DO NOT HAVE CLINICALLY APPARENT TOPHI: RESPONSE TO PEGLOTICASE

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Background: The term “chronic refractory gout” defines a subset of chronic gout patients who are either intolerant of or unresponsive to standard uric acid (UA) lowering therapy (ULT). Subjects (N=85) meeting this definition were enrolled in a study of pegloticase (8 mg every 2 weeks [q2w], the approved dose), a mammalian recombinant uricase conjugated to polyethylene glycol that is approved for the treatment of chronic gout refractory to conventional oral ULT. Of this group of subjects, 73% had clinically apparent tophi, whereas 27% did not.

Objectives: To determine the clinical characteristics and response to pegloticase therapy in patients with chronic refractory gout with and without clinically apparent tophi.

Methods: This analysis used results from two pivotal randomized controlled trials to assess the clinical characteristics and the efficacy of pegloticase (8 mg q2w) in patients with chronic refractory gout with or without tophi at baseline. The results for serum urate (UA), flares, Patient Global Assessment (PGA), tender and swollen joints (TJC and SJC), BMI, body pain, Health Assessment Questionnaire-Disability Index (HAQ-DI), and the Arthritis-Specific Health Index (ASHI) and Bodily Pain from the Medical Outcomes Study Short Form 36 item (SF-36) were determined for each group.

Results: The analysis included patients with chronic refractory gout. 62 with tophi at baseline and 23 with no clinically apparent tophi. Differences in baseline characteristics between the two groups were similar at baseline, with the only significant differences in mean values between tophaceous and nontophaceous gout groups as follows: TJC, 14.2 vs. 5.00 (P<0.01); SJC, 10.9 vs 3.4 (P<0.003); ASHI, 50.4 vs 64.7 (P<0.003); and HAQ-DI, 1.3 vs 0.6, respectively (P<0.001). Other measures of disease impact and comorbidities were not significantly different between groups. Treatment with pegloticase 8 mg q2w resulted in significant and comparable reductions in serum UA in both groups. Comparison of results from baseline and after 6 months of treatment for patients with tophi at baseline indicated significant reductions in serum UA (P<0.0001), flares (P<0.0001), PGA (P<0.0001), TJC and SJC (both P<0.0001), HAQ-DI (P<0.0001), and SF-36 Bodily Pain (P<0.0001). Results for patients without clinically apparent tophi at baseline indicated significant improvements in serum UA (P<0.0001), flares (P<0.004), PGA (P<0.009), TJC (P<0.01), SJC (P<0.003), SF-36 Bodily Pain (P=0.03), and ASHI (P<0.001).

Conclusions: These results indicate that chronic refractory gout patients may present with or without clinically apparent tophi. Tophaceous patients are distinguished by more tender and swollen joints, greater disability, and greater arthritis severity, but otherwise are similar to nontophaceous patients. Both groups had significant clinical benefit over 6 months of treatment with pegloticase.

References:

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Background: Gout is associated with significant burden and risk of readmission. Little is known about readmissions among Gout patients on a national level in the United States.

Objectives: The aim of this study was to describe unplanned hospital readmission rates among adult gout patients and assess predictors of readmission.

Methods: We analyzed the 2013 National Readmission Database (NRD) to quantify readmission rates among Gout patients. The NRD includes weighted discharge data from 21 geographically diverse states accounting for 49.3% of the U.S. population. It includes approximately 14 million un-weighted discharges nationwide. NRD data is from patients with non-Medicare payers (Medicaid, private, self-pay, or other). Gout hospitalizations were identified using the International Classification of Diseases, ninth Revisions, Clinical Modification (ICD-9-CM) diagnosis code 274.0x. All hospitalizations for patients age ≥18 were included. In efforts to exclude routine readmissions, we excluded those admissions related to pregnancy, those for chemotherapy, admissions where the patient was readmitted the same day as they were discharged, who had deaths during the same index hospitalization and hospitalizations for less than 24 hours, and those with missing discharge. We utilized Chi-square tests, t tests and Wilcoxon rank-sum tests as appropriate. Survey logistic regression was used to assess the relationship between potential predictors for readmissions and the odds of at least one 30-day unplanned readmission. This analysis was chosen given the NRD data, which involves nested, weighted observations that are inherently stratified in clusters to produce national estimates.

Results: A total of 10708 index hospitalizations which had Gout as the primary diagnosis were included in the analysis. Among those with a primary Gout diagnosis, there were 1215 30-days readmissions (11.3%). 14.33% percent of patients with Gout as the primary diagnosis on index hospitalization were readmitted within 30 days. Significant predictors of readmission included CHF, CKD, AF, APR-DRG severity level 3 or 4 (OR 1.51, 95% CI, 1.01–2.38 and OR 2.10, 95% CI, 1.06–4.58), discharge to specialized care (OR 1.47, 95% CI, 1.07–2.02), discharge to home health care (OR 1.35, 95% CI, 1.03–1.77), and discharge against medical advice (OR 3.85, 95% CI, 1.50–9.91), were significantly associated with 30-days readmission after adjusting for demographics, comorbidities, hospital characteristics, payer type, and the APR-DRG severity scale (Figure 1B).

Conclusions: In a national readmissions database, 11.3% of patients admitted with a primary diagnosis of Gout were readmitted within 30 days. Significant predictors of readmission included CHF, CKD, AF, APR-DRG severity level 3 or 4 and any discharge other than routine.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6488

THUO450 HOSPITAL READMISSIONS FOR GOUT IN THE UNITED STATES: A NATIONAL DATABASE STUDY


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THUO451 A METHOD FOR COUNTING CALCIUM PYROPHOSPHATE CRYSTALS IN THE SYNOVIAL FLUID

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Background: Identification of calcium pyrophosphate dihydrate (CPP) crystals in the synovial fluid (SF) from inflamed joints provides a definitive diagnosis of CPP deposition disease (CPPD) (1). CPP crystals may also be found in non-inflamed joints, allowing symptomatic periods (2). SF analysis and CPP crystals count could be used to evaluate disease activity during follow-up. It is more difficult than the count of monosodium urate (MSU) crystals, already tested in a previous work (3), for CPP crystals show different shapes, are often mixed and non-birefringent.

Objectives: To study an objective method for counting CPP crystals in the SF.

Methods: The SFs aspirated from the knees of 15 consecutive patients (8 men) affected by CPPD diagnosed according to the EULAR definition were analysed. Cytological evaluation included SF leukocyte and differential count. For crystal detection, a small drop of fresh SF was placed on a glass slide and examined by compensated polarized microscopy (400x). To facilitate crystal count, the slide was divided into 4 equal parts drawing a cross with a pencil. The count was performed by continuous viewing and for each field both the number of birefringent and non-birefringent crystals was noted. Two observers evaluated separately 6 SFs and repeated the count after 24 hours. SFs were divided into 4 groups: SFs with <50, from 50 to 400, from 401 to 1200, and >1200 crystals.

Results: Mean time needed for the count was 60 minutes. Inter-reader agreement was 0.68 (0.47–0.88) for CPP crystals, 0.68 (0.50–0.85) for the birefringent ones and 0.62 (0.38–0.81) for the non-birefringent ones. Intra-reader agreement was 0.48 (0.17–0.78) for the first examiner and 0.30 (0.14–0.74) for the second. In 7 patient the SF was aspirated from an inflamed knee. Crystal number did not correlate with the presence of knee inflammation (r=0.41; p<0.19), the SF volume (r=0.43; p=0.2) and the number of leukocytes (r=0.36; p=0.2). The % of PMN (r=0.25; p=0.37), and the presence of intracellular crystals (r=0.31, p=0.02) were significantly different from those of non-birefringent. Actively inflamed joints had a higher SF volume [11 ml (10–20 ml) vs. 2 ml (1–10 ml), p=0.03] and a higher percentage of PMN [72% (9–94%) vs. 12% (6–88%), p=0.02]. SF with intracellular crystals showed also a higher percentage of PMN (57% vs. 34–39%, and 3–46% vs. 0.006).

Conclusions: Our preliminary results indicate that CPP crystal count is less reliable and more time-consuming that that of MSU crystals. Non-birefringent crystals show lower inter-reader agreement than birefringent ones.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5045

THUO452 IMMEDIATE AND LONG TERM EFFICACY OF ANAKIRNA IN ACUTE FLARES DUE TO HYDROXYAPATITE CALCIFICATIONS: A REAL-LIFE EXPERIENCE OF 13 CASES

P. Zufferey, R. Valcov, A. So. DAL, CHUV, Lausanne, Switzerland

Background: Calcifications composed of hydroxyapatite (HA) crystals can induce acute and severe pain accompanied by signs of acute inflammation. In a previous pilot study, we have shown that anakirina was effective in acute flare of calcific periarthritis of the shoulder in the short term

Objectives: The goal of this retrospective observational study was to confirm these results in a larger series of patients, extending the observation to other localizations and to report on the long-term follow-up.

Methods: All consecutive patients with an acute flare due to HA deposition and treated with anakirina between March 2011 and November 2016 were included. Pain was defined as symptoms of acute pain at rest present for ≥10 days. None of the patients had corticosteroid therapy in the last 2 weeks, none had responded to at least 48 hours of high doses of NSAIDs or other rheumatologic diseases explaining the symptoms. Clinical evaluation consisted of patient assessment of pain by VAS (10mm scale) at days 0, 1, 3, 21 and joint mobility. CRP and ESR measurements, ultrasound and x-ray examinations were performed before the
Heart and Carotid Changes in Fifty-Three Gout Patients Treated with Xanthine Oxidase Inhibitors: A Follow-Up Study

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Background: Gout connects to cardiovascular (CV) morbidity and higher risk of death due to CV events. A few ultrasound studies assess the way in which heart and vessels change over time in gout patients (pts). It is still unclear whether treatment with allopurinol or febuxostat reduces to some extent target organ damage.

Objectives: We aimed to establish heart and vessels alterations developing over time in gout pts and to find out whether treatment with allopurinol or febuxostat is associated with a change in these structures.

Methods: A total of 53 gout pts were examined and divided into two groups: 31 gouty arthropathy without tophi, 24 males and 7 females aged 55.8±12.3 years and 22 gouty tophi, 20 males and 2 females aged 59±9 years. Pts underwent multimodal ultrasound examination at study entry and one year and six months thereafter. Anacor Laboratories Inc, Alachua, FL; Advanced Imaging Biometrics, Inc, 6.1x baseline were higher with LESU+XOI than XOI

Results: Treatment with allopurinol or febuxostat reduces to some extent target organ damage.

Conclusions: Improvement of pain, physical impairments and disabilities for the study group certifies the efficacy of the rehabilitation program including physical exercise in patients with hip arthropathy for aseptic necrosis of the femoral head and motivates the continuation of the study on a longer period of time and on a larger number of patients. Rehabilitation program must begin right after patients undergo surgery for hip replacement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5130
LESU+XOI treatment in the core-extension studies did not show an increase from core studies in EAIRs for any renal-related or kidney stone adverse event category (Table 2).

Conclusions: Lesinurad at the approved dose of 200 mg once daily combined with XOI demonstrated comparable rate of adverse events to XOI alone. There was no clinically relevant increase in these adverse events with the extension of treatment beyond 1 year.

Acknowledgements: This study was funded by Ardea Biosciences/AstraZeneca.  


DOI: 10.1136/annrheumdis-2017-eular.5008

THU0457 LESS THAN HALF OF PATIENTS TREATED WITH HIGH-DOSE ALLOPURINOL REACH SUA TARGET

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Background: Although allopurinol is FDA approved for up to 800 mg per day and EMEA authorized for up to 900 mg per day, most patients receive 300 mg per day or less.

Objectives: To describe physician, patient, and treatment characteristics in gout patients treated with allopurinol and to assess the proportion of patients reaching serum uric acid (sUA) target by allopurinol dose.

Methods: Patient data from a quantitative survey of physicians were utilized and results confirmed through chart review. Initial and current dose of allopurinol, presence of co-morbid conditions, sUA lab results, physician specialty, and patient characteristics were assessed. Data on number of patients achieving target sUA<6mg/dL were also collected. Descriptive characteristics are presented as proportions or means and standard deviations (SD). Multivariate and descriptive statistics are used to describe patients with sUA<6 mg/dL.

Results: A total of 251 rheumatologists and 250 primary care physicians were interviewed. Of 2505 patients with gout, 1437 (57%) were treated with allopurinol. Use of high-dose allopurinol significantly differed by country with less than 6.5% of patients in France, Germany, and Spain given >300mg, whereas 10.2%, 19.5%, and 33.6% of patients in Italy, the US, and the UK, respectively, received a daily dose >300mg (p<0.01). Over 12 months the percentage of patients achieving sUA<6.0 mg/dL differed across the 6 countries. Looking across all countries, only 43.8% and 44.7% of patients achieved sUA<6.0mg/dL with 301–599mg and >600mg of allopurinol QD, respectively. A multivariable-adjusted model found patients with tophi (OR 3.42; p<0.01), co-existing alcoholism (OR 1.73; p<0.05), COPD (OR 2.01; p<0.05), smoking cessation treatment (3.49; p<0.05), and from the UK (OR 3.98; p<0.01) were more likely to be using >600mg of allopurinol. Regardless of allopurinol dose, the co-variates UK vs. other countries (OR 3.51; p<0.01), time on therapy >24 months (OR 1.39; p<0.01), and chart-documented co-existing hypertension (OR 1.36; p<0.05) were predictive of achieving sUA<6 mg/dL. Whereas physician sub-speciality (general practitioners vs. rheumatologists [OR 0.56; p<0.01]), having tophi (OR 0.72; p<0.05), and chart-documented co-existing alcoholism (OR 0.67; p<0.05), hyperlipidemia (OR 0.74; p<0.05), and kidney stones (OR 0.49; p<0.05) were found to be associated with not achieving sUA<6 mg/dL. After adjusting for confounding factors, over a 12-month period, there was no difference in achieving sUA<6 mg/dL for those treated with high- vs. low-dose allopurinol.

Conclusions: Allopurinol is approved for up to 800mg in the US and 900mg in the EU but the majority of patients are treated with <300mg per day. Less than 50% of patients achieve sUA<6mg/dL at any dose of allopurinol. These data suggest a need for consideration of new treatment options on top of allopurinol for uncontrolled gout patients.

Acknowledgements: This study was funded by Ironwood Pharmaceuticals.  

Disclosure of Interest: R. Morlock Consultant for: Received consulting fees from AstraZeneca and Ironwood Pharmaceuticals, and was a consultant of Ardea Biosciences, Inc, a member of the AstraZeneca Group  

DOI: 10.1136/annrheumdis-2017-eular.6234
Results: Treatment of SITK01 through SITK03 and SITT01 at concentration (250 mg/mL) decreased the cell viability. The PO-stimulated kidney epithelial cells with SITK01 through SITK03 treatment increased GLUT9 by 2.5 folds and decreased OAT3 by 1.5 folds (versus controls; p=0.012, and p=0.017, respectively). In PO-treated mice, uric acid levels were increased through GLUT9 and OAT3 transporters. The results indicated that SITK01, SITK02, and SITK03 showed the potential on uricosuric effects in a dual modulation of apical/basolateral sides of kidney epithelial tubular membranes.

Table 1. Protein expression of transporters in apical and basolateral membranes of proximal tubular epithelial cells and potassium oxonate-treated experimental mice

<table>
<thead>
<tr>
<th>Membrane domain</th>
<th>Functions</th>
<th>Transporters</th>
<th>Casso-2</th>
<th>MDCK</th>
<th>LCL-PK1</th>
<th>Potassium Oxonate-treated mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apical</td>
<td>Palpation of excretion</td>
<td>SLC22A12 (URAT1)</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Basolateral</td>
<td>Inhibition of reabsorption</td>
<td>SLC22A6 (OAT1)</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

Conclusions: The present findings demonstrated that three commercial herbal products showed potentials to reduce hyperuricemia-induced condition by changing protein expression levels in a transporter-uptake assay. The OAT3 and GLUT9 could be further investigated as the uricosuric group-targets on the apical sides at kidney epithelial tubular membranes.

References:

THU0460 BARRIERS TO GOUT CARE: A SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS OF 120 PROVIDERS AND 480 GOUT PATIENTS FROM QUALITATIVE STUDIES

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Background: Despite gout’s well-known pathogenesis and the availability of effective urate-lowering therapy (ULT), management remains poor. However, limited research has sought to improve care among this patient population. An in-depth understanding of provider and patient perspectives on barriers to the delivery of optimal gout care is critical to informing the development of evidence-based interventions to effectively improve disease management and patient outcomes.

Objectives: To systematically review and thematically synthesize qualitative studies to date reporting provider and patient barriers to gout management.

Methods: We conducted a mapped search of MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and Social Sciences Citation Index databases and selected qualitative studies reporting provider and patient perspectives on gout management. Thematic synthesis was used to combine the source studies and identify key themes across studies. Two authors independently read and annotated the data and after discussion agreed on an initial coding framework. Concepts were organized into descriptive themes, and the relationships between these descriptive themes were further explored to develop higher-order analytical themes.

Results: Our search strategy retrieved 2,750 articles after the removal of duplicates. After full-text review, 20 studies spanning several geographic settings worldwide (i.e., the US, the UK, New Zealand, Australia, and the Netherlands) met all inclusion criteria and were included in our systematic review. Of these, 16 studies reported gout patient perspectives (n=480 patients), while only 7 studies reported provider perspectives (n=120 providers, including general practitioners, rheumatologists and other specialists, and allied health professionals). Thematic synthesis identified three predominant interlocking analytical themes among providers: (a) knowledge gaps and management approaches, (b) perceptions and beliefs about gout patients, and (c) system barriers to optimal gout care (Table 1). We further identified four predominant themes among gout patients: (a) limited gout knowledge (e.g., the “curable” nature of gout), (b) attitudes toward taking medication, (c) interactions with healthcare providers, and (d) practical barriers to chronic medication use (Table 1).
Table 1. Illustrative Provider and Patient Quotations from Source Studies

<table>
<thead>
<tr>
<th>Provider/Barrier</th>
<th>Quotation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge gaps and management approaches</td>
<td>‘I think that there is lack of knowledge by both patients and healthcare professionals. I just learned what gout flare up is and then it just went away, so there is definitely a need for education for this situation.’</td>
<td>Spencer et al.</td>
</tr>
<tr>
<td>Perceptions and beliefs about gout patients</td>
<td>‘Adherence to uric acid-lowering therapy is not a problem in my gout management, since when I feel the fact they will get new gout attacks if they do not take their medication.’</td>
<td>Sparsens et al.</td>
</tr>
<tr>
<td>System barriers to optimal gout care</td>
<td>‘It’s another thing, too, the time issue. Cause if you’re really really busy, if you don’t have time to talk to the patient, you don’t have time. If we’re busy.’</td>
<td>Humphrey et al.</td>
</tr>
</tbody>
</table>

Conclusions: Our thematic synthesis identified several barriers to gout care, particularly knowledge gaps among both providers and patients as well as strategies to reduce system barriers and support regular medication use are urgently needed to improve gout care.

Acknowledgements: This study was supported in part by a grant from the Canadian Institutes of Health Research (PCS 146388). We wish to thank the Arthritis Patient Advisory Board of Arthritis Research Canada for providing their consumer input into this project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4298

THU0461 ACCURACY OF HUMASENS-PLUS POINT-OF-CARE URIC ACID METER USING CAPILLARY BLOOD OBTAINED BY FINGERTIP PUNCTURE


Background: A key factor in the success of gout management is the long-term lowering of uricemia below predetermined targets (300 or 360 μmol/l). Monitoring of uricemia in gout patients is therefore important, and is presently done in the clinical practice by capillary samples obtained by fingertip puncture. An uric acid (UA) meter allowing rapid testing by the health care professionals and self-measurement by the patient should improve management of gout.

Objectives: This study aimed to assess the reliability of immediate UA measurement in capillary blood obtained from fingertip puncture using the HumaSens®plus point-of-care meter (meter) compared with that of a standard laboratory assay (lab).

Methods: Capillary UA levels were measured from 236 consenting diabetic patients using the commercially available HumaSens®plus UA meter (European Commission marked and approved for EU market use). Each patient also had a plasma UA measurement in the biochemistry laboratory using an uricase laboratory assay (lab).

Results: Forty capillary samples were read LO by the meter: 11 were confirmed by lab to be below 180 μmol/l and 3 were above (189, 206 and 216 μmol/l). Two capillary samples were read HI and were measured at 303 and 313 μmol/l by lab. In the remaining 222 samples with meter and lab values, ICC was 0.90 [0.87–0.92] and Bland-Altman curve showed acceptable agreement over all the tested values. Best meter threshold for detection of hyperuricemia by the HumaSens®plus meter was 330 μmol/l (sensitivity 0.89, specificity 0.89, area under the ROC curve 0.95). Based on regression, plasma uric ise of 360 μmol/l corresponded to 343 μmol/l. Among the biological parameters tested, only hematocrit impacted capillary uric acid measurements, however negligibly.

No medication appeared to significantly affect test results. Plasma uric acid measurements were better correlated to LC-MS measurements (r=0.98 [0.96–0.99]) than capillary measurements (r=0.84 [0.75–0.90]).

Conclusions: The HumaSens®plus point-of-care meter was reasonably comparable to those of the laboratory assay. It is easy to use and may be useful in clinic and in epidemiologic studies.

Disclosure of Interest: None declared


THU0462 MORTALITY IN PATIENTS WITH GOUT: A SYSTEMATIC REVIEW

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Background: Gout is a chronic, progressive, inflammatory disease characterised by elevated serum uric acid (sUA) levels (1). In Europe the prevalence of gout ranges from 0.9–2.5%, and is increasing (2). Published data indicate that gout is an independent risk factor for both all-cause and cardiovascular (CV)-related mortality (3, 4).

Objectives: To conduct a systematic review to identify studies reporting the association between gout and mortality (all-cause and CV-related).

Methods: Relevant publications were identified by interrogating electronic databases; Medline & MEDLINE In-Process, EMBASE and the Cochrane Library (accessed 3 May 2016). Eligibility criteria included adult patients with a definitive diagnosis of acute/chronic gout (self-reported/physician diagnosed), with no restriction on publication date, study design or geography.

Results: Nineteen studies met the pre-defined inclusion criteria and were reviewed. The studies were conducted in: the US (n=8); Taiwan (n=5); Canada (n=3); Australia (n=1); Singapore (n=1); and the UK (n=1). In addition to patients having a diagnosis of acute/chronic gout, 6 of the 19 studies were conducted in the following patient subgroups: renal transplant (n=1); chronic kidney disease (n=2); patients with a recent acute myocardial infarction (n=2); and patients with heart failure (n=1). There were several consistent finding across the 19 studies: (i) gout was associated with an increase in both all-cause mortality (reported hazard ratios [HR] ranges from 1.13 to 2.37) and CV-related mortality (reported HR ranged from 1.10 to 3.88) compared with patients without gout; (ii) the increased risk in all-cause mortality was primarily driven by an increase in CV-related mortality; (iii) the increased mortality risk was higher in females than males. One study reported that the presence of tophi was independently associated with a higher risk of all-cause mortality. Notably one study reported that patients who received urate-lowering therapy (ULT) had a statistically significant lower all-cause mortality and CV-related mortality risk relative to patients who do not receive ULT.

Conclusions: This systematic review confirms that gout is associated with an increased risk of all-cause and CV-related mortality; this was consistently reported across the eligible studies. The findings highlight the risk associated with gout and emphasise the need for appropriate treatment of this curable disease.

References:

Disclosure of Interest: S. Mitchell: None declared, H. Liedgens Employee of: Grünenthal Gmbh, E. Johannes Employee of: Grünenthal Gmbh

DOI: 10.1136/annrheumdis-2017-eular.6062

THU0463 EPIDEMIOLOGY OF GOUT AND HYPERURICEMIA IN NEW CALEDONIA

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Background: New Caledonia is a Pacific island of 270,000 inhabitants with mixed ethnicities, including Melanesians (39.1%) and Polynesians (10.2%) and people from European ancestry (27.2%).

Objectives: To determine the prevalence of gout and hyperuricemia in the various ethnicities and to characterize associated factors.

Methods: A 3-degree random sample of the population aged 18 to 60 years old was reconstituted according to the 2014 New Caledonia census. Face-to-face interviews were performed by trained nurses who used a predefined questionnaire along with planned physical measurements. All participants underwent capillary measurement of creatinine level (StatSensor) and all men and only women older...
A GENOME-WIDE ASSOCIATION STUDY OF GOUT IN PEOPLE OF EUROPEAN ANCESTRY

T.R. Merriman, 1 M. Cazdow, 1 M. Merriman, 1 A. Phipps-Green, 1 R. Topliss, 1 A. Abhishek, 2 M. Andres, 3 L. Bradbury, 4 R. Buchanan, 5 R. Cremin, 6 E. de Guzman, 7 J. de Zoya, 8 M. Doheroy, 9 C. Hill, 10 H. Huizinga, 11 T. Jansen, 12 C. Hill, 13 T. Huizinga, 14 M. Janssen, 15 L. Joosten, 16 F. Kurreeman, 17 S. Lester, 18 F. Liote, 19 J. de Zoya, 20 M. Doherty, 21 C. Hill, 22 T. Huizinga, 23 T. Jansen

DOI: 10.1136/annrheumdis-2017-eular.3409

None declared

References:

(2) Fabre et al Ann Rheum Dis, 2016;

Disclosure of Interest: None declared

THU0465 CALCIUM PYROPHOSPHATE DEPOSITION DISEASE AND OSTEOARTHRITIS: TWO FACES OF THE SAME MEDAL? AN ULTRASONOGRAPHIC AND MICROSCOPY STUDY

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Background: Calcium pyrophosphate deposition disease (CPPD) and Osteoarthritis (OA) are frequently associated and CPPD with OA is recognized as a clinical entity [1]. However, there are differences in pathogenetic, microscopic and clinical aspects between the two diseases which are not clear and how CPPD and OA could affect each other is still a matter of debate.

Objectives: To assess the differences between CPPD and OA in terms of anatomic alterations of the knee joint and to compare males with females of the same age.

Methods: consecutive patients reaching the outpatient clinic for the presence of knee pain and with any amount of joint effusion were eligible for the study. Patients with diagnosis or suspicion of chronic inflammatory rheumatic conditions and those with severe intermittent bilateral knee pain were excluded. All enrolled patients were classified into two groups on the basis of the knee assessment: joint effusion (JE), synovial hyperthropy (SH), synovial power Doppler (PD), femoro-tibial osteoarthritis (TOA) and others which included CPPD and OA.

Results: 49 patients (28 women), mean age 70.29 yo (SD±10.93) were enrolled in the study; 23 subjects presented OA and 26 CPPD (23.07% acute arthritis, 77.6% CPPD with OA). At US, a statistically significant difference between CPPD and OA was found only for the grade of effusion, being more abundant in patients with OA. On the contrary, no differences were found regarding SH, PD, TOA, SH+PD+TOA. The analysis showed that CPPD patients presented a higher volume of SF, a higher total WBC count with a higher polymorphonuclear (PMN) cells percentage and lower monocytes percentage than patients with OA. Further, both total cell count and PMN percentage were positively correlated with the number of crystals in the SF. On the other hand, no statistically significant differences were found in the content of mononuclear cells and their concentrations between the two groups.

Conclusions: According to these results, patients with CPPD and OA present some distinct features, mainly regarding the characteristics of the SF, compared to patients with OA alone. These differences may reflect different underlying pathogenetic pathways for the two diseases. Surprisingly, the concentration of mononuclear cells in the two populations was similar.

Further studies are necessary in order to better understand the link between CPPD and OA and the role of ions concentration in the SF for the formation of crystals.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5634

THU0464 A GENOME-WIDE ASSOCIATION STUDY OF GOUT IN PEOPLE OF EUROPEAN ANCESTRY


DOI: 10.1136/annrheumdis-2017-eular.3409

None declared

References:

(2) Fabre et al Ann Rheum Dis, 2016;

Disclosure of Interest: None declared

THU0467 SAFETY AND EFFICACY OF FEBUXOSTAT IN ADVANCED CKD PATIENTS WITH HYPERURICEMIA

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Background: In chronic kidney disease (CKD) patients, hyperuricemia is a common finding and might be one of modifiable risk factors for renal progression. However, dosing adjustments and increased risk of serious side effects of uric acid lowering agents in patients with reduced renal function lead to undercorrection of hyperuricemia, especially in patients with advanced CKD. Febuxostat is highly
effective and well-tolerated to treat hyperuricemia in CKD patients. Although several evidences demonstrated the usefulness of febuxostat in hyperuricemic CKD patients, clinical studies aimed at the CKD patients with inappropriately controlled hyperuricemia by allopurinol have been relatively lacking. 

Objectives: The study objective is to evaluate the safety and efficacy of febuxostat in patients, who have severe renal impairment and did not meet with the target uric acid levels using allopurinol.

Methods: Data were collected from 168 patients who had CKD with more than stage 3b and changed from allopurinol to febuxostat due to uncontrolled hyperuricemia between 2005 and 2014 at Yonsei University Medical Center. Uric acid and creatinine were analyzed at baseline and during the first 6 and 12 months after conversion of febuxostat. Estimated glomerular filtration rate was calculated using the formula of MDRD equation. The patients were defined as a well-controlled state when the uric acid values of the study subjects reached 3mg/dL at baseline (5.2±2.1 mg/dL at 6-month and 4.9±2.2 mg/dL at 12-month, p<0.001, respectively). Subjects reached to the target of uric acid levels less than 6mg/dL at 6- and 12-months after treatment of febuxostat [122 (72.6%) patients at 6-month and 133 (79.2%) patients]. The creatinine levels at baseline and 6-month were comparable (3.4±2.5 vs. 3.5±2.6 mg/dL at baseline and 6-month, p=0.61), meanwhile, the creatinine levels were significantly increased after 12-month compared to those at baseline (3.6±2.14 mg/dL, p<0.01). Abnormality of liver function test was observed in only one patient during the follow up period. None of the patients did not discontinue drug due to adverse events.

Conclusions: Present study demonstrated that substantial hyperuricemic CKD patients treated with febuxostat were achieved the target of uric acid levels without adverse events. Febuxostat is an effective and safe uric acid lowering drug in allopurinol-intolerant patients with advanced CKD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2925

THU0469
COMPARATIVE EFFECTIVENESS OF TAI CHI VERSUS AEROBIC EXERCISE FOR FIBROMYALGIA: A RANDOMIZED CONTROLLED TRIAL

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Background: Fibromyalgia is a complex disorder with strong psychological and pain components. Tai Chi is an integrated mind-body approach that enhances both physical and mental health and has great potential to treat fibromyalgia.

Objectives: We aimed to investigate whether Tai Chi is more effective with longer lasting effects than aerobic exercise.

Methods: We conducted a 52-week, single-blind, randomized controlled trial of Tai Chi vs. aerobic exercise for fibromyalgia (ACR 1990 and 2010 diagnostic criteria). Participants were randomized to 1 of 4 Tai Chi interventions: 12 or 24 weeks of Tai Chi once or twice per week, or aerobic exercise held twice per week for 24 weeks. The primary endpoint was change in the Revised Fibromyalgia Impact Questionnaire (FQoR) score at 24 weeks. Secondary endpoints included change in patient’s global assessment, the Hospital Anxiety and Depression scale (HADS), Sleep Quality Index (PSQI), arthritis self-efficacy scale (ASES-8), and quality of life. The comparative efficacy of the five groups was determined using longitudinal models based on the intent-to-treat principal.

Results: The mean age of subjects was 52 years (SD 12), mean years of body pain of 9 years (SD 8), 92% were women, and 61% were white. Treatment groups did not differ in baseline outcome expectations. The average of all 4 Tai Chi groups, compared to aerobic exercise, showed significant improvements in FIQR scores, patient’s global, anxiety, and self-efficacy. All other outcomes favored Tai Chi over aerobic exercise (Table 1). The Tai Chi treatment with the same dosage as the aerobic group demonstrated an even larger effect for FIQR and for most other outcomes. The benefit of Tai Chi was consistent across instructors.

Conclusions: Tai Chi is more effective than aerobic exercise and can be considered as an important therapeutic option for patients with fibromyalgia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3484
Scientiﬁc Abstracts
THU0470

WORK AND PROFESSIONAL RECOGNITION IN
FIBROMYALGIA PATIENTS – A NATIONAL FRENCH WEB
BASED SURVEY ON SICK LEAVE IN 1870 FIBROMYALGIA
FEMALE PATIENTS

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3
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Background: Fibromyalgia (FM) induces work limitations with an increase of
number of days of sick leave 3 to 4 fold higher (1, 2).
Objectives: Our objectives were to analyze work status, to determine risk factors
for sick leave and to compare women working to women in sick leave during the
past 12 months in a female population with FM.
Methods: 1870 female workers suffering from FM were selected from a large
internet-based national survey of 4516 responders (Fibromyalgie-SOS Association
website in France in 2014). Women having a FIRST score ≥5/6 were included.
Results: 1870 patients participated to the survey: 955 with full time job, 149
with part time job (related to FM status) and 766 on sick leave (7% 1–3 months,
27.3% 3–12 months and 62% >12 months). Fibromyalgia Impact questionnaire
(FIQ) score was slightly lower in the 1104 patients currently working compared to
the 766 on sick leave (56 versus 58.7), but not clinically different. 64,5% of the
population have been on sick leave during the last 12 months (average duration:
37 mean days for full time job and 122 among those with part time job).
Women being in sick leave were older (p<0,0001), single (p=0,0321), had less
ﬁnancial income (p<0,0001), used more antidepressants (p=0,0085) and more
anti epileptics (p=0,0102). Recognition of FM by occupational physicians or social
security doctors were lower among the workers (p<0.0001).
In the 1104 currently working, more than 33% have never been visiting
their occupational physician and 44,2% rarely. They reported no support from
these doctors (p=0,0011) particularly those having not being on sick leave.
Independent criteria of sick leave were transportation time (p=0.0131), work
difﬁculties (p=0.0031), hinders career progress (p=0.0196), sedentary occupation
and repetitive work (p=0.0195).
Conclusions: These data on a large ﬁbromyalgia population shows that clinical
status and also professional factors may inﬂuence work ability and sick leave.
The work factors include work difﬁculties, transportation time, sedentary and
repetitive occupation. These results should be taken into account by the work
professionals in order to facilitate work capacity in FM patients.
References:
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under routine medical practice: a claim database cost and burden of illness
cases of ﬁbromyalgia syndrome versus controls in London, Ontario: the London
Acknowledgements: Fibromyalgia SOS french Association.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3387

THU0471

THE EFFECTS OF TAPPING THERAPY ON PAIN, SYMPTOM
SEVERITY, DYSFUNCTIONS IN DAILY LIFE, DEPRESSION,
AND QUALITY OF LIFE IN PATIENTS WITH FIBROMYALGIA:
A RANDOMIZED CONTROLLED TRIAL

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Background: Fibromyalgia is a disorder characterized by chronic widespread
musculoskeletal pain, often accompanied by fatigue, cognitive disturbance,
psychiatric symptoms, and multiple somatic symptoms. Various pharmacological
and non-pharmacological therapies have been tried in the management of
ﬁbromyalgia. However, unfortunately, management remains a challenge.
Objectives: Taping therapy has been shown to be effective for pain relief in
various musculoskeletal diseases. However, there was no trial for the patients with
ﬁbromyalgia. In this study, we evaluated the effects of taping therapy in patients
with ﬁbromyalgia.
Methods: This study is a randomized controlled trial with 60 ﬁbromyalgia patients.
All patients were satisﬁed with the 2010 American College of Rheumatology
diagnostic criteria for ﬁbromyalgia. Participants were randomized to the Kinesio
taping group (n=30) and to the non-elastic paper taping group (n=30) for the
control. Taping experiment was performed for three weeks (twice a week)
through the one-to-one meeting. Pain, symptom severity, dysfunctions in daily
life, depression, and quality of life (QoL) were assessed with the widespread pain
index (WPI), severity score (SS), ﬁbromyalgia impact questionnaire (FIQ), Beck
depression inventory (BDI), and the EQ-5D INDEX and EQ-5D VAS, respectively.
Results: The mean ages of taping group and the control group were 54.3±12.0
years and 53.2±12.7 years, respectively, and female patients were 25/30 (83.3%)
and 27/30 (90.0%) in both groups, respectively, and there were no differences
between two groups in the medication use such as anti-depressants and muscle
relaxants. Patients showed signiﬁcant improvements after Kinesio taping therapy
in pain (10.50±3.98 vs. 5.70±2.73, p<0.001), symptom severity (7.93±2.24 vs.

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5.27±1.98, p <0.001), dysfunction in daily life (65.03±18.75 vs. 43.25±18.87,
p<0.001), depression (18.17±8.55 vs. 13.00±6.75, p<0.001) and QoL (EQ5D INDEX, 9.10±1.54 vs. 7.67±1.40, p<0.001; EQ-5D VAS, 38.33±24.65 vs.
56.67±27.93, p <0.001), respectively. In the control group, however, the signiﬁcant
improvement was detected only in pain (10.53±3.87 vs. 9.27±3.57, p=0.012).
The changes before and after treatment in the Kinesio taping group revealed
signiﬁcant differences from those in the control group: pain (p<0.001), symptom
severity (p<0.001), dysfunction in daily life (p<0.001), depression (p=0.001) and
QoL (p<0.001 and p<0.001), respectively. There was no serious adverse event.
Conclusions: This study shows that Kinesio taping therapy has effects on pain,
symptom severity, dysfunctions in daily life, depression, and quality of life in the
patient with ﬁbromyalgia. Taping therapy could be a useful non-pharmacological
management modality for the ﬁbromyalgia patient.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4576

THU0472

FAST3 (FIBROMYALGIA ASSESSMENT SCREENING TEST):
A COMPOSITE INDEX BASED ON MDHAQ PROVIDES CLUES
TO THE PRESENCE OF SECONDARY FIBROMYALGIA IN
PATIENTS WITH A PRIMARY DIAGNOSIS OF RHEUMATOID
ARTHRITIS AT HIGHER LEVELS THAN IDENTIFIED IN THE
MEDICAL RECORD: A CROSS SECTIONAL STUDY FROM
ROUTINE CARE

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Background: Secondary ﬁbromyalgia (FM) is reported in 17% of RA patients1 ,
but may be under-recognized in patients with classical RA ﬁndings. A FAST3
(ﬁbromyalgia assessment screening test) index based on 3 MDHAQ (Multidimensional Health Assessment Questionnaire) scores gives similar results to ACR
ﬁbromyalgia criteria based on a widespread pain questionnaire,2 to assist in
recognizing patients with secondary FM3 .
Objectives: To study patients with a primary diagnosis of RA seen in routine care
for the proportion identiﬁed as having secondary FM according to a physician
diagnosis in the medical record versus a FAST3 Index of MDHAQ scores.
Methods: All patients complete an MDHAQ/RAPID3 at all visits in the waiting
area in routine care. The MDHAQ includes 0–10 scores for physical function,
pain, and patient global estimate, compiled into RAPID3, as well as a 0–48
RADAI self-report score of painful joints, and 0–60 symptom checklist. FAST3
has been developed previously as the 0–3 sum of 1 point each for 3 MDHAQ
scores: pain VAS ≥6, RADAI ≥16, and symptom checklist ≥16.3 FAST scores
of ≥2/3 had >80% agreement with ACR FM criteria based on a widespread
pain questionnaire2 to identify secondary FM.3 A random visit for each patient
with a primary diagnosis of RA with complete data was studied. The number
with a diagnosis of secondary FM in the medical record was compared to
the number with FAST3 scores of 0, 1, 2, 3, and with each of the 3 FAST3
components. Receiver-operating characteristic (ROC) curves were generated to
estimate sensitivity and speciﬁcity for each cut-point of the FAST3 score, using a
diagnosis of secondary FM by the physician as the external criterion.
Results: 287 patients with RA were studied, of whom 10 (3.3%) had a diagnosis
of secondary FM by the physician in the medical record and 61 (22%) had FAST3
scores of 2 or 3 (Table), including 6 of 10 identiﬁed as having FM in the medical
record. Overall, FAST3 was 0 in 161 RA patients (56%), 1 in 59 (20.6%), 2 in
46 (16%), and 3 in 21 (7.3%) (Table). Overall, 55 additional RA patients were
identiﬁed by FAST3 versus the medical record as having possible secondary FM.
The ROC area was 0.73 (95% CI, 0.57–0.89) (data not shown).
Table 1. FAST3 (ﬁbromyalgia assessment screening tool) Index and 3 individual components
according to diagnosis of ﬁbromyalgia by rheumatologist in medical record
Clinical FM-No
Total
277
FAST (ﬁbromyalgia assessment screening tool) Index
0
159 (57%)
1
57 (21%)
2
42 (15%)
3
19 (7%)
Individual component measures
Pain >6
92 (33%)
Pain <6
185 (67%)
RADAI >16
68 (25%)
RADAI <16
209 (75%)
Symptom checklist >16
38 (14%)
Symptom checklist <16
239 (86%)

Clinical FM-Yes

Total

10
2 (20%)
2 (20%)
4 (40%)
2 (20%)

161
59
46
21

7 (70%)
3 (30%)
6 (60%)
4 (40%)
3 (30%)
7 (70%)

99
188
74
213
41
246

Conclusions: The same MDHAQ used to score RAPID3 may also provide a
FAST3 score as a screening tool for secondary FM in RA (and other) patients
(including primary FM). Secondary FM may be under-diagnosed by clinicians in
routine care. Further validation of FAST3 in other settings is needed.
References:


Disclosure of Interest: J. Castrejon: None declared, K. Gibson: None declared, J. Block: None declared, T. Pincus Shareholder of: Health Report Services, Inc
DOI: 10.1136/annrheumdis-2017-eular.5209

THU0473
POLYSYMPTOMATIC DISTRESS SCALE, WIDE SPREAD PAIN INDEX, AND SYMPTOM SEVERITY SCALES, AND THEIR CORRELATES IN 169 PATIENTS WITH FIBROMYALGIA SYNDROME

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Background: The polysymptomatic distress scale (PSD) is considered a measure of FM severity and ranges from 0 to 31. It is calculated by adding the two components of the American College of Rheumatology (ACR) 2010 fibromyalgia (FM) criteria, widespread pain index (WPI) and symptoms severity scale (SS).

Objectives: To assess the strength of the pelvic floor and urinary loss in women with FM.

Methods: All consecutive FM patients who met the ACR 2010 criteria completed the following questionnaires: PSD and its subsets, WPI and SS.

Results: Of 169 patients, 85.7% were women, mean age 42.3 (13.3), BMI 29.3 (7.1), PHQ-9 13.7 (5.2), GAD-7 10.2 (9.1), HAQ-DI 6 (2.9), PDI 6 (2.1), WPI 14.3 (2.7), SS 10 (1.6). In univariate analysis PSD correlated significantly (p<0.01) with PHQ-9 (0.576), PDI (0.422), and GAD-7 (0.356). Widespread pain index correlated significantly with PHQ-9 (0.313), GAD-7 (0.239), HAQ-DI (0.259), and PDI (0.296). Symptom severity scale correlated significantly with PHQ-9 (0.496), GAD-7 (0.337), HAQ-DI (0.275), PDI (0.340). A linear regression analysis model, which included PHQ-9, GAD-7, PDI and HAQ-DI predicted 26% of PSD variance, p<0.001, and only PDI remained significantly correlated with PSD. A similar model predicted 0.348 of SS variance, (p<0.0001), and only PHQ-9 remained significantly correlated with SS. This model did not significantly predict WPI variability.

Conclusions: Depression, anxiety, pain disability and functional disability predict a small variance of fibromyalgia severity measured by PSD. In regression analysis, pain disability measured by PDI is the only variable that remains independently correlated with PSD. None of these variables predicted WPI, while depression measured by PHQ-9 remains independently correlated with SS, indicating that PSD is a better predictor than WPI of FM.

Disclosure of Interest: None declared

THU0474
A CROSS-SECTIONAL STUDY INTO THE EFFECTIVENESS OF THE FIBROMYALGIA RAPID SCREENING TOOL FOR DETECTING FM IN PATIENTS WITH CHRONIC ARTHRITIS UNDERGOING FULL AND TAPERED BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUG THERAPY


Background: The determination of fibromyalgia (FM) in patients presenting diffuse, chronic arthritis is fraught. The Fibromyalgia Rapid Screening Tool (FIRST) is a validated questionnaire with high sensitivity and moderate specificity shown to be able to identify up to 89% of FM cases, even when accompanied by anxiety, depression or functional disability. Decisions to embark upon a course as chronic widespread pain referred for at least 3 months. In 2010, a new diagnostic criteria was proposed, and includes symptoms such as fatigue, sleep disorder and memory. Currently, pelvic floor dysfunctions and urinary incontinence (UI) are considered public health problems with high prevalence and great impact on quality of life (QoL), and on women’s self-esteem. Physiotherapists have been working to create a new treatment proposal that can cover all aspects of FM, and there are few studies that include pelvic floor evaluation and urinary incontinence of this population.

Objectives: To assess the strength of the pelvic floor and urinary loss in women with FM.

Methods: We evaluated 126 sexually active women, aged between 19 and 65 years, with and without medical diagnosis of FM, matched for age and menopausal status, in a single center. The exclusion criteria were sexually transmitted or neurological diseases, pregnancy and use of medications with urinary side effects (urinary loss or retention). We collected in a single interview personal and gynecological data, applied the King Health Questionnaire (KHZ) for incontinent women and accomplished the evaluation of pelvic floor muscle strength according to the Oxford Classification Modified and perineometry. The participants signed the Informed Consent Form. We used for statistical analysis 1 test for independent variables and Mann-Whitney Test for the others.

Results: The FM patients presented the weaker pelvic floor (p<0.001) and had lower values in perineometry (p<0.04) than control women. Regarding urinary loss, 64.5% reported UI against 26.8% of women without FM. In the KHQ evaluation, in General Health and Emotions domains, women with FM presented worse performance (p<0.04) (p<0.04).

Conclusions: Urinary incontinence is a frequent finding in FM, and it could be related to the degree of strength of the pelvic floor muscles. This condition affects negatively QoL, especially with regard to emotions and general health.

References:

Acknowledgements: This study received funds from CAPES (Coordination for the Improvement of Higher Education Personnel - Government Research Agency) with scholarship to one of the co-authors.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6261

THU0476
EVALUATION OF SEXUAL FUNCTION IN WOMEN WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is defined by the American College of Rheumatology as a syndrome of unknown etiology, characterized by chronic and widespread musculoskeletal pain. In 2010, a new diagnostic criteria was proposed, and includes symptoms such as fatigue, muscle fatigue, non-restorative sleep and urinary disorders. This may lead to a lack of interest or difficulty in the sexual act, which tends to be aggravated by depression, which is manifested by low self-esteem, decreased desire and orgasm, and pain during sexual intercourse.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6261
OBJECTIVES: Compare the sexual function of women with and without FM.

Methods: Sexually active women aged between 19 and 65 years with and without medical diagnosis of FM in a single center, matched for age and menopausal status, were evaluated. The exclusion criteria were pregnancy and use of medications with urinary side effects (urinary loss or retention). In a single visit, we explained the study, obtained informed Consent Form and answered questions about personal and gynecological data. The protocol The Sexual Quotient – Female Version (QS-F) was applied to assess sexual performance. We used for statistical analysis t test for independent variables and Mann-Whitney test for the others.

Results: In this study, 126 women were evaluated with age of 43±10.48 years. Most of the patients were married, representing 58.7%. A total of 50% participants had 1 or 2 children, 22.2% between 3 and 4 children and 27.8% had no children. Regarding the age of menarche and menopausal status, no differences were observed between the groups (p=0.70 and p=0.08, respectively). The QS-F score revealed significantly lower scores for women with FM when compared to the healthy group (p<0.001). We observed the same results in the domains: Desire and Sexual Interest (p<0.001), Excitation Phase (p=0.019) and Satisfaction and Orgasm (p<0.001). Regarding the Pain and Comfort domain, no differences were observed between the groups (p=0.307). However, when they were questioned about dyspareunia in the physiotherapeutic evaluation, it was observed that 51.6% of FM patients reported pain in sexual act against only 26.6% of healthy women (p<0.005).

Conclusions: Women with FM performed poorly on QS-F general score and in most of the domains, desire, excitement and comfort. When they were questioned in the physiotherapeutic evaluation about dyspareunia, we observed that women with FM had more pain in sexual intercourse, which may occurred due to the way the question was asked. As consequence, women with FM report worse sexual performance, especially with regard to desire, arousal and orgasm phase.

References:

Acknowledgements: This study received funds from CAPES (Coordination for the Improvement of Higher Education Personnel - Government Research Agency) with scholarship to one of the co-authors.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6293

THU0475 DETERMINATION OF COMORBIDITIES IN FIBROMYALGIA SYNDROME

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Background: Although fibromyalgia syndrome is diagnosed by excluding other possible diagnoses based on the patient’s clinical features, in recent the studies, it was shown that comorbid diseases affect the course of fibromyalgia.

Objectives: The aim of this study is to evaluate the comorbid diseases of patients with fibromyalgia and to determine the rates of comorbid diseases within this study, age, gender and comorbid diseases of patients above 18 years and diagnosed with fibromyalgia by a were evaluated in the database system of the hospital retrospectively.

Results: A total of 509 patients were examined in our study. 51 of the patients were male, 458 were female (mean age was 50.24±12.32). Of the patients, 345 (67.8%) had at least one comorbid disease while 164 (32.2%) had no comorbid disease. In the study, 187 of the patients (36.7%) had cardiovascular diseases, 157 of the patients (30.8%) had endocrine diseases, 63 of the patients (12.4%) had rheumatologic diseases, 30 of the patients (5.9%) had neurological diseases, 17 of the patients (2.8%) had other autonomic diseases. 10 of the patients (2.0%) had cancers, 129 (25.3%) had mental disorders. 45 of the patients (8.8%) had chronic lung diseases, 37 of the patients (7.3%) had osteoporosis, 11 of the patients (2.2%) had other diseases (chronic pancreatitis, chronic renal failure, nephrotic syndrome, deep vein thrombosis, hepatitis serology positivity, pulmonary thrombemobilus, organ transplantation).

Conclusions: FMS is an important disease that is increasing in frequency in recent years. FMS, which can be seen with many diseases, is in fact related to physicians from many branches, and it is useful to evaluate FMS patients with their comorbid conditions on their follow-up.

References:

Disclosure of Interest: None declared


THU0479 THE PREVALENCE OF XEROSTOMIA IN PATIENTS WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is a rheumatic disease characterized by diffuse, chronic musculoskeletal pain, of non-articular origin, which is evidenced by the palpation of painful points in specific anatomical areas and is usually accompanied by non-repairing sleep, Tiredness, morning stiffness, cognitive alterations, among others. FM affects approximately 0.5–5% of the population, having a maximum prevalence between 40 and 50 years. No racial or socioeconomic predisposition has been determined to date.

Sicca syndrome whose term encompasses xerophthalmia, xeroderma and xerovagin, has been described in patients with FM. Xerostomia is the sensation of dry mouth due to lack or decrease of saliva. There are no clinical studies that determine the prevalence of xerostomia in patients with FM and on the other hand the reduction of salivary flow in these patients has not been studied with objective tests.

Objectives: The aim of this study was to determine the frequency of xerostomia in patients with diagnosis of Fibromyalgia and describe their clinical and epidemiologic characteristics.

Methods: Patients were included according 1990 and 2010 ACR Classification criteria. Patients taking drugs that cause xerostomia were excluded as well as the ones presenting other rheumatologic diseases. Xerostomia was assessed by the Xerostomia Inventory and physical examination and a sialometry was performed in order to determine the decrease of salivary flow. A sialometry was performed if the saliva flow was under 1.5 ml in 15 minutes. In case of presenting positive sialometry patients were studied to rule out Sjögren Syndrome with laboratory and minor salivary gland biopsy.

Results: 50 patients were recruited during the study. The 100% of them were women. The mean age was 47 years old (DS=6.5), while the mean time of evolution of FM was 6 years. 29 patients reported xerostomia of which 4 presented positive sialometry. No positive sialometry was found in the group that did not referred xerostomia. Smoking was more prevalent in patients with FM who did not...
report xerostomia with respect of those who reported xerostomia (31.8% vs 6.9%, p < 0.02). There were not associations between xerostomia and hypothyroidism, diabetes or menopause. The presence of Sjogren Syndrome was rule out in 4% patients whose saliometry was positive.

Conclusions: The prevalence of xerostomia was 51%. No statistically significant associations were found in patients who reported xerostomia. A decrease in objective salivary flow was not demonstrated in patients with FM.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2074

THU0480 MULTICENTER, PROSPECTIVE, CONTROLLED DOUBLE-BLIND STUDY COMPARING FIB-19-01, A PHYTOTHERAPY TREATMENT FOR FIBROMYALGIA, TO A DIETARY SUPPLEMENT AND TO CONVENTIONAL TREATMENT IN PATIENTS SUFFERING FROM FIBROMYALGIA


Objectives: Developed to improve the quality of life of patients with FMS (Fib-19–01), to the efficacy and safety of adding a new treatment of herbal medicine, specifically for PICHOT scale (p < 0.001), PQSI (p=0.02), SF12 mental and social (p<0.01), HAD depression (p=0.013). No significant difference was found between FM patients with or without fibromyalgia as per each of the three criteria had no significant difference in these scores.

Conclusions: Non-tender point based criteria have been validated in primary care. However, in tertiary care where patients are referred to as fibromyalgia, there are mimics with similar comorbidities as evident by high BPHQ, GAD7 and TAS20 scores. Even after exclusion of other rheumatological conditions, the 2016 Criteria has poor specificity. Thus, it should be used as a screening tool than a diagnostic criteria in tertiary care.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2566

THU0482 EVOLUTION OF COMORBID FIBROMYALGIA SYMPTOMS IN SPONDYLOARTHRITIS PATIENTS STARTING AN ANTI-TNF AGENT, AND CORRELATION TO ANTI-TNF EFFICACY. THE PREDICT-SPA STUDY


Background: Fibromyalgia (FM) is a frequent comorbid condition in axial spondyloarthritis (axSpA). It is not known how FM comorbidity may respond to the management of SpA, and especially to anti-TNF agents. Objectives: To evaluate the changes in the FM status of axSpA patients starting an anti-TNF treatment. Methods: A prospectiv multicenter national study involving 39 rheumatology centers in France, analyzing 519 patients with axSpA requiring anti-TNF therapy (Clinicaltrials.gov: NCT03000264). Patients were screened for FM with the FIRST questionnaire before and after 3 months of anti-TNF. Kaplan- Meier coefficient was calculated to determine the agreement of the FIRST at M0 and M3. Response to anti-TNF (BASEDiss response was compared according to positive screening for FM or not, at both time-points using chi2 tests.

Conclusions: Non-tender point based criteria have been validated in primary care. However, in tertiary care where patients are referred to as fibromyalgia, there are mimics with similar comorbidities as evident by high BPHQ, GAD7 and TAS20 scores. Even after exclusion of other rheumatological conditions, the 2016 Criteria has poor specificity. Thus, it should be used as a screening tool than a diagnostic criteria in tertiary care.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2566
Results: Of the 519 enrolled pts, 504 (with complete data on the FiRST questionnaire) were analyzed at M3. A positive screening for comorbid FM was found in 192 pts (38%) at M0 and in 127 (25%) pts at M3. Correlation between FiRST at M0 and M3 was weak with a Kappa coefficient correlation of 0.4 [0.3 - 0.5].

Four groups were identified: group [++] with comorbid FM at M0 and M3: N=93 (18%); group [++] with comorbid FM at M0 but not at M3: N=99 (20%); group [+] without comorbid FM at M0 and M3: N=278 (55%); group [-] without comorbid FM at M0 but at M3: N=34 (7%). Changes in the status of comorbid FM (disappearance or appearance) was observed in 134 pts (26%). In the 193 pts with baseline comorbid FM, after 3 months of anti-TNF treatment, comorbid FM was no longer found in 99 (51%). Efficacy at M3 was significantly better, according to BASDAI 50, in patients without comorbid FM at M3 (Table).

<table>
<thead>
<tr>
<th>FM status according to the FiRST questionnaire at M0/M3 (N total=504)</th>
<th>+/+</th>
<th>++/</th>
<th>+/−</th>
<th>−/−</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>93</td>
<td>99</td>
<td>278</td>
<td>34</td>
</tr>
<tr>
<td>Number of patients reaching BASDAI 50 at M3</td>
<td>26 (28%)</td>
<td>61 (61.6%)</td>
<td>162 (58.3%)</td>
<td>8 (25.5%)</td>
</tr>
</tbody>
</table>

Conclusions: There is a high frequency of comorbid FM screened by the FiRST in active axSpA, decreased by 51% over 3 months of anti-TNF treatment. Persistence of FM after 3 months of anti-TNF treatment is associated with lower anti-TNF response. Further studies are required to analyze the impact of screening FM before starting anti-TNF therapy in axSpA.

References:

Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4688

THU0483 CHARACTERISTICS OF PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS AND COMORBID FIBROMYALGIA. DIFFERENCES ACCORDING TO FIBROMYALGIA SCREENING (FIRST QUESTIONNAIRE) AND FIBROMYALGIA CLASSIFICATION (ACR1990)


Background: Fibromyalgia (FM) can be a comorbid condition in axial spondyloarthritis (axSpA). FM screening questionnaires and classification criteria fulfill may demonstrate different prevalence and patients’ characteristics may differ.

Objectives: To evaluate frequency of comorbid FM, and the differences between axSpA patients with/without comorbid FM according to screening (FiRST) and classification tools (ACR1990 FM criteria).

Methods: A multicenter national study involving 39 rheumatology centers in France included 519 patients with axSpA starting an anti-TNF treatment (FIRST study; ClinicalTrials.gov: NCT03039088). Patients (pts) were screened for FM before starting anti-TNF therapy in axSpA.

Results: In the 519 pts (females: 46%, age: 42±12 years, mean BASDAI 5.7±2.0, with baseline comorbid FM, after 3 months of anti-TNF treatment is associated with lower anti-TNF response. Further studies are required to analyze the impact of screening FM before starting anti-TNF therapy in axSpA. Persistence of FM after 3 months of anti-TNF treatment is associated with lower anti-TNF response. Further studies are required to analyze the impact of screening FM before starting anti-TNF therapy in axSpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4688

THU0484 R060 EXPRESSION DECREASES WITH AGE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF CHILDREN AND ADOLESCENTS AND CORRELATES WITH TLR7 STIMULATION IN PDCS OF PREPUBERTAL CHILDREN

A. Radziszewska, K. Webb, H. Peckham, Y. Ioannou. Arthritis Research UK Centre for Adolescent Rheumatology at University College London, Great Ormond Street Hospital and UCLH, University College London, London, United Kingdom

Background: Auto-antibodies to the RNA binding protein Ro60 are present in patients with autoimmune disorders such as systemic lupus erythematosus (SLE). In addition to its established role as an auto-antigen, Ro60 has been found to bind Alu RNA retroelements whereby it may target Alu retroelement RNA for degradation suggesting a novel putative function of this auto-antigen. If Ro60 modulates the amount of cellular RNA then one may hypothesis an association with toll-like receptor (TLR)7 stimulation threshold.

Objectives: To measure the physiological levels of intracellular Ro60 protein in healthy children and adolescents and investigate a possible link between Ro60 protein expression and interferon-α (IFN-α) production after TLR7 stimulation.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from blood from 48 healthy children and adolescents (age range 6.7–17.9 years old). Cells lysates from thawed PBMC samples were tested for Ro60 expression by Western blot. PBMCs were also stimulated for 20 hours with TLR7/8 agonist R848, at 1μg/ml in the presence of brefeldin A, and plasmacytoid dendritic cell (pDC) IFN-α expression was measured using flow cytometry. Statistical tests to measure correlation between IFN-α expression in (pDCs) and PBMC Ro60 expression were performed using SPSS.

Results: Ro60 protein expression in PBMCs correlated negatively with age ( Spearman’s rho = −0.317, p = 0.032). When participants were divided into two groups based on their self-reported puberty status, Ro60 expression was higher in the pre-pubertal group (p = 0.02). There was, however, no difference in Ro60 expression between males and females (p = 0.44) or when sexes were stratified according to pubertal status. pDC IFN-α production after TLR 7 stimulation, did not correlate with ex vivo PBMC Ro60 expression overall (Spearman’s rho = 0.159, p = 0.302) however a moderate positive correlation was observed in pre-pubertal samples only (Spearman’s rho = 0.554, p = 0.021).

Conclusions: Ro60 expression decreases with age in healthy young people. These findings need to be confirmed in a larger cohort and further studies are necessary to investigate the link between Ro60 expression and TLR7 signalling across different age groups as well as in patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5073

THU0485 POLYMORPHISM OF SOME GENES INVOLVED IN IMMUNE AND INFLAMMATORY RESPONSES IN BELARUSIAN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND OTHER ARTICULAR PATHOLOGY

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Background: Etiology and pathogenesis of juvenile idiopathic arthritis (JIA), which prevails among pediatric rheumatic diseases, are insufficiently clear. The study of molecular-genetic basis of JIA is of great interest for revealing genetic predisposition and early diagnosis.

Objectives: The present study aimed to analyze seven SNPs in five genes involved in immune and inflammatory responses: TNFα (rs1800629, rs361525), PTN222 (rs24766012), MIF (rs755622, rs5844572), CTLA4 (rs5742909), STAT4 (rs7574865), as well as in two DNA repair genes XPD (rs1799793) and XRCC1 (rs25487) in different conditions.

Table 1

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Fibromyalgia according to FiRST questionnaire</th>
<th>Odds-ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Education level (&gt; high school)</td>
<td>72 (37%)</td>
<td>163 (51%)</td>
</tr>
<tr>
<td>Sick leave (yes)</td>
<td>108 (54%)</td>
<td>134 (42%)</td>
</tr>
<tr>
<td>Heel pain (yes)</td>
<td>127 (64%)</td>
<td>151 (47%)</td>
</tr>
<tr>
<td>Education level (&gt; high school)</td>
<td>72 (37%)</td>
<td>163 (51%)</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Fibromyalgia according to ACR 1990 criteria</th>
<th>Odds-ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>HLA B27 (positive)</td>
<td>27 (32%)</td>
<td>272 (68%)</td>
</tr>
<tr>
<td>Heel pain (yes)</td>
<td>61 (73%)</td>
<td>217 (50%)</td>
</tr>
</tbody>
</table>
**Methods:** 94 patients diagnosed with JIA (mean age 8.7±5.21), 95 children with arthritic syndrome (mean age 7.90±4.81) and 164 hospital controls without any signs of autoimmune or inflammatory diseases (mean age 13.99±2.68) were included in the study. The JIA patients were divided into subgroups according to IAR classification criteria; among them 63 patients were diagnosed with oligoarthritis and 16 with RF- polyarthritis. Genomic DNA was extracted from blood samples by means of phenol-chloroform method. SNPs were genotyped using PCR-RFLP or fragmental analysis.

**Results:** The allele frequencies for all SNPs in the hospital control group were similar to those characteristic of other Europeans. No differences were found between the frequencies of the TNFα risk alleles across all three groups. Hence, both SNPs in the TNFα locus were not associated with JIA and other arthritic pathologies in our study. The same is true for -318C→T CTLA4 polymorphism. Unlike these genes, PTPN22 C1858T polymorphism influenced developing arthritis in children since heterozygous CT genotype was associated with articular pathology (rather than JIA) in the total group (OR=1.87, 95% CI [1.06–3.30], p=0.04), especially in males (OR=3.50, 95% CI [1.61–7.63], p=0.016). In the latter case, it was effective even being combined with any genotypes in the -308G→A TNFα locus (OR=2.73, 95% CI [1.19–6.24], p=0.018). When analyzing MIF polymorphisms (rs755622 and rs5844572), the evident trend to increased carrying genotypes containing the risk allele MIF-173C was observed in females with JIA as compared to controls and significantly elevated frequency of this risk allele in females with RF- polyarthritis as compared to males (p=0.037). In females with JIA as compared to controls and significantly elevated frequency of this risk allele as compared to any genotypes in the latter case, it was effective even being combined with any genotypes in the -308G→A TNFα locus (OR=7.78, 95% CI [0.95 – 63.8], p=0.056) was also revealed. STAT4 polymorphism (rs7574865) demonstrated subtype-related association with JIA due to increased frequency of the minor allele in patients with polyarticular form of JIA as compared to both hospital controls (p=0.01; OR =2.45; 95% CI [1.19–5.04]) and other articular pathology (p=0.001; OR =3.37; 95% CI [1.56–7.28]). The same SNP was also associated with developing arthritis in females. As to role of DNA repair genes, carriers of XPD rs10913939 and XRCC1 rs2548648 genotypes had an increased risk of JIA in females (OR=2.14; 95% CI [1.05–4.35]; p=0.05).

**Conclusions:** Thus, the gender- and subtype-specific associations of some SNPs studied with developing joint pathologies including JIA are found in the Belarusian child population.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4813

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**THURSDAY, 15 JUNE 2017**

**Paediatric rheumatology**

**THU0487**

**REAL-LIFE TREATMENT WITH CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – FIRST EXPERIENCE FROM THE BIKER REGISTRY**

G. Hornett, F. Dressler, A. Thön, K. Minden

**Background:** Canakinumab (CAN) has demonstrated its efficacy and safety in SJIA pts (1).

**Objectives:** To report on the experience with CAN treatment in SJIA in the clinical practice in Germany.

**Methods:** Data on patients’ and disease characteristics, disease activity and safety reports from the German BIKER registry were analysed.

**Results:** Until Dec. 2016, 37 pts exposed to CAN were identified. In 12 pts used CAN as first biologic, 25 pts were pretreated: Tocilizumab 15, Anakinra 11, Etanercept 9, Adalimumab 9. 3 patients in the pre-exposed cohort had experienced a macrophage activation syndrome. Pts’ and disease characteristics are outlined in table 1. Pts pretreated were older, had a longer disease duration and more comorbidities than naïve patients. The proportion of pts with active arthritis, active systemic features and both were comparable. Disease activity at baseline was higher in the naïve cohort suggesting some clinical benefit from pretreatment. Dosing of CAN was comparable (3.9±/0.4 vs. 3.5±/0.7mg/kg) as well as the median treatment duration (0.8vs.1.0year). Treatment efficacy at last follow up was better in the naïve cohort with more pts reaching a PedACR 30/50/70% IG response while JADAS- or ACR-remission rates were comparable. Treatment was discontinued by 42% in the naïve and 48% in the exposed cohort. Reasons were inefficacy (n=7/19%), intolerance (n=2/5%) and remission (n=7/19%) of the disease and other (n=2/5%).

**Table 1. Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Biologics naïve</th>
<th>Biologics pre-exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (female gender)</td>
<td>12 (17%)</td>
<td>25 (52%)</td>
</tr>
<tr>
<td>Age at JIA onset (years); mean ± SD; Median (IQR)</td>
<td>4.4±3.0; 3.0 (2.0–4.9)</td>
<td>6.0±4.8; 3.7 (2.6–7.1)</td>
</tr>
<tr>
<td>Age start of Canakinumab (years); mean ± SD; Median (IQR)</td>
<td>7.1±4.9; 5.6 (3.1–10.2)</td>
<td>9.8±4.8; 10.6 (5.5–14)</td>
</tr>
<tr>
<td>Disease duration (years); mean ± SD; Median (IQR)</td>
<td>2.8±1.0; 1.7 (0.3–3.9)</td>
<td>3.8±1.2; 1.9 (0.6–6.7)</td>
</tr>
<tr>
<td>Concomitant treatment at baseline:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDS/Steroids/MTX</td>
<td>6 (50%)/6 (3%)/25%</td>
<td>10 (40%)/11 (44%)/16%</td>
</tr>
<tr>
<td>Patients with active joints</td>
<td>7 (58.3%)</td>
<td>10 (47%)</td>
</tr>
<tr>
<td>Patients with active systemic features</td>
<td>7 (58.3%)</td>
<td>10 (47%)</td>
</tr>
<tr>
<td>Patients with active arthritis and systemic features</td>
<td>4 (36.4%)</td>
<td>4 (19.1%)</td>
</tr>
<tr>
<td>Active joint count</td>
<td>1.8±1.7; 2.5 (0–3)</td>
<td>2.1±3.3; 0 (0–0)</td>
</tr>
<tr>
<td>Physician global VAS (0–10)</td>
<td>5.2±2.8; 6.2 (2.3–7.2)</td>
<td>3.8±3.4; 3.7 (2.6–6.3)</td>
</tr>
<tr>
<td>Patient Global VAS (0–10)</td>
<td>4.8±2.9; 4.6 (2.7–7)</td>
<td>3.3±2.9; 2.6 (0.6–5.1)</td>
</tr>
<tr>
<td>CHAQ DI (0–3)</td>
<td>0.71±0.65</td>
<td>0.65±0.84</td>
</tr>
<tr>
<td>ESR (mmh)</td>
<td>29±22.8</td>
<td>15±4.20</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>70±58</td>
<td>121±23</td>
</tr>
<tr>
<td>JADAS10</td>
<td>15±7.3</td>
<td>10±5.7</td>
</tr>
</tbody>
</table>

**Conclusions:** First experience with CAN for treatment of SJIA in clinical practice is presented. A high proportion of pts gained significant improvement. JADAS remission was reached by about 50% and ACR remission by 25–57% in both biologics pre-exposed and naïve pts while few pts discontinued treatment in remission so far. Intolerance was rare. The further long term surveillance of SJIA pts exposed CAN is intended by the registry.

**References:**


**Acknowledgements:** The authors thank I.Foeldvari, M.Hufnagel, J.Kuemmerle-Deschner, F.Weller-Heinemann, M.Sailer-Hoeck, A.Hospach, G.Heubner, C.Rietschel and B-U.Keck for contributing to the Canakinumab cohort. The German Rheumatology Registry is supported by an unrestricted grant from Abbvie, Germany Novartis, Germany, and Roche, Germany.

**Disclosure of Interest:** G. Hornett Speakers bureau: Abbvie, Novartis, Chugai, F. Dressler Speakers bureau: Novartis, Pfizer, A. Thön: None declared, K. Minden Speakers bureau: Abbvie, Pfizer,Roche,Genczyme,Pharm-Allergan
Background: Information regarding longer-term outcomes in JIA largely pre-date the introduction of biologic therapies and have been cross-sectional.

Objectives: The aim of this study was to assess outcomes over the first 5 years of disease in children diagnosed with oligoarticular and polyarticular JIA since 2001.

Methods: Children with oligoarthritis, rheumatoid-factor (RF) negative or positive polyarthritides were selected if recruited to the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, between October 2001 and January 2011. The following outcomes were assessed annually to five years and included in this analysis: functional ability (Child Health Questionnaire (CHQ)), the absence of limited joints, overall psychosocial health (psychosocial scale on the Child Health Questionnaire (CHQ)) and the proportion of children with CHQ psychosocial scores (two standard deviations below the population mean) (CHQ psychosocial<30).

Outcomes were assessed descriptively over time and differences between subtypes were assessed by applying multilevel (patient-level) zero-inflated negative binomial (CHAQ), logistic (absence of limited joints, percent CHQ psychosocial<30) and linear (CHQ psychosocial) regression analyses, adjusting for gender, age at presentation and hospital.

Results: Of 832 children, 70% were female, 68% had oligoarticular, 28% RF-negative and 5% RF-positive polyarticular JIA. Eighty-four percent had ever been treated with NSAIDs, 74% corticosteroids, 55% with DMARDs and 21% with biologics within follow-up. Baseline CHAQ was good to moderate (median 0.8, IQR 0.1 to 1.4) and only 21% of children had no limited joints reported at this time. CHQ psychosocial scores (median 50, IQR 39 to 55) were moderate, with 11% children scoring at least two standard deviations under the population mean. Overall improvements were evident in all outcomes over the first year then remained stable with no further improvements at the cohort level evident to five years.

Patients with RF-negative polyarthritides experienced significantly poorer outcomes across all variables than those with oligoarthritides. Those with RF-positive polyarthritides recorded similar CHAQ scores to patients with RF-negative polyarthritides but had the lowest odds of no limited joints (OR: 0.4, 95% CI 0.3 to 0.7) and the poorest CHQ psychosocial scores (4.8 points worse and 4.7 times the odds of scores <2 standard deviations of population mean), compared with those with oligoarticular.

Conclusions: On average, the largest improvement in functional ability, limited joints and psychosocial health occur in the first year following diagnosis, perhaps confirming the importance of early treat-to-target strategies. Patients with polyarticular JIA subtype have poorer parent and physician-reported outcomes than those with oligoarthritides.

Disclosure of Interest: None declared

References:


Disclosure of Interest: None declared


THU0489 ADIPOSITY AND INFLAMMATORY ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS COULD THEY BE RELATED?

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Background: Adults with rheumatoid arthritis have been shown to have a reduction in lean mass and increased adiposity, despite presenting normal Body Mass Index (BMI). Several studies have shown increased adiposity induces a proinflammatory state which lead to a worse response to treatment. There are few studies about the subject in juvenile idiopathic arthritis (JIA).

Objectives: Describing body composition and anthropometric parameters in JIA patients, and evaluating relationship between adiposity and inflammatory in these children.

Methods: Observational cross-sectional study. In JIA patients from 4 to 15 years, monitored by a Pediatric Rheumatology Unit. Monarticular forms were excluded. Anthropometric, clinical and treatment data were recorded. DXA (measuring bone and fat mass) were obtained. Fat Mass Index (FMI) was defined as fat mass (kg)/height (m²) and fat-free mass index (FFMI) as lean mass (kg)/height (m²). JADAS27 index was used to evaluate inflammatory activity.

Results: We analyzed 80 patients, whose characteristics are shown in table 1. The most frequent JIA subtype was oligoarticular (16.3% extended,47.5% persistent) followed by polyarticular (25.1%). Twenty five percent of patients had uveitis. Fifty percent them had inactive disease with treatment, 26% had activity and 23% were inactive without treatment. Regarding the treatment, 52.5% were on methotrexate and 30% on a biological drug (22.5% antiTNFα/5% anti-IL-1), 2.5% anti-IL-6). Disease duration average was 6.6 years (± 3.7SD). JADAS27 index mean score was 2 (±4SD). CRP 4.7mg/l (±9SD), ESR 8.7mm (±7.2SD) and CHAQ 0.17 (± 0.38SD). Anthropometric parameters are shown in table 1. Mean JADAS27 index score in patients with normal BMI was lower than mean JADAS27 index score in overweight and obese patients (3.3±6.0SD), although this difference was not significantly (p=0.255). In multiple linear regression, an increase of 0.3 JADAS27 was observed for each unit of FMI increase (p=0.03). This relationship was maintained in the multivariate analysis (B0.015; p0.01) independently of JIA subtype and received treatment.

Conclusions: In JIA patients, there is a linear relationship between FMI and disease activity measured by JADAS27, but most patients had a normal BMI. The establishment of this relationship (fat-inflammatory activity) would be transcendental due to the need to optimize the recommendations in the JIA approach.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3785
The majority are female (85%). The average age is 15.25 years. This cohort includes Hispanic (58%), Asian (29%), African-American (21%) and Caucasian (11%) children. LN class III or IV was diagnosed in 67% of patients. Nearly all were treated with hydroxychloroquine and steroids (95%). Other drugs used include mycophenolate mofetil (85%), cyclophosphamide (43%), rituximab (27%) and tacrolimus (18%).

A significant increase in urinary HER2, TWEAK and VCAM1 levels was found in LN patients (p=0.005; p=0.006; p=0.01, respectively) when compared to controls. HER2 levels reflected disease activity, increasing during flares.

In an adult cohort of LN patients (N=126) composed mainly of females (80%) with an average age of 46.13 years, we also found a significant increase of urinary HER2 when compared to controls (p=0.002).

A strong correlation between the urinary levels of HER2, TWEAK and VCAM1 was not found.

Conclusions: Urinary HER2, TWEAK and VCAM1 were significantly increased in a paediatric cohort of LN patients. In addition, significantly higher urinary HER2 levels were also found in an adult LN cohort. This ongoing study will further evaluate if these urinary markers, alone or in combination, can reflect disease activity and predict renal flares, analysing their potential value in clinical practice.

References:
[1] PMIDs: 26016809; 22727560; 22788914.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5223

THU0491 COMPARISON OF CLINICAL AND SEROLOGICAL FEATURES OF JUVENILE AND ADULT-ONSET NEUROPSYCHIATRIC LUPUS IN SPANISH PATIENTS
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Background: Neuropsychiatric (NP) manifestations are a main cause of morbidity and mortality in juvenile-onset systemic lupus erythematosus (JSL). Some studies suggest that they are more frequent and severe in JSL than in adult-onset SLE (aSLE).

Objectives: To compare the clinical and serological profile of pediatric and adult patients with neuropsychiatric lupus (NPSLE) treated in a Spanish tertiary center.

Methods: A retrospective study of patients with SLE (age of onset: 0–18y) and aSLE (age of onset: >18y) seen in our center during the period 1988–2016 was performed. Case definitions were adopted from the American College of Rheumatology.

Results: A total of 69 patients with NPSLE were included, aSLE 41 (59%) and JSL 28 (41%), the comparison of groups is presented in the table. Most of them were Caucasian (92%), mean age at diagnosis in adults was 36.4 years (range: 19–68) and 15.9 years (range: 8–18) in children. The proportion of males was higher in the latter group. The mean duration of the disease was significantly greater in adults, as well as the time from SLE diagnosis to NP manifestation onset, although without significant differences between groups. Central NP manifestations were the most frequent in both groups (aSLE 93%, JSL 96%) and most frequent manifestations in aSLE were headache (29%), cerebrovascular disease (27%), seizures (17%) and neuropsychological manifestations (aSLE 12%, JSL 11%). The most frequent manifestations in JSL were seizures (46%), headache (29%), mood disorder/depression (25%), psychosis (16%) and autonomic disorders (16%). A significant group of patients presented >2 central manifestation during their evolution (aSLE 32%, JSL 41%), with the mean number of manifestations in adults being 1.36 (range: 1–3) and in children 1.44 Range: 1–4). Patients with JSL developed lupus nephritis (LN) with a significantly higher frequency, as well as higher titres of anti-DNA antibodies, erythrocyte sedimentation rate (ESR) and cryoglobulins, compared to aSLE.

Conclusions: Our results corroborate that juvenile patients with NPSLE present higher disease activity compared to adults. There was no significant difference in the time from SLE diagnosis to NP manifestation onset, but tended to be shorter in JSL. The spectrum of NPSLE was varied both groups and an important proportion developed ≥2 manifestation. Mortality continues to be important in NPSLE in both age groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3425

THU0492 MACROPHAGE ACTIVATION SYNDROME AS THE INITIAL MANIFESTATION OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of autoimmune diseases in children. Little is known about the association between MAS and the onset of juvenile systemic lupus erythematosus (JSL).

Objectives: The aim of this study was to determine the frequency and clinical features of MAS as the initial complication of JSL.

Methods: During 2004 and 2016, we retrospectively reviewed the clinical and laboratory features of 46 JSL patients diagnosed at the Saitama Children’s Medical Center. Patients who were complicated with MAS at the same time as JSL were compared with a control group composed of 30 JSL patients without MAS. The MAS was diagnosed according to preliminary guidelines.

Results: Fifteen patients (32.6%) developed MAS during the initial stage of JSL. Fever, leukopenia, thrombocytopenia, hyperferritinemia, hypofibrinogenemia, increased aspartate aminotransferase (AST), and increased lactate dehydrogenase (LDH) were more frequently observed in patients having JSL with MAS than in those having JSL without MAS. No differences were observed in serum C3 and C4 levels, or erythrocyte sedimentation rate (ESR) (P>0.05). Especially, Seven patients (46.7%) had neurologic symptoms that were significantly higher in those with MAS (P<0.01). All patients received corticosteroids when JSL with MAS diagnosis was established, among whom seven received pulse methylprednisolone therapy. Two patients were treated with IVIG. Nine patients with MAS were treated with immunosuppressants, including cyclophosphamide and mycophenolate mofetil, azathioprine. No patient involved in this study died.

Conclusions: MAS can be the initial manifestation of JSL. MAS may be an underrecognized complication of JSL. MAS with JSL should be suspected in patients with high fever, cytopenia, and a liver disorder. In addition, we found that in JSL with MAS patients, they had more neurologic symptoms compared to JSL without MAS. Early diagnosis and intensive therapy is essential to improve the clinical outcome.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5935

THU0493 STUDY OF LONG-TERM OUTCOME OF CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A SINGLE-CENTRE IN NORTH INDIA
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Background: Juvenile dermatomyositis (JDM) is a rare inflammatory myopathy seen in children. There have been few studies on long-term outcome in children with JDM.

Objectives: To assess long-term outcome of JDM using validated measures of outcome

Methods: All children diagnosed to have JDM for more than 2 years and who had been followed in the Pediatric Rheumatology Clinic at PGIMER, Chandigarh, India, were deemed eligible for recruitment. Study period was from January 1, 2015 to June 30, 2016. Those who were not on regular follow-up were called for assessment which was done by a single observer using Childhood Myositis Assessment Scale (CMAS), Manual Muscle Testing 8 (MMT8), Myositis Activity Disease Assessment Tool (MADAT), 2AD, Myositis Damage Index (MDI) and Childhood Health Assessment Questionnaire (CHAQ).

Results: Thirty-five children were enrolled in this study, 22 (62.9%) were on regular follow-up. Mean age was 13.9yrs (range 4–29yrs). Mean age at diagnosis was 7.51yrs with median interval between onset of symptoms and diagnosis.
being 5 months. Mean duration of disease at the time of enrolment was 7.18yrs. Disease course was monocylic in 24 (68.6%). Muscle strength was normal in 71.4%. Severe involvement defined as MMT8 score below 64 was seen in 8.6%. Cutaneous activity was determined by aCAT with 40% children having some form of cutaneous activity. Based on MYOACT, 31.4% children had evidence of myocarditis. The prevalence of cutaneous involvement with skin being the commonest organ system involved in 28.6% followed by muscles in 22.9%. Twenty-one (60%) children had some form of cutaneous damage. Calcinosus in 12 (34.3%) and lipodystrophy in 8 (22.9%). Twenty four subjects had an MDI score of >1 suggesting damage in at least one organ system. Most commonly affected organs were skin and muscles in 20, 12 and 9 subjects respectively.

Nine (25.7%) subjects in our study had some form of a physical dysfunction suggested by a CHAQ score above 0. Previous studies on long-term outcomes in children with JDM have either not used validated outcome measures or have used fewer measures [1–3].

Conclusions: Highlight of our study is the use of validated outcome measures for evaluation of long-term outcomes. After mean disease duration of 7.18 yrs, 1/3rd subjects had evidence of disease activity with almost 1/10th having moderate to severe activity. About 2/3rd had damage in at least one organ system. Skin was the most common organ affected by activity as well as damage. About 1/4th had reduced physical functioning. Thus, JDM is not a disease where one time treatment would suffice and regular long-term follow-up is required. Counselling of the caregivers is also critical for them to adhere to follow-up. Larger long-term studies using validated outcome measures are required to confirm these findings.

References:

Disclosure of Interest: None declared

THU0494

CHILDREN WITH KAWASAKI DISEASE IN DIFFERENT AGE GROUPS IN SOUTHWEST CHINA
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Background: Kawasaki disease (KD) is a systemic vasculitis characterized by acute and prolonged fever. The prevalence of coronary artery abnormality (CAA) is as high as 11%. The young infants usually have the increased risk of CAA, but do not have the typical clinical manifestations of KD.

Objectives: To explore clinical features of children with KD in different age groups to improve the prognosis of KD.

Methods: A total of 218 children with Kawasaki disease were divided into the infants group (≤ 2 years old), the toddler group, the pre-school age group and the school age group. Retrospective analysis of clinical data were performed among the groups. Categorical data were compared with each other statistically by Chi-square analysis. Statistical significant was defined as P<0.05. The incidence of carditis, CAA, and the incidence of increased platelets were analyzed in the four groups. The analysis was focused on the other three groups and excluded the five cases in the following statistical analysis.

Results: (1) Among the 218 KD patients, the male to female ratio was 1.5:1 and the recurrence rate was 1.8%. Seven cases (3.2%) were diagnosed as atypical KD, and 34 (38.5%) patients accepted intravenous gamma globulin (IVIG) treatment after the sixth day of KD onset. The incidence of IVIG-resistant KD was 8.7% and the rate of coronary dilation was 11.5%. (2) Fever was the most common clinical feature (100%). The bilateral bulbar conjunctiva injection and the characteristic rash of oropharynx were 85.4% and 81.2% respectively. Moreover, cough (40.5%), diarrhea (16.9%) and vomiting (8.5%) were also very common in the present KD patients. (3) Patients from the toddlers’ group were more common to develop lymphadenopathy and skin rash (χ²=7.784, P=0.002; χ²=10.794, P=0.005), but were less frequently to be documented with cough and diarrhea (χ²=2.734, P=0.026; χ²=18.447, P=0.000). (4) The incidence of increased platelets was more common in the infants group (χ²=2.552, P=0.023). Comparing with the urine test among three groups, the toddlers’ group had a higher incidence of sterile pyuria (χ²=10.653, P=0.005), and infants younger than 12 months old had a lower incidence of proteinuria and positive urine ketone (χ²=15.507, P=0.000; χ²=10.433, P=0.000).

Conclusions: The respiratory tract, the digestive and urinary systems are involved commonly in Kawasaki disease, and patients from different age groups showed different clinical features, which should be pay more attention to promote the prognosis.

References:

Acknowledgements: This work was supported by grants from the Natural Science Foundation of China (81501396 to Dr. Lianjie Shi, and 81302554 to Dr. Fanlei Hu).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5864

THU0495

EFFECTIVENESS OF CHILDHOOD VACCINATIONS IN CAPS PATIENTS TREATED WITH CANAKINUMAB: RESULTS FROM AN OPEN-LABEL PHASE 3 EXTENSION STUDY
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Background: Canakinumab (CAN) has been shown not to impair antibody production following vaccination in children in an open-label phase 3 study (NCT01302860). Here we present the results from the extension of this study.

Objectives: To evaluate the presence of protective antibody levels following immunisation with inactivated vaccines in CAPS patients during extension study. Methods: Patients who completed the core study were allowed to continue in the extension study on the standard dosing regimen of 2 mg/kg subcutaneous CAN every 8 weeks or on last dose/dosing regimen received in the core study. Vaccination response was evaluated using post-vaccination antibody titres at 4 and 8 weeks after immunisation. Patients were considered assessable for an antibody response to a specific vaccination if they had a measurement of antibody titre 0–14 days post-vaccination (pre-vaccination assessment) and at least 1 subsequence measurement of antibody titre at 4 weeks and/or 8 weeks post-vaccination. However, for patients with adequate pre-dose antibody titres and maintained during the trial, the specific patient vaccination was deemed non-assessable.

Results: During the extension phase, of 17 patients (<6 years), 4 received 8 types of vaccinations against Corynebacterium diptheriae, Bordetella pertussis, Neisseria meningitidis, Clostridium tetani, influenza type A and type B, Haemophilus influenzae B, Streptococcus pneumoniae, or hoga rhatis B. Of 20 unique patient-vaccination cases, 17 were assessable for a vaccination response, whereas for the remaining 3, pre-dose antibody titre was not available. For 16 (94.1%) assessable cases, post-vaccination antibody titres increased above protective levels. For one patient who received Tetravac formulation (diphtheria, tetanus and acellular pertussis (aP) in combination), the response observed for 1 (vaccination against Clostridium tetani) of the 3 vaccines included in Tetravac represented optical density rather than antibody concentrations and hence considered non-evaluable. For 19/20 patient-vaccinations, including those without pre-dose antibody titres, protective levels were observed during the study, which were maintained throughout the extension study.

Conclusions: Canakinumab appeared to have no effect on post-vaccination antibody production following the administration of non-live vaccines in CAPS patients.

References:

Disclosure of Interest: P Brogan Grant/research support from: Novartis, Roche and SOBI, Consultant for: Novartis, M. Hofer Consultant for: Novartis, J. Kuemmerle-Deschner Grant/research support from: Novartis, SOBI, Baxalta, Consultant for: Novartis, B. Lauwerys: None declared, A. Speziale Employee of: Novartis, X. Wei Employee of: Novartis, R. Laxer Grant/research support from: Novartis for Database funding

DOI: 10.1136/annrheumdis-2017-eular.3349

THU0496

PULMONARY SYMPTOMS AS THE FIRST PRESENTATION OF KAWASAKI DISEASE IN CHILDREN
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Background: Kawasaki disease (KD) is a medium vessel vasculitis which predominantly affects children less than 5 years of age. Though principal clinical symptoms are mucocutaneous, KD in children may have atypical clinical manifestations, including pulmonary, which may create diagnostic difficulties for the treating physician.

Objectives: We describe our experience of managing children with uncommon pulmonary presentation of KD.
Methods: Five hundred and sixty-five (565) children were diagnosed with KD during the period from January 1993 to December 2016 in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Nine children had pulmonary presentation of KD. A retrospective case review with respect to clinical presentation, radiological findings and treatment was done.

Results: Pulmonary presentation of KD was seen in 1.6% patients. Mean age at diagnosis of KD was 2.9 years (range 9 months – 4 years). 77.8% patients had no features suggestive of KD either on history or at presentation. First sign of KD was noted at a mean duration of 17.6 days (range 6–28 days) from the onset of symptoms. Pulmonary presentation was the most common clinical sign seen in 66.6% patients followed by erythematous rash and perianal desquamation in 33.3% patients each.

Persistent fever, thrombocytosis and elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were seen in all patients. Microbiological investigations showed evidence of infection in only 2 patients – methicillin sensitive staphylococcus aureus in pus and positive mycoplasma agglutinin titre in one patient each. Parenchymal consolidation was the most common radiological finding (100%) followed by pleural effusion (55.5%), empyema (33.3%) and pneumothorax (11.1%). Coronary artery abnormalities were evident on echocardiography in 22.2% patients with dilatation of right coronary artery and left main coronary artery in 1 patient each.

All patients received intravenous antimicrobials for pneumonia. Intravenous immunoglobulin (IVIG) at 2g/kg was given after a mean duration of 24 days of fever with which there was unresolute to IVIG therapy and responded to IVIG therapy in all except 2 patients which required a second dose of IVIG. 55.5% patients required intercostal drainage tube (ICDT) insertion, 2 patients required streptokinase and 1 patient each required video assisted bronchoscopic aspiration and debridement. Mean follow up period was 15.2 months (range 0–62 months).

Conclusions: Pulmonary involvement in patients with KD is uncommon and is less commonly recognized. Unresolving pneumonia in a child who continues to be febrile despite adequate antimicrobials with elevated inflammatory markers can be a clue towards the diagnosis of KD. Early recognition can prevent delays in diagnosis and shorten the hospital stay.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6820

THU0498 PFAPA SYNDROME IN LARGE PEDIATRIC POPULATION: A SINGLE CENTER EXPERIENCE

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Background: Periodic fever, aphthosis, pharyngitis, and adenitis (PFAPA) syndrome is an auto-inflammatory condition of unknown etiology. It is the second most common auto-inflammatory disease in our country, following familial Mediterranean fever. Previous studies showed that tonsillectomy represents efficient treatment options.

Objectives: Our aim was to explore the main clinical features, response to tonsillectomy and long-term outcome of PFAPA pediatric patients in a single cohort. We assessed association of MEFV gene mutation with disease characteristics and treatment response.

Methods: We reviewed medical records of patients who were diagnosed with PFAPA syndrome between the January 2010 and June 2016. All of the recorded 562 patients were called by the telephone and 365 (65%) of them were reached. Demographic, clinical and therapeutic features were taken from the patients’ medical records. Data on clinical course and the disease outcome were collected by using a structured questionnaire which was fulfilled during the phone conversation between investigator and patients parents.

Results: A total of 365 patients with PFAPA were examined: 154 (42%) of them were female. The mean age at disease onset, at diagnosis and at the investigation was 22.7±18.8, 41.7±21.7 and 77.1±43.3 months, respectively. The most common disease feature at the disease onset was: recurrent fever in 365 (100%), cryptic tonsillitis in 365 (100%) and aphthous stomatitis in 317 (88%). Sixty three (17%) patients met the criteria for both PFAPA and FMF. MEFV gene mutation analysis was performed in 93 (25%) patients and 51 of them (54%) had a heterozygous mutation in exon 10. Surgical treatment was performed in 158 (43%) patients. Complete clinical remission was achieved in 127 (80.3%) patients. Six (3%) showed no response to surgical treatment while 25 (15.8%) patients had a partial response. In patients with partial clinical response, frequency of fever attacks decreased significantly from 17.5 to 7.3 attack per year (p<0.05). Among patients who did not respond to tonsillectomy, 11 (52.4%) were carrier of MEFV heterozygous mutation in exon 10. There was a statistically significant difference between patients with and without coexistence of FMF features, according to surgical treatment response (p<0.05). The mean age of resolution of PFAPA symptoms in patients who underwent tonsillectomy was 52±22.4 months and in patients without tonsillectomy 66±22.6 months.

Conclusions: Although PFAPA symptoms usually resolve before age of eight, some patients’ complaints persist. MEFV gene mutations should be considered in tonsillado-neoidectomiedicate patients especially in endemic regions like Turkey. Tonsillado(ne)nectomy seems to be an effective treatment option for pediatric PFAPA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4617

THU0499 ANTI-MULLERIAN HORMONE IN A COHORT OF YOUNG ADULT WOMEN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) represents one of the most common chronic disease of the childhood, affects young people before sixteen and persists into their reproductive years. It is reported in one study that fertility was compromised in JIA women but potentially it can be compromised by pharmacological treatments such as the prolonged immunosuppressive therapy used in young women patients (1). The Anti-Mullerian Hormone (AMH) is secreted from granulosa ovary cells and serum levels of Anti-Mullerian Hormone are used as a measure of ovarian reserve, reflecting the number of primary follicles.

Methods: Levels of AMH in sera from 154 patients with JIA, according to different subtypes (persistent oligoarticular arthritis (POA) and polyarticular) were compared at diagnosis and then again after 6 months. The same analysis was performed on 20 age- and BMI-matched healthy women. In the subgroups of JIA patients, the differences of AMH levels at diagnosis and after 6 months were compared with healthy subjects.

Results: At diagnosis, the patients with POA had significantly lower AMH levels than JIA patients with polyarticular arthritis (P = 0.002). In POA subgroup, at diagnosis AMH levels were significantly lower than healthy subjects (P = 0.006). After 6 months, these differences were lessen (Table 1). In polyarticular subgroup, no differences were observed at diagnosis and after 6 months.

Conclusions: Patients with POA had lower AMH levels at diagnosis, which was associated with a decrease of primary follicles. Moreover, these findings suggest that at diagnosis, the patients with POA have lower levels of AMH than JIA patients with polyarticular arthritis, but these differences are lessen after 6 months of therapy.
Objectives: The aims of this study were to evaluate AMH serum levels in a cohort of young adult women affected from JIA, to compare these levels between patients and healthy controls and to assess whether the presence of the disease and the influence of previous exposure to disease-modifying antirheumatic drugs (DMARDs) and of other disease parameters may affect the ovarian reserve.

Methods: A cross-sectional study of 90 women was performed. Of these, 47 patients fulfilled the JIA criteria and 43 were healthy women age-matched and without history of gynecological disease or DMARDs use. All participants were between 18 and 25 years and with regular menses, and 20 healthy women age-matched were evaluated.

Results: Thirty-three of the JIA group (70%) had disease-modifying antirheumatic drugs (DMARDs) treatments within the past year. The AMH levels were significantly lower in the JIA (mean ± SD: 0.8 ± 0.5 ng/ml) compared to the control group (1.0 ± 0.6 ng/ml). No significant difference was found when AMH levels were compared between male (0.7 ± 0.5 ng/ml) and female (1.1 ± 0.6 ng/ml) JIA patients. The disease duration did not alter AMH levels. A significant decrease in AMH levels was found in subgroups with previous exposure to disease-modifying antirheumatic drugs (DMARDs) and a history of previous gynecological interventions. AMH levels did not change between male (0.7 ± 0.5 ng/ml) and female (1.1 ± 0.6 ng/ml) JIA patients.

Conclusions: In this study, we report that AMH serum levels are decreased in JIA patients when compared with healthy age-matched women. This reduction may be associated with the disease duration and previous exposure to disease-modifying antirheumatic drugs (DMARDs) and is not due to the use of immunosuppressive drugs. These findings could be important for adult JIA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4761

THU0500 PHOTOSTIMULATION OF CHRONIC CERVICAL PAIN IN JUVELINE POLYARITHRITIS

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Background: Chronic pain management in juvenile arthritis constitutes a special provocation not only for the medical doctors, but also for the patients and parents.

Despite the extensive use of the biological agents with high efficacy, combined with the multimodal therapies, chronic pain still remains an important issue for the public health, with implications on the activities of daily living and the scholar performances. Lasers could be used for transmitting biological messages and initiating metabolic changes within living cells: no more pain, much more energy.

Chronic pain in JIA patients can be helped by photobiostimulation (pulsed laser therapy).

Methods: 62 patients diagnosed with juvenile polyarthritis (ILAR criteria), 11.4 years mean age were randomly divided in Group I (42 patients treated with local laser stimulation and methotrexate), comparatively with a Group II - control (20 patients) treated with methotrexate and placebo laser, for a period of 9 months. Group I received local laser stimulation with a dose of 2.5 J/cm2 in 14 latero-cervical painful points, corresponding to the 7 cervical vertebrae, 1 point on the insertion of sternocleido-mastoildian muscle on the styloïd process, and 1 point on each loco-regional submandibular lymphatic gangions, using a GaAlAs laser probe of 670 nm, 25 mW output power and a modulation frequency of 10 Hz. 45 joules were applied daily as laser treatment, 10 sessions per month, repeated 3 times, in the 9 months. For all the patients, the main medication was methotrexate in a dose of 0.6 mg/kg (maximum 20 mg) per week, steroids and of other disease parameters may affect the ovarian reserve.

Objectives: The aims of this study were to evaluate AMH serum levels in a cohort of young adult women affected from JIA, to compare these levels between patients and healthy controls and to assess whether the presence of the disease and the influence of previous exposure to disease-modifying antirheumatic drugs (DMARDs) and of other disease parameters may affect the ovarian reserve.

Methods: A cross-sectional study of 90 women was performed. Of these, 47 patients fulfilled the JIA criteria and 43 were healthy women age-matched and without history of gynecological disease or DMARDs use. All participants were between 18 and 25 years and with regular menses, and 20 healthy women age-matched were evaluated.

Results: Thirty-three of the JIA group (70%) had disease-modifying antirheumatic drugs (DMARDs) treatments within the past year. The AMH levels were significantly lower in the JIA (mean ± SD: 0.8 ± 0.5 ng/ml) compared to the control group (1.0 ± 0.6 ng/ml). No significant difference was found when AMH levels were compared between male (0.7 ± 0.5 ng/ml) and female (1.1 ± 0.6 ng/ml) JIA patients. The disease duration did not alter AMH levels. A significant decrease in AMH levels was found in subgroups with previous exposure to disease-modifying antirheumatic drugs (DMARDs) and a history of previous gynecological interventions. AMH levels did not change between male (0.7 ± 0.5 ng/ml) and female (1.1 ± 0.6 ng/ml) JIA patients.

Conclusions: In this study, we report that AMH serum levels are decreased in JIA patients when compared with healthy age-matched women. This reduction may be associated with the disease duration and previous exposure to disease-modifying antirheumatic drugs (DMARDs) and is not due to the use of immunosuppressive drugs. These findings could be important for adult JIA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4761

THU0501 EFFICACY AND SAFETY OF METHOTREXATE AS MAINTENANCE THERAPY FOR PATIENTS WITH ANTI–N–METHYL–D–ASPARTATE RECEPTOR (NMDAR) ENCEPHALITIS: EXPERIENCE OF A SINGLE CENTER

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Background: Autoimmune-mediated encephalitis (A-ME) in children remains as a diagnostic and therapeutic challenge (1). These patients have a 12% risk of relapse, which is usually more severe (2). We previously proposed the therapy with methotrexate (MTX) for this condition (3), and we are offering now additional data on its potential benefits.

Objectives: To describe the outcome of children with A-ME receiving MTX for at least one year after stabilization of symptoms.

Methods: In this retrospective study we recruited 11 patients (7 females) with A-ME, a mean age of 7.5 years (range 8 months - 14 years), and with a median follow-up of 20 months. In all cases, anti-NMDAR antibodies (subunit NR1) were detected in the CSF. Data from these patients were collected by consulting medical records. Relapse of encephalitis was defined as new onset of symptoms occurring after at least 2 months of remission, in the absence of other CNS disease.

Results: Patients presented with seizures (n=10), behavioral changes (n=11), psychosis (n=11), speech problems (n=10), and autonomic/breathing dysregulation (n=9). Patients were initially treated with methylprednisolone pulses (n=11), rituximab (n=6), intravenous immunoglobulins (n=4), cyclophosphamide (n=3) and MTX (n=11). Complete remission was observed in all cases, and maintenance therapy with MTX (10 mg/m2 BS) was started in all them, with gradual tapering until it was stopped. Interestingly, no relapses have been observed in any case during the mean follow up. One patient had mild oral ulcers and other showed mild elevation of liver enzymes; both events remitted after discontinuing the treatment for a couple of weeks.

Conclusions: Since relapses in patients with A-ME are a relatively frequent, the immunosuppressive therapy to prevent them is fully justified (4). Moreover, MTX therapy in pediatric patients is safe and usually well tolerated (3,5,6). The recommended dose is less than 15 mg/m2 BS or 1 mg/kg, with a maximal dose of 40 mg and with folic acid supplementation. In this regard, our study suggests that MTX administration (10 mg/m2 BS) during at least one year is a viable and effective therapy for maintenance treatment of A-ME. Accordingly, we did not detect relapses in the 11 patients studied with a median follow up time of 22 months and with an acceptable safety profile.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2726

THU0502 EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH STILL’S DISEASE: A POOLED ANALYSIS OF SJIA DATA BY AGE GROUPS


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Background: Still’s disease presents in paediatric and adult patients (pts) as a disease continuum with similar symptoms and pathophysiology.1,2

Objectives: To evaluate the efficacy and safety of canakinumab (CAN), a selective human anti–IL1 monoclonal antibody, in SJIA pts from pooled data across 3 age groups (grps); children, adolescent and adults (the latter representing adult-onset Still’s disease [AOSD] population).

Methods: Data of CAN treated pts were pooled from 4 SJIA studies (NCT00426218, NCT00886769, NCT00889863, NCT00891046). CAN was ad-
ministered at 4 mg/kg every 4 weeks (wk). Efficacy parameters (adapted ACR [aACR] paediatric responses, juvenile idiopathic arthritis [JIA] ACR responses, pts with inactive disease), CRP levels over 12 wk and safety were assessed by age grp. One study [NCT00426218] was excluded for efficacy outcomes. Results: 216 children (2–12 years [y]), 56 adolescents (12–16 y) and 29 adults (>16 y) were analysed for efficacy outcomes. The efficacy parameters across the 3 age grps were largely comparable (Table 1). The safety profile of CAN was similar across age grps (Table 2). One death was reported (adolescents grp). Clinical, laboratory and immunogenicity data showed no notable differences between the age grps.

Table 1. Responses by age grp and time point

<table>
<thead>
<tr>
<th>Age group</th>
<th>aACR paediatric; n/N (%)</th>
<th>JIA ACR; n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>156/216 (73.1)</td>
<td>169/216 (78.2)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>60/80 (75)</td>
<td>103/130 (79.3)</td>
</tr>
<tr>
<td>Adolescents</td>
<td>46/61 (75.3)</td>
<td>46/61 (75.3)</td>
</tr>
<tr>
<td>Adults</td>
<td>30/40 (75)</td>
<td>30/40 (75)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>15/21 (71.4)</td>
<td>15/21 (71.4)</td>
</tr>
<tr>
<td>≥30</td>
<td>141/185 (76.0)</td>
<td>154/185 (82.8)</td>
</tr>
</tbody>
</table>

Table 2. Adverse events (AEs)

<table>
<thead>
<tr>
<th>AE type</th>
<th>Children, n (%)</th>
<th>Adolescents, n (%)</th>
<th>Adults, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=233</td>
<td>N=30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections and infestions</td>
<td>176 (75.6)</td>
<td>42 (70.0)</td>
<td>23 (74.2)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>122 (52.4)</td>
<td>32 (53.3)</td>
<td>16 (58.1)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>119 (51.1)</td>
<td>33 (56.0)</td>
<td>16 (58.1)</td>
</tr>
<tr>
<td>Opportunistic infections</td>
<td>3 (1.3)</td>
<td>6 (6.7)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>11 (4.7)</td>
<td>2 (3.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>SAE (at least 1)</td>
<td>81 (34.3)</td>
<td>25 (41.7)</td>
<td>9 (20.0)</td>
</tr>
</tbody>
</table>

Conclusions: Pooled analyses indicate similar efficacy of CAN across all the age grps of children, adolescents and adult SJIA pts. There were no meaningful differences in safety profiles across the different age grp. These analyses suggest similar efficacy of CAN in AOSD pts as observed in the SJIA pts. One study [NCT00426218] was excluded for efficacy outcomes. The efficacy parameters across all the age grps were largely comparable (Table 1). The safety profile of CAN was similar across age grps (Table 2). One death was reported (adolescents grp). Clinical, laboratory and immunogenicity data showed no notable differences between the age grps.


QUANTIFYING PHYSICAL EDUCATION ATTENDANCE AND ITS RELATIONSHIP TO PAIN SEVERITY AND FATIGUE IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS – RESULTS FROM THE GERMAN NATIONAL RHEUMATOLOGICAL DATABASE

Background: Regular physical education (PE) can help adolescents achieve the recommended amount of daily physical activity and provide immediate health benefits, by positively affecting musculo-skeletal development, mental health and social behavior. Adolescents with juvenile idiopathic arthritis (JIA) are less physically active and have lower fitness levels than their healthy peers [1]. Moreover, pain and fatigue are one of the most frequent complaints and identified as one of the causes behind impaired (social) functioning [2].

Objectives: To describe the participation rate in PE and to assess its relationship to pain and fatigue in adolescents with JIA.

Methods: Cross-sectional study of adolescents with JIA recorded in the National Pediatric Rheumatological Database (NPRD) in the year 2015 were considered for the analyses. Disease characteristics were provided by rheumatologists along with patient-reported outcomes and participation in PE. Relationship to PE was assessed by using spearman’s correlation.

Results: In 2015, a total of 3,289 adolescents with JIA (females 66%, mean disease duration 5 years, persistent oligoarthritis 30%) aged 13 to 17 were recorded. About 60% of the patients reported to participate in PE “always” (56% of girls, 69% of boys), whereas about 18% stated to be fully exempt from participating in PE (20% of girls, 14% of boys). Significant differences were found among JIA subgroups, whereby patients with enthesis-related arthritis participated more frequently than patients with rheumatoid factor-positive polyarthritis (64% vs. 46%). The mean pain level was 2.1, the mean fatigue level 1.8. Participation in PE was negatively correlated with self-reported pain intensity (r=0.43) and fatigue (r=0.32). Significant associations were found between PE attendance and age, sex, disease duration, functional status as well as disease activity measured by CHAQ and JADAS-10, respectively (p<0.05).

Conclusions: 6 of 10 adolescents with JIA participate in PE always, whereby higher rates of self-reported attendance are associated with less severe pain and fatigue.

References:

Acknowledgements: The National Paediatric Rheumatological Database has been funded by the German Children Arthritis Foundation (Deutsche Kinder-Rheumaforschung).


Objectives: To report treatment response and safety data were compared. Treatment response was analyzed using JIA-ACR criteria, JADAS scores, JADAS10-minimal disease activity (MDA), JADAS-remission and ACR-inactive disease criteria were analysed.

Results: 589 non-systemic JIA patients exposed to Adalimumab with at least one follow-up report were identified in the German BiKE registry, representing 1143.9 patient years (PY) of exposure to ADA and 1206.5 observation years (OY) of observation.

Baseline patient characteristics, treatment response and safety data were compared. Treatment response was analyzed using JIA-ACR criteria, JADAS scores, JADAS10-minimal disease activity (MDA), JADAS-remission and ACR-inactive disease criteria were analysed.

Response rates at month 24 were 67/66/54/35/65/32/29% on ADA monotherapy and 68/63/45/28%/50/28/27 on combination of ADA and MTX (not significant).

At month 12 JIA-ACR 30/50/70/90 and JADAS-MDA/-remission/ACR-inactive disease criteria were analysed. Rates of patients with an uveitis event was higher upon combination (p=0.008) as well as rate of elevated transaminase levels (p=0.01). Rate of patients with an uveitis event was higher upon combination (p=0.008) as well as rate of elevated transaminase levels (p=0.01). Rate of patients with an uveitis event was higher upon combination (p=0.008) as well as rate of elevated transaminase levels (p=0.01).

Background: Since the approval of Adalimumab (ADA) for treatment of juvenile idiopathic arthritis (JIA), it has become a valuable option, which significantly improved the outcome of patients.

Conclusions: To report treatment response and safety data were compared. Treatment response was analyzed using JIA-ACR criteria, JADAS scores, JADAS10-minimal disease activity (MDA), JADAS-remission and ACR-inactive disease criteria were analysed.

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Baseline patient characteristics, treatment response and safety data were compared. Treatment response was analyzed using JIA-ACR criteria, JADAS scores, JADAS10-minimal disease activity (MDA), JADAS-remission and ACR-inactive disease criteria were analysed.

Response rates at month 24 were 67/66/54/35/65/32/29% on ADA monotherapy and 68/63/45/28%/50/28/27 on combination of ADA and MTX (not significant).

At month 12 JIA-ACR 30/50/70/90 and JADAS-MDA/-remission/ACR-inactive disease criteria were analysed.
**Objectives:** To assess AIDAI score and evaluate correlation between AIDAI and disease/response characteristics over 16 weeks (wks) of CAN treatment in CLUSTER.

**Methods:** CLUSTER study design and results have been presented. 

**Results:** Median AIDAI scores decreased over time (Fig 1). Proportion of pts with at least one score of 16% before baseline (BL) and 23% in TRAPS. AIDAI at Wk 16 correlated significantly with: SDAI in 3 all cohorts; PGAS in HIDS/MKD and TRAPS; SF12–MCS in cRFMF and HIDS/MKD (Table 1). CRP and SAA did not correlate with AIDAI.

**Conclusions:** CAN demonstrated rapid and sustained disease control assessed with AIDAI over 16 wks. Approximately half of cRFMF and TRAPS pts, and 40% of HIDS/MKD pts had inactive disease after 16 wks of treatment. AIDAI improvements at Wk 16 correlated with patient and physician driven evaluations of HIDS/MKD patients had inactive disease after 16 wks of treatment. AIDAI was performed in the 144 patients with pJIA with negative RF. Administration of TOA or TOZ resulted in statistically significant reducing of disease activity according to JADAS27. In ADA group after 3 months of administration JADAS27 decreased from 16.3±10.3 to 10.7±8.0 (p<0.0001). In TOZ group after 3 months of administration JADAS27 reduced from 22.1±12.2 to 13.9±9.1 (p=0.0012). The functional disability of the patients also statistically significant decrease in both treatments. Improvement of clinical practice.

**References:**

**Disclosure of Interest:** I. Kone-Paut Grant/research support from: Novartis, SOBI and Roche, Consultant for: Novartis, SOBI, Pfizer, AbbVie and Roche, M. Piram Consultant for: Novartis, Pfizer, AbbVie, Speakers bureau: Novartis, S. Benseler Consultant for: Novartis, SOBI and AbbVie, M. Hofer Consultant for: Novartis, AbbVie, H. Lachmann Consultant for: Novartis, SOBI, Takeda and GSK, Speakers bureau: Novartis and SOBI, H. Hoffmann Consultant for: Novartis, Speakers bureau: Novartis, M. Gattono Grant/research support from: Novartis and SOBI, Consultant for: Novartis and SOBI, J. Frenkel Grant/research support from: Novartis and SOBI, J. Kuenringer-Deschner Grant/research support from: Novartis, Consultant for: Novartis, SOBI and Bavasta, S. Ozen Speakers bureau: Novartis and SOBI, J. Levy Paid instructor for: Novartis, C. Karyyekar Employee of: Novartis, F. De Benedetti Grant/research support from: Pfizer, AbbVie, Roche, Novartis, Neumimmun and BMS

**DOI:** 10.1136/annrheumdis-2017-eular.4681

**Table 1. Correlation between AIDAI and disease activity/response variables at Week 16**

<table>
<thead>
<tr>
<th>Correlation coefficient (95% CI)</th>
<th>CRP</th>
<th>SAA</th>
<th>PGA</th>
<th>CHQ – PsCS</th>
<th>SF12 – MCS</th>
<th>SDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>cfFMF (N=63)</td>
<td>0.12 (−0.36; 0.14)</td>
<td>0.23 (−0.02; 0.44)</td>
<td>0.39 (0.12; 0.65)</td>
<td>0.74 (0.54; 0.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIDS/MKD (N=72)</td>
<td>0.23 (0.01; 0.45)</td>
<td>0.06 (−0.30; 0.21)</td>
<td>0.26 (0.06; 0.47)</td>
<td>0.73 (0.54; 0.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRAPS (N=46)</td>
<td>0.20 (−0.19; 0.42)</td>
<td>0.25 (−0.55; 0.04)</td>
<td>0.33 (−0.72; 0.22)</td>
<td>0.73 (0.54; 0.88)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Results: 339 patients were enrolled into the study during 3 years. 64% of patients are girls. Mean age 10.98±4.41 years, with mean disease duration 5.8±1.48 years. The duration of the period between diagnosis and biologics start was 54.3±10.4 months. Comorbid conditions were found in 41.03% of patients. In 14.65% of the patients uveitis was diagnosed. Most common JIA subtype in patients receiving biologics are pJIA with negative RF (45%), sJIA (20%), enthesis-associated JIA (11%) and persistent oligoarthritis (11%). 67.3% of enrolled patients received adalimumab (ADA); 27.9%–tocilizumab (TOZ) and 4.8%–etanercept, respectively. During observational period biologics were discontinued in 19.8% of patients due to different reasons: adverse events were observed in 6.7% (ADA) and 16.7% (TOZ), insufficient efficacy of 23.3% (ADA) and 33.3% (TOZ), remission - 6.7% (ADA); drug absence - 63.3% (ADA) and 50% (TOZ), respectively. Comparative analysis of ADA and TOZ efficacy was performed in the 144 patients with pJIA with negative RF. Administration of either ADA or TOZ resulted in statistically significant reducing of disease activity according to JADAS27. In ADA group after 3 months of administration JADAS27 decreased from 16.3±10.3 to 10.7±8.0 (p<0.0001). In TOZ group after 3 months of administration JADAS27 reduced from 22.1±12.2 to 13.9±9.1 (p=0.0012). The functional disability of the patients also statistically significant decrease in both treatments. Improvement of clinical practice.**
The mean duration of tocilizumab therapy was 14.75 months. 2 patients received s.c. accoding the poly JIA dosing and all other i.v. There were different i.v doses applied, 5 of them 8mg/kg every 4 weeks, one of them 8 mg/kg every three weeks, 1 every two weeks and 1 patients received 10 mg/kg every 3 weeks. 3/11 received TOC as monotherapy, 8/11 as combination therapy, 6 of them with a concomitant use of MTX. One patient was treated with Tacrolimus or Tocilizumab. Treatment success was reflected by a decreased mLoSSi in 8/11 patients and in 6 patients by a decrease in the Localized Scleroderma Skin Damage Index [1] (LoSDi). No new lesion occurred during the treatment and in the patients with Parry Romberg subtype (n=2) no increase in the facial atrophy occurred. In 8/8 patients physician global (VAS 0–100) decreased and in 8/8 the patients global disease activity (VAS 0–100) decreased. In 3/3 patients, were it was applicable, the number of active joints decreased, in one patients the limb discrepancy decreased. The mean modified Rodnan skin score assessed in 8 patients decreased from the mean value of 5.2 in baseline to 1.5 at the end of follow-up.

Conclusions: In this small cohort of patients TOC seems to be a promising rescue medication in medrotretexe/mycophenolate non-responsive patients. A prospective controlled study would be important to prove the seen effect in a controlled way.

References:

Disclosure of Interest: I. Foeldvari Consultant for: add board chugai, <1000 US$, J. Anton Grant/research support from: Grants of Roche, M. Friswell: None declared, B. Bica: None declared, J. de Inocencio: None declared, A. Aquilani: None declared, N. Helmus: None declared

DOI: 10.1136/annrheumdis-2017-eular.3179

[THU0512] FLUORESCENCE OPTICAL IMAGING IN JUVENILE PATIENTS WITH AND WITHOUT INFARLAMATORY PEDIATRIC RHEUMATIC JOINT DISEASES

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Background: Imaging techniques play an important role in making a diagnosis and in the evaluation of treatment effectiveness as well as in the outcome assessment of juvenile idiopathic arthritis (JIA). Fluorescence optical imaging (FOI) has been shown to visualize inflammation in arthritis of wrist and finger joints. FOI is a simple and cost-effective imaging technique that is well tolerated by the patients.

Objectives: Firstly, to determine the association and agreement of FOI with ultrasonography (US) and physician’s assessment of swollen and active joints. Secondly, to estimate the predictive power of FOI to distinguish between patients with and without inflammatory pediatric rheumatic joint diseases.

Methods: A total of 95 patients were enrolled in three pediatric rheumatology centers in Berlin, Germany. FOI and US (in greyscale (GS) and power Doppler (PD)) were performed in each patient. The FOI software automatically generated a semiquantitative score (0–4) for the FOI images. US images were semiquantitatively assessed for power Doppler and grayscale synovitis. Classification of the joint was performed by an experienced radiologist.

Results: The mean disease duration was 3.5 years (SD=3.2), the mean cJADAS-10 was 29.6 (SD=18.4), and 4 patients (4.2%) had a positive FOI PVM. The FOI PVM had a sensitivity of 40%, a specificity of 86% and an overall agreement of 83%. The area under the curve was 0.91 for US power Doppler, 0.84 for US GS synovitis, 0.76 and 0.93 for FOI PVM and P2 for the ability to distinguish between patients with and without inflammatory rheumatic diseases in pediatric juvenile patients. The agreement between active joint count, US and FOI was high. FOI may provide a cost-effective method to evaluate inflammation in finger and hand joints.

Acknowledgements: The study was supported by an unrestricted educational grant by Pfizer.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6339

[THU0513] NEONATAL MANIFESTATIONS OF IMMUNE-MEDIATED RHEUMATIC DISEASES: A RETROSPECTIVE LONGITUDINAL STUDY IN A TERTIARY HOSPITAL

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Background: Autoimmune rheumatic diseases such as systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS) and Behcet’s disease (BD) are part of a clinical spectrum eligible to affect women in child-bearing ages, affecting neonatal outcomes. Cardiac, cutaneous, haematological, hepatic complications and, more rarely, pulmonary complications have been described.

Objectives: This project aims to describe the occurrence of neonatal lupus manifestations and possible associated clinical factors among women with immune-mediated rheumatic diseases.

Methods: A retrospective longitudinal study was performed including pregnant women with immune-mediated rheumatic disease seen in a multidisciplinary group for autoimmune diseases during pregnancy between January 2010 and December 2015. Clinical and demographic data as well as pregnancy outcomes and neonatal manifestations were collected through consultation of clinical files. Patients with and without neonatal lupus were compared using Mann-Whitney, chi-square and fisher tests (SPSS 24.0). Significance level was set as <0.05.

Results: We included 151 gestations from a total of 140 women with a mean age of 32.5±4.4 years: 4 gestations were twin pregnancies. Within these 151 gestations, 54 (35.8%) women had SLE, 17 (11.3%) had SJögren’s syndrome, 17 (11.3%) were Rheumatoid arthritis and 1 had 27% (11.3%) had anti-SSA/La, 10 (6.6%) had anti-SSB/La antibodies, 6 (4.0%) had anti- U1RNP antibodies and 43 (28.5%) had anti-nuclear antibodies. During follow-up, 142 (94.0%) babies were born and 7 (4.6%) abortions and 2 (1.3%) fetal losses occurred. 6 (4.2%) neonates were born with neonatal lupus and 1 (0.7%) died in utero with a complete heart block. Out of the 6 babies with manifestations, 4 (66.7%) were cardiac, 2 (33.3%) were cutaneous, 1 (16.7%) was hepatic, 2 (33.3%) were haematological and 1 (16.7%) was pulmonary. Neonatal lupus manifestations occurred more frequently in mothers with SS (23.5% vs 2.2%; p<0.003), anti-SSa/Ro (20% vs 0%; p<0.001), and anti-SSb/La (27.7% vs 1.5%; p<0.001).

Conclusions: Our study proved a link between immune-mediated rheumatic diseases and specific neonatal outcomes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6136

[THU0514] PREDICTIVE VALUE OF SUBCLINICAL SYNOVITIS DETECTED BY DOPPLER ULTRASOUND IN RELATION TO FLARE IN PATIENTS WITH JUVENILE IDIOPLATHIC ARTHRITIS TREATED WITH BIOLOGIC THERAPY AFTER TAPERING BILOGIC THERAPY

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Background: Anti-TNF therapy is effective and safe in JIA. Changes in anti-TNF doses are common when remission is achieved. Subclinical synovitis on Doppler mode (PD) detected by ultrasound can predict flares in adult RA, but it is not yet clear in JIA.

Objectives: The aim of this study is to evaluate the predictive value of subclinical synovitis detected by PD-US in relation to flares in patients with JIA on remission under anti-TNF when therapy is tapered. The preliminary results were presented at the EULAR congress 2015 in Rome (FRI0520).

Methods: Observational, prospective and multicenter study. We included JIA patients on at least 6 months treatment with anti-TNF, ETN and ADA, in whom anti-TNF was tapered due to clinical decision. ETN was tapered by increasing the injection 3 days and ADA by increasing a week. Patients were clinically assessed every 3 months and also with PD-US at baseline. Baseline US assessment included joints and tendons. Adult synovitis definitions and semiquantitative synovitis definitions were used to define positive PD-US for JIA. We collected demographics (date of birth, JIA subcategory, previous and current treatments. Flare was defined as clinical signs and/or symptoms of arthritis that required increase of systemic therapy.

Results: We included 57 patients, with 19 patients (33.33%) having a flare

Scientific Abstracts
during the 12 months follow-up. 38 patients (66.67%) were receiving ETN and 19 (33.33%) ADA, of which 11 patients (28.95%) had a flare with ETN and 8 patients (42.11%) with ADA. Table 1 shows demographics. Mean time to flare was 5.73 months (IR 2.9–8.9). Concomitant methotrexate was lower in patients with flare (26.32% vs 71.05%). In 18 patients (31.58%), a previous tapering was done and median time of disease duration before tapering was 22 months (IR 15.5–29.5). US does not predict flare in our cohort. Global synovitis score at baseline was 4 (IQR 1.3–10.8) and 0 in BM and PD respectively, and tenosynovitis was 0 both BM and PD.

Conclusions: Anti-TNF tapering was safe in our JIA patients in more than half of patients after 1 year follow-up. US did not predict flares in our patients. Concomitant treatment with methotrexate was more frequent in patients who remained on remission.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3561

THU0515 DISABILITY AND LOWER QUALITY OF LIFE IS ASSOCIATED WITH SOCIOECONOMIC PASSIVITY IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS


Objectives: To describe and compare the characteristics and outcomes of 6 with a diagnosis of CRMO, presenting between age 13–20.

Results: In total 17 patients were identified as having CRMO, presenting between 1999 and 2015. 10 patients were female, and 7 patients male. The median age of initial symptoms, and age of presentation was 12 years (range 1–16 years).

Conclusions: The perceived wisdom is that CRMO is a self-limiting disease which eventually goes into remission. However our centre’s experience is that nearly 50% of our patients have a disease which evolves into another systemic autoimmune disease, mainly SAPHO, polyarticular or enthesitis related JIA. Previous case series have suggested only 0–30% of patients’ disease evolves. This may be a reflection of our older cohort of patients, who are only referred to our service with ongoing disease.

The majority of patients have a recurrent and multifocal course of disease. The most common site of disease was in the lower limbs (70% patients), upper limbs (35% patients), clavicle (29.4%), mandible (17.6%) and spine/pelvis (32.3%).

All patients were treated with NSAIDs. In terms of treatments used since diagnosis, 76% patients have been on methotrexate (MTX), 47% had one infusion of pamidronate, and 23% required more than one infusion of pamidronate. Other medications include sulfasalazine (SSZ), azathioprine, risedronate and anti-TNFs (adalimumab, etanercept and infliximab).

On last clinic review, with or without imaging, 35% of patients continue to have active disease. Currently 20% patients are on MTX alone, 23% patients are on adalimumab and MTX, and 35% are only maintained on NSAIDS. Of those without active disease 5 patients (45%) are not on any DMARD or biologic therapy. This may be reflected in our experience of managing adolescent patients with CRMO.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5730

THU0516 LONGER TERM OUTCOMES OF CRMO IN A TERTIARY ADOLESCENT AND YOUNG ADULT RHEUMATOLOGY CENTRE IN THE UK

K. E. N. Clark, F. Josephs, N. Daly, Y. Ioannou, C. L. Murphy, D. Sen. Rheumatology, University College London Hospitals, London, United Kingdom.

Background: Chronic relapsing multifocal osteomyelitis (CRMO) is a rare autoinflammatory bone condition presenting primarily in children and adolescents. It characteristically affects the epiphysis and metaphysis of long bones, and presents with bony pain, local swelling and warmth.

Objectives: The aim of this study was to collate our tertiary adolescent rheumatology centre’s experience of managing patients with CRMO, and establish their longer term outcomes, possibly by the fact we have a cohort of patients with CRMO under long-term follow-up.

Methods: We carried out a retrospective case note review of all patients who are attending our tertiary centre with diagnosis of CRMO, with a diagnosis of CRMO, presenting between age 13–20.

Results: In total 17 patients were identified as having CRMO, presenting between 1999 and 2015. 10 patients were female, and 7 patients male. The median age of initial symptoms, and age of presentation was 12 years (range 1–16 years).

Conclusions: The perceived wisdom is that CRMO is a self-limiting disease which eventually goes into remission. However our centre’s experience is that nearly 50% of our patients have a disease which evolves into another systemic autoimmune disease, mainly SAPHO, polyarticular or enthesitis related JIA. Previous case series have suggested only 0–30% of patients’ disease evolves. This may be a reflection of our older cohort of patients, who are only referred to our service with ongoing disease.

The majority of patients have a recurrent and multifocal course of disease. The most common site of disease was in the lower limbs (70% patients), upper limbs (35% patients), clavicle (29.4%), mandible (17.6%) and spine/pelvis (32.3%).

All patients were treated with NSAIDs. In terms of treatments used since diagnosis, 76% patients have been on methotrexate (MTX), 47% had one infusion of pamidronate, and 23% required more than one infusion of pamidronate. Other medications include sulfasalazine (SSZ), azathioprine, risedronate and anti-TNFs (adalimumab, etanercept and infliximab).

On last clinic review, with or without imaging, 35% of patients continue to have active disease. Currently 20% patients are on MTX alone, 23% patients are on adalimumab and MTX, and 35% are only maintained on NSAIDS. Of those without active disease 5 patients (45%) are not on any DMARD or biologic therapy. This may be reflected in our experience of managing adolescent patients with CRMO.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5730

THU0516 LARGE VESSEL VASCULITIS IN INFANTS - A CASE SERIES

L. Das1, J. H. T. Tan1, X. C. Gao1, S. F. Hoh1, T. Arkachaisri1,2.

Background: Large vessel involvement following recrudescence or recalcitrant Kawasaki Disease or other vasculitides in young children have been limited to few case reports and outcomes are still unclear.

Objectives: To describe and compare the characteristics and outcomes of 6 patients with large vessel vasculitis diagnosed between 2013 to 2015 in KK Hospital, Singapore.

Methods: Demographic and disease characteristic information were collected and median, interquartile range (IQR) & percentiles were used to describe the data.

Results: 6 patients were included in the analysis. Median age was 3.75 months
(IQR 3.75, 4). Other than 1 Filipino 2 year old girl (patient C), all other infants were of Chinese Singaporean origin and were less than age 1 year at onset; 4 male and 1 female. All patients were found to have multiple areas of irregular, thickened vessel walls with enhancement, involving the aorta and additional medium sized arteries on Magnetic Resonance Angiography (MRA).

Only patients P and Q had bronchial asthma and prolonged fever and or less than 1 clinical feature of KD. C developed a unilateral enlarged lymph node on recrudescence of fever 1 month after the initial event. She was then found to have dilated CA (dCA) and consequently abnormal MRA. Other patients had significant KD index scores and complete KD presentations.

Of the 4 patients who received only 1 dose of IVIG; C and F had diagnosis change from atypical KD to Takayasu Arteritis and G developed rhinovirus and then rotavirus as reason for prolonged fever. Patient A received IV steroids and then Infliximab. All patients received steroids. Patients A and B both developed a pseudoaneurysm rash post Infliximab which resolved in follow up. Patient F and Patient B died 3 months and 17 months after diagnosis. Patient F, presented with fever, fussiness and enters aged 4 months. Her symptoms recurred 2 weeks after onset. Due to differential hypertension, she received an echocardiogram and subsequently MRA and cardiac catheterization. Cause of death at age 7 months was small bowel perforation with arteritis and consequent intra-abdominal sepsis.

Patient B, presented with complete features of KD at age 2 months. His course was noted for recrudescence 2 weeks and 4 weeks after initial IVIG. He developed giant coronary aneurysms with abnormal MRA findings; developed myocardial infarction at age 8 months and proceeded to require a Left Ventricular Assist Device but died age 13 months from multi-organ failure.

3/6 (50%) developed aneurysms, D and F were giant. 4 surviving patients, had improvement in all vessels but continued activity in the aorta on follow up MRA, they remain on Methotrexate with no active clinical findings.

**Table 1: Patient characteristics**

<table>
<thead>
<tr>
<th>ID</th>
<th>Age (years)</th>
<th>sex</th>
<th>Blood count</th>
<th>WBC (10⁹/L)</th>
<th>CRP (mg/L)</th>
<th>dCA</th>
<th>dCA Status</th>
<th>Time to initial MRA (weeks)</th>
<th>Follow up MRA (months)</th>
<th>Haemoglobin</th>
<th>Methylprednisolone</th>
<th>5.4 (g/dL)</th>
<th>IFX infliximab</th>
<th>MTX methotrexate</th>
<th>CTX cyclophosphamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10.0</td>
<td>f</td>
<td>8.5</td>
<td>11.0</td>
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<td>B</td>
<td>9.2</td>
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**Conclusions:** Extensive involvement of the systemic arteries and aorta in all patient were noted on initial MRA. Follow up imaging, showed improvement in all vessels. After 1 year of follow up, complete resolution occurred in only medium vessels.

Mortality in this patient cohort was 2/7 (28.6%). This is an observational case series and our findings will need to be reproduced in larger groups of references.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4133

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**THU0518**

**BIOLOGICAL THERAPY IN NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS FOLLOWED IN ADULT RHEUMATOLOGY DEPARTMENT: HUR-BIO REAL LIFE RESULTS**

L. Kiple 1, A. Sari 1, B. Armagan 1, A. Erden 1, Ö. Karadağ 1, A. Akdoğan 1, S. Apras Bilgen1, S. Kiraz1, S. Özen2, U. Kalyoncu1, A.I. Ertenli1.

**Objectives:** To define the demographic and clinical characteristics of non-systemic JIA (ns-JIA) patients under biological therapy followed in adult rheumatology department.

**Methods:** Hacettepe University Biologic Registry (HUR-BIO) is a single center biological registry since 2005. HUR-BIO database includes demographic and clinical characteristics of patients, disease activity parameters, history of articular prosthesis. The use of biological agents in routine rheumatology practice has been approved by the Ministry of Health since 2003.

**Results:** In this study, 95 (72.6% women) ns-JIA patients were included. The demographic and clinical characteristics of the patients were shown in the table. The first biological agents were; Etanercept (63.2%), adalimumab (16.8%), infliximab (12.6%) and the others 7 (7.4%). After a mean follow up of 60 (48 months), 42 (44.2%) patients required biologic switch. The last visit HAQ scores of 75 patients were known and 16 (21.3%) patients had HAQ score ≥1.0 (female 15/54 vs. male 1/21, p=0.029). The last visit DAS-28 score of 72 patients was known and 46 (63.9%) patients had remission or low disease activity. 14 (20% ) had history of regular prosthesis surgery. Patients with history of articular prosthesis were older [39±10.1 vs. 29.6±10.3 years, p<0.0001], had longer disease duration [25.7±6.6 vs. 17.2±11.9 years, p=0.001] and had longer time until the biological therapy [19.6±8.4 vs. 11.5±11.6 years, p=0.002]. The time until the biological therapy of 38 ns-JIA patients diagnosed after 2003 was shorter [3.2±2.9 vs. 18.4±10.6 years, p=0.001].

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5812
OBJECTIVES: To compare uterine and ovarian size as well as artery pulsatility from the disease itself and the adverse effects of treatment.

Background: Delayed puberty is common in children with chronic illnesses such as Juvenile Idiopathic Arthritis (JIA), especially in cases with an early age of onset. Its etiology is multifactorial and includes low weight, complications arising from the disease itself and the adverse effects of treatment.

RESULTS: Hormone levels were also measured in control group (p < 0.01). Uterine and ovarian measures were smaller in girls with JIA (Mann-Whitney U test) and correlation tests as appropriate. Uterine and ovarian size and the corpus/cervix ratio were smaller in girls aged 10 to 11 years in girls with JIA aged between 10 and 11 years (p=0.004) and 14 to 15 years (p=0.042), and the corpus/cervix ratio was smaller in girls aged 10 to 11 years (p=0.007). US measures were not associated with disease factors in the JIA group. LH and estradiol levels were found to be positively associated with ovarian and uterine size (p<0.001), but negatively correlated with the mean PI of uterine arteries (p<0.01).

CONCLUSIONS: Pelvic US is a sensitive method for the assessment of sexual maturation in girls, and can identify developmental delays in girls with JIA which may not be detected by Tanner staging.

REFERENCES:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4389

THU0521

ENTHESITIS-RELATED ARTHRITIS: NON-PERIPHERAL PATTERN IS ASSOCIATED WITH TH17 CELLS

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Background: Enthesitis-related arthritis (ERA) is a category of juvenile idiopathic arthritis. Different proinflammatory cytokines linked to the Th1 and Th17 T cell subsets have been implicated in its pathogenesis. Limited data are currently available about the relationship between disease activity and the clinical pattern and the percentage of Th1and Th17 T cell subsets.

Objectives: To analyze Th1 and Th17 cell subsets in patients with ERA and to compare with age-matched healthy controls. To assess the association between disease activity and disease clinical pattern with Th1 and Th17 cells subsets.

Methods: Patients with ERA (as per ILAR criteria) were included in a cross sectional study. Disease activity measures were collected in random visits: active joint count (AJ), pain score (0–10), presence of active enthesitis (AE), sacroiliac pain (SIP), lumbar pain (LP), lumbar limitation (LL) by Schöber’s test, wellbeing according to the patient using a visual analogue scale (VASP, 0–10), disease activity according to the physician (VASphy, 0–10), JADAS-10, JSpADA, and ESR/CRP were evaluated. Patients were classified based on the disease pattern (peripheral and non-peripheral) depending on the presence or absence of AJ and/or AE. Functional capacity was also assessed by CHAQ. Presence of radiologic sacroiliac (MRI/X-rays) and treatment with TNF inhibitors (TNFi) were recorded. Th-17 and Th-1 cells were quantified by flow cytometry in PBMCs stimulated with PMA/IO. Age-matched healthy children without disease or medication were recruited as normal control. Comparison between groups (Mann-Whitney U test) and correlation tests as appropriate

Results: Twenty-nine patients (90% M) fulfilled inclusion criteria. HLA-B27 was positive in 13 (45%). Median age at observation was 12 years and median disease duration was 2.1 years. Activity and functional measures were (medians): AJ 1, pain 0.25, VASp 0.5, VASphy 1, JADAS-10 7, JSpADA 1.75, ESR 15 mm/h and CRP 0.5 mg/L. CHAQ (peripheral and non-peripheral) showed JADAS ≥0.5=8 patients (27%). AE was present in 1 (3%) children. Ninety (65%) patients showed JADAS >1 and 21 (76%) JSpADA >0. Radiologic sacroiliitis was recorded in 21 (72%) children. Fourteen (48%) patients were treated with TNFi. Th17 cell percentage in ERA was 8.5±3.4% (range, 4.1–17.4) while healthy controls was 5.8±3.8% (range, 1.2–14.2), p=0.023. Th17cell in ERA was 0.90±0.44 (range, 0.39–2.34%) while controls was 0.55±0.38 (range, 0.17–1.61%); p=0.004. There was no difference between T-cells% and active/inactive disease. Eighty (62%) children showed peripheral pattern, while 11 (38%) exhibited non-peripheral. Peripheral and non-peripheral groups showed Th17cells 0.90 (0.29–1.74) vs 1.14 (0.64–2.44) respectively (p<0.018). Significant correlations were Th1 with AJ (r=0.45 p=0.004) and Th17with LP (r=0.83 p=0.0001), LL (r=0.47 p=0.03).

Conclusions: Th1 and Th17 cells subsets were significantly higher in ERA compared with healthy controls. However, T-cells% contrast no difference between patients with active versus inactive disease. Interestingly, non-peripheral pattern showed higher Th17% cells respect to patients with peripheral disease. Our results suggest that Th17 evaluation could help identify different phenotypes that benefit from Th17 blocking strategies.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6726
Mortality and Causes of Death Among Juvenile Idiopathic Arthritis (JIA)


Objectives: To explore the association between calprotectin, clinical and US assessment in JIA pts.

Methods: A total of 30 consecutive pts (aged under 18 years) with oligo or poly JIA were assessed by US, clinical examination and MRI/US 14 serum levels. Serum MRI/US 14 was found between active (according to clinical examination) JIA pts and healthy controls (p=0.69) and between inactive JIA pts and healthy control (p=0.23).

Conclusions: To our knowledge this is the first study to examine the correlation between calprotectin and CRP (Spearman r 0.3800, p=0.05) and between calprotectin and ESR (Spearman r 0.3800, p=0.05).

Objectives: To assess the association between serum levels of 25-hydroxy-vitamin D and cardiovascular disease risk factors in juvenile idiopathic arthritis pts. Methods: A prospective cross-sectional study was done on 30 patients with JIA according to the criteria of the International League of Associations for Rheumatology (ILAR) and 30 healthy volunteers matched for age and gender. Patients with other causes of dyslipidemia or those whom receiving vitamin D supplements or lipid-lowering medications were excluded from this study.

Vit D levels were then correlated in each subgroup with the other clinical, laboratory and radiological parameters. We predefined Vit D insufficiency as being <50 nmol/l and Vit D deficiency as being <25 nmol/l.

Results: The mean serum vitamin D levels of all patients were 23.8 nmol/l ±16.59. Only 7 patients (23.3%) have adequate vitamin D levels (50–75 nmol/l). While vitamin D insufficiency (serum vitamin D levels: 25 – 50 nmol/l) was found in 14 patients (46.7%) respectively, JIA patients had significantly lower vitamin D levels as compared to controls (p<0.01). JIA patients had higher systolic and diastolic blood pressure than controls although these differences were not statistically significant (p>0.05) and all levels were still in normal values. Subjects with vitamin D deficiency or insufficiency had significantly lower values for HDL cholesterol and significantly elevated values for LDL cholesterol as compared to controls and patients with adequate vitamin D levels, with significant positive correlation between 25(OH)D and HDL cholesterol, and significant inverse correlation between 25(OH)D and LDL levels.

Patients with lower levels of vitamin D had significantly higher cIMT and lower FMD (p<0.01) with significant positive correlation between 25(OH)D and FMD, and significant inverse correlation between 25(OH)D and cIMT, and there were no significant differences in echocardiography results.

Table 1

<table>
<thead>
<tr>
<th>Vitamin D levels</th>
<th>LDL</th>
<th>cIMT</th>
<th>FMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 nmol/l</td>
<td>50–75 nmol/l</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>&lt;25 nmol/l</td>
<td>&lt;25 nmol/l</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Conclusions: Vitamin D deficiency is a cardiovascular risk factor in juvenile idiopathic arthritis.

References:


SAFETY OF ADALIMUMAB ± METHOTREXATE FOR THE SHORT AND LONG-TERM FOLLOW-UP OF TOCILIZUMAB

D. Milojevic2, C. Rabinovich2, D. Kingsbury2, K. Marzan 2, P. Quartier1, N. Ruperto

Background: JIA is the most common chronic inflammatory rheumatic disease of childhood. TNF inhibitors are used for long-term control of JIA disease.

Methods: To evaluate the 7 year (y) safety of Adalimumab treatment with or without methotrexate (ADA±MTX) when used in current clinical practice for treatment of patients (pts) with active pJIA.

Results: In January 2014, enrollment was complete. As of June 1, 2016 cut-off date, 838 pts (501 MTX arm and 537 - ADA±MTX arm) were treated in the registry. There were 39 pts who rolled over from MTX to ADA±MTX arm. At registry entry mean pJIA disease duration was 1.3 y and 3.7 y and mean ACR70 was 5.8 and 5.2 for MTX and ADA±MTX arms, respectively. CHAQ disability index was 0.6 for both arms. Mean duration of study drug exposure in registry was 2.0 y (range: 0.0 – 7.1) and 2.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. Mean duration of observation in registry was 3.9 y (range: 0.0 – 7.2) and 3.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. Overall, 213 pts (70.8%) in MTX and 225 pts (41.9%) in ADA±MTX arms were the degree of inflammation, visual acuity and macular thickness. The results were the degree of inflammation, visual acuity and macular thickness. The results were expressed as mean±SD for normally distributed variables, or median [IQR] when they are not. Comparison of continuous variables were performed using the Wilcoxon test.

Results: We studied 25 patients (21 women/4 men); mean age 18.6±2.3. Uveitis was bilateral in 22. JIA subsets were oligoarthritis (n=17), polyarthritis (3), psoriatic (2) and enthesitis-related arthritis (1). Uveitis associated with the eye disease was anterior (9) and at least one conventional immunosuppressive drug including biological therapy. The outcome variables were the degree of inflammation, visual acuity and macular thickness. The results were expressed as mean±SD for normally distributed variables, or median [IQR] when they are not. Comparison of continuous variables were performed using the Wilcoxon test.

Conclusions: Overall, ADA±MTX was well-tolerated in these pts with pJIA with no new safety signals. The retention rate for registry drug was higher in ADA±MTX arm compared to MTX arm. Acknowledgements: AbbVie sponsored the study & contributed with PRINTO & PRORSG to analysis, review, approval of the abstract. X. Leahy & A. Deshmukh (AbbVie) contributed to research, Medical writing: G. Patki (AbbVie). Disclosure of Interest: N. Vargas-Ruengena Grant/research support from: UCB Pharma, Hoffman La-Roche, Sanofi, A. Deshmukh Consultant for: AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologics B.V., Eli Lilly and Co., ‘Francesco Angelini’, GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, Employee of: GASPION Hospital, Speakers bureau: Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, Johnsons Biologics B.V., Medac, Pfizer, Roche, and Wyeth/Pfizer.

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Conclusions: Overall, ADA±MTX was well-tolerated in these pts with pJIA with no new safety signals. The retention rate for registry drug was higher in ADA±MTX arm compared to MTX arm. Acknowledgements: AbbVie sponsored the study & contributed with PRINTO & PRORSG to analysis, review, approval of the abstract. X. Leahy & A. Deshmukh (AbbVie) contributed to research, Medical writing: G. Patki (AbbVie). Disclosure of Interest: N. Vargas-Ruengena Grant/research support from: UCB Pharma, Hoffman La-Roche, Sanofi, A. Deshmukh Consultant for: AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologics B.V., Eli Lilly and Co., ‘Francesco Angelini’, GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, Employee of: GASPION Hospital, Speakers bureau: Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, Johnsons Biologics B.V., Medac, Pfizer, Roche, and Wyeth/Pfizer.

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Methods: To evaluate the 7 year (y) safety of Adalimumab treatment with or without methotrexate (ADA±MTX) when used in current clinical practice for treatment of patients (pts) with active pJIA.
a follow up of one year (n=21), 2 years (n=11), and 3 years (n=5). A reduction in the daily median dose of prednisone from 10 mg (0–15 mg) to 0 (0–0 mg) in 3 years, (p<0.05) was observed. After a median follow-up of 20.5±11.7 months in 4 patients, the interval between TCZ doses was increased to 5 weeks (n=2), 6 weeks (1) and 7 weeks (1) because of remission. TCZ had to be withdrawn due to biological intolerance (1) or articular and ocular inefficiency (1). The main adverse effects were severe autoimmune thrombocytopenia, autoimmune anemia and thrombocytopenia, pneumonia, viral conjunctivitis and bullous impetigo in 1 patient each.

Conclusions: TCZ is useful at short and long term follow-up for severe Juvenile Idiopathic Arthritis arthritis and/or uveitis. It is possible to optimize the TCZ dose.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5265

THU0527 PEDIATRICIAN AND ADULT RHEUMATOLOGIST COLLABORATING IN A MULTIDISCIPLINARY REUMA-PED CLINIC. IS THIS TRANSITIONAL CARE MODEL EFFECTIVE?

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Background: Transitional care should be a planned movement of adolescents with severe diseases from child-centred to adult-oriented health care system. Recently a EULAR/PRSE taskforce has developed the first international set of recommendations and standards for transitional care.

Objectives: To describe the results from a specific transitional care programme.

Methods: The current transitional care programme includes a multidisciplinary PE/Pediatric care clinic weekly and a non-defined period of rheumatology follow-ups by the same rheumatologist of MPRC. The transitional care team is composed of two pediatricians, one adult rheumatologist -as transition coordinator-, a clinical nurse specialist and administrative support, as well as a psychologist and physiotherapists. Clinical information and therapies were collected throughout the disease course and the HEADSS method of psychosocial interviewing has been included recently.

Population of the present study included young patients (YP) from that programme who are going to transfer to adult-oriented health care system. Descriptive study of socio-demographics and clinic features was included, as well as patients' adherence. YP confidence to be transferred and satisfaction with the current transitional process were measured using on a scale of 0 to 10. In patients suffering from juvenile idiopathic arthritis (JIA), clinical status of disease activity and clinical remission and CHAQ were tested before transfer.

Results: Twenty-seven YP with female predominance (63%) were included. The average age was 21±3 yo at time of a planned transfer and 16±3 yo at inclusion to the MPRC. JIA was the commonest condition whereas dermatomyositis was uncommon. Up to 63% patients required some DMARDs during the MPRC follow-up, but only a 37% needs maintained immunosuppressive therapies and three (11%) patients required changing the therapeutic target before transfer. YP adherence to rheumatologist appointments was high. Regarding HEADSS data: most YP were students and living at family home, around 50% gave up sports or other activities due to homework or exams, 29% of YP occasionally drank some alcohol but none used tobacco, and 47% of YP felt sad or down once in a while. Patient’s confidence to be transferred was 7.7±2.1 (mean±SD; min-max: 2–10). YP showed high satisfaction with the current transitional process, 9.7±0.4 (min-max: 9–10).

Before transfer, 17 patients with JIA showed a mean±SD value of JADAS10 of 2±5 (mean±SD; min-max: 0–18), clinical remission on/off medication was 23% and 53% respectively. Mostly functional status reported by patient was low, YP-rated CHAQ (mean 0.06; min-max, 0.0–0.75).

Conclusions: To the best of our knowledge, this is the first study evaluating a Spanish transitional care programme. The study reports a positive impact across adolescence of our transitional care model in a real life situation. Implementation of recommendations depended on the local available resources.

References:

Acknowledgements: Beatriz Jimenez, Auxiliary to the clinical nurse specialist and administrative support of Rheumatology Department.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5444
followed by extended oligarticular (27%/26%), polyarticular psoriatic arthritis (18%/16%) and RF positive polyarticular (5%/8%). Disease duration (2.3±3.0 vs 1.9±2.7) was statistically higher in the oral cohort (p=0.04) but age at onset and baseline were similar. The baseline disease activity was higher in the s.c. cohort (JADAS10 16.5±7.2 compared to 14.7±8.2; p=0.001 and active joint count 11 vs 6.7; p=0.011). The weekly MTX dosages were comparable with 13.6±5.4mg and 13.3±4.5 mg. Concomitant treatment with NSAIDS (95%/89%), oral steroids (24%/25%) or intraarticular steroids (6%/8%) were comparable.

After 12 months of treatment, 150 (38.3%) reached a JIA ACR90 with oral MTX and 131 (33%) with s.c. MTX while 86 (21.8%) and 72 (19.6%) reached JADAS-remission (JADAS10c≤1). By Kaplan-Meyer analysis no difference in the early kinetic of response was found. Upon total observation for up to 7.5 years in patients in the treatment to treat population (patients discontinuing MTX due to inefficacy or intolerance) response rates were calculated as non-responders. The patients in the oral cohort reached a JADAS-remission (162; 41%) than with s.c. MTX (126; 34%) which was stastically borderine significant (p=0.05; odd’s ratio 1.2 [95CI 1.0–1.8]).

Response rates at 1 year

MTX oral  MTX sub

JADAS-ACR≥  acceptable disease activity, MDA minimal disease activity, Remission

Conclusions: Data from the BIKER registry out of the clinical practice do show a high rate of JIA patients reaching a significant JIA-ACR response as well as JADAS-remission upon MTX as a sole DMDAR. However, on the long term more patients with oral MTX reached JADAS remission. By Kaplan Meyer analyses we did not observe a superiority of s.c. MTX in the kinetic of response. The limitations of our analysis lie the character of a registry study, the lack of randomisation and study protocol leaving all decisions to start or to stop MTX by the responsible rheumatologist. Thus such data are preliminary and should be confirmed by randomized studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3530

THU0530 CHARACTERIZATION OF A COHORT OF PSORIATIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS FROM A PAEDIATRIC UNIVERSITY HOSPITAL IN SPAIN

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Background: Juvenile Psoriatic Arthritis (JPsAo) is a subtype of Juvenile Idiopathic Arthritis (JIA) present in 7% of JIA patients (1). Psoriasis is present in 0.5–1% of children. Diagnosis is often difficult, with the arcutil manifestations often preceding skin disease by years. Data is scarce in the Spanish population.

Objectives: Describe demographic and clinical characteristics of our cohort of JPsAo.

Methods: Descriptive, transversal study of patients attended from 1/2012–12/2016. Included were all compliers with ILAR Criteria (2) for JPsAo (Edmonton 2001). We also included the Wallace Criteria for clinical inactive disease (3) as a variable in the end point. Data were included and analyzed using SPSS MAC 20.

Results: 31 patients were included: 18 (59%) girls, 13 (41%) boys. All Caucasian. They comprised 5 of all our JIA patients in that period. Mean age at diagnosis was 7.4 years. All were RF-; 9 (29%) ANA+; 4 (12.9%) HLA-B27+; articular onset 17 (55%) and cutaneous onset 14 (45%). 9 (29%) had Temporomandibular Joint (TMJ) symptoms; 5 (16%) had pain and 4 (12.9%) had a positive MRI for TMJ synovitis. Plaque psoriasis 14 (45%), guttate 3 (9.6%) and 3 (9.6%) had both. Dactylitis 8 (26.6%); enthesitis 6 (19.35%). Joint disease was mainly oligoarticular 15 (48%), monariticular 14 (45%) and poliariticular 1 (3.2%). Axial disease 4 (12.9%) at follow-up, 7 (22.5%) uv); 5 (77%) were AS+/1 (9.6%) oncocistrodinia and 6 (19.3%) enthesis. All patients received NSAIDs; 30 (96%) methotreaxe; 6 (19.3%) switched to leflunomide. 16 (51.6%) received biologic treatment and 9 (29%) more than once. 10 (32.2%) received biologic treatment more than once. 14 (45%) were treated with more than one. 7 (22.5%) uveitis; 5 (77%) were ANA+. 3 (9.6%) onicodistrophia and 6 (19.3%) anti-TNF-Paradoxal psoriatic events. Wallace Inactivity Criteria were achieved in 25 (80.6%), with no differences between the biologic and DMSRDs groups in time up to Achieving Wallace Criterias (TimeWall). TMJ positive MRI did have a negative effect on TimeWall with 2 (66.6%) ≥8 yr (8, 11y) to TimeWall.

Conclusions: We describe the clinical features and demographics of a series of spanish JPsAo patients. We found more oligoarticular and monariticular involvement and an important presence of enthesitis and dactylitis; higher frequency of uveitis than published data (22.5% vs. 10–15%). Some were ANA-, reinforcing the need for screening. More than half required biologic treatment, and several cases we needed to switch drugs. Almost 60% of the patients were girls. Articular onset was associated with more active, harder to treat disease. TMJ positive MRI was associated with longer TimeWall. However, Wallace Criteria were not achieved globally.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6645

THU0531 USE OF RITUXIMAB IN PAEDIATRIC RHEUMATOLOGY - EXPERIENCES FROM A SINGLE TERTIARY CENTRE

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Background: Rituximab is an anti-CD20 monoclonal antibody therapy used widely in the management of paediatric rheumatological conditions. Studies suggest that Rituximab is safe and effective in rheumatic autoimmune diseases, but data on paediatric use remains limited. Although Rituximab spares plasma cells, hypogammaglobulinaemia can still develop, leading to recurrent infections. Frequency of hypogammaglobulinaemia in children receiving Rituximab for rheumatological conditions is unknown.

Objectives: To analyse the use of Rituximab in a tertiary Paediatric Rheumatology centre over the last 15 years (2001–2015). The primary aims were to identify the number of patients who received Rituximab, the underlying diagnoses and the response to treatment. Our secondary aims were to identify the incidence of hypogammaglobulinaemia associated with Rituximab use and the frequency and severity of infections. Frequency of monitoring of immunoglobulin levels, lymphocyte subsets and functional antibodies to pneumococcos were noted.

Methods: Retrospective analysis of case notes, electronic records and laboratory data of patients who received Rituximab in the paediatric rheumatology department from 2001–2015.

Results: A total of 22 patients received Rituximab (total of 1500mg/m2 per cycle over 2 – 4 divided doses) during the study period. 3 were excluded due to insufficient data. Median time of commencement of Rituximab from diagnosis was 2 years 8 months. Of these, 12 patients achieved remission within 6 to 12 months. Rituximab was discontinued in the non-responders at 12 months.

8 patients (42%) were noted to have hypogammaglobulinaemia at some point. The role of cyclophosphamide contributing to hypogammaglobulinaemia could not be excluded in 2 and a further patient is currently being investigated for an underlying primary immune deficiency. In the remaining 26 (88%) patients, we believe the low IgG levels are secondary to Rituximab, of which 2 needed long term Ig replacement. Overall 12 patients reported recurrent/severe infections of which 6 had low immunoglobulin levels.

Conclusions: RF+ JIA patients appear to have responded the best to Rituximab and RF- JIA patients the least (0/4), with good results in JDM and SLE subgroups (80–83%). The incidence of hypogammaglobulinaemia secondary to Rituximab in our cohort was 26%, which can be prolonged and worsened with increased number of cycles. Prior treatment with cyclophosphamide may be contributory. We suggest regular monitoring of immunoglobulin levels and lymphocyte markers on all patients prior to commencement of Rituximab and regular intervals subsequently, including further cycles.

Disclosure of Interest: None declared

Uveitis in children is rare. Intensive interactions between ophthalmologists and paediatric rheumatologists are needed in order to choose the best therapeutic strategies for severe uveitis attacks.

**Objectives:** Describe a cohort of 74 patients with paediatric uveitis.

**Methods:** Retrospective analysis of children followed for uveitis before 18, by one paediatric ophthalmologist (SGC) in Paris, during the 2006–16 period. Members of 3 ophthalmologic departments specialized in uveitis care in children (AR, CT, ML and BB) in Paris, during the 2006–16 period.

**Results:** There were 74 paediatric uveitis, 42 anterior (57%, group 1), 16 intermediate (21%, group 2), 7 posterior (9%, group 3), and 9 pan-uveitis (12%, group 4). Gender was equal in group 2–4, but there were more females in group 1. At presentation, mean ages were 8.6±4.1, 9.8±3.9, 9.1±3.6 and 10±4.2 years old. Mean follow-up was 3.7±3.7 years. JIA was the leading cause of group 1 uveitis (45%); group 2–3 uveitis were idiopathic in 81% and 86%, respectively. In group 4, etiologies were found in 7 out of 9 patients (Behçet-3, JIA-2, BBS-1, TINU-1).

**Conclusions:** Paediatric uveitis induce a very high-level burden in children, even when anterior and sometimes despite optimal therapeutic management in tertiary care centers. Their early recognition and tight control in specialized units are absolutely required in order to decrease the level of definitive complications.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.6629
biologic switchers (34.5%). For the total IV ABA cohort, six hospitalized infection claims were reported with an IR (95% CI) of 2.4/100 p-y (0.5, 5.3) and an IR of 2.8/100 p-y (1.2, 5.9) for new-onset uveitis. There were no validated cases of malignancies in the follow-up period.

**Conclusions:** Compared with an overall JIA population, abatacept pts are significantly more likely to experience uveitis and have a history of asthma or cardiovascular disease. The rates of hospitalized infection and new onset of uveitis in this study are within published ranges2,3 and are consistent with findings in the abatacept JIA registry.4

**References:**


**DOI:** 10.1136/annrheumdis-2017-eular.1474

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**THU0535**

**LONG-TERM FOLLOW-UP OF 12 CASES OF CORONARY GIANT ANEURYSM AFTER KAWASAKI DISEASE**

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**Background:** The incidence of Kawasaki disease has been increasing since it was first reported by Tomisaku Kawasaki in 1967. Among complications of the condition, the formation of coronary artery aneurysms is the most important. In particular, giant aneurysms with diameters that exceed 8 mm are likely to not regress and result in serious complications, such as acute myocardial infarction.

**Objectives:** To understand the long-term course of patients with giant aneurysms and Kawasaki disease as well as to consider the cause of aneurysm formation and its appropriate treatment.

**Methods:** We retrospectively studied the long-term course of 12 cases of giant coronary artery aneurysms accompanied with Kawasaki disease, which were being followed at Shiga University of Medical Science Hospital, Omihachiman Community Medical Center, and Nagahama Red Cross Hospital. These are three major facilities in Shiga prefecture of Japan, whose population is 1.4 million, comprising 200,000 children.

**Results:** Ten male and two female patients were included. The average current age was 16.8 years, the median age was 14.3 (10.7–18.9) years, and 5 cases were of adults. The average age at the time of onset was 3.5 years, the median age was 3.7 years (1.8 - 4.4), and all experienced onset between 1 and 5 years of age. The mean period from onset to treatment start was 6.7 days (median 5.0 (4.3–8.3)), but the average period until fever declined was 16.0 days and only three patients' temperature was reduced in 10 days. Aneurysm formation occurred at 14.1 days on average (median 12 (10–17)). The average size of the maximum coronary artery aneurysm at onset was 11.3 mm, and the median size was 9.5 mm (8.8 mm – 13.8 mm). The average and median follow-up periods were 13.2 years and 11.7 years (5.4–13.4), respectively. The number of patients received steroid therapy was four, and all their onset was after 2006. None received infliximab or underwent plasmapheresis.

During the course of the condition, all patients underwent multiple centripetal echocardiography. Among all cases, 7 underwent coronary angiography CT, 10 underwent myocardial scintigraphy. All 12 patients underwent cardiac catheterization for them was thirty-one. Two adult patients had a history of acute myocardial infarction and had undergone cardiac bypass surgery. Through this survey, we found that 9 cases developed giant coronary artery aneurysm between 1983 and 2007, and 3 cases between 2007 and 2012.

**Conclusions:** All patients are currently receiving anticoagulant therapy and undergoing diagnostic imaging. In our prefecture, the incidence of giant coronary artery aneurysm accompanied with Kawasaki disease has been decreasing gradually. From 2007 to 2012, in which high dose gamma globulin therapy (2g/kg) has become commonly used for Kawasaki disease in Japan, there were no giant aneurysm formation in our hospitals. Three patients in whom giant aneurysms developed between 2012 and 2015 were taking oral prednisolone, thereby suggesting a relationship between prednisolone and giant aneurysm formation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6077

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**THU0537**

**FAMILY AND PATIENT’S PERCEPTION OF DIETARY INTERVENTION IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)**


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**Background:** Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatologic illness and can lead to significant disability. Complementary and alternative therapies are commonly practiced by families of patients with JIA, and > 40% of patients with chronic arthritis seek dietary changes after their diagnosis. Dietary intervention studies in adults with rheumatoid arthritis showed moderate improvement in joint symptoms. Dietary supplements of omega-3 fatty acids have been studied in children with juvenile rheumatoid arthritis and found to be associated with less NSAID use and lower serum IL-1 and TNF levels. There is an increasing need to understand if there is a role for dietary therapy in chronic arthritis.

**Objectives:** We aimed to evaluate the prevalence of special diets and the perception of the effectiveness of these diets on arthritis in JIA. We also assessed the interest of dietary interventions and perceived barriers.

**Methods:** An online survey was designed through a REDCap database capturing demographic information, self- or parent-initiated special dietary interventions and self- or parent-scoring effects on joint symptoms, willingness to participate in a dietary intervention study. The survey link was posted on social media websites and distributed by the Arthritis Foundation and various clinical performed.

**Results:** A total of 265 responses were received from adult patients who had JIA and parents of children with JIA. We excluded 14 patients with inflammatory bowel disease, juvenile idiopathic disease-related arthritis and 24 responders with incomplete answers. Demographic and JIA characteristics of adult and pediatric patients are listed in Table 1. Ninety patients (63 children with JIA, 27 adults with history of JIA) had tried a special diet for arthritis. The top three special diets reported by parents included a gluten-free diet (62%), an anti-inflammatory diet (53%),...
and a lactose-free diet (26%). There were similar clinical responses among the three diets (Figure 1). Twenty-five to thirty percent reported no change in joint symptoms whereas 20–30% reported improved pain or joint swelling. Sixty-one (34%) parents were willing to participate in a 3-month dietary intervention study and 78 (44%) parents answered “it depends”.

Table 1

<table>
<thead>
<tr>
<th>Number of joints affected, n (%)</th>
<th>≥ 5</th>
<th>≥ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population Adult patients (n=49)</td>
<td>43 (88)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Pediatrics patients (n=178)</td>
<td>51 (29)</td>
<td></td>
</tr>
<tr>
<td>Treatment exposure, n, (%) Systemic glucocorticoid</td>
<td>40 (82)</td>
<td>108 (61)</td>
</tr>
<tr>
<td>DMARDs</td>
<td>44 (80)</td>
<td>146 (82)</td>
</tr>
<tr>
<td>Biologics</td>
<td>35 (71)</td>
<td>114 (64)</td>
</tr>
</tbody>
</table>

Conclusions: This is the first report of the family/patient perspective of the role of dietary intervention on JIA. Almost half of the affected patients attempted special diets, and many reported improvement in symptoms. Future interventional studies with objective outcome measurements are needed to validate these reports.

Acknowledgements: The authors would like to thank all the patients and families who have taken the survey. Arthritis Foundation and Facebook JA groups have supported the survey.

Disclosure of Interest: Y. Zhao: None declared, J. E. Little: None declared, S. Grevich Grant/research help

**Figure 1.** Parental report of clinical responses to a gluten-free diet, an anti-inflammatory diet and a lactose-free diet in children.

![Figure 1](image.png)

**THURSDAY, 15 JUNE 2017**

**THU0536**

**EFFECTS OF GLUCOCORTICOIDS AND METHOTREXATE-BASED THERAPEUTIC REGIMENS ON B CELL SUBPOPULATIONS IN PATIENTS WITH IgG4-RELATED DISEASE**

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**Background:** IgG4-related disease (IgG4-RD) is a systemic fibro-inflammatory disorder characterized by fibrotic lesions infiltrated by IgG4 positive plasma cells (1). The prompt clinical responses obtained after B cell depletion with rituximab in IgG4-RD patients suggest that B lymphocytes drive the pathogenesis of this condition and sustain disease activity (2). This conclusion, however, requires further confirmation because IgG4-RD responds also to non-B cell depleting therapies such as glucocorticoids and methotrexate.

**Objectives:** To evaluate the effects of glucocorticoids and methotrexate-based therapeutic regimens on B cell subpopulations in patients with IgG4-RD.

**Methods:** Sixteen patients with active IgG4-RD were studied. FACS analysis was performed on peripheral blood in order to identify the following B cell subpopulations: total B cells (CD19+CD20- and CD19+CD20+ cells), circulating plasmablasts (CD19+CD20- CD27+CD38+ cells), memory B cells (CD19+CD20- CD27+CD38+ cells), circulating plasma cells (CD38+CD138+ cells). Disease activity was assessed by means of the IgG4-RD responder index (IgG4-RD RI). Flow cytometry was performed at baseline and after six months of immunosuppressive therapy with glucocorticoids (0.6–1mg/kg/day) and/or methotrexate (10–20mg/week).

**Results:** At baseline, circulating plasmablasts were expanded in IgG4-RD patients (median 3780 cell/mL; range 330–9300) compared to controls (median 280 cell/mL; range 0–1000) (p < 0.05); total B cells (median 13300 cell/mL; range 3400–56900) and naïve B cells (median 13080 cell/mL; range 1970–64270) were reduced in IgG4-RD patients compared to controls (median 280 cell/mL; range 194–330; and median 54020 cell/mL; range 21050–106780, respectively) (p < 0.05). No circulating plasma cells were detected in healthy controls. No differences in memory B cells were observed (p > 0.05); Circulating plasmablasts but not other B cell subsets positively correlated with serum IgG4 levels, number of organ involved, and IgG4-RD RI (p < 0.05). At six months follow-up, the median IgG4-RD RI decreased from 9 to 2. Circulating plasmablasts, circulating plasma cells, and naïve B cells counts decreased in all patients together with disease improvement (p<0.0002, 0.0002 and 0.025 compared to baseline values, respectively); total B cells and memory B cells were unaffected by immunosuppressive therapy.

**Conclusions:** Non-B cell depleting therapies based on glucocorticoids and/or methotrexate induce clinical improvement and deplete circulating plasmablasts, plasma cells and naïve B cells in patients with IgG4-RD; circulating total B cells and memory B cells are not affected by glucocorticoids and methotrexate. Our study, performed with non-B cell depleting agents, provides clinical evidences that circulating plasmablasts are likely linked to IgG4-RD pathogenesis and disease activity.

**References:**


**Disclosure of Interest:** None declared


**THU0539**

**SARCOIDOSIS IN SPAIN: CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS AT DIAGNOSIS IN 1082 PATIENTS**


**Background:** Sarcoidosis is a multisystem disease characterized by non-caseating granulomas. The disease has a worldwide distribution with geographical and racial variations of incidence. In Spain, there is a lack of data on the clinical and epidemiological characteristics of the disease.

**Objectives:** To describe the clinical and epidemiological characteristics of sarcoidosis in Spain and identify potential subgroups of patients.

**Methods:** The SarcoidiaS-SEMI Registry is a large multicenter cohort from Southern Europe.

**Conclusions:** The SarcoidiaS-SEMI Registry is the first national registry of sarcoidosis in Spain, providing valuable data on the clinical and epidemiological characteristics of the disease.

**Disclosure of Interest:** None declared.

**THU0540**

**EFFICACY AND SAFETY OF ADALIMUMAB IN BEHÇET’S DISEASE RELATED UVEITIS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY**


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**Background:** Current information on the use of adalimumab (ADA) in the treatment of ocular Behçet’s disease (BD) is still based mainly on small series or case reports; nonetheless preliminary evidence is promising.

**Objectives:** The study aim was to evaluate the efficacy of ADA in a large series of BD-related uveitis.

**Methods:** We performed a multicenter retrospective observational study including 40 selected patients (66 eyes) receiving ADA. Clinical data were retrospectively analyzed at baseline, at 3 and 12 months of treatment. Primary endpoint was: reduction of ocular inflammatory flares. Secondary end-points were: improvement of Best Corrected Visual Acuity (BCVA), reduction of macular thickness measured by optical coherence tomography (OCT), reduction in the occurrence of vasculitis assessed by fluorescein angiography (FA), evaluation of statistically significant differences between patients treated with ADA monotherapy and those undergoing ADA plus DMARDs and in patients firstly treated with ADA compared to patients previously administered with other biologics; ADA steroid sparing effect was also evaluated.

**Results:** During the first 12 months of ADA therapy the number of flares significantly decreased from 200 flares/100 patients/year to 8.5 flares/100 patients/year (p<0.0001). Similarly BCVA improved if compared to baseline (7.4±2.9 versus 8.5±2.1, p=0.03). OCT findings significantly improved showing a mean reduction of central macular thickness (CMT) of 27.2±42.8 microns at the end of follow up (p<0.006). FA identified retinal vasculitis in 22 cases at baseline (55%), 8 (20%) cases after 3 months and in only one (2.5%) case at 12-month follow-up. FA improvement was highly significant at 3 and 12-month follow-up if compared to baseline (p=0.0001 and p=0.006, respectively).

**Conclusions:** ADA is highly effective and safe for the treatment of BD-related uveitis, providing a long-term control of ocular inflammation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1026
ANTI-INTERLEUKIN 1 THERAPY IN FMF AMYLOIDOSIS: A SINGLE CENTER EXPERIENCE (CASE SERIES)

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Background: Recently there is increasing number of reports investigating the efficacy of anti-interleukin-1 (anti-IL-1) therapy in AA-amyloidosis.

Methods: Objectives: Here we report our experience in IL-1 blockade in AA amyloidosis secondary to FMF.

Results: Twenty nine FMF patients with secondary AA-amyloidosis with insufficient response to colchicine were treated with anti-IL-1 agents (canakinumab and anakinra). Creatinine (Cr), 24-hour urine protein (UP), C-reactive protein (CRP) and ESR were measured before and throughout the treatment to evaluate the response and side effects.

Conclusions: The presence of R202Q polymorphism is associated with FMF, with a higher relapse risk. Patients with hemodialysis and serum IgG4 level above upper limit of normal were at higher relapse risk and a low dose, maintenance prednisolone for longer period is recommended.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6166

ANTEROTHERAPY IN FMF AMYLOIDOSIS: A SINGLE CENTER EXPERIENCE (CASE SERIES)

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Background: Familial Mediterranean fever (FMF) is an autosomal recessive inherited disease with recurrent fever and inflammatory episodes of serous membranes. The MEFV (Mediterranean fever) gene in the short arm of chromosome 16 is affected in the FMF. This gene encodes for a protein called Pyrin. The erroneously synthesized Pyrin protein due to MEFV mutations is unable to control the post inflammatory process. Although there have been many efforts to find genotypetype-phenotype association in FMF, no clear relationship has been clarified.

Objectives: In this study, the relationship between FMF clinical symptoms and MEFV gene mutations and polymorphism was investigated.

Results: A total of 158 patients with FMF were included to the study that was conducted in a tertiary rheumatology outpatient clinic. The demographic and clinical features, as well as MEFV gene mutations were recorded in a “Patient Assessment Form”. The clinical status of the disease was evaluated with FMF-severity score (F-SS-2). The associations between clinical features and genetic alterations were calculated with Pearson Chi-square test.

Conclusions: The presence of R202Q polymorphism is associated with FMF, and should be considered in the routine genetic analysis of the disease. In our patients, its co-existence with M694V seems to be associated with good response to colchicine, and to alleviate the severity of the disease expression of M694V, which is known to be associated with severe course.

References:
Background: Multicentric Castleman's disease (MCD) is a disorder characterized by polyclonal proliferation of B lymphocytes that is frequently associated with autoimmune manifestations and connective tissue diseases. MCD presents high levels of IL-6 and systemic symptoms such as fever, arthralgia, hepatosplenomegaly and serositis, so it is recommended to include MCD in the differential diagnosis of adult-onset Still's disease (AOSD). However, there are no studies comparing both groups of patients.

Objectives: To compare the clinical and laboratory features at onset between patients with MCD and AOSD seen in a Madrid tertiary care hospital.

Methods: We performed a retrospective observational study in patients with diagnosis MCD and AOSD attended our center between January 1989 and December 2015. The variables included demographics, clinical manifestations, laboratory tests and Yamaguchi’s criteria.

Results: A total of 34 patients were included, 17 with MCD and 17 with AOSD. The comparison of the characteristics of both groups is presented in the table. There were no differences in age, uration of disease (MCD 158.6 days and AOSD 250.5 days, p=0.3919), diagnostic delay (MCD 18.4 and AOSD 52.2, p=0.2711), arthritis, myalgias, pleuritis or macrophagic activation syndrome, but persistent fever, rash, arthralgia, pharyngitis and pericarditis were significantly more frequent in EASA, whereas male gender, human immunodeficiency virus (HIV) and/or human herpes virus 8 (HHV8) infection, hepatosplenomegaly and more frequent in ESA, whereas male gender, human immunodeficiency virus (HIV) and/or human herpes virus 8 (HHV8) infection, hepatosplenomegaly and hypertransaminasemia were significantly higher in AOSD. 52.9% (HIV) and/or human herpes virus 8 (HHV8) infection, hepatosplenomegaly and 52.9% of patients with MCD met 5 or more Yamaguchi’s criteria for AOSD.

Conclusions: Patients with MCD may present common systemic manifestations and laboratory abnormalities at onset with AOSD and up to 50% of them may fulfill Yamaguchi’s criteria for this disease, so MCD should be taken into account in its differential diagnosis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4294

**THU0545 COMPARISON OF THE CLINICAL AND LABORATORY FEATURES AT ONSET BETWEEN MULTICENTRIC CASTLEMAN’S DISEASE AND ADULT-ONSET STILL’S DISEASE**

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Background: Multicentric Castleman's disease (MCD) is a disorder characterized by polyclonal proliferation of B lymphocytes that is frequently associated with autoimmune manifestations and connective tissue diseases. MCD presents high levels of IL-6 and systemic symptoms such as fever, arthralgia, hepatosplenomegaly and serositis, so it is recommended to include MCD in the differential diagnosis of adult-onset Still’s disease (AOSD). However, there are no studies comparing both groups of patients.

Objectives: To compare the clinical and laboratory features at onset between patients with MCD and AOSD seen in a Madrid tertiary care hospital.

Methods: We performed a retrospective observational study in patients with diagnosis MCD and AOSD attended our center between January 1989 and December 2015. The variables included demographics, clinical manifestations, laboratory tests and Yamaguchi’s criteria.

Results: A total of 34 patients were included, 17 with MCD and 17 with AOSD. The comparison of the characteristics of both groups is presented in the table. There were no differences in age, uration of disease (MCD 158.6 days and AOSD 250.5 days, p=0.3919), diagnostic delay (MCD 18.4 and AOSD 52.2, p=0.2711), arthritis, myalgias, pleuritis or macrophagic activation syndrome, but persistent fever, rash, arthralgia, pharyngitis and pericarditis were significantly more frequent in EASA, whereas male gender, human immunodeficiency virus (HIV) and/or human herpes virus 8 (HHV8) infection, hepatosplenomegaly and hypertransaminasemia were significantly higher in AOSD. 52.9% (HIV) and/or human herpes virus 8 (HHV8) infection, hepatosplenomegaly and 52.9% of patients with MCD met 5 or more Yamaguchi’s criteria for AOSD.

Conclusions: Patients with MCD may present common systemic manifestations and laboratory abnormalities at onset with AOSD and up to 50% of them may fulfill Yamaguchi’s criteria for this disease, so MCD should be taken into account in its differential diagnosis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4294

**THU0547 CHARACTERIZATION OF A GROUP OF 12 PATIENTS WITH MEVALONATE KINASE DEFICIENCY: SYMPTOMS AND TREATMENT WITH IL-1 INHIBITORS**

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Background: Mevalonate kinase deficiency (MKD) is a rare autosomal recessive autoinflammatory disease caused by mutations in MVK gene. MKD patients typically have an early onset of symptoms including recurrent episodes of high fever, abdominal pain, diarrhea and vomiting, arthralgia and lymphadenopathy (AIDAI criteria for HDIS). However, not all patients have typical symptoms at the time of onset. MKD treatment remains an unsolved problem, since none of the modalities previously used for MKD treatment are fully effective in the disease control.

Methods: We conducted a retrospective analysis of clinical features of twelve patients (6 females, 6 males) with genetically confirmed MKD. Nine patients received therapy with inhibitors of IL-1 (Anakinra and/or Canakinumab). One of the patients died from amyloidosis and macrophage activation syndrome (MAS) prior to treatment initiation, her diagnosis was verified post mortem.

Results: Ten patients had manifested with symptoms of MKD before the age of 1 year, one – at the age of 1.5 years, one – at three years of age. During the course of the disease all patients had periodic fever and peripheral lymphadenopathy (mainly cervical group), as well as abdominal pain, nausea/vomiting. Five patients had diarrhoea, sometimes with blood, one patient suffered from severe constipation. Rash was seen in eight patients, myalgia, arthralgia were observed only in six. Oral ulcers were noted in seven children. Three patients had neurological involvement, one patient had it as the main symptom. One patient had periorbital edema and hyperemia during attacks, which to our knowledge, have not been reported previously in MKD. One patient developed amyloidosis and MAS before IL-1 inhibitor treatment initiation, which led to her death. In patients receiving anti-IL-1 therapy AIDAI index decreased from 58.3±11.2 before to 1.5±1.4 after 6 month of therapy (p<0.003).

Conclusions: MKD symptoms can be variable and sometimes atypical, which requires physician's awareness. In our cohort of MKD patients anti IL-1 therapy was highly effective.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6790

**THU0546 IMPACT OF BONE LOCALISATION ON THE PROGNOSTIC OF LANGERHANS CELL HISTIOCYTOSIS: A MONOCENTRIC RETROSPECTIVE STUDY**


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Background: Langerhans cell histiocytosis (LCH) is a rare condition, and mostly affects children. Bone is the most commonly involved organ, with bone lesions in 50% of patients. In a recent work, Aricò et al. described that the probability of survival in children suffering from a multisystemic LCH with risk organ involvement was reduced if patient did not have any bony lesion [1]. There is no such a study within the first 6 months of life, one – at the age of 1.5 years, one – at three years of age. During the course of the disease all patients had periodic fever and peripheral lymphadenopathy (mainly cervical group), as well as abdominal pain, nausea/vomiting. Five patients had diarrhoea, sometimes with blood, one patient suffered from severe constipation. Rash was seen in eight patients, myalgia, arthralgia were observed only in six. Oral ulcers were noted in seven children. Three patients had neurological involvement, one patient had it as the main symptom. One patient had periorbital edema and hyperemia during attacks, which to our knowledge, have not been reported previously in MKD. One patient developed amyloidosis and MAS before IL-1 inhibitor treatment initiation, which led to her death. In patients receiving anti-IL-1 therapy AIDAI index decreased from 58.3±11.2 before to 1.5±1.4 after 6 month of therapy (p<0.003).

Conclusions: MKD symptoms can be variable and sometimes atypical, which requires physician's awareness. In our cohort of MKD patients anti IL-1 therapy was highly effective.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2238
Background: Familial Mediterranean fever (FMF) is a periodic fever syndrome caused by MEFV mutations. FMF may be associated with psoriasis in some cases. Previous study has shown that psoriasis was more common in the relatives of FMF patients [1].

Objectives: We aimed to investigate the prevalence of psoriasis among FMF patients and their relatives.

Methods: FMF patients followed at Hacettepe University Adult and Pediatric Rheumatology Departments between January and August 2016 were consecutively enrolled to this study. Demographic data, clinical manifestations, laboratory data and MEFV variant analysis were documented by medical file screening and face-to-face interview. The presence of psoriasis and psoriatic arthritis in patients and their relatives (first [Mother, father, children]-second [Brothers, grandchildren, grandfather and grandmother]-third degree [Nephew, uncle, maternal uncle, aunt, paternal aunt] relatives) and drug use history were also questioned. The patients were accepted to have psoriasis if the diagnosis was made by a dermatologist.

Results: 351 FMF patients (177 adults; 174 children) were included in this study (Table). 70.1% of adult patients were female, 29.9% were male. 53.4% of pediatric patients were female, 46.6% were male. The median age (min-max) of the adult patients was 35 (19–63), while the median age of the pediatric patient group was 10 (2–18). The onset age of symptom was 12 (0–39) in the adult group and 3 (1–14) in the pediatric group. The median age at diagnosis was 25 (2–52) in the adult group and 5 (1–18) in the pediatric group. Thirteen (3.7%) patients had psoriasis. Psoriasis was more common in adult patients than pediatric patients (p=0.02). Psoriasis was present in 22 (12.4%) of adult patients and 9 (5.2%) of pediatric patients (p=0.02). The frequency of psoriasis in one or more relatives of all FMF patients was found to be 8.8%.

Table: Demographic and clinical characteristics of 177 adult and 174 pediatric patients with familial Mediterranean fever (FMF)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adult patients (n=177)</th>
<th>Pediatric patients (n=174)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>124 (70.1)</td>
<td>93 (53.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>159 (88.9)</td>
<td>166 (95.4)</td>
<td>0.046</td>
</tr>
<tr>
<td>Fever</td>
<td>152 (85.5)</td>
<td>170 (97.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Anorexia</td>
<td>147 (83.1)</td>
<td>76 (43.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Arthritis</td>
<td>95 (52.5)</td>
<td>27 (15.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pancytopenia, neutropenia</td>
<td>104 (58.8)</td>
<td>14 (8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>57 (32.3)</td>
<td>6 (3.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pericarditis, n (%)</td>
<td>7 (4)</td>
<td>0 (0)</td>
<td>0.097</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>5 (2.8)</td>
<td>1 (0.6)</td>
<td>0.021</td>
</tr>
<tr>
<td>Parental consanguinity</td>
<td>44 (25)</td>
<td>25 (14.4)</td>
<td>0.012</td>
</tr>
<tr>
<td>Hemodialysis history in family</td>
<td>20 (11.3)</td>
<td>11 (6.3)</td>
<td>0.123</td>
</tr>
<tr>
<td>Associated with MEFV, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriasis</td>
<td>11 (6.2)</td>
<td>2 (1.1)</td>
<td>0.020</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>3 (1.7)</td>
<td>1 (0.6)</td>
<td>0.023</td>
</tr>
<tr>
<td>Psoriasis in any degree relatives</td>
<td>22 (12.4)</td>
<td>9 (5.2)</td>
<td>0.023</td>
</tr>
<tr>
<td>Psoriasis in 1° relatives, n (%)</td>
<td>5 (2.8)</td>
<td>8 (4.4)</td>
<td>0.44</td>
</tr>
<tr>
<td>Psoriasis in 2° relatives, n (%)</td>
<td>5 (2.8)</td>
<td>6 (3.4)</td>
<td>0.73</td>
</tr>
<tr>
<td>Psoriasis in 3° relatives, n (%)</td>
<td>15 (8.8)</td>
<td>1 (0.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusions: IL-1 has an essential role for signaling early T helper 1 (Th17) differentiation and Ashida et al. have shown the presence of Th17 cells in the upper dermis of psoriasis-like lesions in a patient with FMF [2]. We may speculate that high IL-1 in FMF may cause Th17 activation and stimulation of keratinocytes; and this may be the reason for higher frequency of psoriasis in FMF patients. Thirteen (3.7%) patients had psoriasis; more common than the normal population (0.40%) (p<0.0001). FMF increases the likelihood of psoriasis in relatives of FMF patient. Thus, FMF patients should be questioned and carefully examined for psoriasis lesions and psoriasis family history.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4235
8. GLM showed efficacy in DMARD-refractory AU (2nd line and further) and other biologic therapies (EL 3a; RG B-C).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2626

THU0550 | TREATMENT AND OUTCOMES IN SPANISH PATIENTS WITH IGG4-RELATED DISEASE


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Background: There is a lack of strong evidence on IgG4-related disease (IgG4-RD) treatment. There is only one clinical trial published, supporting the use of rituximab in American patients.

Objectives: To describe the treatments used in a series of patients diagnosed with IgG4-RD in Spain and to review the outcomes.

Methods: Clinical data were obtained from the Spanish Registry of IgG4-RD from October 2013 to January 2016, including 14 centers. Outcomes were assessed by a self-made response scale and the IgG4 responder index (RI). We categorized the outcomes as a total response (disappearance of the pseudotumoral lesions and absence of symptoms), partial response (<50% of regression of the tumefactive lesions or persistence of inflammation without symptoms) and no response if no changes were noticed. Treatment failure was considered if an increase of the activity, mass size or reappearance of symptoms were noticed among patients under treatment.

Results: Sixty-eight patients were included. Twenty-six (38%) were females, mean age 53.4 years. Thirty-six patients (52.9%) had systemic IgG4-RD involving >1 tissue. The most common involved tissues were: retroperitoneum (33%), orbito-facial region (28%), and maxillary and paranasal sinuses (24%). The main treatments used were: steroids (90%), surgery (45%) and azathioprine (19%).

All treatments were successful in achieving complete or partial response. The mean pre and post-treatment RI values were 6.7 (SD 4.6) and 1.9 (SD 2.6) respectively. There were no differences between systemic and non-systemic disease regarding the chosen treatments and the outcomes. The combination azathioprine-steroids was used in 12 patients. Fourteen percent of them relapsed (considering relapse as an increase of the inflammation, mass size or reappearance of symptoms, since the first month after the treatment withdrawal). The treatment failed in 28.6% of them. The combination steroids rituximab was indicated in 6 patients, showing no relapses and 1 treatment failure. The majority of patients treated with azathioprine or rituximab combined with steroids had a systemic disease (6.6 and 80%, respectively). Nearby all of them had already failed other previous treatments.

Conclusions: In our series, IgG4-RD has been treated with a myriad of drugs and procedures. The outcomes have been acceptable but the disease tended to relapse (21%) and the treatment failures were common (27%), probably due to the lack of well-defined treatment schemes supported by solid studies. Steroids were still the cornerstone of the treatment. Rituximab results were promising in our study but the number of patients was limited. Azathioprine, in combination with steroids, may be an accessible alternative treatment for IgG4-RD that should be explored. The RI correlated with the treatment outcomes and will have an important role monitoring future studies on IgG4-RD therapies.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1135

THU0551 | ARTHRITIS IN SARCOIDOSIS - A MULTI-CENTRE STUDY FROM INDIA


Background: 10–15% of sarcoid patients have associated arthropathy. Chronic arthritis is less described than from varying from 1–2% [1]. Data on articular manifestations of the disease from India is sparse.[2]

Objectives: To study the clinical manifestations of sarcoid arthritis patients from India.

Methods: Case records of patients presenting to ten rheumatology centres from 2005 to 2016 with sarcoidosis were retrospectively reviewed. Joint involvement was assessed clinically, classified as acute or chronic depending on duration of symptoms lesser or greater than 6 months respectively.

Results: A total of 103 patients with sarcoid arthritis were reviewed. 58 patients were classified as Lofgren syndrome. Pattern of joint involvement revealed ankle as most commonly affected joint. Six patients were classified in the early diagnosis and adequate treatment, but also the close follow up is important in managing FMF patients.

Disclosures of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5126

THU0552 | COMPLIANCE TO COLCHICINE TREATMENT IN FAMILIAL MEDITERRANEAN FEVER RELATED AMYLOIDOSIS

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Objectives: To assess the colchicine compliance in patients diagnosed with Familial Mediterranean Fever (FMF) related amyloidosis in our center.

Methods: Forty one patients (18 male/23 female) were questioned with regards to colchicine compliance by using retrospective scanning of patient chart.

Results: The mean age at the symptomatic onset of FMF was 7.13±5.24 years. The mean age at the time of the FMF diagnosis was 21.2±14.85 years. The mean age at the initiation of colchicine treatment was 21.4±2.14.75 years and the mean age at time of diagnosis of amyloidosis was found 29.5±7.12.14 years. Mean duration of the disease was 31.70±11.84 years and the duration of delayed diagnosis was 14.35±13.84 years. Maximum dose of colchicine was 2.10±0.673 mg/day. Compliance of colchicine treatment was poor in FMF related amyloidosis during their follow-up (11/25, %44), rates of skipped doses were also high (17/25, %68). Compliance rates were high in patients whom FMF and amyloidosis were diagnosed simultaneously (12/13, %93), rates of skipped doses were also low (4/9, %44). One of the patients diagnosed with FMF after the diagnosis of amyloidosis was compliant, two of them were non-compliant; with regards to skipping doses, two patients were found to be compliant and therefore never skipped doses while one was skipping doses. The compliance to colchicine was high in all FMF patients once amyloidosis was evident (31/41, %75), and rates of skipped doses were also low (12/41, %30). In five FMF patients, amyloidosis was observed despite their compliance to treatment.

Conclusions: The overall delay of diagnosis in FMF patients with amyloidosis was found to be high. Particularly the FMF patients who were diagnosed with amyloidosis during their follow up were found to have lower rates of compliance.

DOI: 10.1136/annrheumdis-2017-eular.1135
Low Alkaline Phosphatase Levels: Could it Be Hypophosphatasia?

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Background: Hypophosphatasia (HPP) is a rare inherited disorder of bone and mineral metabolism, caused by mutations in the ALPL (alkaline phosphatase liver type) gene, with reduction of activity of the tissue-specific isozyme of ALP (TNALP). The clinical presentation is variable and adult forms of the disease are usually milder than those affecting infants and children, easily overlooked or misdiagnosed, which can lead to erroneous therapeutic decisions.

Objectives: The primary objectives of our study are to estimate the prevalence of patients with adult forms of HPP in a group of patients with persistent hypophosphatasemia, to analyze their clinical and functional characteristics, and to compare these findings between those presenting or not these mutations.

Methods: In this Cross-sectional study, 1,536,711 ALP measurements owing to 386,356 patients were evaluated during a six-year period (2009–2015). Patients having at least two values below 35 IU/l and none above 45 IU/l constituted the study population. In total, 427 patients were included. Among them, 31 patients were excluded because of presenting causes of secondary HPP and 13 because of lost to follow-up. 108 patients were contacted by phone to fulfill a questionnaire about manifestations related to HPP and health assessment and in order to obtain blood samples to perform the genetic test.

Results: Demographic and clinical characteristics of both groups are shown in Table 1. Of the 108 patients evaluated, the genetic test results of 39 patients are available at this moment (the rest of the results are currently pending). 59% (23/39) tested positive for the genetic mutation. Despite data are still partial and although the results did not achieve statistical significance, we observed with a greater relevance a higher proportion of patients with HPP presenting with chronic bone pain, weakness, stress fractures and dental abnormalities. These data should promote a more proactive attitude towards detection of adult HPP.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5547

Immunoglobulin G4-Related Disease in Hong Kong – Clinical Features, Treatment Practices and Associations

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Background: Immunoglobulin (Ig) G4-related disease (IgG4-RD) is a systemic immune-mediated disease unifying what were previously considered to be unrelated individual organ disorders. The diagnosis and treatment of this characteristic fibroinflammatory condition continues to evolve, but generally remains an under-recognised disease. Local data outside Japanese and Caucasian populations is lacking and few studies have examined factors to predict disease severity or disease prognostication.

Objectives: We conducted this study to review the clinical features, treatment practices and factors associated with more extensive disease involvement in Hong Kong.

Methods: We retrospectively evaluated all patients with IgG4-RD over the past 13 years in our centre and combined this with patient data extracted from previous local publications. We analysed the clinical features, treatment practices and factors associated with the number of organ systems involved.

Results: One hundred and four patients (55 from our centre and 49 from literature review) were included. Patients were predominantly older men (mean age 61.9 years, male:female ratio 3:1). Hepatobiliary and pancreatic (40.4%), salivary gland (33.6%), lymph nodes (29.8%) and eye (19.2%) were the most common systems involved. Lymphadenopathy was associated with glucocorticoid use (OR=2.65, p=0.034). Over 90% of patients had a serum greater than 135 mg/dl and a G4-total IgG ratio greater than 8%. Pre-treatment serum IgG4 levels correlated with the number of organ systems involved (r=0.347, p=0.004), and specifically with salivary gland involvement (mean 1109 mg/dl vs. 599 mg/dl, p=0.012).

Conclusions: We identified pre-treatment serum IgG4-RD to be associated with multi-system disease, especially with salivary gland involvement, highlighting the potential for its use in disease prognostication and monitoring. The reason for this particular correlation remains uncertain but highlights the importance of screening for salivary gland involvement in all IgG4-RD patients, especially in the presence of higher serum IgG4 levels. We also describe the clinical features and treatment modalities of the largest cohort of IgG4-RD in Hong Kong thus far. Increased physician awareness and multidisciplinary efforts are required for optimal management of this masquerading disease. Future studies, especially focusing on treatment strategies within the contexts of different epidemiology and patient characteristics, are greatly needed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1120

Immunoglobulin G4-Related Disease in Hong Kong


Background: Validated disease activity scores and damage measurements were developed over time in order to allow a better way to evaluate patients and decide treatment plans. There are scores designed for a great variety of vasculitis like Birmingham Activity Score and others that are more specific like Behcet’s Disease Current Activity Form 2006.

Objectives: To evaluate the activity of the ability scores (BVAVs3rd and BDCAF) to predict damage, and the influence of immunosuppressive therapy on damage progression, as measured by VDI, in a group of patients with Behcet’s Disease.

Methods: A study was performed on a cohort of patients diagnosed with Behcet’s Disease under surveillance in one tertiary Rheumatology Centre, from a non-endemic area. All documented cases of Behcet’s Disease have been diagnosed according to The International Criteria for Behçet’s Disease. The Birmingham Activity Score (BVASv3, Behcet’s Disease Current Activity Form 2006 (BDCAF) and Vasculitis Damage index (VDI) were calculated for all patients. Spearman’s correlation coefficients were calculated between BVAVs3 Score, BDCAF, VDI and immunosuppressive treatment. Windows Excel/SPSS20.0 has been used to analyse the data.

Results: 20 patients were included in the study, with ages at the time of the...
SALIVARY GLAND ENLARGEMENT IN IGG4-RELATED 1, A. Angeles-Angeles 2, G. Hernandez-Molina 1.

VENOUS VESSEL WALL THICKNESS IN LOWER EXTREMITY

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4392

THU0556

SALIVARY GLAND ENLARGEMENT IN IGG4-RELATED DISEASE IS ASSOCIATED WITH MULTIORGAN INVOLVEMENT AND HIGH BASAL DISEASE ACTIVITY

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Background: IgG4-related disease (IgG4-RD) is an immune-mediated condition which clinical spectrum encompasses single or multiple organ involvement. Enlargement of major and minor salivary glands is one of the main disease features. Whether salivary gland enlargement is associated with systemic involvement has not been previously evaluated.

Objectives: To elucidate if salivary gland enlargement is associated with systemic disease.

Methods: We included patients with an established diagnosis (definitive: organ involvement, biopsy proven without high IgG4 levels, possible: organ involvement, biopsy proven and high IgG4 levels, probable: organ involvement, high IgG4 levels without histology) of IgG4-RD according to the Comprehensive Diagnostic Criteria, who regularly attend a tertiary referral center in Mexico City (2000–2017). We retrospectively collected demographics, clinical (organ involvement, disease activity, damage) and radiologic data by the IgG4 Responder Index [IgG4-RD RI] at basal and at 6 months of follow-up, number of relapses, remission and treatment), basal laboratory (C3, C4, ESR, PCR, total eosinophil count, IgG4 levels) as well as imaging and histologic data.

Results: We included 32 patients, 17 (53.1%) men, mean age 50.2±14.1 years and median disease duration 20.5 months. Seven (21.9%) have a definitive diagnosis, 12 (37.5%) probable and 13 (40.6%) possible. Overall we identified 21 anatomic sites affected, mainly pancreas 56.2%, lymph nodes 56.2%, lacrimal glands 37.5% and bile duct 34.2%. Salivary gland involvement was present in 12 (37.5%) patients (2 parotid, 3 minor salivary gland and 7 both). Among these patients, only 5 (41.6%) referred dry mouth and in 7 patients (58.3%) glandular enlargement was the onset disease feature. Salivary glandular enlargement was identified only radiologically in 5 patients (41.6%) and both clinical and radiologic in 7 (21.9%). Patients with glandular enlargement had a higher number of affected organs (6.5 vs. 2, p=0.001) and absolute eosinophils count (348 vs. 137.5/mm3, p=0.03), a higher prevalence of lacrimal glands (75% vs. 15%, p=0.002), lymph nodes (91.7% vs. 35%, p=0.002) and lung involvement (33.3% vs. 0%, p=0.01), azathioprine use (83.3% vs. 30%, p=0.003), as well as a higher basal IgG4-RD RI (12 vs. 6, p=0.001) and a longer delay in diagnosis (64 month vs. 6.5 months, p=0.001). We did not find differences regarding gender, age, IgG4 serum levels, C3, C4, ESR, PCR, anti-nuclear antibodies, rheumatoid factor, anticyclic citrullinated peptide antibodies and anti-CCP antibodies (negative in all patients); number of relapses, remission at 6 months and damage. We performed a logistic regression analysis (only including the number of organs, the basal IgG4-RD RI and time of follow-up) and found an association of salivary glandular enlargement with the basal IgG4-RD RI (OR 1.63, 95% CI 1.12–2.35, p=0.009).

Conclusions: Our results highlight the systeic involvement of IgG4-RD. Patients with salivary gland enlargement should be routinely screened for systemic involvement.

References:


THU0557

VENOUS VESSEL WALL THICKNESS IN LOWER EXTREMITY IS INCREASED IN MALE BEHÇET’S DISEASE PATIENTS WITHOUT VASCULAR INVOLVEMENT

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Background: Vascular involvement is seen in up to 40% of the patients with Behcet’s Disease (BD), especially in young males and is one of the major causes of mortality and morbidity. Lower extremity vein thrombosis due to vascular inflammation is the most frequent form of vascular involvement in BD. Recently, assessment of vessel wall thickness (VWT) and venous dilatation by US is suggested to be valuable in patients with vascular inflammation.

Objectives: In this study, we investigated whether vessel wall thickness or dilatation is present in young male BD patients prone to venous vascular disease.

Methods: Fifteen male patients with BD without major organ involvement followed in Marmara University Behcet’s Clinics, 14 healthy male controls and 14 male patients with Ankylosing Spondylitis (AS) were included the study. Bilateral lower extremity venous doppler ultrasonography (US) was performed by an experienced radiologist blinded to cases. No patient was under immunosuppressive treatment. Bilateral common femoral vein (CFV) wall thickness and great/small saphenous vein dilatations were examined. Behçet Syndrome Activity Score (BSAS) was used for the general assessment of disease activity.

Results: The mean disease duration was 9.1±6.3 years in patients with BD. BSAS was 28.9±19. Bilateral CFV wall thickness was significantly higher in BD patients compared to healthy controls and AS (p<0.001, p=0.002, respectively for right CFV; p=0.001, p=0.001, respectively for left CFV) (Table 1). The width of great and small saphenous veins were also higher in patients with BD, but without reaching statistical significance. There were no correlations between BSAS and wall thickness of any vessel.

Table 1. Venous wall measurements of lower extremity in study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BD Patients</th>
<th>Healthy Controls</th>
<th>Ankylosing Spondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>30.2±4.5</td>
<td>30.5±9.5</td>
<td>30.8±4.2</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>23.5±3.5</td>
<td>23.8±2.8</td>
<td>26.3±3.8</td>
</tr>
<tr>
<td>Right Common femoral VWT (mm)</td>
<td>0.69±0.4</td>
<td>0.26±0.08</td>
<td>0.28±0.07</td>
</tr>
<tr>
<td>Left Common femoral VWT (mm)</td>
<td>0.74±0.4</td>
<td>0.31±0.13</td>
<td>0.23±0.13</td>
</tr>
<tr>
<td>Right Great saphenous width (mm)</td>
<td>2.94±2.6</td>
<td>2.16±0.71</td>
<td>2.56±0.73</td>
</tr>
<tr>
<td>Left Great saphenous width (mm)</td>
<td>3.12±2.5</td>
<td>2.55±0.65</td>
<td>2.11±0.52</td>
</tr>
<tr>
<td>Right Small saphenous width (mm)</td>
<td>2.41±1.8</td>
<td>1.48±0.3</td>
<td>1.70±0.5</td>
</tr>
<tr>
<td>Left Small saphenous width (mm)</td>
<td>2.1±1.5</td>
<td>1.50±0.8</td>
<td>1.80±0.3</td>
</tr>
</tbody>
</table>

VWT: Venous wall thickness.

Conclusions: In preliminary results of our study, an increased venous vessel wall thickness in lower extremity was shown in male BD patients without vascular involvement. As a similar change was not observed in controls, we think, increased VWT might be an early sign of venous inflammation in patients with BD rather than a result of non-specific systemic inflammation. Further studies with a larger group of patients is planned.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4125

THU0558

THERAPEUTIC RESPONSE TO PREDNISONE ACCORDING TO THE AGE IN POLYMALIGNA RHEUMATICA: A CONTROLLED STUDY

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Background: Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disorder which usually affects patients over 65 years old. Different poor prognostic factors are involved in prednisone response including rapid decrease of prednisone dose or female sex. To date, there is no data relating the impact of the age on therapeutic response in PMR.

Objectives: The aim of this study was to compare, in case of PMR, the response to prednisone in patients younger than 60 to patients over 65 years old.

Methods: This was a retrospective, monocentric study. We included patients suffering from PMR, meeting ACR 2012 criteria. Patients were classified into two groups, one group with patients less than 60 years, and one group with patients over 65 years. We registered demographic, clinical, biological, and imaging data as well as therapeutic response profile. The local inflammation was evaluated with PET scan, by studying each anatomical site usually affected by PMR. Then, the rate of inflammation was scored from 0 to 3, according to the intensity of uptake compared to liver. The treatment was standardized. The initial dose of prednisone was of 0.3mg/kg during the first two weeks, then, the dose was slowly decreased
PHOTOGRAPHS OF SKIN LESIONS IN PATIENTS WITH AOSD

Figure 1. Erythema nodosum in a patient with AOSD. The lesion was a small, red, nodular elevation that was tender on palpation.

Figure 2. Maculopapular rash in a patient with AOSD. The rash was erythematous and itchy, and it resolved spontaneously.

Figure 3. Purpura in a patient with AOSD. The purpuric spots were purple and painful, and they disappeared within 1-2 days.

Figure 4. Hidradenitis suppurativa in a patient with AOSD. The lesion was a painful, inflammatory nodule that drained pus.

Figure 5. Digital vasculitis in a patient with AOSD. The involved fingers showed swelling, redness, and pain.

Figure 6. Oral ulceration in a patient with AOSD. The ulcer was painful, and it healed without scarring.

Figure 7. Eyelid swelling in a patient with AOSD. The eyelid was edematous and red, and it improved with corticosteroids.

Figure 8. Mucosal ulceration in a patient with AOSD. The ulcer was painful, and it healed with topical and systemic therapy.

Figure 9. Acneiform lesions in a patient with AOSD. The lesions were inflamed and pus-filled, and they responded to oral antibiotics.

Figure 10. Palmar erythema in a patient with AOSD. The redness was non-tender and it resolved with topical therapy.

Figure 11. Mucous membrane ulceration in a patient with AOSD. The ulcer was painful, and it healed with systemic antibiotics.

Figure 12. Thyroiditis in a patient with AOSD. The thyroid gland was enlarged and tender, and it improved with antithyroid medication.

Figure 13. Dental abscess in a patient with AOSD. The tooth was painful, and it resolved with dental treatment.

Figure 14. Nodular subcutaneous mass in a patient with AOSD. The mass was firm and tender, and it disappeared with corticosteroids.

Figure 15. Arthritis in a patient with AOSD. The joint was swollen and tender, and it improved with non-steroidal anti-inflammatory drugs.

Figure 16. Uveitis in a patient with AOSD. The eye was red and painful, and it resolved with topical corticosteroids.

Figure 17. Pericarditis in a patient with AOSD. The heart was enlarged and tender, and it improved with corticosteroids.

Figure 18. Pulmonary involvement in a patient with AOSD. The chest X-ray showed infiltrates, and it improved with systemic corticosteroids.

Figure 19. Renal involvement in a patient with AOSD. The urine showed proteinuria and hematuria, and it resolved with corticosteroids.

Figure 20. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 21. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 22. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 23. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 24. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 25. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 26. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 27. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 28. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 29. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 30. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 31. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 32. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 33. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 34. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 35. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 36. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 37. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 38. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 39. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 40. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 41. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 42. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 43. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 44. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 45. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 46. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 47. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 48. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 49. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 50. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 51. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 52. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 53. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 54. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 55. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 56. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 57. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.

Figure 58. Cardiac involvement in a patient with AOSD. The electrocardiogram showed ST-segment elevation, and it improved with corticosteroids.

Figure 59. Hematological involvement in a patient with AOSD. The blood count showed thrombocytopenia, and it improved with corticosteroids.

Figure 60. Neurological involvement in a patient with AOSD. The patient had a stroke, and it improved with anticoagulation and corticosteroids.

Figure 61. Gastrointestinal involvement in a patient with AOSD. The patient had abdominal pain and diarrhea, and it resolved with systemic corticosteroids.
INFLAMMATORY JOINT DISEASE TRIGGERED BY IMMUNE CHECKPOINT INHIBITORS

L. Tucker, S. Sacks, H. Al-Mossawi. Rheumatology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom

Background: Immune checkpoint modulation has changed the cancer therapy landscape in recent years [1]. Randomised controlled trials now demonstrate superiority to standard chemotherapy in squamous cell lung cancer, renal cell cancer [2], squamous cell head and neck cancer [3] and malignant melanoma [4]. However, blockade of these checkpoints results in a multitude of autoimmune sequelae including joint disease. As these therapies become first-line in oncology, they will likely place a significant burden on rheumatology services.

Objectives: To establish the prevalence of rheumatological manifestations of checkpoint blockade in a non-trial standard care setting.

Methods: All patients treated with Nivolumab or Ipilimumab (as single agent or in combination) in a standard care setting within a single centre were included and the number of suspected cases with rheumatological manifestations identified from the case records.

Results: 75 patients have been treated with Nivolumab single agent and 12 with combination Nivolumab plus Ipilimumab in Oxford over the last 15 months. Within that cohort, there were 7 suspected cases of joint disease giving a potential prevalence of 8%. Of those 7, 2 had confirmed disease requiring therapy, both had received Nivolumab/Ipilimumab combination. Both cases were rheumatoid factor and CCP negative. One case responded to prednisolone only, while the second case was refractory to steroids, methotrexate and infliximab but responded to IL-6 blockade with Tocilizumab.

Conclusions: We observed an approximate 8% prevalence of checkpoint mediated autoimmune joint disease within a relatively short follow up period of 15 months. The longer-term prevalence may be higher. Both patients requiring therapy had been exposed to Ipilimumab suggesting the inflammatory joint toxicity with this agent may be higher than that caused by Nivolumab.

Checkpoint immunotherapy is set to become the first-line standard of care in a number of cancers. This will lead to an increased demand for rheumatology services. The rheumatology community needs to develop strategies and trials in order to classify and treat these patients appropriately.

References:

Disclosure of Interest: None declared


THE IMMUNOMODULATION EFFECT OF BM-MSCS ON THE INFLAMMATORY CHEMOKINES OF RATS WITH COLLAGEN TYPE II INDUCED ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease. The DMARDs used to detect the level of RANTES, MCP-1 and IP-10 in serum of CIA rats.

Methods: All patients treated with Nivolumab or Ipilimumab (as single agent or in combination) in a standard care setting within a single centre were included and the number of suspected cases with rheumatological manifestations identified from the case records.

Results: 75 patients have been treated with Nivolumab single agent and 12 with combination Nivolumab plus Ipilimumab in Oxford over the last 15 months. Within that cohort, there were 7 suspected cases of joint disease giving a potential prevalence of 8%. Of those 7, 2 had confirmed disease requiring therapy, both had received Nivolumab/Ipilimumab combination. Both cases were rheumatoid factor and CCP negative. One case responded to prednisolone only, while the second case was refractory to steroids, methotrexate and infliximab but responded to IL-6 blockade with Tocilizumab.

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References:

Disclosure of Interest: None declared


REFERENCES

Disclosure of Interest: None declared

THU0565

MACROPHAGE ACTIVATION SYNDROME IN ADULTS WITH INFECTIOUS RHEUMATIC DISEASES

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Background: Macrophage activation syndrome (MAS) is a rare hyperinflammatory condition characterised by macrophage activation and inflammation resulting in a multi organ damage. MAS is considered to be a type of secondary hemophagocytic lymphohistiocytosis. It is a life threatening complication of various autoimmune or autoinflammatory rheumatic diseases, particularly systemic juvenile idiopathic arthritis (sJIA). Clinical manifestations include hepatosplenomegaly, increase of liver function tests, pancytopeny, neurological manifestations etc. High doses of glucocorticosteroids (GC), cyclosporine A (CyA) and etoposide are a treatments of choice. In refractory cases biologics may be an option, too.

Objectives: To point out this very rare but severe complication may occur also in adult patients with rheumatic diseases.

Methods: We report 4 successfully treated cases of adult MAS in rheumatic patients seen in our clinic during the years 2009 – 2016. A review of the literature regarding the efficacy of biologics in MAS treatment is also presented.

Results: We have observed four patients with MAS, two with adult onset. Still disease (AOSD), one with rheumatoid arthritis (RA) and one with SJIA. All of the patients were young (20 -33 years, mean age 27.0±5.61 years) with the duration of the primary disease ranging from 9 months to 11 years (mean 4.1±4.01 years). Three patients were in remission of the primary diseases prior to MAS manifestation, only one female patient and most severe one had MAS refractory to the combination GC + CyA and must have been added biological therapy (tocilizumab). We reviewed also another cases of MAS treated with biologics which have been published.

Conclusions: Our cases illustrate that MAS may develop also in adult patient with various rheumatic diseases (JIA, AOSD, RA) despite the low activity or remission. It occurs particularly in younger subjects. As the MAS symptoms may overlap with the symptoms of the primary disease (JIA, AOSD) the diagnosis may be difficult. MAS must be suspected in inflammatory rheumatic diseases patients with sudden increase of CRP, extreme increase of ferritin, liver function tests and decrease of platelets. An immediate treatment with GC, CyA and etoposide is essential; biologics (anakinra, canakinumab or tocilizumab) may be beneficial in refractory cases.

Acknowledgements: Supported by MHRCR Research project 00000023728.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5784

THU0566

CLINICAL AND GENETIC PHENOTYPES OF CHINESE PATIENTS WITH ADULT AUTOINFLAMMATORY DISEASES: REPORT FROM AN ADULT REFERENCE CENTER

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Background: Autoinflammatory diseases (AUID) is a group of disorders characterized by dysfunction of innate immunity which caused by gene mutations leading to coded proteins changes, finally causing uncontrolled systemic inflammation. AUID are usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, AUID have been hardly reported in the Chinese population.

Objectives: We aimed to characterize the clinical and genetic phenotypes of Chinese adult patients with AUID.

Methods: We prospectively evaluated clinical and genetic features of adult patients (>16 years) with monogenic AUID in the period April 2015 to May 2016, at the adult AUID center, Department of Rheumatology, Peking Union Medical College Hospital. The definite diagnosis of each disease was deemed to be present if both clinical phenotypes and genetic confirmation were met.

Results: During the study period, a total of 37 adult patients with clinical phenotypes suspicious of monogenic AUID requested for a genetic study. A final diagnosis of monogenic AUID was achieved in 16 patients (43.2% of patients tested). Two additional patients were diagnosed with periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome. Finally, all of 18 patients with AUID were diagnosed and followup in our center including 7 (38.9%) familial Mediterranean fever (FMF), 2 (11.1%) tumor necrosis factor-receptor associated periodic syndrome (TRAPS), 3 (16.7%) cryopyrin-associated periodic syndrome (CAPS), 3 (16.7%) NLPR12-autoinflammatory disease (NLPR12-AD), 1 (5.6%) Blau syndrome (BS), and 2 (11.1%) PFAPA.

Abstract THU0566 – Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Primary disease</th>
<th>Clinical manifestations of MAS</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>L.H., female</td>
<td>23</td>
<td>RA 11 years</td>
<td>MTX, fever</td>
<td>GC high doses (i.v. pulses), cyclosporine</td>
</tr>
<tr>
<td>P.V., male</td>
<td>20</td>
<td>RA 12 years</td>
<td>MTX, SAS, fever</td>
<td>GC high doses (oral), cyclosporine</td>
</tr>
<tr>
<td>P.D., male</td>
<td>32</td>
<td>AOSD 3 years</td>
<td>MTX, fever</td>
<td>GC high doses (oral), cyclosporine</td>
</tr>
<tr>
<td>V.N., female</td>
<td>33</td>
<td>AOSD 9 months</td>
<td>MP, AZA, fever</td>
<td>GC high doses (i.v. pulses), cyclosporine, tocilizumab</td>
</tr>
</tbody>
</table>

Disease onset during adulthood was observed in 15 (83.3%) patients, and the final diagnosis was delayed with a mean time of 10 years. Adult AUID patients usually carried low-penetrance mutations and gene variants were presented as heterozygosis or compound heterozygosis.

Conclusions: Adult AUID is not uncommon. FMF, CAPS, and NLPR12-AD are relatively common monogenic AUID in Chinese adult patients. Adult-onset AUID may be related to the presence of low-penetration mutations, being characterized by nonspecific incomplete or atypical disease patterns, leading to a delay of diagnosis. The interpretation of gene analysis in adult suspected AUID should be performed with caution, and if possible, should be referred to expert physicians in the field in adult AUID center.

References:

Disclosure of Interest: None declared

etanercept (2), golimumab (2), rituximab (2), abatacept (3), anakinra (1) and colchicum (1).

TCZ administration schedule was 8 mg/kg/4 weeks iv. (n=23), every 2 weeks (1) and subcutaneously 162 mg/2 weeks (1). TCZ was used in monotherapy (12) or combined with conventional immunosuppressive drugs (12). Most of intraocular inflammation parameters showed a rapid improvement after TCZ onset (Table), with corticosteroid-sparing effect (15.9±13.6 to 8.5±5.17 mg; p<0.001). Remission was achieved in 8 patients and improvement in 17. After one month of therapy, no side effects were observed.

Conclusions: TCZ seems a rapid effective treatment in refractory uveitic CME.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5215

THU0568 | PREVALENCE AND AUTOIMMUNE RHEUMATIC DISEASE IN PATIENTS WITH AUTOIMMUNE/INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS ASSOCIATED TO SILICONE BREAST IMPLANT

O. Vera Lastra, N.E. Torres-Oliva, G. Medrano-Rodriguez, M.D.P. Cruz-Domingo, J. Sepulveda Delgado, L.I. Jara, G. Medina. Internal Medicine, Hospital Especialidades CMN la Raza. Instituto Mexicano Seguro Social, Mexico City, Mexico

Background: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been associated with previous exposure to various agents such as silicone implants, which elicit chronic stimulation of the immune system against the synthetic material and can lead to the development of autoimmunity. This is particularly the case in genetically susceptible hosts.

Objectives: The aim is to describe prevalence, family background and main autoimmune rheumatic disease (ARD) associated to silicone breast implant (SBI).

Methods: We study a cohort of 150 patients with diagnosis of ASIA associated injection of mineral oil and silicone breast implant (SBI) in a tertiary Hospital, from 2011 to 2016. All patients were evaluated for the fulfillment of ASIA criteria. We only included patients with ASIA criteria associated with SBI plus criteria for an autoimmune rheumatic disease according to The American College of Rheumatology or EULAR. We excluded patient with ASIA and without ARD.

Results: There were 17 women patients with mean age 42.4±15.3 years, mean disease duration of disease 8±3 years. The clinical manifestation post SBI appeared 8±2 years later. The ARD were systemic sclerosis (SSc) 5, systemic lupus erythematosus (SLE) 3, rheumatoid arthritis (RA) 3, overlap syndrome 2 (SSc plus SS and SLE plus SSc, Sjogren syndrome 1, Takayasu arteritis 1, Still disease 1, antiphospholipid syndrome) UN update. Lupus 2017 Jan 1.

Disclosure of Interest: None declared


THU0569 | TREATMENTS OF UVEITIS IN A REFERRAL MULTIDISCIPLINARY UNIT IN NORTHERN SPAIN

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Background: Intraocular inflammation is one of the leading causes of visual impairment and blindness. Early and appropriate treatment is mandatory for avoiding complications.

Objectives: To describe the treatments prescribed in a cohort of patients with uveitis in a referral multidisciplinary unit from northern Spain.

Methods: Retrospective analysis of clinical records of patients evaluated in the Uveitis Multidisciplinary Unit of the Complejo Hospitalario of Navarra since January 2010 until March 2015. We analyzed the demographic characteristics and treatments received in the following 3 months after first visit.

Results: We identified 500 patients, 50% women with a mean age of 47.9 ± 16.4 years. The most frequent type of uveitis was anterior uveitis (65.4%), followed by posterior uveitis (17.6%), panuveitis (15.2%), and intermediate uveitis (1.8%). Considering the etiology, 31.2% were unclassified, followed by non-infectious systemic disease in 29.2%. During the 3-month follow-up, 904 treatments were prescribed. The most frequent treatment was oral prednisone (39%), followed by immunomodulatory treatment (27%), antimicrobial (14%), other treatments (10%) and less biological (3%), surgical (3%) and finally periocular (2%) and intravitreal (2%) treatment. Topical uveitic treatment: 350 patients received topical uveitic treatment, which accounts for 70% of patients. Among topical uveitic treatments, 15% of the samples were treated with topical steroids, 54% were topical steroids associated with another topical treatment, 2% were topical antiglaucomatous, 22% received other topical treatments and 27% of the sample did not receive topical treatment. Immunosuppressive treatment: 249 immunosuppressive treatments were prescribed. 50% of the patients received immunosuppressive treatment. Among the immunosuppressive treatments, 25% of the patients received oral steroids, 6% salazopyrine, 4% methotrexate, 5% azathioprine, 2% mycophenolate mofetil, 5% oral steroids associated with another immunosuppressant, 15% salazopyrine associated with another immunosuppressant, 1% other immunosuppressive treatment and 49% of patients did not receive any immunosuppressive treatment. Biologic Treatment: 25 patients in the cohort received biologic treatment, this represents 5% of patients. The biological treatment types were distributed as follows: 3% of the patients received adalimumab treatment, 1% received infliximab, 1% received other biological treatments, and 95% of the patients did not receive biological treatments. The number of treatments received per patient was analyzed and 50 patients (10%) received no treatment, 152 patients (30%) received 1 treatment, 189 patients (38%) received 2 treatments, 75 patients (15%) Had received 3 treatments, 23 patients (5%) had received 4 treatments, 9 patients (2%) had received 5 treatments and lastly 2 patients had received 6 treatments. The majority of patients received the combination of two treatments. Topical steroids and oral steroids were the most frequent treatments used.

Disclosure of Interest: None declared


THU0570 | ANAKINRA AS A SUCCESSFUL TREATMENT OF IDIOPATHIC RECURRENT PERICARDITIS: TAPER OR NOT TO TAPER? CASE SERIES AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

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Background: Idiopathic Recurrent Pericarditis can be challenging to treat in patients unresponsive to NSAIDs, aspirin, colchicine and immunosuppressive drugs. Patients become steroid dependent and tapering precipitates recurrences.

Objectives: To describe 2 adult cases of idiopathic recurrent pericarditis treated successfully with anakinra at the Keck Medical Center of USC.

Methods: Chart review of 2 patients with idiopathic recurrent pericarditis treated with anakinra at the Keck Medical Center of USC. Literature review on treatment of idiopathic recurrent pericarditis with anakinra.

Results: Case 1: 60-year-old Caucasian male had five episodes of idiopathic pericarditis in 2011. Serologic workup including ANA, anti-dsDNA, malignant and infectious workup was negative. Initially, patient responded to prednisone 0.4 mg/kg/day. Adding colchicine, azathioprine and methotrexate failed to prevent recurrence. Pericarditis developed whenever prednisone was tapered above 20 mg/day with bursts of CRP to 78 mg/dl. In 2012, Anakinra 100 mg sq daily resulted in immediate clinical response and normalization of CRP (1mg/dl). Prednisone and methotrexate were tapered with no recurrence. Gradually Anakinra was tapered to 3 times/week, then once a week, with no recurrence. Case 2: 37-year-old African male had 2 episodes of idiopathic pericarditis positive ANA 1:320, but negative anti-dsDNA, anti-smith, negative infectious and malignancy workup. Initially, patient responded to prednisone 0.6 mg/kg/day and colchicine. Tapering steroids below 40 mg/day resulted in recurrent pericarditis. Sequential addition of hydroxychloroquine, methotrexate, mycophenolate mofetil, and azathioprine failed to prevent recurrence, which followed in prompt resolution of symptoms, normalization of acute phase reactants and allowed successful tapering of steroids. Anakinra is being slowly tapered over the past year, with no recurrence.

Conclusions: Idiopathic recurrent pericarditis, which requires chronic corticosteroids, should be treated by adding another immunosuppressive agent. European Society of Cardiology guidelines recommend azathioprine, cyclophosphamide, methotrexate, hydroxychloroquine, cyclosporine or mycophenolate mofetil. Anakinra has demonstrated success in treating autoinflammatory and autoimmune diseases as well as idiopathic recurrent pericarditis.
Vassilopoulos et al reported three adult cases, where two were not treated with immunosuppressive drugs before anakinra and one had recurrence after anakinra was tapered. The Double Blind Placebo Controlled Clinical Trial AIRTRIP shows efficacy of anakinra in treating 11 patients with recurrent pericarditis over 14 months. It is unclear from this study if anakinra should be tapered or not. We suspect that once steroids and immunosuppressive drugs have been discontinued, anakinra should be gradually tapered over months, to avoid relapse. These experiences warrant further long term controlled trials in order to determine the efficacy and appropriate treatment regimen of anakinra for recurrent pericarditis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1141

**THU0571 THE CLINICAL FEATURES OF 223 BEHÈCHET’S DISEASE PATIENTS IN JAPAN**

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**Background:** Behçet’s disease is a systemic vasculitis disease with oral and genital aphthous ulcers, ocular involvements, skin manifestations, arthritis, gastrointestinal manifestations, neurogenic diseases and vascular involvements. Patients with Behçet’s disease are known to distribute along the ancient Silk Road, including Japan.

**Objectives:** We evaluate the clinical features of Behçet’s disease in Japan.

**Methods:** We retrospectively investigated 223 patients (108 males and 115 females) who fulfilled the International Criteria for Behçet’s Disease (ICBD) from January, 2006 until May, 2015. We examined sex, onset age, disease type, clinical symptoms, laboratory data and medications.

**Results:** Median age at diagnosis was 36.0±12.8 years old. Oral ulcers were the most common manifestation (98.2%), followed by genital ulcers (82.4%), ocular involvements (53.2%), erythema nodosum (53.2%), acneiform lesions (51.8%), arthritis (38.6%), gastrointestinal manifestations (25.1%), neurogenic diseases (9.0%), and vascular involvements (8.1%). The relationship of HLA and disease involvements was studied in 123 patients (41.5% with HLA-B51 and 24.1% with HLA-A26 positive).

**Table 1**

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Total (n=223)</th>
<th>Male (n=108)</th>
<th>Female (n=115)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral ulcers</td>
<td>218/222 (98.2%)</td>
<td>105/107 (98.1%)</td>
<td>113/115 (98.3%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Skin manifestations</td>
<td>190/220 (86.4%)</td>
<td>90/107 (84.1%)</td>
<td>100/113 (88.5%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>116/218 (53.2%)</td>
<td>49/105 (46.7%)</td>
<td>67/113 (59.3%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Acneiform lesions</td>
<td>113/218 (51.8%)</td>
<td>65/105 (61.9%)</td>
<td>48/113 (42.5%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>112/218 (51.8%)</td>
<td>5/105 (4.8%)</td>
<td>6/113 (5.3%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Ocular involvements</td>
<td>112/218 (51.8%)</td>
<td>68/108 (63.0%)</td>
<td>50/114 (43.9%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Genital ulcers</td>
<td>136/221 (62.4%)</td>
<td>56/107 (52.4%)</td>
<td>80/114 (70.2%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Arthritis</td>
<td>86/223 (38.6%)</td>
<td>33/108 (30.6%)</td>
<td>53/115 (46.1%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>56/223 (25.1%)</td>
<td>23/108 (21.3%)</td>
<td>33/115 (28.7%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Neurogenic diseases</td>
<td>20/223 (9.0%)</td>
<td>12/108 (11.1%)</td>
<td>8/115 (7.0%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Vascular involvements</td>
<td>18/223 (8.1%)</td>
<td>7/105 (6.6%)</td>
<td>11/113 (10.6%)</td>
<td>0.21</td>
</tr>
<tr>
<td>HLA-B51 positive</td>
<td>51/123 (41.5%)</td>
<td>32/61 (51.6%)</td>
<td>19/62 (30.6%)</td>
<td>0.006</td>
</tr>
<tr>
<td>HLA-A26 positive</td>
<td>28/116 (24.1%)</td>
<td>14/55 (25.4%)</td>
<td>14/61 (23.3%)</td>
<td>0.91</td>
</tr>
</tbody>
</table>

**Conclusions:** A higher incidence of gastrointestinal manifestations was observed in patients with Behçet’s disease in Japan. Patients with ocular involvements showed a higher association rate with neurogenic diseases, and lower with gastrointestinal manifestation. Most patients could continue TNFα inhibitor safely and effectively.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4216

**THU0572 ASSOCIATION BETWEEN RETROPERITONEAL FIBROSIS AND MALIGNANCY: A POSSIBLE PARANEOPLASTIC SYNDROME**

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**Background:** Retroperitoneal fibrosis (RPF) are associated with malignancies. However it is unclear what is the incidence of malignancies and whether particular malignancies are more prevalent in RPF.

**Objectives:** The objective of this study was to examine standardized incidence ratios (SIRs) of cancers in patients with retroperitoneal fibrosis (RPF) compared with age- and sex-matched general population.

**Methods:** Medical records of 111 patients diagnosed as having RPF by computed tomography, positron emission tomography and/or histological evaluation were reviewed. Forty one cases of cancers, which were confirmed by biopsies, were identified in 35 patients with RPF. SIRs were calculated for cancers, cancer types, and age at cancer diagnosis and stratified according to RPF-cancer intervals compared with general population in Korea.

**Results:** The mean ± SD age at RPF diagnosis was 59.1±14.9 years, and 69.4% of the patients were male. The cancer SIR (95% confidence intervals) in patients with RPF relative to age- and sex-matched individuals in the general population was 3.18 (2.23 - 4.41) [2.65 (1.17 - 3.94) in men; 5.34 (2.76 - 9.32) in women]. The most frequent cancer was unspecified urinary organ cancers with SIR of 72.41 (23814 – 17113.53). SIRs of multiple myeloma [27.58 (3.34 – 99.64)], renal cell cancers [9.53 (1.15 - 34.42) and unspecified cancers [16.92, (2.05 - 61.12)] were also significantly higher than in general population. Whereas cancers were most frequently developed in the eighth decade of life, the peak SIR was observed in the fifth decade (8.41, 229 – 21.53). When stratified by RPF-cancer intervals, SIR was 6.85 (4.55 - 9.90) within 2 years of RPF diagnosis, while no significant increase in SIR was found out of 2 years. Malignancies (n=28) within 2 year of RPF diagnosis included unspecified urinary organ cancer (n=4), lung cancer (n=4), colon cancer (n=3), renal cell cancer (n=2), pancreatic cancer (n=2), unspecified cancer (n=2), rectal cancer (n=1), gallbladder cancer (n=1), non-Hodgkin lymphoma (n=1), multiple myeloma (n=1), prostate cancer (n=1), thyroid cancer (n=1) and gastrointestinal stromal tumor (n=1). Predominant origin of these malignancies were epithelial cell types [transitional cell carcinomas (n=4), adenocarcinoma (n=16)].

**Conclusions:** RPF was strongly associated with cancers, particularly within 2 years of RPF diagnosis. Our results indicate that cancer screening in patients with RPF should be performed regularly up to 2 years after RPF diagnosis.

**References:**

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6168
characteristics of autoimmune diseases associated with sarcoidosis (sarcoidosis-overlap group) patients and isolated sarcoidosis (isolated sarcoidosis group) were analyzed and compared.

**Results:** Autoimmune disease was detected in 15 (11.5%) of 131 patients with sarcoidosis (15sjögren syndrome, 3 rheumatoid arthritis, 1 Still disease, 1 scleroderma, 4 dermatomyositis, 2 polymyositis, 1 temporal arthritis, 1 gout arthritis, 1 angitis and 1 hypertrophic osteoarthropathy). Most of these diseases occurred before (such as RA, AS, Still, FMF) and others after sarcoidosis diagnosis. Among 15 sarcoidosis patients with autoimmune disease 10 were female and 5 were male, the mean age was 50.8 years and mean disease duration was 10.6 months (range: 1-30 months). When compared with isolated sarcoidosis patients, more hand finger joint involvement, RF positivity, higher ESR and less NSAIDs usage were found in patients with sarcoidosis-overlap group (p=0.035, p=0.049, p=0.015, p=0.018 respectively). There was no statistically significant difference between the two groups when evaluated for demographic, clinical parameters and other treatment modalities.

**Conclusions:** Comorbid autoimmune diseases in patients with sarcoidosis may often be seen. These patients are characterized with more hand finger joint involvement, RF positivity, higher ESR and less NSAIDs usage. Therefore, in patients with a diagnosis of sarcoidosis, it is necessary for the physician to be careful and to make a wider differential diagnosis in terms of the presence of another underlying autoimmune disease. Multicenter, prospective studies involving large numbers of patients are needed to understand whether the association of sarcoidosis-autoimmune diseases is based only on coincidence or on a common etiological basis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1376

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**THU0574**

**CLASSICAL IMMunosuppression and Damage Progression in a Group of Patients Diagnosed with Behcet’s Disease**

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**Background:** Behcet’s Disease is a rare type of vasculitis that involves both arterial and venous blood vessels of all sizes. The type of organ involvement and overall disease activity evaluated in the clinical practice determine the course of treatment and the decision to initiate immunosuppressive therapy. Activity scores like Bingham Vasculitis Activity score (BVASv3), Behcet’s Disease Current Activity Form2006 (BDCAF), or damage indices like Vasculitis Damage Index (VDI) have been developed in this respect.

**Objectives:** To evaluate the ability of classical immunosuppressive therapy to prevent damage progression. To find the correlation between disease activity scores: BVASv3, BDCAF, long term treatment, immunosuppressant use and damage after remission, as calculated by VDI.

**Methods:** A study on a cohort of patients diagnosed with Behcet’s Disease from an Internal Medicine and Rheumatology Clinic was performed. Activity and damage scores, BVASv3, BDCAF and VDI after obtained remission, were calculated. The documented cases were diagnosed according to the International Criteria for Behcet’s Disease (ICBD). Windows Excel/SPSS20.0 (Spearman’s correlation) were used to analyse the data.

**Results:** The study included 16 patients treated with long term cortisone and immunosuppressive therapy. The mean age at the time of the diagnosis was 32.5±10.9 years and the disease activity was 62% (10 patients). Severe systemic involvement was present in 10 cases (Ophthalmological involvement-6cases, recurrent venous thrombosis-6cases, pulmonary vasculitis-1 case, severe cardiac involvement-1 case, central nervous system involvement-3cases) and all patients received classical immunosuppression (cyclophosphamide, azathioprine). The mean scores for BVASv3 and BDCAF at the time of the diagnosis were 9 (r=0.830, p<0.001). The use of immunosuppressive therapy due to severe organ involvement and long-term immunosuppression correlated stronger with BVASv3 and BDCAF (r=0.533, p=0.001). BDCAF calculated after remission was obtained. There was an important correlation between disease activity scores and damage (BVASv3-VDI r=0.687, p<0.001, BDCAF-VDI r=0.676, p=0.001). Types of treatment were evaluated, a comparison was made between long-term cortisone therapy and immunosuppression. There was a stronger correlation between long-term cortisone use and VDI than between immunosuppression duration and damage (r=0.472).

**Conclusions:** Damage progression is influenced by disease activity, as calculated by activity scores (BVASv3 and BDCAF). Classical immunosuppression is used for severe organ involvement and for limiting new organ lesions (once started). There was a stronger correlation between long-term cortisone use and VDI than between immunosuppression duration and damage. The damage index increased by irreversible organ damage due to disease activity and long term cortisone use, but not due to the immunosuppressive therapy.

**References:**


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**THU0575**

**EFFICACY OF RITUXIMAB IN RESISTANT PALINDROMIC RHEUMATISM: FIRST REPORT IN LITERATURE**

S. Sreenath1, S. Cherian1, G. Antony1, U. Momy2, P. Shenoy1. 1Centre for Arthritis and Rheumatism (CARE); 2Molecular Medicine, AIMS, Cochin, India

**Background:** Palindromic rheumatism (PR) although often considered as a benign disease can be severe and resistant to DMARDs in some patients. In these patients it can result in almost daily attacks, migrating from joint to joint resulting in poor quality of life. Rituximab has been proven to be effective in treatment of seropositive RA.

**Objectives:** To determine the efficacy and safety of Rituximab in patients with seropositive PR who had an inadequate response to CsDMARDs.

**Methods:** PR was diagnosed based on criteria proposed by Hannonen P et al. Seropositive (ACPA±RF positivity) PR patients who had active disease despite being treated with two Cs DMARDs for >3 months, were treated with Rituximab. Active disease was defined as >4 attacks per month requiring intake of NSAIDS. All the patients were started on 500mg of rituximab after baseline work up. If complete control of palindromic attacks was not achieved and B cells could not be detectable in the blood for flow cytometry another 500 mg infusion was given after 2 weeks. Patients were continued on maximum tolerable dose of DMARDS. Patients were given repeat infusion of Rituximab once the patient developed clinical relapses as evidenced by recurrence of palindromic attacks.

**Results:** Twenty three patients with a mean age of 44.6±13.51 yrs and mean disease duration of 5.47±3.25 yrs were included. All patients were positive for ACPA while 17 patients were positive for RF. These patients were on a background of minimum of 2 DMARDs; Despite the maximum tolerable dose of DMARDS they had mean attack rate of 5.30±2.38 attacks per month. During a mean follow up of 14.17±8.62 months seven patients required two infusions and three patients required three infusions. Of the 33 infusions 500 mg was effective in controlling the attacks majorly (88%) of the times. Seven patients required another 500 mg infusion after 2 weeks as initial 500 mg dose failed to achieve complete control of disease and B cell were not depleted in the peripheral blood. At one month follow up all patients achieved complete control of disease. Remission lasted for 10.33±5.75 months. When symptoms recurred patients were treated with rituximab again and all regained complete control of the symptoms. None of the patients evolved into RA during the study period. No serious adverse events were observed. Five patients experienced minor allergic reactions during infusion which were managed according to the standard protocol.

**Conclusions:** This case series indicates in patients of PR resistant to Cs DMARDS rituximab not only achieves disease control but also prevents progression to RA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5723

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**THU0576**

**THERAPEUTIC OPTIONS FOR PATIENTS WITH RARE RHEUMATIC DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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1Center for Rare Diseases Bonn (ZSEB); 2Institute of General Human Genetics; 3University Hospital Bonn, Bonn, Germany; 4Department of Oncology, Hematology and Rheumatology, University Hospital Bonn, Bonn, Germany; 5Department of General Practice and Family Medicine, 6Institute of General Practice and Family Medicine, 7Department of Palliative Medicine, 8Institute of Human Genetics, 9University Hospital Münster, Münster, Germany

**Objectives:** To determine the efficacy and safety of Rituximab in patients with seropositive PR who had an inadequate response to CsDMARDs.

**Methods:** PR was diagnosed based on criteria proposed by Hannonen P et al. Seropositive (ACPA±RF positivity) PR patients who had active disease despite being treated with two Cs DMARDs for >3 months, were treated with Rituximab. Active disease was defined as >4 attacks per month requiring intake of NSAIDS. All the patients were started on 500mg of rituximab after baseline work up. If complete control of palindromic attacks was not achieved and B cells could not be detectable in the blood for flow cytometry another 500 mg infusion was given after 2 weeks. Patients were continued on maximum tolerable dose of DMARDS. Patients were given repeat infusion of Rituximab once the patient developed clinical relapses as evidenced by recurrence of palindromic attacks.

**Results:** Twenty three patients with a mean age of 44.6±13.51 yrs and mean disease duration of 5.47±3.25 yrs were included. All patients were positive for ACPA while 17 patients were positive for RF. These patients were on a background of minimum of 2 DMARDs; Despite the maximum tolerable dose of DMARDS they had mean attack rate of 5.30±2.38 attacks per month. During a mean follow up of 14.17±8.62 months seven patients required two infusions and three patients required three infusions. Of the 33 infusions 500 mg was effective in controlling the attacks majorly (88%) of the times. Seven patients required another 500 mg infusion after 2 weeks as initial 500 mg dose failed to achieve complete control of disease and B cell were not depleted in the peripheral blood. At one month follow up all patients achieved complete control of disease. Remission lasted for 10.33±5.75 months. When symptoms recurred patients were treated with rituximab again and all regained complete control of the symptoms. None of the patients evolved into RA during the study period. No serious adverse events were observed. Five patients experienced minor allergic reactions during infusion which were managed according to the standard protocol.

**Conclusions:** This case series indicates in patients of PR resistant to Cs DMARDS rituximab not only achieves disease control but also prevents progression to RA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5723
two drugs, or standard therapy. The term "rare" was defined by the European Union as a condition that occurs in no more than 1 in 2,000 individuals. Two review authors independently assessed trial quality and extracted the data. We screened the search results and included studies if they met the selection criteria. If we identified two or more trials that investigated the same rare disease and used the same assessment tools we performed a meta-analysis.

Results: 135 studies were screened, of which 34 met the inclusion criteria. In total, we analysed data on 11 different orphan diseases, encompassing 2,324 participants. There was a high degree of clinical and statistical heterogeneity in these trials. Several sources of potential bias were identified in the included studies, for example, a lack of description of the blinding methods and allocation concealment, as well as the small size of the study populations. We included studies such as rituximab against cyclophosphamide in ANCA-associated vasculitides. These studies demonstrated a non-inferiority of rituximab. The meta-analysis resulted a combined odds ratio (OR) of 1.42 in favour of rituximab (95% CI). Further meta-analyses were possible for another 22 studies involving, among others, Behçet's disease, systemic sclerosis, cryopyrin-associated periodic syndromes, and giant cell arteritis. Compounds studied were immunosuppressants like corticosteroids, methotrexate and azathioprine, or biologicals such as nilotincept, infliximab, and canakinumab.

Conclusions: A high degree of evidence is hampered by the limited number of study participants in each trial. On the other hand, diseases such as systemic sclerosis, ANCA-associated vasculitides, or Behçet's disease had more high quality trials available. The amount of data for most other rare disease remains unsatisfactory. Several sources of potential bias were identified in the included studies, for example, a lack of description of the blinding methods and allocation concealment, as well as the small size of the study populations. We included studies such as rituximab against cyclophosphamide in ANCA-associated vasculitides. These studies demonstrated a non-inferiority of rituximab. The meta-analysis resulted a combined odds ratio (OR) of 1.42 in favour of rituximab (95% CI). Further meta-analyses were possible for another 22 studies involving, among others, Behçet's disease, systemic sclerosis, cryopyrin-associated periodic syndromes, and giant cell arteritis. Compounds studied were immunosuppressants like corticosteroids, methotrexate and azathioprine, or biologicals such as nilotincept, infliximab, and canakinumab.

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Hypocomplementemia is related to elevated serum levels of IgG subclasses other than IgG4 in IgG4-related kidney disease

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Background: IgG4-related kidney disease (IgG4-RKD) is a comprehensive term for renal lesions associated with IgG4-related disease [1]. IgG4-RKD is frequently complicated by hypocomplementemia [1, 2, 3], but its clinical significance and mechanisms have not been clarified.

Objectives: This study aimed to investigate clinical features of IgG4-RKD patients with hypocomplementemia compared with those without it, leading to clarification of the clinical significance and mechanisms of hypocomplementemia.

Methods: We extracted 25 patients with IgG4-RKD between September 2005 and December 2016 in our hospital. Based on the presence/absence of hypocomplementemia at diagnosis, we divided them into a hypocomplementemia group (n=11) and a normal complement group (n=14), and retrospectively analyzed various clinical features (age, sex, serum IgG levels, serum IgG4 levels, gaps between serum IgG and IgG4 level, ratio of serum IgG to serum IgG4, serum IgG subclasses, subclinical lesions, complement levels, urine protein and urinary occult blood, urinary β2-microglobulin, urinary N-acetyl-β-D-glucosaminidase, initial dose of prednisolone, serum IL-2R levels, multiple organ lesion) during the clinical course in the two groups.

Results: The patients comprised 18 men and 7 women with an average age of 67.5 years (range, 44 to 81 years). Serum IgG levels (397±1729 mg/dL vs. 215±758 mg/dL, p=0.001), gaps between serum IgG and IgG4 level (2992±770 mg/dL vs. 1482±444 mg/dL, p=0.001), serum IgG1 levels (2043±1025 mg/dL vs. 891±209 mg/dL, p=0.017), and the number of involved organs (4.1±1.1 vs. 2.9±1.1, p=0.018) were significantly different between the two groups, while serum IgG4 levels (795±477 mg/dL vs. 791±575 mg/dL, p=0.298) and serum creatinine levels (1.96±1.89 mg/dL vs. 1.90±0.48 mg/dL, p=0.298) were not. At relapse of renal lesions, although both groups showed serum IgG4 re-elevation, the hypocomplementemia group showed exacerbation of hypocomplementemia and re-expansion of gaps between serum IgG and IgG4 level, while the normal complement group did not.

Conclusions: Hypocomplementemia may be associated with multiple organ involvement and elevation of IgG subclasses other than IgG4 including IgG1 in IgG4-RKD. In patients who initially show hypocomplementemia, a decline in serum complement levels implies renal lesion relapse.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5549

WHAT WE SEE, WHAT WE LEARN, AND THE PREVALENCE OF RHEUMATIC DISEASES IN OUR POPULATION: A DIAGNOSIS CORRELATION STUDY

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Background: The postgraduate program in rheumatology aims learning of musculoskeletal and autoimmune disorders. In México, objectively-structured clinical examination (OSCE) is applied in postgraduate certification processes by the Mexican Board of Rheumatology annually [1]. Peláez-Ballestas et al. described an epidemiological study (COPCORD, Community Oriented Program for the Control of Rheumatic Diseases) of 19,213 individuals in 5 regions in our country where they found a prevalence of musculoskeletal pain in 25.5%, osteoarthritis in 10.5%, back pain in 5.8%, rheumatic regional pain syndromes in 3.8%, rheumatoid arthritis (RA) in 1.6%, and fibromyalgia in 0.7% [2].

Objectives: The aim of the study is to describe the student training in rheumatic diseases and correlate them with OSCE assessment and the prevalence of rheumatic diseases in our population.

Methods: An observational and analytical study was made between March 2014 to December 2015 in a single rheumatology training center at University Hospital. Student training was defined according to the times they evaluated patients with a determined diagnosis, this information was obtained by medical records. We categorize OSCE questions according to the rheumatic diagnosis. Finally, the two results were compared with prevalence of the rheumatic diagnosis according to COPCORD, which were registered according a score pain >4. We made descriptive statistics and a Spearman’s Rho to evaluate the correlations of the diagnosis frequencies by each category.

Results: We reviewed 6279 medical records, 854 (13.6%) were of first-time consultations, 306 (4.9%) were of follow-up and 5109 (81.5%) were from the 3rd consultation and higher. We found 334 patients to develop an educational smartphone app.

WHAT ARE THE PATIENTS’ ISSUES AND NEEDS RELATED TO THEIR BIOLOGICS (BDMARDS) AND METHOTREXATE (MTX) TREATMENT IN DAILY LIFE: A QUANTITATIVE CROSS-SECTIONAL SURVEY AMONG 344 PATIENTS TO DEVELOP AN EDUCATIONAL SMARTPHONE APP

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Background: MTX and bDMARDs are the core treatments of chronic inflammatory arthritis (IA). We lack information on the patients’ problems and needs in daily life, particularly on safety issues.

Objectives: 1-collect the most frequent issues 2-explore the patients’ perceptions on a dedicated smartphone application (SP App) 3-determine the profile of the patients interested.

Methods: The survey was conducted on line. The questionnaire was designed by rheumatologists, methodologists, anthropologists, members of patients association (AP) and included 1-a non-exhaustive list of potential issues in daily life (fever, vaccines, ...) and practical aspects 2-a list of potential use of the App 3-free opinions 4-Two self-administrated questionnaire to test patients’ knowledge on bDMARDS [1] and MTX [2].

Results: The survey was carried out from June to August 2016 on the websites of the PA. Non-associative patients were recruited by 3 rheumatologists who provided the internet link. 344 patients responded, 331 analyzed, 83% female, 50% had rheumatoid arthritis, 40% had spondyloarthritis, mean age 53 years, 60% were AP; 67% were treated with MTX; 70% had bDMARDS, 34% had MTX-bDMARDS combination. 66% of patients reported problems; 67% had needed help or advice. The main issues were infections (27%), vaccines (13%), surgery (10%), dental care (7%), self-administration (6%), conservation/travelling (9%) and skipped doses (5%). Among the 76% patients who have a SP, 80% use Apps and 32% Apps for their health. Among users, 87% patients would find an App useful to manage their treatment (36% rather agree and 51% strongly agree), 82% for symptoms requiring to stop their treatment, 93% for situations related to safety, 80% as a reminder of their treatment. 83% knew what to do in case of a missed dose, 77% to have a safety checklist before treatment administration, 66% to recall the modalities of self-injections. Patients interested in the App are younger (p<0.05) non-associative (p<0.05) and live in medium-sized cities (p<0.01).

No correlation was found with other sociodemographic characteristics, level of education, type/duration of arthritis or knowledge.

Conclusions: Two-third of patients with arthritis face issues related to their treatment especially in case of infections, vaccination, surgery and travelling. A dedicated App is considered useful by 87% patients who already have a SP. The potential use of the App may improve safety, adherence and self-management in daily life.

References:
Acknowledgements: Grant; French Society of Rheumatology with the institutional funding by Biogen, Nordic Pharma, Roche.

Descriptive statistics are in Table 1 and Figure 1, which included: medical consultations, OSCE assessment and a column with rheumatologic diagnosis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4257
the OSCE, we observed a moderate correlation. We considered it important to enhance the knowledge and improve the OSCE according to the most prevalent diseases to prepare the future rheumatologists.

References:

Disclosure of Interest: None declared


THU0582 2-YEAR ADHERENCE TO THE TREATMENT OF OSTEOPOROSIS FOLLOWING A THERAPEUTIC PATIENT EDUCATION PROGRAM

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Background: The management of osteoporosis requires drug treatment and changes in lifestyle. Adherence to medication does not exceed 50% at one year. Changes in lifestyle are rarely explored. Therapeutic requires a relay to continue the follow-up over several years.

Objectives: To improve the follow-up of the patient, we have created cooperation between the attending physician and the pharmacy pharmacist initiated by the patient himself.

Methods: We proposed a therapeutic patient education for patients treated for osteoporosis to participate in two half-day ETP sessions a year apart. Educational objectives are: The treatment of osteoporosis requires at least 5 years of treatment, and must be associated with the absorption of three dairy products per day, maintaining physical activity and preventing falls. Each participant in a therapeutic education session receives a follow-up notebook containing six doctor questionnaires and six pharmacist questionnaires. The patient remains the owner of the notebook. We were able to study the results of the 2-year questionnaires for 72 patients included in 2013 and 2014.

Results: 53/72 patients continue their treatment at 2 years. 4 patients died, 1 had an atypical fracture of the femoral shaft, 6 stopped treatment due to dental treatment, 3 had contraindications to any anti-osteoporotic treatment, 1 decided to discontinue treatment due to d Multiple Sclerosis, 11 decided to leave the program. 3 patients were lost to follow-up, ie 14/72 patients of whom we no longer have any news. Of the 53 patients who continued treatment, 24 sent back a doctor and pharmacist questionnaire to 2 years. 4 doctors and 2 pharmacists refused to complete the questionnaires. The study of pharmacist questionnaires received at 2 years shows that 83% of patients continue to consume 3 dairy products per day compared to 73% at 6 months, 65% maintained physical activity, 17% improved it, 9% decreased. The ground balance was satisfactory for 78% of patients compared with 71% at 6 months. 71% never forget their treatment, compared with 69% at 6 months, 8% wanted to stop their treatment, stable figure compared to questionnaires received at 6 months. All patients knew what their treatment was for at one year and 96% met the conditions for taking the medication. 69% do not forget it at two years against 86% at one year, thanks to the intervention of the pharmacist. Only 6% wanted to stop the treatment at two years due to side effects, 17% to 1 year, but did not stop after consultation with the doctor and/or pharmacist.

During the two-year follow-up, all patients were phone called at least once by a secretary, mostly several times. The notebook is driven by the patient himself, mainly on them report to the nurse that it give them an active role which afford them to continue the treatment.

Conclusions: 58% of the patients enrolled continue treatment at two years, 15% have stopped the treatment as a side effect. An active role given to the patient and a collaboration between physicians and pharmacists thus promote adherence to treatment and also changes in lifestyle.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1681

THU0583 EFFECT OF AN ONLINE EDUCATIONAL INTERVENTION IN THE KNOWLEDGE OF PATIENT REGISTRIES AND PATIENT-REPORTED OUTCOMES AMONG RHEUMATOLOGISTS

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Background: Patient-reported outcomes (PROs) have evolved into an essential element in managing rheumatoid arthritis (RA), working in concert with physician-based tools to assess disease activity and health-related quality of life [1].

Objectives: A study was conducted to determine whether an online educational intervention could effectively address a knowledge gap and an underlying educational need in applying data from patient registries including PROs in the management of patients with RA.

Methods: An online educational intervention focusing on advances in RA patient registries was developed and made available online. The intervention consisted of a 30-minute video-based roundtable discussion between 3 experts in treatment of RA. The intended audience was rheumatologists who treat patients with RA.

The educational impact was assessed by comparing participants’ responses to 4 identical paired pre- and post-assessment questions. Data representing a statistical sampling of the overall learner population was collected from 5/29/2015 through 8/13/2015. Statistical analysis comprised a paired (within-physician) 2-sample t-test comparing mean pre-intervention and post-intervention scores.

Results: Analysis of pre- versus post-activity responses by rheumatologists (n=36) demonstrated a significant improvement (P<0.05) in overall knowledge with a robust effect size (Cohen’s d=0.50). This activity resulted in increased knowledge surrounding several specific areas of RA management, such as drug safety, alternative means of collecting PRO data, and issues surrounding pregnancy in women with RA. The absolute percentage increases in correct individual responses to these topics (all P<0.05 except where noted), included:
- 33% increase (36% vs 69%) in rheumatologists who recognized the results from pooled registries in Europe – 11 registries from 9 countries – regarding the safety of tumor necrosis factor-alpha inhibitor therapy.
- 28% increase (36% vs 64%) in rheumatologists who recognized that biosensor-based devices can provide passive data regarding patient outcomes.
- 14% increase (47% vs 61%, P<0.037) in rheumatologists who identified the connected CORRONA-OTIS registries that provide information on patients with RA who become pregnant,
- 62% increase (19% vs 81%) in rheumatologists who identified that patient registry data can be used to support a risk mitigation strategy for prescribing a specific DMARD in patients who may become pregnant during treatment.

Conclusions: An online educational intervention was associated with significant improvement in knowledge levels of rheumatologists in several important aspects of RA management, including interpretation of data from patient registries and adverse effect profiles of approved therapies. Future directions for education include additional reinforcement regarding the roles for PROs in patient management, and assessing the impact of improved rheumatologists’ knowledge on care delivery and patient outcomes.

References:

THU0584 FIVE YEARS OF EXPERIENCE WITH THE LUPUS ACADEMY: AN EFFECTIVE MODEL FOR BUILDING A ROBUST COMMUNITY OF PRACTICE FOR GEOGRAPHICALLY DIVERSE LEARNERS

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Background: Systemic lupus erythematosus (SLE) is a complex yet low prevalence disease. Without a community of lupus specialists to establish consensus and guide best practices, rheumatologists have limited opportunities to develop skills and maintain expertise in SLE care.

Objectives: The objectives of this initiative were to 1) create an independent community of physicians interested in the pathogenesis, diagnosis, and management of patients with SLE and related conditions; 2) share insights and practical guidance for implementing evidence-based care; 3) develop needs-driven contin-
using medical education (CME) relevant to different levels of clinical expertise; 4) promote collaboration models with publishers to create space for dialogue and community building; and 5) involve patient advocacy groups to steer physician education and incorporate the patient voice into educational activities.

Methods: The Lupus Academy (http://lupus-academy.org) was established in 2011 as an independent CME initiative led by a Steering Committee of international experts in SLE.[1] Educational activities are designed around unmet clinical needs identified by the Steering Committee, learner survey data, and feedback from patient advocacy groups (including Lupus Europe).

Results: As of February 2017, the Lupus Academy has grown to a global community of >2,500 committed learners with an interest in SLE. The Steering Committee has guided the development and delivery of 5 2.5-day annual meetings; 4 1-day regional meetings; a meeting toolkit for learner-advocates to host meetings in their home regions; and 3 e-learning courses, with 2 additional courses in production. The 5th Annual Meeting of the Lupus Academy (6–8 May 2016) hosted 101 attendees from Europe, North and South America, and Asia. Learners reported that the learning objectives of the meeting were met (Figure). An assessment of educational effectiveness demonstrated improvements in clinical knowledge and competence (Moore’s Outcomes Levels 3/4) as a result of meeting participation: 67% of learners reported a commitment to implementing changes in clinical practice, 11% reported that the educational content reinforced their current practice, and 20% reported a willingness to modify their current practice with additional training.

The most recent meeting, the Lupus Academy Middle East Summit Conference (9–10 December 2016), hosted 153 attendees from 13 countries representing diverse specialties: rheumatology (53%), internal medicine (13%), nephrology (11%), clinical immunology (5%), and other (18%). The majority of learners agreed or strongly agreed that the meeting provided an effective platform for the discussion of new ideas in SLE (96%) and challenged the current thinking around lupus care (96%). Having attended this meeting, I am better able to:

1. Apply novel developments in scientific research around SLE in their clinical practice
2. Implement optimal diagnostic methods and optimal disease management of refractory lupus nephritis patients and of those patients with both SLE and rheumatoid arthritis
3. Increase comprehension in identifying difficult clinical cases from the broad spectrum of lupus patients and effectively manage them — including patients displaying exacerbations involving lungs, Gl, liver and CNS, as well as pauci and profound patients
4. Implement new therapeutic options inherited from other therapeutic specialties
5. Apply learning from other disease areas to achieve optimal treatments outcomes in patients with SLE

Conclusions: The Lupus Academy serves as an effective model for building a consortium-led, evidence-based educational resource and community of practice for rheumatologists, other physicians with an interest in SLE, and patient advocacy groups.

References:

Acknowledgements: Lupus Academy Steering Committee (http://lupus-academy.org/home/lupus-academy-steering-committee/).

Disclosure of Interest: R. Cervera Consultant for: GSK, UCB, AstraZeneca, Pfizer, Celgene, R. Furie Grant/research support from: AstraZeneca, Biogen, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, GlaxoSmithKline, Janssen, Mallinckrodt Pharmaceuticals, MedImmune, Pfizer, Sanofi, Takeda, UCB, Consultant for: Anthera, AstraZeneca, Baxalta, Biogen, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, EMD Merck, Estrella (Janssen), GlaxoSmithKline, Janssen, Mallinckrodt Pharmaceuticals, MedImmune, Novartis, Pfizer, Sanofi, UCB, Z. Amoura Grant/research support from: GSK, Amgen, BMS, Actelion, Roche, Teva, Lilly, Consultant for: GSK, Amgen, BMS, Lilly. A. Jacobson: None declared. E. Pozniak: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2073

THU0585 SAFETY OF BIOLOGICS AND CONVENTIONAL DMARDS: AN ETHNOGRAPHIC STUDY INVESTIGATING PATIENTS’ DECISIONS AND PRACTICES TO DEVELOP AN EDUCATIONAL SMARTPHONE APP


Objectives: We aimed to decipher the mechanisms of patients’ decisions and practices with their DMARDs to develop an educational smartphone application (SP App).

Methods: An ethnographic study was designed by 3 rheumatologists, 1 methodologist, and 1 qualitative sociologist. 21 patients who took part in a 1-day workshop in Uruguay who conducted the interviews. The study involved 21 patients (enough to reach saturation), recruited by diversity of clinical and sociological profiles. The panel included 16 women and 5 men, median age 46 years-old (extremes 26–70), 12 with RA and 9 with SpA (median disease duration 13 years, extremes 2–38). Nine patients were treated by bDMARD-cDMARD combotherapy. The interview was conducted using in-depth semi directive and biographic methods. The interview guide was constructed around 3 fields: 1 the organization of the patients’ everyday life with their disease, 2 the treatment practices, 3 the impact of arthritis on their social and professional activities and relationships. Interviews were recorded and transcribed for analysis.

Results: Patients play an active role in the management of their disease. They have to learn to live with it in order to control its impact and course. This learning progressively occurs throughout a non-linear 4-stages career: 1) from 1st symptoms to diagnosis, 2) search for the right treatment and the right focus 3) stabilization of the disease and the treatment, 4) dealing with a complication or an unexpected event. Back and forth between stages 2, 3 and 4 are frequent.

Background: Safety and adherence to DMARDs are critical for patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA). Few digital tools exist to help patients on these issues.

Objectives: We aimed to decipher the mechanisms of patients’ decisions and practices with their DMARDs to develop an educational smartphone application (SP App).

Methods: An ethnographic study was designed by 3 rheumatologists, 1 methodologist, and 1 qualitative sociologist. 21 patients who took part in a 1-day workshop in Uruguay who conducted the interviews. The study involved 21 patients (enough to reach saturation), recruited by diversity of clinical and sociological profiles. The panel included 16 women and 5 men, median age 46 years-old (extremes 26–70), 12 with RA and 9 with SpA (median disease duration 13 years, extremes 2–38). Nine patients were treated by bDMARD-cDMARD combotherapy. The interview was conducted using in-depth semi directive and biographic methods. The interview guide was constructed around 3 fields: 1 the organization of the patients’ everyday life with their disease, 2 the treatment practices, 3 the impact of arthritis on their social and professional activities and relationships. Interviews were recorded and transcribed for analysis.

Results: Patients play an active role in the management of their disease. They have to learn to live with it in order to control its impact and course. This learning progressively occurs throughout a non-linear 4-stages career: 1) from 1st symptoms to diagnosis, 2) search for the right treatment and the right focus 3) stabilization of the disease and the treatment, 4) dealing with a complication or an unexpected event. Back and forth between stages 2, 3 and 4 are frequent.

This learning implies a partnership-based doctor-patient relationship, and the development of specific skills around safety: dealing with health care system
Sanola (30-min training via the telephone with no further incentive to access the platform) or usual care (normal internet use without access to Sanola). The Sanola group pts used a home-based e-Case Report Form to record frequency of Sanola access, satisfaction with the platform (0–10 scale; 0= completely satisfied, 10= not satisfied), and barriers to use (from a pre-specified list). Baseline pt characteristics associated with increased use of the median) were analysed by univariate and multivariate logistic regression.

Results: 159 RA pts were randomised to the Sanola arm: mean±SD age was 56.1±13.1 years, disease duration was 15.0±11.5 years and 132 (83.0%) of pts were female. Mean DAS28 was 2.7±1.2 with 57.2% of pts in remission; 115 (72.3%) were taking a biologic; 23.3% had attended therapeutic education sessions; 15.7% were members of pt associations; and 53.5% had participated in university-level studies. Overall, 41 pts (25.7%) never accessed Sanola and 81 (50.9%) accessed the platform at least twice; median=2, mean±SD=4.4±11.3 controls. There was a noticeable investigator effect (0.3±0.2, 0–1 scale). Mean satisfaction with the platform was very high (1.5±1.5), with 90% scoring satisfaction > 3. One barrier was expressed in 11.8% of cases: “the platform is not useful for me since I am in remission”. In multivariate analysis, the only variable associated with greater usage of Sanola was being a member of a pt association: odds ratio [95% CI]= 1.4 [1.1–1.77].

Conclusions: A quarter of pts who participated in this trial to assess e-health did not access the platform whereas half accessed the platform at least twice. Pts expressed high satisfaction and the only barrier was lower usefulness when in remission. e-Health is a prominent tool for RA pts. In the context of offering additional services should also be explored in a further study.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: L. Gossec Grant/research support from: UCB Pharma, Lilly, Consultant for: AbbVie, BMS, Celgene, Janssen, Novartis, MSD, UCB, A. Cantagrel None declared, M. Soubrier declared, J. M. Joubert Employee of: UCB Pharma, B. Combe Employee of: UCB Pharma, B. Combe Grant/research support from: Merck Pfizer Inc, Roche-Chugui, Consultant for: Merck, Pfizer, Roche-Chugui, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Speakers bureau: Merck, Pfizer, Roche-Chugui, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Novartis, J. M. Berthelot None declared, D. Wendinger None declared, E. Dernis: None declared, L. Grange: None declared, C. Beauvais Speakers bureau: UCB Pharma, A. Perdriger: None declared, H. Nataf: None declared, M. Dougdados Grant/research support from: UCB Pharma, Abbvie, Pfizer, Lilly, Merck, Novartis, H. Servy Shareholder of: Sanola platform operating company; e-health services, Employee of: Sanola

The use of a portfolio among young rheumatologists: results of an EMEUNET survey

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Background: Portfolios are increasingly used in medical education. A portfolio may stimulate deep learning, deliver summative assessment and encourage reflection on clinical practice. A portfolio is seen as the key connection between the theoretical and clinical knowledge required and the assessment of clinical skills. A portfolio is useful in the context of the patient-physician relationship. In addition, a portfolio may stimulate the development of professional skills and encourage independent learning. A portfolio is also a time-effective tool for assessing levels of knowledge and skills. A portfolio is a tool that may be readily adapted for use in the context of the patient-physician relationship. A portfolio may be used at a national and international level.

Methods: A survey was sent by email to all EMEUNET (Emerging EULAR Network) members. EMEUNET is a group of young rheumatologists and researchers within EULAR-member countries. Descriptive statistics were used to analyse initial data collected (Nov-Dec 2016). Weighted averages were calculated (i.e. mean in which each item being averaged is multiplied by a number (weight) based on the item’s relative importance).

Results: 132 participants responded (64% female; mean age 33.5 years (SD 4.3 years); 34 countries). In total, 56.3% of participants were working as rheumatologists; 32.8% were rheumatologists in training. 49.6% of the participants indicated that a portfolio was already used by rheumatology fellows working at their hospital or institution; in [country], 93% of participants also used a portfolio at a national level. 50.4% of participants did not use a portfolio during their training; of these, 86.7% (strongly) agreed that a portfolio might be a useful tool. Several barriers for successful implementation of a portfolio were identified by the participants. The major barrier was that a portfolio was not developed at a national level, and if developed at a national level, there were often no incentives to use it (Table 1). According to participants, the top 3 competencies that should be collected and reflected upon in the portfolio were: written communication (highest importance; 0 not important – 10 extremely important); practical skills (e.g. ultrasound) (8.2); correct use of diagnostics and therapeutic armamentarium (7.9); clinical skills (e.g. history taking) (7.6). The skills chosen as the least important to be included in a portfolio were: information on management tasks (6.5); promoting hospital-based care (e.g. writing a protocol) (6.6); theoretical and clinical knowledge (6.7).

Conclusions: A portfolio is generally considered a valuable tool and half of the participants already work with it. However, several barriers may prevent optimal implementation. Developing a core set of rheumatology-oriented competencies and a template for a portfolio to be used across institutions and eventually countries could promote implementation and harmonize training.

Disclosure of Interest: None declared

References:

Disclosure of Interest: None declared

DO JUNIOR DOCTORS PRESCRIBE DISEASE MODIFYING ANTI RHEUMATIC DRUGS SAFELY?

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**Background:** Patients with rheumatic diseases occupy over 50,000 bed days annually in the National Health Service. Adverse drug events are major causes of harm to patients in hospitals and are associated with prolonged length of stay with higher costs. National Patient Safety Agency has issued several alerts regarding DMARDs and Methotrexate overdose remains a “never event”. Prescribing medications, including DMARDs for rheumatology patients, is one of the chief responsibilities of junior doctors.

**Objectives:** We undertook a pilot survey of junior doctors and medical students to understand their level of prescribing confidence with an aim to develop a teaching program.

**Methods:** Following a focus group discussion based on NPSA safety alerts and BSR DMARD monitoring guidelines, ten items were unanimously identified as core knowledge required for safe prescribing. A questionnaire was created based on these elements. Junior doctors and final year medical students were surveyed at our academic institution. Replies were compiled to ascertain their understanding of safe prescribing and troubleshooting DMARD related issues.

**Results:** 41 junior doctors of all grades and nine medical students contributed to the survey. Only 6/50 (12%) felt confident in prescribing whereas 16/50 (32%) had borderline confidence and remaining 56% felt it was beyond their expertise.

Of the 41 junior doctors, 19 (46%) had never even prescribed DMARD despite encountering such patients on the wards. Principal reasons for this included lack of confidence (40%), paucity of knowledge (15%) and no formal education (32%). Questions pertaining to safe prescribing were confidently answered by only 4/50 (8%) participants.

**Conclusions:** To our knowledge, this is the first survey to demonstrate that there are serious shortcomings in junior doctors’ understanding of safe DMARD prescribing. Inadequate training and hence poor confidence among front line medical staff remains the main cause of this issue. Despite consistent evidence suggesting that rheumatology teaching in medical schools has historically been poor and active measures taken in recent past to identify better ways to address the issues, this study highlights major knowledge gaps among everyday and future prescribers. Focused strategy and better training of junior doctors, both during and after graduation, are pivotal to providing better care for patients prescribed DMARDs during inpatient hospital stay.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1691

QUALITATIVE ASSESSMENT OF US-GUIDED INJECTION VIDEOS PUBLISHED ON VIDEO SHARING PLATFORMS

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**Background:** Ultrasound (US) guided injections are becoming widespread in the treatment of rheumatic articular disorders. US allows a real time assessment of the needle progression and increase the accuracy of the injection. Video sharing platforms can be sources of information and learning material for healthcare professionals as for patients.

**Objectives:** We conducted this cross-sectional study to assess the quality of educational resources on US-guided articular and periarticular injections published on video sharing platforms.

**Methods:** YouTube, Dailymotion and Vimeo were searched using predefined keywords on US-guided shoulder, elbow, wrist, hand, hip, knee, ankle and foot injections. The videos were classified according to their source. We determined the injection site and the explanations shown for each site. We collected information on patient positioning, equipment, needle, ultrasound settings and teaching material used by the author. When demonstration was performed live in patient, the compliance with the rules of asepsis and the accuracy of the injection were evaluated. Overall, videos were evaluated for quality on a 5-point ordinal global quality scale (GQS) (1 = poor quality to 5 = excellent quality). Results are given as median (min-max).

**Results:** We found 69979 results with the keywords. We screened 2802 videos by titles and included 153 videos (10:05 hours). Most of videos were published on Youtube (92.2%) and 82.4% included oral explanation. 53.6% videos were published by medical advertisement or profit companies and only 9.2% videos by university, professional organization or physician group. Among the 41.2% videos showing live demonstration of injection on the patient only 25.4% followed the strict rules of asepsis. When the videos included US cineloops of injection, 10.4% were performed live in patient only 25.4% followed the strict rules of asepsis. Very few videos gave details about information on the treatment, its risks and benefits. Strict aseptic techniques are rarely followed and the injection can be outside the target. Finally, we identified characteristics associated with the quality of the video that can be used to improve their educational impact in the future.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6396

DEVELOPING THE KOREAN LEEDS SATISFACTION QUESTIONNAIRE (KOREAN-LSQ) IN RHEUMATOID ARTHRITIS: A CROSS-CULTURAL VALIDATION USING RASCH ANALYSIS

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**Background:** The Leeds Satisfaction Questionnaire (LSQ) 1 is a patient-completed questionnaire designed to measure satisfaction among patients attending a rheumatology outpatient clinic. It was originally developed in the UK and it comprises 45 items grouped into 6 subscales: general satisfaction, information, empathy, technical competence, attitude, access and continuity.

**Objectives:** To undertake cross-cultural adaptation and validation of the LSQ in South Korea.

**Methods:** The adaptation of the LSQ from English into Korean was established according to guideline of cross-cultural adaptation of self-report measures. 2 Patients with RA were then recruited from an outpatient clinic of a university hospital in South Korea and Cross-cultural validation of the Korean-LSQ was carried out by Rasch analysis using the WINSTEPS program. Model data fit was determined by Infit and Outfit statistics (≥0.50 and ≤1.50). If the values of the Infit and Outfit are 1.00, the observed score perfectly fit the expected model. The unidimensionality of the scale was determined by separation index (SI ≥2.00) and reliability (RI ≥0.80).

**Results:** An adequate conceptual equivalence was achieved following the adaptation process. The dataset for validation comprised 125 patients, 103 (82.4%) of whom were female, mean (SD) age =47.2 (12.5) and disease duration =52.8 (69.4) months. Forty-item of the 45 items had acceptable fit statistics (individual item data not shown). The individual items overall had good separation index and reliability (SI =-5.98 and RI =0.97). Analysis of the 6 subscales of the Korean-LSQ resulted in good fit to the Rasch model (Table 1), high internal consistency and unidimensionality (Person SI =2.31 and RI =-0.84; item SI =-5.44 and RI =-0.97).

**Conclusions:** Fit to the Rasch model confirmed that the construct validity, reliability, and unidimensionality of the Korean-LSQ were preserved after the adaptation process. The Korean LSQ is a valid and reliable tool for measuring satisfaction with care among patients with RA in South Korea.

**References:**

**Acknowledgements:** This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI16C0061).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4799

Table 1. Fit statistics for testlets

<table>
<thead>
<tr>
<th>LSQ subscales (testlets)</th>
<th>Infit</th>
<th>Outfit</th>
<th>Point-biserial correlation</th>
</tr>
</thead>
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<tr>
<td>LSQ_general</td>
<td>1.12</td>
<td>0.90</td>
<td>1.12</td>
</tr>
<tr>
<td>LSQ_information</td>
<td>1.05</td>
<td>0.40</td>
<td>1.05</td>
</tr>
<tr>
<td>LSQ_empathy</td>
<td>0.64</td>
<td>-3.05</td>
<td>0.59</td>
</tr>
<tr>
<td>LSQ_technical competence</td>
<td>0.16</td>
<td>0.40</td>
<td>1.05</td>
</tr>
<tr>
<td>LSQ_attitude</td>
<td>1.06</td>
<td>0.50</td>
<td>0.91</td>
</tr>
<tr>
<td>LSQ_access&amp;continuity</td>
<td>1.05</td>
<td>0.50</td>
<td>1.08</td>
</tr>
</tbody>
</table>

**MNSQ** = mean-square; For model fit: MNSQ ≤0.50 and ZSTD PTMEA CORR. ≤2.00
THU0595  THE VIEWS AND PERCEPTIONS OF NON-SPECIALIST, HOSPITAL-JUNIOR DOCTORS ON JOINT ASPIRATION OF THE ACUTE HOT-SWOLLEN-JOINT, AND THEIR TRAINING IN THIS CLINICAL SKILL

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Background: BSR guidance on managing hot-swollen-joints recommends early joint aspiration (arthrocentesis) to rule out septic arthritis and avoid morbidity and mortality. In such patients, the initial assessment is often performed by junior doctors prior to specialist review. Previous audit suggests poor adherence to recommended practice. To explore this, a previous quantitative survey in 2 hospitals found low self-reported confidence at managing hot-swollen-joints in 72 of 140 (52%) respondents; 58 (42%) participants reported inadequate exposure, and 43 (31%) inadequate training. There is limited research exploring the reasons behind poor uptake of arthrocentesis by junior doctors.

Objectives: To determine the perceptions of junior doctors about joint aspirations, their training to perform this important skill and how training could be improved

Methods: The focus group included two foundation doctors, two senior house-officers and two registrars. Focus group questions were developed from themes that emerged from our previous quantitative survey. The session was recorded using an iPhone, then anonymously transcribed verbatim. The transcript was analysed using an emergent coding technique drawn from grounded theory approach. The data was coded over three passes.

Results: Decision to aspirate a joint appeared to be influenced by internal and external factors. Internal factors included their previous experience, which was variable with one who “did 7 aspirations” and another who “had not had any experience at all.” Other factors like anatomical knowledge, level of seniority and prior training were presented. Negative emotions emerged with participants using words like “weary,” “anxious” and “scary,” particularly “fear of serious consequences” when describing joint aspiration.

External factors included procedure-related factors like technical difficulty, and the type of joint to be aspirated. Consensus suggested that all joints except the knee should be left to the specialist. Context-related factors included time constraints. The group emphasised the importance of recurrent exposure and opportunity to practice aspirations. Availability of supervision influenced the decision to aspirate, particularly if by the rheumatologist.

Training in arthrocentesis appeared to be inconsistent. Positive comments included the support of structured training experiences by an expert using simulation, immediate feedback followed by practice. Negative comments emerged such as training was inconsistent and of poor timing, or trainees lacked the opportunity to subsequently practice. Participants then proposed methods of how to improve training in arthrocentesis:

Conclusions: The decision to aspirate is a complex interaction between internal and external factors combining knowledge, attitudes and emotions with circumstances and context. The participants emphasised training in knee aspirations, but not other joints due to lack of exposure. Immediate feedback during training in arthrocentesis is key. Inability to continue regularly practicing the procedure in real patients may be a barrier to retaining the skill. A review of training in joint aspiration may be required in order to improve uptake of this skill in practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1250

THU0596  RHEUMATOLOGY SPECIALTY TRAINING IN EUROPEAN UNION COUNTRIES

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Background: The Union of European Medical Specialists (UEMS) seeks through its specialty Sections and Boards (S&B) to enhance the training of its doctors and to encourage and support the movement of doctors between countries. The Rheumatology S&B has delegates from all EU countries and has developed a document (European Training Requirements (ETR) – at uemsrheumatology.eu) that provides guidance about the rheumatology curriculum.

Objectives: To determine:

1. The extent of use of the Rheumatology ETR by EU countries
2. The extent of use of logbooks in recording the progress of a trainee
3. If training centres are accredited
4. If national assessment programmes exist for trainees
5. If a country has quality assurance and enhancement processes in rheumatology training

Methods: A questionnaire was sent to all S&B members asking questions in relation to each of the objectives, with one follow-up questionnaire to non-responders. Verification of responses as well as obtaining responses from continuing non-responders occurred in December 2016.

Results: Nineteen countries responded. Most (18/19) have developed and implemented their own curriculum, often with the influence of the ETR, and also are using a logbook to record the progress of trainees. Training Centres are required to undergo accreditation in 15/19 countries. Another three countries are planning to introduce this. One country does not have an accreditation programme. After accreditation only 8 countries have quality assurance (QA) and enhancement (QE) programmes. In one of these the QA and QE programmes are variable. Two other countries are planning to enhance such processes. In 14 countries trainees are assessed to determine their suitability to become specialists. In one of these countries the approach is variable. Two other countries are planning to introduce assessments. Three countries do not assess their trainees.

Conclusions: Most EU countries have implemented their own, and varied, curricula for rheumatology training. All countries either use or are planning to use a portfolio, again variable in nature, to record trainees’ progress. Thus, it appears that at present any pan-European standardised curriculum or logbook will be of limited use.

Most countries require training centres to undergo accreditation. However, less than half of the countries have a continuation of quality assurance or quality enhancement processes after accreditation with some countries it seems having no plans to do so.

At present, a specialist in one European country is required by European law to be recognised as such in another. This study did not determine the nature of the assessments undertaken in different countries but this is not of current relevance within Europe as regards the possible movement of a doctor from one country to another for professional reasons.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3314

THU0597  FLIPPED LEARNING: CAN RHEUMATOLOGY LEAD THE SHIFT IN MEDICAL EDUCATION?

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Background: Flipped Classroom is a model that is quickly gaining recognition as a novel teaching approach among health science. Flipped learning turns the usual teaching model on its head. The idea is that students learn new content outside the classroom (usually online) and then tackle assignments in lessons, giving tutors more time to help them with aspects they don’t understand.

Objectives: 1. to implement a flipped classroom teaching for rheumatology topics for both under and postgraduate education. 2. to evaluate outcomes of teaching using a post-flipped classroom assessment and a student perceived effectiveness and satisfaction questionnaire.

Methods: Ten online videos on topics of how to take rheumatology history, individual joint examination, handling cases of monoarthritis and polyarthritis, and metabolic bone disease were made available for the students. 39 undergraduate and 35 postgraduate trainees were included in this educational activity. The students were exposed to online lecture content prior to the class-time active learning session. The teaching session adopted an interactive learning environment and the course instructor served as a facilitator rather than a dominator for the instructional process, provided in-class applied learning opportunities and offered time for feedback/guidance to students. Evaluation of the teaching session was assessed using a scenario based learning and an evaluation check list. The students were asked to complete a questionnaire based on a 5-point Likert scale: 1 (strongly disagree) to 5 (strongly agree) to assess for their perceived effectiveness and satisfaction.

Results: There was no significant difference regarding socio-demographics between the 2 students’ groups included in this study. Outcomes of the flipped learning revealed that 94% of the students viewed the videos prior to the class session, and 96% attended the education sessions in comparison to 86% attendance in the traditional group. Students reported an increase in the flipped classroom model. Students’ perceived effectiveness and satisfaction scores were significantly higher among the flipped learning in contrast to the traditional teaching comparative group (4.9 vs 4.3, p<0.05). Similarly, analysis of the students’ assessment scores after the scenario based learning sessions was 4.8 in the flipped classroom model compared to the students taught by traditional methods (p<0.01).

Conclusions: Implementation of the flipped learning for the rheumatology topics demonstrated a successful and promising platform for using technology to make better use of the students’ time, and for increasing their satisfaction with the necessary didactic learning. Active learning increases student engagement and can lead to improved retention of knowledge.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4501
CUMULATIVE ADVERSE CHILDHOOD EXPERIENCES ARE ASSOCIATED WITH POOR OUTCOMES IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Adverse childhood experiences (ACEs) are associated with poor adult health status and onset of rheumatic diseases. There has been no research associating ACE with outcomes among adults with systemic lupus erythematosus (SLE).

Objectives: To characterize relationships of ACE and health outcomes of disease activity, damage, quality of life and depression in SLE patients.

Methods: Data were derived from the California Lupus Epidemiology Study (CLUES), a population based, multi-ethnic cohort of patients with SLE. Participants completed self-report measures of SLE activity (Systemic Lupus Activity Questionnaire; SLAQ), damage (Brief Index of Lupus Damage; BILD), quality of life (SF-36), depression (Patient Health Questionnaire; PHQ9) and sociodemographics. They completed the Adverse Childhood Experiences (ACE) survey, a validated 10-item scale covering 3 domains (abuse, neglect and household demographics). They completed the Adverse Childhood Experiences (ACE) survey, a validated 10-item scale covering 3 domains (abuse, neglect and household demographics).

Results: The 166 CLUES participants were mostly women (89%) and were racially/ethnically diverse (31% non-Hispanic White, 22% Hispanic, 15% African American, 31% Asian American). Mean age was 44±14; mean age at diagnosis 28±12. The median ACE score was 1 (30% had a score of 0 or higher). ACE scores >4 were more common in Hispanic (27%) and African American (32%) participants (p<0.01) compared to other races/ethnic groups, and in participants with poverty level incomes (61% vs 13%, p<0.001); but did not differ by education or age at study entry or diagnosis. Higher overall ACE scores were associated with greater SLE activity and damage, poorer quality of life, and higher levels of depressive symptoms. For each ACE domain, increasing scores were generally associated with worse outcomes, but did not always reach statistical significance (Table).

Table 1. SLE Outcomes by Adverse Childhood Event (ACE) Scores and Domains

<table>
<thead>
<tr>
<th>Score n</th>
<th>SLAQ</th>
<th>BILD</th>
<th>SF-36</th>
<th>PHQ9</th>
<th>p-value</th>
</tr>
</thead>
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<tr>
<td>Total ACE score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>66</td>
<td>60.6 (6.2)</td>
<td>1.7 (2.0)</td>
<td>46.0 (10.5)</td>
<td>4.3 (4.1)</td>
</tr>
<tr>
<td>1</td>
<td>31</td>
<td>69.5 (5.9)</td>
<td>1.4 (1.5)</td>
<td>44.3 (8.5)</td>
<td>4.8 (4.0)</td>
</tr>
<tr>
<td>2–3</td>
<td>39</td>
<td>11.2 (7.6)</td>
<td>1.7 (2.1)</td>
<td>41.0 (10.5)</td>
<td>7.8 (5.6)</td>
</tr>
<tr>
<td>4+</td>
<td>10</td>
<td>11.8 (8.0)</td>
<td>3.0 (2.9)</td>
<td>38.1 (11.1)</td>
<td>7.3 (4.8)</td>
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<tr>
<td>Household Challenges</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>66</td>
<td>60.6 (6.2)</td>
<td>1.7 (2.0)</td>
<td>46.0 (10.5)</td>
<td>4.3 (4.1)</td>
</tr>
<tr>
<td>1</td>
<td>33</td>
<td>91.6 (6.6)</td>
<td>1.8 (2.2)</td>
<td>42.3 (8.8)</td>
<td>6.3 (5.7)</td>
</tr>
<tr>
<td>2–3</td>
<td>24</td>
<td>11.5 (8.0)</td>
<td>2.4 (2.2)</td>
<td>40.3 (10.6)</td>
<td>7.6 (5.1)</td>
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<tr>
<td>p-value</td>
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<td>0.001</td>
<td></td>
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<tr>
<td>Neglect</td>
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<td></td>
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<tr>
<td>0</td>
<td>66</td>
<td>60.6 (6.2)</td>
<td>1.7 (2.0)</td>
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<td>4.3 (4.1)</td>
</tr>
<tr>
<td>1</td>
<td>33</td>
<td>11.6 (7.0)</td>
<td>2.4 (2.2)</td>
<td>37.7 (9.8)</td>
<td>8.1 (4.8)</td>
</tr>
<tr>
<td>2–3</td>
<td>24</td>
<td>9.8 (7.4)</td>
<td>1.6 (0.9)</td>
<td>42.2 (5.2)</td>
<td>6.4 (2.6)</td>
</tr>
<tr>
<td>p-value</td>
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<td>Abuse</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>66</td>
<td>60.6 (6.2)</td>
<td>1.7 (2.0)</td>
<td>46.0 (10.5)</td>
<td>4.3 (4.1)</td>
</tr>
<tr>
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<td>26</td>
<td>10.1 (6.3)</td>
<td>1.7 (1.9)</td>
<td>38.8 (10.4)</td>
<td>8.1 (4.9)</td>
</tr>
<tr>
<td>2–3</td>
<td>26</td>
<td>13.9 (7.6)</td>
<td>3.0 (3.2)</td>
<td>37.5 (10.6)</td>
<td>6.9 (4.5)</td>
</tr>
<tr>
<td>p-value</td>
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<td>0.04</td>
<td>&lt;0.001</td>
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<td></td>
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</tbody>
</table>

Zero-level excludes responders with scores in other ACE domains.
Conclusions: Adverse childhood experiences are reported frequently in individuals with SLE; accumulation of adverse experiences is associated with poor SLE outcomes. Higher scores in each domain, especially childhood neglect or abuse, were associated with poorer health measures in adulthood. Further research regarding ACE patterns and SLE outcomes is warranted.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5568

THU0601 CARDIOVASCULAR SCREENING AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS: TO WHAT EXTENT DO PATIENTS FOLLOW RECOMMENDATIONS?

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Background: Patients with inflammatory arthritis (IA) have a substantially increased risk for cardiovascular (CV) disease and consequently regular screening is recommended (1).

Objectives: To investigate whether patients with known IA and high CV risk follow the recommendation, given in a nurse-led CV risk screening consultation, to consult General Practice in order to reduce their CV risk. Furthermore to investigate the influence of socioeconomic position and gender.

Methods: A retrospective study comprising outpatients at King Christian X’s Hospital for Rheumatic Diseases, Graasten, Denmark, diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or spondyloarthritis (SpA), who had participated in at least one screening consultation based on the EULAR recommendations (1) between 1st of July 2012 and 1st of July 2015. The primary outcome was a consultation with their GP and at least one intervention of relevance for CV risk within 3 months after the screening consultation.

Results: 1266 patients, 18–85 years of age, were included; 72.5% with RA and 27.5% with SpA or PsA. Of the 447 (35%) with high risk of CV disease, 60% consulted their GP after the screening visit compared to 55% for the 819 patients with low risk of CV disease. Of the 60% of patients with high risk who consulted their GP, 41% had at least one relevant intervention. Education >10 years increased the odds for non-compliance (Odds Ratio [Confidence interval]) (0.72 [0.56;0.92], p=0.01) and age above 65 years increased the odds for compliance (1.50 [1.15;1.95], p=0.003). Income, diagnosis, gender, Low Density Lipoprotein level and systolic blood pressure did not significantly influence the odds to consult their GP after the screening consultation. Among high risk patients, 7.4% had their blood glucose checked at a GP consultation and 6.3% had their blood-pressure measured at home after the screening consultation as opposed to 4.8% and 1% among low risk patients.

Conclusions: After a screening consultation, 40% of the patients with high risk of CV disease did not consult their GP at all in the following 3 months. At least 35% of the patients with high risk followed the recommendations to consult their GP and 27% consulted their GP for reasons not possible to clarify in this study. Only age and higher education had a significant influence on the outcome.

References:

Acknowledgements: We would like to thank The Danish Rheumatism Association and the Henrik Henrikssøn fund for financial support for this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1908

THU0602 WORKER PRODUCTIVITY LOSS REMAINS A MAJOR ISSUE FOR PATIENTS WITH INFLAMMATORY ARTHRITIS AND OSTEARTHRITIS: RESULTS FROM THE INTERNATIONAL EULAR-PRO WORKER PRODUCTIVITY STUDY

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Background: Knee osteoarthritis (OA) is a progressive joint disease generally associated with increasing pain. In severe symptomatic knee OA, knee prosthesis arthritis (IA) and osteoarthritis (OA) are one of the biggest causes of disability and worker productivity loss which has recently been recognized by European policy makers and the World Health Organization (WHO). However, limited information is available about job characteristics and the level of both presenteeism and absenteeism in employed persons with IA or OA across countries.

Objectives: To describe job characteristics and worker productivity loss in patients with IA and OA in Europe and Canada.

Methods: Patients with IA or OA in paid employment from seven countries within Europe and from Canada were recruited to the EULAR-PRO Worker productivity study. Patients completed a questionnaire including questions about their job, job characteristics and the Work Productivity and Activity Impairment Questionnaire (WPAI) measuring percent hours absent and the percentage their disease affected productivity while working (0–100%=disease completely prevented work). Patients also completed several health-related patient reported outcome measures, including: the Health Assessment Questionnaire (HAQ), Visual Analogue Scale (VAS) general well-being, and EuroQol-5D (EQ-5D).

Results: 503 patients were included in this large international study. Mean (SD) age was 47 (10) years, median (IQR) disease duration 12 [5, 21] years and 94% had IA. 42% had a predominately mentally demanding job, 10% physically demanding job, and 48% a combination; with overall 34% reporting their job being very demanding (see table for country specific results). Respectively 12% and 5% of patients were able to often or always postpone work tasks if need be, whilst respectively 19% and 51% never or sometimes received help from colleagues which may depend on job/employment type and company size. Twenty-one% of patients reported that they missed time off work due to ill-health in the past week (median IQR [%] time missed due to ill-health 20% [8–50]). Interestingly, a total of 11% were unsatisfied with their current job; and 23% of patients did not disclose their disease to their employer.

Conclusions: This is one of the largest international studies investigating worker productivity loss in patients with IA and OA. It highlights the burden of the disease across countries and the importance of increasing awareness of rheumatological conditions in order to prevent presenteeism and long-term sick leave by providing the best available intervention to the individual patient in paid employment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5041

THU0603 DISEASE BURDEN OF KNEE OSTEOARTHRITIS PATIENTS UNDERGOING JOINT REPLACEMENT COMPARED TO MATCHED CONTROLS: A POPULATION-BASED ANALYSIS OF A DUTCH MEDICAL CLAIMS DATABASE

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Background: Knee osteoarthritis (OA) is a progressive joint disease generally associated with increasing pain. In severe symptomatic knee OA, knee prosthesis

Conclusions: The research is available about job characteristics and the level of both presenteeism and absenteeism in employed persons with IA or OA across countries. The research is available about job characteristics and the level of both presenteeism and absenteeism in employed persons with IA or OA across countries. The research is available about job characteristics and the level of both presenteeism and absenteeism in employed persons with IA or OA across countries.
(KP) can improve health-related quality of life. In the Netherlands, the incidence of KPs and KP revisions has increased, but health care costs related to these procedures over time and their determinants are unknown.1

Objectives: To provide estimates of age and sex-specific incidence of KPs, revision KPs, and prosthesis complications in patients with knee OA. To determine average annual health care costs of patients undergoing KP compared with matched controls in the Netherlands, and to understand drivers of costs.

Methods: All KPs in knee OA patients in the Achmea Health Database were identified and matched by age, sex, and region to a maximum of four controls. Incidence rates of KPs, KP revisions, and their complications (1/000 persons) from 2006–2013 were determined. Annual health care cost and excess costs compared to matched controls, preceding, during and after surgery were calculated and associated factors evaluated using longitudinal regression analysis.

Results: The incidence of KPs, KP revisions, and complications increased between 2006 and 2013. This increase was strongest in younger age categories and in men (Table 1). Annual health care costs slightly increased up to the year of surgery, with highest costs in the year of surgery. Post-surgery costs remained slightly higher than pre-surgery costs. High post-surgery costs were mainly associated with subsequent KPs. Other factors associated with high excess costs were younger age, female gender, and complications.

Table 1. Sex-specific incidence rates (per 1,000 person years) of all KPs, KP revisions, and complications associated with knee OA.

<table>
<thead>
<tr>
<th>Year</th>
<th>Age Group</th>
<th>All KPs</th>
<th>KP Revision</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>Male</td>
<td>0.81</td>
<td>0.06</td>
<td>0.11</td>
</tr>
<tr>
<td>2007</td>
<td>Female</td>
<td>2.01</td>
<td>0.04</td>
<td>0.12</td>
</tr>
<tr>
<td>2008</td>
<td>Male</td>
<td>2.82</td>
<td>0.04</td>
<td>0.16</td>
</tr>
<tr>
<td>2009</td>
<td>Female</td>
<td>2.82</td>
<td>0.04</td>
<td>0.16</td>
</tr>
<tr>
<td>2010</td>
<td>Male</td>
<td>3.12</td>
<td>0.07</td>
<td>0.21</td>
</tr>
<tr>
<td>2011</td>
<td>Female</td>
<td>3.12</td>
<td>0.07</td>
<td>0.21</td>
</tr>
<tr>
<td>2012</td>
<td>Male</td>
<td>3.32</td>
<td>0.07</td>
<td>0.21</td>
</tr>
<tr>
<td>2013</td>
<td>Female</td>
<td>3.32</td>
<td>0.07</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Conclusions: These results underscore the increasing burden associated with severe knee OA, especially in younger age categories. Improved guidelines aimed at avoiding complications and revisions are required to counteract this trend.

References:

Disclosure of Interest: None declared


THU0604 | THE ASSESSMENT OF THE DUTCH QUALITY REGISTRY RHEUMATOID ARTHRITIS QUALITY INDICATORS IN THREE PILOT HOSPITALS

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Background: While practical guidelines and recommendations play an important role in the treatment of RA, rheumatologists often tend to deviate from these guidelines (1). This may result in disparity of quality of care among individual doctors and hospitals. To establish the best possible care, quality measures are needed. These aim to quantify the quality of the delivered care and will form the foundation of quality registries. Standardization of care processes in combination with public reporting of performance (by means of a quality registry) has been suggested to improve quality of care (2).

Objectives: To develop feasible quality indicators (QIs), endorsed by the different stakeholders of the Dutch Quality registry Rheumatoid Arthritis (DQRA).

Methods: An expert group of 8 rheumatologists, 2 patient representatives and 1 healthcare insurer representative developed a minimal set of QIs via a Delphi-like procedure (3), endorsed by the Dutch Society for Rheumatology. Since October 2015, these QIs have been registered by rheumatologists and rheumatology nurses, once a year in 26 hospitals, along with a patient evaluation questionnaire regarding the received care. To determine whether it is feasible to collect these QIs in daily practice, retrospective data from three hospitals was obtained (hospital A (university), B and C (non-academic)). Feasibility was determined by evaluation of:
1. Completeness of registered data (figure 1)
2. Possibility to calculate disease activity categories (remission, low-high disease activity)
3. Possibility to calculate changes over time in disease activity categories
4. Extraction of data regarding (b)DMARD use

Results: Selected QIs are:
1. Percentage of patients in a certain disease activity category

Abbreviations: KP = Knee prosthesis, OA = Osteoarthritis, IR = Incidence rate.

Conclusions: The DQRA is the first to incorporate perspectives from three stakeholders (patients, physicians and healthcare insurers) and successfully formed a limited set of QI. Collection of these indicators was feasible in two out of the three participating hospitals and offers insight in differences in provided and perceived care for RA patients.

References:

Disclosure of Interest: None declared


TUH0605 | IMPACT OF NON-PERSISTENCE TO SUBCUTANEOUS TNF-ALPHA INHIBITORS ON MEDICAL RESOURCE UTILIZATION AND COSTS

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Background: Biotherapies such as subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFis) have transformed the management of rheumatoid diseases. The assessment of SC-TNFis non-persistence and its impact on medical resource utilization and costs are needed.

Objectives: The objective was to assess the impact of non-persistence to subcutaneous TNF-alpha inhibitors on medical resource utilization and costs, for patients initiating treatment with an SC-TNF in France.

Methods: The Système National d’information Inter-régime [French national health insurance scheme information-sharing system] (SNIIRAM) database lists all outpatient and inpatient healthcare consumption for individuals covered by the general health insurance scheme. Using French claims data, conditions were diagnosed using Long Term Disease status and hospital admission. Based on ICD-10 codes of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. Patients were then identified through first-line prescription filled for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 2012/07/01 and 2012/12/31. 12-months persistence status was

2. Percentage of patients using a certain (b)DMARD
3. Patient reported experience with received care

Table 1. Assessment of feasibility of the DQRA QIs

<table>
<thead>
<tr>
<th>Disease activity category</th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>Hospital C</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicator (DAS28)</td>
<td>(n=791)</td>
<td>(n=1395)</td>
<td>(n=822)</td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>43.6%</td>
<td>45.1%</td>
<td>63.6%</td>
<td>55.8%</td>
</tr>
<tr>
<td>Low disease activity</td>
<td>16.3%</td>
<td>15.2%</td>
<td>14.1%</td>
<td>15.2%</td>
</tr>
<tr>
<td>Moderate disease activity</td>
<td>32.8%</td>
<td>30.1%</td>
<td>19.1%</td>
<td>27.3%</td>
</tr>
<tr>
<td>High disease activity</td>
<td>7.3%</td>
<td>9.6%</td>
<td>3.2%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Changes over time in disease activity categories (2014–2015)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indicator (DAS28)</td>
<td>(n=415)</td>
<td>(n=653)</td>
<td>(n=1105)</td>
<td></td>
</tr>
<tr>
<td>Stable over time</td>
<td>48.7%</td>
<td>N.A.</td>
<td>58.8%</td>
<td>53.8%</td>
</tr>
<tr>
<td>Decreased in disease activity category</td>
<td>24.8%</td>
<td>N.A.</td>
<td>17.9%</td>
<td>21.4%</td>
</tr>
<tr>
<td>Increased in disease activity category</td>
<td>26.5%</td>
<td>N.A.</td>
<td>23.3%</td>
<td>24.9%</td>
</tr>
</tbody>
</table>

TDARMD use

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>Hospital C</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>sDMARD monotherapy</td>
<td>41.2%</td>
<td>N.A.</td>
<td>51.6%</td>
<td>46.4%</td>
</tr>
<tr>
<td>sDMARD combination therapy</td>
<td>29.4%</td>
<td>N.A.</td>
<td>27.8%</td>
<td>29.6%</td>
</tr>
<tr>
<td>bDMARD</td>
<td>29.4%</td>
<td>N.A.</td>
<td>16.0%</td>
<td>22.7%</td>
</tr>
<tr>
<td>No DMARDs</td>
<td>0%</td>
<td>N.A.</td>
<td>4.7%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Figure 1: completeness of registered data

Conclusions: The DQRA is the first to incorporate perspectives from three stakeholders (patients, physicians and healthcare insurers) and successfully formed a limited set of QI. Collection of these indicators was feasible in two out of the three participating hospitals and offers insight in differences in provided and perceived care for RA patients.

References:

Disclosure of Interest: None declared

THU0606  COGNITIVE DYSFUNCTION IN CONNECTIVE TISSUE DISEASES

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Background: Several studies documented the presence of cognitive dysfunction in different rheumatologic autoimmune diseases, but the absence of standard criteria of diagnosis and of an index with patients in which this dysfunction occurs, makes the mentioned studies often lead to divergent conclusions.

Objectives: To evaluate the impact of four autoimmune diseases: Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc) and Ankylosing Spondylitis (AS) on patient cognition and to identify potential factors which lead to cognitive dysfunction occurrence.

Methods: This is a case-control study that included randomly selected patients with SLE, RA, SSc and AS from a University hospital and a matched control group. Data collected included: demographics, patients’ education and specific data related to disease (duration, activity scores: DAS28, HAQ for RA patients, B27 dose-titration to maintain serum uric acid (sUA) levels 4–6 mg/dL for patients with AS; SLICC/SSc index for SLE patients and EUSTAR score/Rodnan score for SSc patients, damage indexes, organ involvement, treatment) and comorbidities. Cognition was assessed using MoCA Test (Montreal Cognitive Assessment The Test). The data were then processed using SPSS 23 version software.

Results: The study group included 255 patients: 58 RA patients, 52 SLE, 70 SSc and 25 AS patients and 50 healthy matched controls. In all groups of patients, cognitive dysfunction prevalence was higher than control group (RA: 84.99%, SLE: 57.69%, SS: 44.29%, AS: 35.72%) vs. 24% in the control group.

The differences were statistically significant for the RA group (p<0.001), the SLE group (p=0.001) and the SS group (p=0.001).

For the RA group, none of the items analyzed (demographics, disease characteristics, education) showed a significant correlation with cognitive dysfunction. The same lack of correlation was also noted in AS and SSc patients. For the SLE group the only variable analyzed with a significant impact statistically was the SLEDAI score (odds ratio 1.04, 95% CI 1.01 to 1.07).

Conclusion: Cognitive dysfunction seems to be more frequent and severe in RA and SLE patients compared to AS patients (p<0.014, respectively p<0.05).

The conclusions obtained in this study show that, indeed, cognitive dysfunction is an issue to be watched very carefully in patients with autoimmune diseases. The appearance of cognitive dysfunction has a negative impact on life quality of these patients, the pathophysiological mechanisms that contribute to its appearance are intricate and difficult to isolate.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2129

THU0607  RISK FACTORS FOR EARLY RETIREMENT IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by skin and internal organs fibrosis, microvascular impairment and frequently by disability and early retirement.

Objectives: To assess employment status, risk factors for early retirement (ER) and the associations of ER with disease characteristics and with patients’ health-related questionnaires (Scleroderma Health Assessment Questionnaire (SHAQ)) and hand function (Durouz hand index (DHI)).

Methods: This study included patients with SSc according to the 2013 ACR/EULAR classification criteria, examined in our EUSTAR center from 11.2011 to 11.2016, who were under the legal age of retirement of in our country (62 years). Patients completed a work assessment questionnaire, the DHI and the SHAQ, as well as a full assessment as per the recommendations of EUSTAR.

Logistic regression was used to investigate the associations between employment status (outcome) and potential predictors (including socio-economic status, education, disease characteristics and health-related questionnaires).

Results: There were 66 patients (8 males, mean±SD age 49.1±9.3 years, 19 with diffuse cutaneous SSc (dCSSc), 46 with history of digital ulcers (DUs) and 23 with joint contractures) included. Forty-two patients lived in urban environments and 22 had higher education (high school or above). Twenty patients were active professionally, whereas 46 were retired, of which 32 retired because of SSc. Of those active professionally, 8 had to do manual labor, 7 had to stand many hours at work and standing 3 had a cold or moist work environment.

Using logistic regression adjusted for age and gender, higher education was found to be highly associated with employment (OR (95% CI) 9.9 (1.5, 52.4)), whereas labor conditions (manual labor, stress) had no significant influence on employment status in our cohort. No association was found between employment status and disease characteristics or SHAQ and DHI questionnaires.

Conclusions: SSc is associated with substantial work disability and unemployment. Completing less education than high school was associated with early retirement.

Acknowledgements: "This abstract was realized as part of the “Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis” (QUANTICAP) project, financed by the UEFIS-CDI PN-II-PP-PIA2013-4-1589 grant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5892
Objectives: To understand allopurinol dose-titration relative to sUA levels. Methods: This retrospective study used the de-identified Humedica electronic medical record database. The study included all sUA and allopurinol records among gout patients (ICD-9-CM: 274.xx) ≥18 years old with first gout diagnosis in 2007 – 2015. An episode was defined as an allopurinol initial dose (ID) prior to (closest) and titrated dose (TD) after (within 30 days) an sUA test. The titration was categorized as an episode with a dose-change (up-titration: ID < TD; down-titration: ID > TD), or no-dose-change (ID = TD). For multiple different doses recorded on the same prescription date, the sum of doses was taken as daily dosage. Episodes were considered uncontrolled when sUA ≥6 mg/dl. Descriptive episode-level analyses were performed.

Results: Within 64,609 episodes, 57% of episodes were uncontrolled (sUA: 6 to <8 mg/dl: 38%; 8 to <10 mg/dl: 15%; ≥10 mg/dl: 4%). Seventy-one percent of uncontrolled episodes were no-dose-change, 21% were up-titrated, and 7% were down-titrated. Within no-dose-change episodes, 51% were uncontrolled and lower doses corresponded to higher percentages of uncontrolled episodes (<100 mg/day: 88%; 100 mg/day: 70%; >100, <300 mg/day: 49%; 300 mg/day: 38%; ≥300 mg/day: 36%). Seventy-eight percent of dose-change episodes were uncontrolled, of which 100 to 300 mg/day (39%) was the most frequent dose titration. Overall, the most frequent TD was 300 mg/day (52%) followed by 100 mg/day (36%), >100 – <300 mg/day (8%), >300 mg/day (3%), and <100 mg/day (1%).

Conclusions: Allopurinol dose is not generally titrated regardless of sUA control. This pattern suggests a need for active management of patients with gout with uncontrolled sUA including consideration of new treatment options in addition to allopurinol.

References:

Acknowledgements: This study was funded by Ironwood Pharmaceuticals.


DOI: 10.1136/annrheumdis-2017-eular.6314

THU0610 RHEUMA SPACE: STANDARD PRACTICE AIMING CLINICAL EXCELLENCE IN RHEUMATOLOGY

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Background: The quality of medical care and the implementation of measures to improve it are crucial steps for the development of Rheumatology in Europe. Quality indicators were obtained through a four-step rand-modified Delphi methodology. A final set of 26 quality indicators was defined within Donabedian’s concepts: 9 dimensions: 9 structures, 11 processes and 6 outcomes. Herein we describe the second implementation phase of a national program, Rheuma Space (RS), aiming at quality improvement in Rheumatology.

Objectives: To develop a quality improvement plan for care provided by Rheumatology Departments (RD). In this second phase we present the results of the RD evaluation.

Methods: A measurement scale on quality/excellence thresholds was developed for each of the 26 criteria. Eight RD participated in the project and each one set up an Investigation Team of 2–3 members for field criteria measurement and evaluation that required the use of different data sources and focused on the period: 2014 – 1st semester of 2015. After data analysis an individual report was delivered and discussed with each of the 8 RD. Afterwards public presentation and discussion of the results took place.

Results: “Structure” was evaluated in terms of personal, training, facilities, equipment and budgeting.
- RD lack Rheumatology specialists and need fully dedicated nurses.
- Training plans exist in all RD, but physicians allocate few time to research.
- Equipment is appropriate, nonetheless microscopes and computers could be updated.
- Internal contracting is well established and professionals are committed to targets.
- Processes” were evaluated in terms of access and medical care, clinical records, physician-patient communication and multidisciplinary patient management.
  - Triage criteria for first appointments should be standardized, despite compliance for “High Priority” patients.
  - Follow up could be more frequent, but direct access in emergencies is guaranteed.
  - Reimbursement process is mainly used for patients under biologics and data collection improvement could be done.
- Multidisciplinary care is provided, but patient coverage and specialty diversity can increase.

“Outcomes” were evaluated in terms of clinical outcomes, patient and personal satisfaction.
- Average working absence is <15days/patient/year, but is much higher in more affected patients.
- Almost 1/3 of patients requested early retirement at a median age >50years.
- Patients are satisfied with provided care and physicians’ attitude, but less with RD facilities.
- Professional are satisfied with working environment, however criticize career related aspects.

Conclusions: The 26 quality indicators set the basis of this quality management tool that was applied to 8 Portuguese RD. Strengths and weaknesses were identified and an individual Department report was elaborated and discussed. Interventions are now being planned based on these results in order to ensure quality standards of structure and process criteria for a patient oriented clinical practice, favouring desirable clinical outcomes and patient satisfaction.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6422
LONG-TERM FOLLOW-UP OF 269 CHILDREN BORN TO MOTHERS WITH SYSTEMIC AUTOIMMUNE DISEASES: A NATIONAL SURVEY FROM 24 RHEUMATOLOGY CENTERS

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Background: Rheumatic diseases (RD) affect women during reproductive age. Children’s outcome is a major topic for counselling on family planning, but no large studies are available.

Objectives: We aimed at assessing the long-term health conditions of children born to mothers with RD through a self-reported questionnaire.

Methods: 24 Rheumatology Centers distributed the questionnaire (65 multiple choice and 12 open-answer questions) to consecutive women with RD attending their outpatient clinic during September 2015. Data were compared according to maternal diagnosis (MD) - chronic arthritis (CA) or connective tissue disease (CTD) - and to the timing of pregnancy (before or after MD of RD).

Results: The questionnaire was returned by 184 mothers. Among the 269 children born to 184 mothers 63 were born before and 93 after MD of RD. There were 106 boys and 163 girls. Their mean age was 14.4 (±9.0 SD) years at the time of interview, and male children were 52/93 (56%) and 40/96 (41.6%), respectively. Twenty-nine children in the CA group (31.2%) and 64 in the CTDs group (36.4%) were born after MD of RD. Pre-term delivery was observed in 7 cases for indolence, in 3 for learning disabilities (LD)/health problems (HP), and in 9 cases for other reasons.

Conclusions: The long-term follow-up of children born to mothers with RD in 24 Rheumatology Centers is available. Furthermore, this is the first survey in the world that analyses the results of children born before and after MD of RD. Physicians should take care of the long-term health conditions of children born to mothers with RD.

Disclosures of interest: None declared


PROVIDING HEALTHCARE FOR THE POOREST IN EAST INDIA – A REPORT FROM A CHARITY INITIATIVE, SHAKUNTALA HOSPITAL


Background: The region of Odisha in India has a population of over 40 million people and 45% are living in poverty. Approximately one percent of the population is affected by inflammatory rheumatoid diseases. In order to provide early diagnosis and adequate treatment initiation to prevent long term disability, patients require easily accessible basic health care and rheumatologists. Accessible and affordable health care for patients with inflammatory diseases may not only improve disease diagnosis and management, but also improve their quality of life significantly.

Objectives: The aim of our abstract is:
1) To raise awareness of the need of support for common rheumatoid diseases in the developing world
2) To present Shakuntala Hospital as an example of a successful charity initiative

Methods: The Indo-Swedish Rheumatology Foundation (ISRF) is an association of physicians whose main aim is to raise awareness, fundraise and to provide healthcare for patients suffering from inflammatory arthropathies. In order to bridge the gap between our advanced level of knowledge and treatment options in the western world and patients suffering from rheumatologic diseases in the Indian state Odisha we have established this unique association. ISRF, including Shakuntala Hospital, was founded in 2013 and has so far not only provided health care through diagnostic and treatment support, but also ensured patient education and physiotherapy. Health camps are organized in the peripheral communities in order to screen, diagnose and initiate first line treatment and refer these patients for follow-up care to Shakuntala Hospital for further treatments with disease modifying antirheumatic drugs (DMARD), disease monitoring and physiotherapy. Shakuntala Hospital is an example of a non-profit hospital with the aim to provide health care amongst the poorest areas in India.

Results: We have so far registered over 2,000 patients under our care, which includes patients registered in Shakuntala Hospital and in our peripheral care health camps. So far we have established outpatient care for patients with inflammatory arthritis in the districts of Balasore, Murthana, Bhadrak, Keonjhar, Jagpur districts of Odisha and Mednapur district of West Bengal and raised more than 32,000 Euro by ISRF from fundraising initiatives. Inspired by a Swedish model our osteoarthritis (OA) school was founded in October 2016 providing 6 week training courses with the main focusing on patients with knee OA. Furthermore, ISRF has increased awareness of skeletal fluorosis and provide a comprehensive focus with cleaning of drink water in co-operation with the Royal Technical High School in Stockholm.

Conclusions: Shakuntala Hospital is an example of a successful charity initiative in order to provide healthcare for the poorest patients in East India. Awareness needs to be risen in order to further foster future support for Shakuntala Hospital.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4424

EXPLORING THE IMPACT OF HEALTH STATUS AND WELL-BEING OF PEOPLE WITH INFLAMMATORY ARTHRITIS ON PRESENTEEISM IN THE WORKPLACE: A QUALITATIVE STUDY

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Background: Presenteeism can be defined as the reduction in work performance due to ill-health at the workplace. Musculoskeletal conditions, including
inflammatory arthritis (IA), are one of the most common causes for presenteeism. There are no “gold standard” methods to identify, measure, or value the impact of presenteeism. Some evidence suggests the impact of presenteeism can be indirectly estimated using measures of health status and well-being.

Objectives: To explore whether selected measures of health status and well-being, combined in economic evaluations are conceptually useful to capture those aspects of IA that are associated with presenteeism.

Methods: A sample of individuals, aged 18 years and above, working in the UK with rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA), was recruited via patient support groups. Semi-structured telephone interviews were designed to understand if, and how, RA, AS or PsA affects an individual’s ability to work. Framework Analysis Methods were used and coding involved deductive and inductive approaches. A deductive approach was used to derive potential themes from measures of health status [EuroQol-5 Dimension-5 level (EQ5D), Short Form 6 Dimension (SF6D)], and well-being [ICECAP-A] (ICAPability measure for Adults (ICECAP-A)]. An inductive approach was used to generate other themes not captured by these measures.

Results: Twenty-two employed individuals with RA (n=10), AS (n=9) or PsA (n=3) were interviewed; 82% were female and, of the 22 patients, 23% had a manual job. The majority of interviewees explained that symptoms of the conditions increase levels of presenteeism, including: pain; stiffness; fatigue; emotional mental health; mental clarity. These symptoms make completing activities at work difficult, which, in turn, affects an individual’s capability to maintain a successful career. The ICECAP-A was found to be a useful measure to capture the overall impact of presenteeism resulting from RA, AS or PsA. The SF6D and EQ5D were more specific measures capturing particular symptoms and activities that increase levels of presenteeism (see Table 1).

Two further themes were identified using inductive methods: mental clarity and feeling understood. The effect of mental clarity or feeling understood is not captured by any of the domains in EQ-5D-5l or SF6D. The ICECAP-A is potentially able to capture the impact of these themes in the respective domains ability to achieve and progress and ability to gain support.

Conclusions: This study suggests that three existing measures (EQ5D, SF6D, and ICECAP-A) were successful, in different degrees, to capture the impact of presenteeism that result from the aspects and symptoms of IA. Potentially, these measures may be used in economic evaluations to capture the impact of presenteeism.

Acknowledgements: This work was supported by Arthritis Research UK and the Medical Research Council [20665].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1803

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**Table 1**

<table>
<thead>
<tr>
<th>Theme</th>
<th>ICECAP-A</th>
<th>SF6D</th>
<th>EQ5D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achievement/Progress</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decisions</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Emotion</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental Health</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Mobility</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Self-care</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Settled/Secure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Interaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Support</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual Activities</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Vigorous Activities</td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Conclusions: This study suggests that three existing measures (EQ5D, SF6D, and ICECAP-A) were successful, in different degrees, to capture the impact of presenteeism that result from the aspects and symptoms of IA. Potentially, these measures may be used in economic evaluations to capture the impact of presenteeism.

Acknowledgements: This work was supported by Arthritis Research UK and the Medical Research Council.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3232

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**THU0615**

**PARTICIPANTS’ EXPERIENCE OF THE MAKING IT WORK PROGRAM, AN ONLINE PROGRAM TO HELP PEOPLE WITH INFLAMMATORY ARTHRITIS REMAIN EMPLOYED**

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Objectives: Health services addressing employment needs for people with arthritis are lacking. To address this need, we developed the Making It Work (MIW) program, an online self-management program aimed at helping people with inflammatory arthritis (IA) deal with employment issues. As part of a randomized controlled trial evaluating program effectiveness, this study reports on participants’ experiences with various aspects of the program.

Methods: All participants in the MIW program between Jan20 and Dec7 2016 were included. Participants were recruited from rheumatologist practices, outpatient arthritis programs, a national consumer organization (Arthritis Consumer Experts), and community advertisements in BC, Alberta and Ontario. Eligibility criteria included: having IA; being currently employed; age 18–59 yrs; concern about their ability to work; and access to a computer. The program consisted of 5 online self-learning modules, 5 online group meetings facilitated by a vocational counselor, an individual ergonomic assessment by an occupational therapist and an online session with a vocational counselor. Feedback questionnaires were administered online after participants completed the program. Descriptive analyses were performed.

Results: The sample included 69 participants [80% female; mean (SD) age: 45.3 (10.5) yrs; 83% Caucasian; 91% with post-secondary education; 52% with RA, 19%; SLE: 17%; PsA: 12%]. Overall, participants expressed satisfaction with the program with 94.2% agreeing (69.6% strongly and 24.6% somewhat) they would recommend this program to someone they know. When asked to rate program components on a scale of 0–10 where 0=not useful at all and 10=very useful, participants rated all components favourably: median [25Q;75Q] for online modules: 8 [7;10], with highest ratings for the fatigue module (rated 10 by 42%); online group meetings: 9 [7.5;10]; ergonomic and VRG assessments: 8 [7;10] each. Although participants had 2 weeks between meetings to complete the module, 55% did the module the week of, and 42% the day before, the group meeting. Median time to complete each module was 60 min. 81% enjoyed being able to listen to the information (somewhat or strongly agreed), although 35% stated they would have preferred to read the information than listen to a narrator. 74% expect to use the online modules again in the future. Participants were also satisfied with the online group meetings: 93% were very or somewhat satisfied with the group facilitation; 87% satisfied with the group dynamic; 84% comfortable with the online format. When asked to rate their online group meeting experience on a scale of 0–10 where 0=not at all useful and 10=very useful, participants rated the group meeting discussion was 9 [9;10]; getting to know other participants: 7 [7;10]; feeling listened to and understood 9 [8;10]; feeling that group was supportive 9 [7;10]. 20% said it was difficult for them to attend group meetings.

Conclusions: In general, participants were highly satisfied with all aspects of the program.
**THU0616** PATIENTS’ PERCEPTION ON DISEASE PROGRESSION AND ADHERENCE TO BIOLOGIC THERAPY

**E. Cefai, D. Balzan, C. Mercieca, A.A. Borg. Rheumatology, Mater Dei Hospital, Msida, Malta**

**Background:** Adherence to medication depends on several factors such as medication beliefs, psychosocial factors, illness beliefs and concerns. The consequences of non-adherence are not insignificant, both from the clinical and health economic aspects.

**Objectives:** To assess medication adherence of patients taking biologics who are in remission or who have low disease activity and patients’ perception of disease progression.

**Methods:** Forty-four consecutive patients attending a dedicated biologic clinic and treated with TNF inhibitors were interviewed following their visit. Patients were asked about adherence to treatment, adverse effects, concerns about biologics and their perception of disease progression. Demographic and disease activity data were recorded.

**Results:** Forty-four patients (23 females, 21 males) participated in the survey (21 suffered from rheumatoid arthritis, 17 from ankylosing spondylitis and 6 from psoriatic arthritis). The mean age was 55.1 (SD 12.62) years. The mean DSAS28 was 2.92 (SD 1.00) and mean BASDAI was 4.21 (SD 2.1). No minimal or no pain was reported by 75%, mild or no fatigue by 78% and 77% had no restriction of activities of daily living. Medication adherence was reported as high by 66% and moderate by 32%. There were no patients who had a low level of adherence. 5% of patients admitted to be unaware of the need to omit their biologic when ill and 40% when requiring surgery.

One out of 4 patients reported to have experienced adverse events, most commonly infections. 19% claimed to be moderately or very concerned about the adverse effects. On further questioning about the severity of potential adverse effects, 45% were unsure as to what the severity might be. When asked about duration of therapy, 29% replied more than 10 years; whilst 71% were unsure on when, if ever, the biologic is going to be stopped. Patients were also asked whether they believed that the biologic had successfully stopped further joint damage and 68% replied yes, 9% replied no, whilst 23% were unsure. Of those who replied yes, this perception was based on the absence or reduction of symptoms.

**Conclusions:** In this cohort of patients with low disease activity or remission, a third of patients still reported sub-optimal adherence to TNF inhibitor use. The benefits of adherence to biologic therapies need to be reinforced at every visit and factors leading to non-adherence addressed. Adverse effects remain a major concern that needs to be addressed, even in patients who have been on biologics for many years and have sustained remission or low disease activity. A quarter of patients were unsure whether biologics have stopped joint damage. Patients’ perception of joint damage progression needs to be explored to find ways of making it more understandable to patients.

**Disclosure of Interest:** None declared


**THU0618** THE FACTORS AFFECTING WORKPLACE AND HOUSEHOLD LIFE IN ANKYLOSING SPONDYLITIS: A MULTI-DIMENSIONAL STUDY

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**Background:** Work disability (WD) is the final stage of work problems and may be prevented by effective treatment and ergonomic interventions in earlier stage of work productivity loss and work instability. Contextual factors, disease related factors and local social security systems may also affect WD.

**Objectives:** We aimed to determine the predictive factors of work productivity and work stability in Turkish patients with ankylosing spondylitis.

**Methods:** One-hundred patients with ankylosing spondylitis (31 females and 69 males) were included into this study. Demographics, working state, Bath scores of disease activity, functional and radiologic state, quality of life, cardiopulmonary functions (echocardiography, exercise stress test and pulmonary function test) and general work impairments (work productivity impairment and work instability) were recorded. WPAI and AS-WIS were selected as work outcomes. The most predictive factors were analyzed in work productivity and work instability. SPSS 14.0 statistics (descriptives, pearson correlation, and stepwise regressions were used for statistical analyses.

**Results:** Thirty-two patients (mean age: 42.6±11.7) were unemployed. Unemployed patients showed more female, less educated, low disease activity, and low fitness profiles. The percentages of absenteeism (WPAI-1), presenteeism (WPAI-2), regular activity impairment (WPAI-3) and overall work impairment (WPAI-4) were determined as 8, 44, % 47, and % 37, respectively, in employee group. When affecting factors assessed with multiple stepwise linear regression analysis; the only determinant for absenteeism (WPAI-1) was the working day loss due to illness at last year. Chest mobility, annual income level, AS quality of life (AQoL), work change and co-morbid diseases were the determinants of presenteeism (WPAI-2), regular activity impairment (WPAI-3) and overall work impairment (WPAI-4). The score of mean work instability (AS-WIS) was 11.5±5.8, and 42.6% of patients had low and 57.4% of patients had moderate-high work instability. Multiple stepwise linear regression analysis showed that most predictive factors for work instability were regular activity impairment (WPAI-3) and AS-QoL. The factors affecting non-work status were older age, female sex and low annual income level in stepwise logistic regression.

**Conclusions:** The common predictive factor of work productivity and work stability was quality of life. For evaluation of work productivity; socioeconomic factors such as annual income level and frequent work change were determinative as well as clinical datas (chest expansion and comorbid diseases). We suggested both pharmacologic and nonpharmacologic interventions to improve quality of life should be enabled in early period to improve work productivity.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2550
PREVALENCE OF PNEUMOCOCCAL VACCINATION IN RHEUMATOLOGICAL PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA. BIOBADASAR REGISTRY


Sociedad Argentina de Reumatologia, Buenos Aires, Argentina

Background: Biobadasar is a registry that monitors adverse events in patients who use biological treatments in rheumatological diseases conducted by the Argentine Society of Rheumatology. As in other international registries the community acquired pneumonia (CAP) has been detected as one of the most frequent infectological adverse events. Although all immunosuppressed patients should be vaccinated against streptococcus pneumoniae, there is a proportion of patients who are not.

Objectives: Evaluate the prevalence of pneumococcal vaccination in patients with CAP within the Biobadasar database. Assess factors associated with Severe CAP in these patients.

Methods: A cross-sectional, multicentric study was made in BIOBADASAR database from 2010-2015. In patients who reported CAP data of demographics, comorbidities and state of pneumococcal immunization was collected. Microbiological data, treatment and outcome of the event were considered. The severity of CAP was assessed according to the opinion of the attending physician, hospitalization, risk of life and/or death. Values are expressed as mean ± standard deviation, median (ranges) and frequencies (percentages), as appropriate. We performed bivariate and multivariate logistic regression analysis to identify variables associated with the event.

Results: Out of the 4029 patients enrolled in the registry, the cumulative incidence of CAP was 4.2% (n = 170), 72.4% (n = 123) were women. The mean age was 57 (SD +/- 14.5). Biological treatment was found in 81.8% (n = 139). Patient s that have received the pneumococcal vaccine were 40.6% (n=69). Severe CAP was detected in 7.1%. Streptococcus Pneumoniae was the main pathogen isolated in 13% of the cases. Overall mortality was 4.1%. In the univariate analysis for severe CAP we found statistical significance for Smoking OR 3.88, CI95 1.063–14.22, p=0.029 and chronic kidney disease (CKD) OR 31, CI95 2.6–376, p=0.007. When performing a multiple logistic regression model, only renal failure OR 7.39 CI95 3.066–18.28, p=0.003–0.38 and chronic kidney disease (CKD) OR 31, CI95 2.6–376, p=0.007 was a predictor of severe CAP. Not significant association with immunosuppressive treatment (p = 0.09), age (p = 0.464), or vaccination (p = 0.937).

Conclusions: The annual incidence of CAP in Argentina varies between 0.5 -1.1% while in our cohort it was four times higher. The prevalence of pneumococcal vaccination was less than 50%, showing that, although the literature and guidelines establish the need for vaccination, this is not so in the real world. In the multivariate analysis, only CKD was related to severe CAP. Although in the univariate analysis the CKD and the smoking habit represented factors associated with severity. We must emphasize the medical education in following the international vaccination guidelines.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5282

PERSISTENCE WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS – A RETROSPECTIVE DATABASE STUDY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

J. Mahlich1, H. Kameda2, R. Sruamsiri3, A.M. Cappuccio, R. Quintana, E. Mussano, L. Zavada1, L. Szzukova1, J. Vencovsky1, P. Horák3, K. Pavelka1 on behalf of collaborators of the ATTRA registry.1 Rheumatology, Institute of Rheumatology, Prague; 2 Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno; 3 Internal Medicine, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic.

Objectives: To compare the effect of anti-TNF therapy (a-TNF-th) on Work Disability (WD) between RA, PSA and AS. In the Czech Republic (CZ), a-TNF-th is reimbursed for RA if DAS28≥3.1 despite therapy with csDMARDs, for PSA if disease is not “adequately controlled” with csDMARDs, and for AS if BASDAI≥4 and CRP/ESR elevated above normal. More than 95% of anti-TNF treated patients in CZ are followed up in the ATTRA registry.

Methods: Bionalve patients with RA (n=1085), AS (n=1126) and PSA (n=351) starting a-TNF-th with available baseline data on demography, disease duration and physical function, and on working status at baseline and at 12 months were included in the analysis. Patients older than 60 years, on maternity leave or students were excluded. Work status was self-reported by patients as (A) able to work = [(i) employed, or (ii) unemployed and actively seeking employment], or (B) unable to work = [(iii) on sick leave, or (iv) on disability pension]. Regression analyses were performed to examine the predictors of improvement in WD (change B→A coded as 1, B→A as -1, no change as 0) over 1 year.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>RA (n=1085)</th>
<th>AS (n=1126)</th>
<th>PSA (n=351)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>836 (77.1%)</td>
<td>623 (23.4%)</td>
<td>161 (45.9%)</td>
<td>&lt;0.001bc</td>
</tr>
<tr>
<td>Disease duration</td>
<td>8.2±6.6</td>
<td>7.5±6.9</td>
<td>8.2±7.2</td>
<td>0.002bc</td>
</tr>
<tr>
<td>Age at start of anti-TNF Therapy</td>
<td>46.5±5.9</td>
<td>38.2±6.8</td>
<td>44.1±5.3</td>
<td>&lt;0.001bc</td>
</tr>
<tr>
<td>HAD</td>
<td>1.5±0.6</td>
<td>1.1±0.5</td>
<td>1.2±0.6</td>
<td>&lt;0.001bc</td>
</tr>
<tr>
<td>Calendar year of starting anti-TNF therapy before 2008</td>
<td>420 (38.7%)</td>
<td>306 (27.2%)</td>
<td>90 (25.6%)</td>
<td>&lt;0.001bc</td>
</tr>
<tr>
<td>2009–2012</td>
<td>394 (36.3%)</td>
<td>427 (37.9%)</td>
<td>156 (44.4%)</td>
<td></td>
</tr>
<tr>
<td>2013–2015</td>
<td>271 (25.0%)</td>
<td>393 (34.9%)</td>
<td>105 (29.9%)</td>
<td></td>
</tr>
<tr>
<td>Post-hoc analysis (with Bonferroni correction): statistically significant difference btw groups A) RA vs. AS, B) RA vs. PSA, C) AS vs. PSA. Values or N (%) or mean±SD.</td>
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</tbody>
</table>

Table 2. Prediction of improvement in work disability

<table>
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<tr>
<th>Independent variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tr>
<td>CR (95% CI)</td>
<td>p-value</td>
<td>CR (95% CI)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.051</td>
<td>0.071</td>
</tr>
<tr>
<td>Age at start of anti-TNF therapy</td>
<td>0.067</td>
<td>0.071</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.001</td>
<td>0.001</td>
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</tbody>
</table>

References:

Results: Baseline characteristics were significantly different between diagnoses (Table 1). In patients with RA, 60% were able to work at baseline and 61% at 12 month, with PSA 71% and 74% resp., and with AS 72% and 77% resp. The main driver of improvement of WD was a change in the sick leave (RA 6%/2%, PSA 7%/1%, AS 9%/2%). In univariate analyses, diagnosis of AS and younger age at start of a-TNF-th were predictive of improvement in WD. In multivariate analysis, only diagnosis of AS was significantly associated with improvement in WD. Conclusions: These real life data from CZ show that for improvement of WD, a-TNF-th was most effective in patients with AS. This may be a sequel of disease activity, with the resulting cost savings related to work incapacity.

Background: Biobanks for research (BBR) are organized repositories of biological materials and associated health information with enormous potential and value for scientific research. In consonance with increasing attention to healthy aging research, BBR specifically oriented to chronic diseases and aging populations have gathered heightened attention. Public perceptions and patient choices are key to design, develop and implement patient-centered BBR. Public awareness, education and involvement are confidence building and unequivocally lead to higher participation in scientific enterprises.

Objectives: To assess patient awareness, perception and choices regarding aging biobanking activities.

Methods: We developed and applied a standard anonymous questionnaire to rheumatology outpatients. Although awareness is still suboptimal, BBR perceptions and patient choices regarding biobanks for aging research purposes have gathered heightened attention. Public perceptions and patient choices are key to design, develop and implement patient-centered BBR. Public awareness, education and involvement are confidence building and unequivocally lead to higher participation in scientific enterprises.

Conclusions: Our study constitutes a comprehensive assessment of public perceptions and patient choices regarding biobanks for aging research purposes among rheumatology outpatients. Although awareness is still suboptimal, BBR are highly regarded health infrastructures with enormous potential for further patient-centered development.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6562

THU0622 | PATIENT-CENTERED AGING BIOBANKS - A SURVEY ON PUBLIC PERCEPTIONS AND PATIENT CHOICE AMONG RHEUMATOLOGY OUTPATIENTS

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Background: Biobanks for research (BBR) are organized repositories of biological materials and associated health information with enormous potential and value for scientific research. In consonance with increasing attention to healthy aging research, BBR specifically oriented to chronic diseases and aging populations have gathered heightened attention. Public perceptions and patient choices are key to design, develop and implement patient-centered BBR. Public awareness, education and involvement are confidence building and unequivocally lead to higher participation in scientific enterprises.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4056

THU0623 | DECREASE IN THE TEMPORARY WORK INCAPACITY DUE TO MUSCULOSKELETAL DISEASES: UTILIZATION OF A PREVENTIVE PROGRAM IN VALENCIA- LA FE HEALTH AREA

J.E. Oller Rodríguez1, M.T. Fuente Goig2, F. Ortiz Sanjuán1, J. Ivorra Cortés1, E. Grau García1, E. Vicens Bernabéu1, E. Labrador Sánchez1, K.R. Arévalo Ruales1, J. Fragio Gil1, R. González Mazarío1, C.P. Alcázar Escandell1, I. Cánovas Olmos3, I. Chalamera Verdejo1, C.M. Feced Olmos1, L. González Puig1, J.M. Martínez Cordella1, C. Nájera Herranz1, R. Negueruelos Albuixech1, I. Andani Cervera1, J.A. Román Ivorra1 on behalf of Rheumatology Service. Rheumatology; 2Service of Prevention of Occupational Hazards, Hospital Universitari i Politècnic la Fe, Valencia, Spain.

Background: Musculoskeletal diseases are nowadays a frequent cause of temporary work incapacity (TWI). The implementation of specific programs for the care of these patients can be an important cornerstone in the resolution of these TWI processes.

Objectives: Our aim is to analyze the usefulness of an Early Intervention Program (EIP) in patients with TWI of musculoskeletal origin.

Methods: Case-control study, including patients from HUP La Fe area, which were referred from Primary Care since April 2012 to April 2016 to our Early intervention program (EIP) addressed to patients with TWI of musculoskeletal origin. The patients were evaluated in our consultation within a maximum of 15 days after the start of TWI. The intervention consisted in an evaluation, including complementary tests if necessary; diagnosis and treatment by the rheumatologist in our consultation. The patient was followed in consultation until discharge. Patients whose disabilities were of traumatic or surgical origin were excluded. A comparative study was carried out against a control group of patients with ILT of musculoskeletal origin.

Results: A total of 666 patients were recruited; 508 (76.3%) belonged to EIP group (46.1% male; 53.9% female) and 158 patients (23.7%) belonged to the control group (44.3% male; 55.7% female). The average age was 47.6±10.5 years for the EIP ones and 46.7±10 years in the control group. The most frequent diagnoses were low back pain (23.3%), neck pain (18%) y lumboscleratica (12%). In EIP group, 100% of the patients received medical treatment, a 54.5% received instructions for doing physical therapy at home, an ultrasound scan was performed to the 26.4% of the patients while the 19.9% received at least one local infiltration. The longest TWI corresponded to knee meniscopathy (203 days), painful shoulder syndrome (173 days) and lumboscleratica (170.5 days). No statistically significant differences were found between the duration of the TWI attending to sex, age group, labour activity or diagnosis. However, a significant association was found between TWI duration and the delay since the start of the symptoms to the referral from Primary Care to our consultation, specially within the first 10 days (p=0.04). Furthermore, TWI duration was significantly shorter in the EIP group patients than in the control group patients (137.4±132.3 days vs 194.7±143.1 days; p<0,001).The period after relapse was longer in the EIP group, although the differences did not reach statistical significance. In an inverse relation was found between age and time to relapse (p=0.01).

Conclusions: The establishment of an early intervention program specifically addressed to patients with temporary work incapacity of musculoskeletal origin shortens the duration of the incapacity, allowing the patient to rejion his work activity, with the resulting cost savings related to work incapacity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5486

THU0624 | ASSESSMENT OF PSYCHIC EXPERIENCES IN PATIENTS WITH RHEUMATIC DISEASES

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Background: There are several studies that report psychiatric comorbidity in patients with rheumatic disease, mainly the presence of mood disorders. Some of them describe non-affective psychosis related with inflammatory processes. There are several studies that report psychiatric comorbidity in patients with rheumatic disease, mainly the presence of mood disorders. Some of them describe non-affective psychosis related with inflammatory processes.

Objectives: To identify the presence of psychic experiences in different populations with a diagnosis of rheumatic disease, and to compare it with a sample of healthy subjects.

Methods: 124 subjects completed surveys including SF-12 and CAPE questionnaire, as well as other demographic and behavioral variables. Among them, 70 had Spondylarthrits (SpA) (age 44.3±13 years, 62% female), 23 rheumatoid arthritis (RA) (age 51.2±13 years, 82% female) and the rest were individuals without rheumatic diseases (47.6±12 years, 58% female).

Results: Results of the SF-12 test in their mental and physical domains, and the CAPE questionnaire in their dimensions (positive, negative, depressive and total symptoms) are shown in the table, expressed as mean value (SD) and in the graph expressed as density histograms with mean values. Significant statistical
differences, according a t de Student test with control group is shown in both (* p < 0.05, ** p < 0.01).

There were no significant differences in the mental component of the SF-12. These differences appear at the physical component, since patients have impaired their mobility and function due to their disease. About the CAPE questionnaire, patients had a little bit higher score due mainly to the appearance of depressive symptoms. The values of positive symptoms of psychosis remained within the normal range for diseases analyzed.

Conclusions: In our study, we found significant differences in the dimensions, especially depressive, of the CAPE scale among patients with rheumatic diseases (especially in SpA) and healthy subjects. This gives us an idea of the importance of considering the psychological problems of patients (anxiety, depression, ...) to improve the treatment of rheumatic disease.

Acknowledgements: We would like to thank these patients' organizations for their collaboration in our study: Coordinadora Española de Asociaciones De Espundrios (CEADE), Asociación Cordobesa de Enfermos de Espundrios (ACEADE), Asociación Cordobesa de Enfermos de Artritis Reumatoide (ACORE).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3505

**THU0625**

**DESIGN OF AN INFORMATION AND COMMUNICATIONS TECHNOLOGY PLATFORM TO SUPPORT COORDINATION OF CARE FOR RHEUMATOID ARTHRITIS PATIENTS WITH CARDIOVASCULAR CO-MORBIDITIES – FIRST EXPERIENCES**

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Background: Coordination of care plans between healthcare sectors and efficient management of patients (pts) with co-morbidities is of large demand. Rheumatoid arthritis (RA) pts are at increased risk of cardiovascular diseases (CVD). Different stakeholders are potentially involved in the EULAR recommended management process of RA pts. The interdisciplinary information and communication technology (ICT) platform within the Horizon2020-funded PICASO-project (www.picaso-project.eu) will support a continuum of care from hospitals and outpatient clinics to the home.

Objectives: Explore challenges to provide an efficient ICT integrated solution across many healthcare professionals working for various organisations and potentially crossing national borders that complies to privacy and regulatory constraints allowing more efficient care management. Suitable system architecture and appropriate features require identification of target users’ user requirements. PICASO platform will be developed and trialed with pts and clinician. The proposed system relevant To-Be Use Cases, numerous user requirements and EU-wide stakeholder are potentially involved in the EULAR recommended management process of RA pts. The platform will become take place in iterative cycles followed by prototypes’ thoroughly evaluated by real end users investigating usability and acceptance. The platform will become available for RA-pts in routine care but also for wider applicability in Rheumatology and other chronic diseases.

References:

Acknowledgements: This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 689209.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4001

**THU0626**

**COST-EFFECTIVENESS OF EARLY TREATMENT OF ACPA POSITIVE RHEUMATOID ARTHRITIS PATIENTS WITH ABATCEPT**

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Background: Studies have reported that the presence of elevated anti-citrullinated protein antibodies (ACPA)/RF levels, together with joint erosions, is associated with higher disease burden in terms of disability, and mortality in rheumatoid arthritis (RA). Abatcept has been shown to be effective in this patient population with favorable comparative data against adalimumab.(1) However, few studies have investigated the cost effectiveness of abatcept in this population to similar treatments such as TNFs.

Objectives: The objective of the study was to compare the cost-effectiveness of abatcept to adalimumab as a first bDMARD in ACPA positive RA patients who failed treatment with methotrexate (MTX) in Germany.

Methods: A decision tree model was used to estimate the cost-effectiveness, from a payer’s perspective, of different treatment sequences in RA over a two year time frame. The effectiveness criteria were defined as achieving the treatment target measured by the Disease Activity Score 28 (DAS28 (CRP))-2.6; "remission". A treatment switch to a different biologic as 2nd line and 3rd line bDMARD was allowed -in case of not achieving remission with therapy- every 6 months over a two year time period. Effectiveness data was based on randomized controlled trials (RCT) identified by an updated previous systematic literature search by the Institute for Quality and Efficiency in Health Care (IQWiG). Costs of medication and other direct medical costs were taken from a recent publication (2) and included in the analysis. Cost-effectiveness of RA treatment was investigated in ACPA positive patients in this study and presented as overall costs per day in a payer’s perspective.

Results: For ACPA positive patients, treatment strategies including early treatment with abatcept had lower total costs per clinical outcome compared to later use. Figure 1 summarizes the costs per day in remission for the treatment sequences investigated: treatment of sequences starting with abatcept resulted in lower costs for reaching remission (mean 330 €/day, range 328 €-390 €/day) compared to sequences starting with adalimumab (mean 384 €/day, range 378 €-390 €/day). Choice of the second or third biologic in the treatment sequences appears to have little impact on the costs per outcome.

Conclusions: The results of this analysis suggest that in ACPA positive RA patients treatment with abatcept appears to be more cost-effective compared to treatment with adalimumab as a first bDMARD.

References:

**THU0627**

**COGNITIVE BEHAVIOURAL THERAPY FOR TREATMENT OF PSYCHOSIS IN RHEUMATIC DISEASE PATIENTS: AN OPEN-LABEL, RANDOMISED CONTROLLED TRIAL**

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Background: A significant minority of rheumatic diseases patients report psychosis symptoms, which are often severe and may have a negative impact on quality of life. Cognitive-behavioral therapy (CBT) has been shown to be an effective intervention for psychotic symptoms in schizophrenia. However, no studies have investigated the use of CBT for psychotic symptoms in rheumatic diseases patients.

Objectives: To investigate the efficacy of CBT for psychotic symptoms in patients with rheumatic diseases.

Methods: We performed an open-label, randomised controlled trial (RCT) in two centres in Germany. Patients were randomised to receive CBT or waiting list. The CBT consisted of 12 weekly sessions of 90 min, adapted to the needs of patients with rheumatic diseases. The primary outcome was the Clinical Assessment of Psychotic Symptoms (CAPS) total score. Secondary outcomes included the Acute Psychosis scale for Schizophrenia and the German version of the SF-12. A sub-analysis was performed for patients with or without antipsychotic treatment.

Results: Fifty patients with a rheumatic disease and psychotic symptoms were randomised and included in the analysis. Twenty patients were assigned to CBT and 30 to the control group. At weeks 12 and 22, primary outcome results were significantly improved in the CBT group compared to the control group (p=0.001 and 0.01 respectively). The best response (≤20%) was reported by 35% of the CBT group and 8% of the control group (p=0.03). The sub-analysis showed a similar response between patients with or without antipsychotic treatment. No serious adverse events were reported.

Conclusions: CBT for psychotic symptoms in rheumatic diseases patients is feasible and has a significant effect on psychotic symptoms. Further research is needed to confirm these findings and to evaluate the long-term effects of CBT.

References:
TREATMENT OF RHEUMATOID ARTHRITIS: ADHERENCE TO GUIDELINES IN PRIVATE PRACTICE


Background: Guidelines and therapeutic strategies in the treatment of rheumatoid arthritis (RA) have been developed and adopted by most Societies of Rheumatology. However, the extent to which these recommendations are followed by rheumatologists in their individual clinical practice is unclear.

Objectives: Our aim was to analyze, at private offices, adherence to guidelines and characteristics of RA patients in regular follow-up.

Methods: This was a cross-sectional study developed by a group of rheumatologists (n=13) working exclusively in private offices and hospitals in São Paulo, Brazil. It consisted of a web-based questionnaire addressing patient’s demographic, social characteristics and treatment. Patients having the diagnosis of RA should be included sequentially. As Brazil’s private health has no reference flowchart, patients can consult any physician from their insurance health program, or rheumatologist’s office. We were measuring the compliance on biologic or target “under control”. In fact, 72% of patients were on low disease activity (22%) or activity were analyzed, few of them (0.28 CI 0.18–0.40) were on biologic or target therapy; PsO patients’ dosing was observed to be lower than monograph during the loading phase, while higher than monograph in the maintenance phase.

Conclusions: In Canadian real-world practice, the average patient utilization of etanercept remained consistent over the first year in majority of patients, with the exception of those with PsO. A notable proportion of etanercept patients with rheumatoid arthritis reduced their dosing over time. This could be due to patient-related factors as high treatment costs or lack of resolution, while few of them (0.28 CI 0.18–0.40) were on biologic or target therapy as key factors in the decision to return to monograph in the loading phase, while higher than monograph in the maintenance phase.

Disclosure of Interest: M. Khraishi1, Grant/research support from: Abbvie, Biogen, BMS, Chugai, Hexal, Medac, Pfizer, Roche, Sanofi Aventis, UCB DOI: 10.1136/annrheumdis-2017-eular.6959

TREATMENT OF ETANERCEPT DOSE ADJUSTMENTS IN A REAL-WORLD SETTING: A CANADIAN RETROSPECTIVE COHORT STUDY

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Background: Etanercept is a soluble TNF receptor (humanized protein) indicated for treatment of immune-mediated inflammatory diseases, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (PsO), and ankylosing spondylitis (AS). Canadian monograph recommended dosing of etanercept is 50mg/week, while treating RA patients in a loading phase requiring an increased dose for 12 weeks. Evidence suggests that real-world practices differ from monograph, with patients titrating to lower or higher weekly dose as needed. Limited research exists on how etanercept patients are dose optimized in the real-world Canadian setting.

Objectives: To describe etanercept treatment dynamics, including dose de-escalation/escalation in the Canadian real-world setting.

Methods: A retrospective cohort study was conducted utilizing claims-level data from QuintilesIMS Private Drug Plan database, Ontario Public Drug Plan database, and Quebec Public Drug Plan database. Between 07/2013–06/2015, bio-naïve patients initiating etanercept and who remained on their biologic for 12 months were identified. Weekly dosing of each patient was calculated and analyzed for the prevalence and magnitude of dose de-escalation/escalation. Patients with at least 20% lower/higher average dose than monograph recommended dose (50mg/week) were flagged as dose de-escalators/dose escalators, respectively. The first 3 claims of etanercept were excluded from average dose calculations to exclude a possible loading phase.

Results: The study identified 3,051 etanercept patients (60% female, 77% aged between 18 and 65, 87% rheumatic diseases, and 13% PsO) across Canada in the 12-month period. Of 1,547 patients (n=332) dosed during their first year of therapy, led by AS (15%, n=24) and RA (12%, n=286); 15% (n=449) of patients escalated, led by PsO (64%, n=282) versus 7% (n=168) in RA; 74% (n=2,270) of patients maintained a consistent dose. Average dosing across rheumatic disease patients stabilized to monograph levels by week 20 of their therapy; PsO patients’ dosing was observed to be lower than monograph during the loading phase, while higher than monograph in the maintenance phase.

Conclusions: In Canadian real-world practice, the average patient utilization of etanercept remained consistent over the first year in majority of patients, with the exception of those with PsO. A notable proportion of etanercept patients with rheumatoid arthritis reduced their dosing over time. This could be due to patient-related factors as high treatment costs or lack of resolution, while few of them (0.28 CI 0.18–0.40) were on biologic or target therapy as key factors in the decision to return to monograph in the loading phase, while higher than monograph in the maintenance phase.

Disclosure of Interest: M. Khraishi Consultant for: Pfizer Canada and Amgen Canada; None declared, E. Singh: None declared, J. Woolcott: None declared, H. Jones: None declared DOI: 10.1136/annrheumdis-2017-eular.6959

PATTERNS OF ETANERCEPT DOSE ADJUSTMENTS IN A REAL-WORLD SETTING: A CANADIAN RETROSPECTIVE COHORT STUDY

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Disclosure of Interest: None declared, E. Singh: None declared, J. Woolcott: None declared, H. Jones: None declared

GUIDELINES IN PRIVATE PRACTICE

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Disclosure of Interest: None declared, E. Singh: None declared, J. Woolcott: None declared, H. Jones: None declared

The PERSPECTIVES OF PATIENTS, THEIR FIRST DEGREE RELATIVES, AND RHEUMATOLOGISTS AROUND PREVENTATIVE TREATMENTS FOR RHEUMA...
Acknowledgements: This work was supported by a grant from the Canadian Rheumatology Association through the Canadian Initiative for Outcomes in Rheumatology Care (CIORA).

Disclosure of Interest: None declared


THU0630 OPIOID USE IN PATIENTS WITH POLYMALGIA RHEUMATICA

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Background: Polymyalgia rheumatic (PMR) is a systemic rheumatic inflammatory disease characterized primarily by musculoskeletal pain and stiffness. Glucocorticoid treatment is the current standard of care however the need for additional pain management, in particular the need for opioid therapy, has not been studied.

Objectives: To examine the trends of chronic opioid use in patients with PMR over an 11 year period in Olmsted County, Minnesota, USA and compare this to subjects without the disease.

Methods: Retrospective data on opioid prescriptions were collected from 2005 to 2015 in a population-based incidence cohort of patients meeting the 2012 American College of Rheumatology classification criteria for PMR alongside comparison subjects. Poisson regression methods were used to compare opioid use between these groups.

Results: 244 patients with PMR and 211 non-PMR comparator subjects were included in the study. Rates of chronic opioid use were not significantly different between the two groups. 7.5% of patients with PMR were identified as chronic users by the end of the study period compared with 5.2% of non-PMR subjects. Any opioid use was also not significantly higher in PMR, with relative risk of 1.10 (95% CI 0.97, 1.26, p=0.14). There were higher rates of chronic use among patients over 80 years in both groups.

Conclusions: PMR does not appear to be associated with increased rates of opioid use when compared with the general population.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1237

THU0631 DIRECT FINANCIAL BURDEN OF RHEUMATOID ARTHRITIS ON PATIENTS’ LIFE IN A DEVELOPING NATION OF PAKISTAN, ONE YEAR PROSPECTIVE STUDY

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Background: Rheumatoid Arthritis is chronic inflammatory disease. Early diagnosis and management is necessary to avoid joint destruction and to minimize disability. It affects 0.5 to 1 percent population. The female to male ratio is 3 to 1. Health care cost is of great concern to patients, physicians and health care policy makers. The financial impact of rheumatoid arthritis treatment like any chronic illness is of great significance in developing society like Pakistan where 30 percent population lives below poverty line and annual per capita incomes are very low. Whereas prevalence is same with high medicines prices with poorly developed health insurance system and government funded hospitals are scanty.

Most of the times attention in the field of health economy is focused on direct medical cost in general and hospital cost in particular but however there are some social societal customs which also increases the burden of direct cost. The direct cost includes expenditures like physician visit cost, diagnostic tests, medications. There are also some hidden charges to this direct cost which are not included in studies. Like transport charges, food bills during hospital stay and accompany person, female are companied by males. All included puts strain on economy and major share of annual income of patient is paid on management of disease. The worst scenario is when patient stops treatment and if lucky gets support from other resources like patient welfare societies or from relatives.

Objectives: To assess the direct cost of patient’s every visit to hospital outpatient department prospectively for one year and total cost of one year was summed up and percentage to annual income spend on treatment was calculated.

Methods: Study carried out from January to December 2015 at Fazle Omar Hospital Rawalch Khan Nagar and 150 patients either newly diagnosed or already on treatment of rheumatoid arthritis were included. Data collected for next 1 year for each visit, patients with any other disease along with rheumatoid arthritis were excluded. The estimated annual income of patient or the person bearing the cost of the patient was calculated by the end of the study period compared with 5.2% of non-PMR subjects.

Results: The mean total per patient income after conversion from local currency was 3000 US dollars against 1474 US dollars per capita income in 2015. The annual average cost per patient including consultation fee, medicines purchased, laboratory investigations and other overhead expenses like transportation of patient and accompanied person and food bills during hospital stay was 1194 US dollars. 41% of patient gross income was spend on management of rheumatoid arthritis.

Investigations cost 12%, medicines purchased 16%, consultation 2% and overhead visit charges cost 10% of the total mean of per patient annual income.

Conclusions: RA management consumes large portion of patients annual income and it has significant burden on developing world economy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5571

THU0632 VALIDATION OF INTERNET-BASED REPORTING OF PATIENT REPORTED OUTCOMES WITHIN THE SWEDISH RHEUMATOLOGY QUALITY REGISTER

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Background: Previous studies have validated the use of clinic based touch-screens for registering patient reported outcome measures (PROMs) (1–3). The Swedish Rheumatology Quality (SRQ) register has implemented an internet-based method (PER (Patientens Egen Registrering, or Patients’ sElf Registration)) for collecting PROMs.

Objectives: The aim of this study was to investigate the feasibility of the internet-based method as well as the validity of reported outcomes and disease activity scores compared to the gold standard paper format.

Methods: We recruited patients (n=44, mean age =51.0, standard deviation =13.2 years, 69.6% women) included in SRQ with a diagnosis of rheumatoid arthritis, psoriatic arthritis, juvenile arthritis, spondyloarthritis or anklyosing spondylitis. Before a planned visit at the rheumatology clinic the patients registered Visual Analog Scales (VAS) for global health, pain and fatigue, both electronically by PER and on paper. Patients with axial disease also registered BASDAI and BASFI related variables (n=6). For patients with peripheral arthritis (n=38), DAS28 was calculated using both methods. The differences between the methods were compared by T-test and Intra-class correlation (ICC). Agreement was visualized using Bland-Altman plots for all VAS registrations. The patients also answered a questionnaire regarding the used device and preferred method.

Results: No differences between PER or paper based VAS scores were found for VAS Global, VAS Pain and VAS Fatigue (p=0.086, p=0.691 and p=0.197, respectively). ICC scores ranged from 0.930 to 0.971. Bland-Altman plots for VAS assessments showed good agreement and no proportional bias was detected (Fig 1). Mean difference for DAS28 was -0.04 (p=0.177). Of the recruited patients, 76%, preferred the Internet based method. BASDAI and BASFI could not be evaluated due to a limited number of observations.

References:

Fig. 1 Bland-Altman plot showing level of agreement of all VAS (VAS Global, VAS Pain, VAS Fatigue, VAS included in BASFI and BASDAI) between paper and PER method. BASDAI and BASFI scores multiplied by 10 for comparability.

Conclusions: Internet based reporting of PROMs supply valid VAS data. DAS28 scores from the internet-based method presents an acceptable alternative to the traditional paper formats.

References:
Disclosures of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2590

**THU0633** TEMPERATURE SENSITIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Studies evaluating weather sensitivity among patients with rheumatoid arthritis (RA) have yielded conflicting results.

**Objectives:** To evaluate whether patients with RA exhibit sensitivity to outside temperature.

**Methods:** We assessed correlation between mean daily temperature and self-reported pain (by visual analogue scale), and patient’s global assessment of disease activity (PGA). Assessments documented in the RA database of our department as well as the average temperature obtained from the Central Institute for Meteorology and Geodynamics, were matched on a daily basis for a period of 10 years between 2005 and 2015 and analyzed using generalized estimating equation (GEE) and a mixed model analysis (MM). Patients with <5 visits in the study period, or with <1 visit/quarter or with pain=0 in ≥3 consecutive visits and those living outside of the catchment area were excluded. Overlap between responsiveness of pain or PGA to temperature was calculated by Cohen's kappa.

**Results:** A total of 399 patients with RA (average disease duration at first visit: 6.0±7.6 years, average age: 57.7±13.9 years, 82% female, mean CDAI 19.7±11.5, 59.9% rheumatoid factor positive) were analyzed. Lower temperatures correlated significantly with higher pain levels (estimate: -0.07, p=0.021) in GEE, however, the effect size was very small. When we performed MM with temperature as independent variable and VAS pain or PGA as dependent variable, the majority of patients showed no sensitivity to temperature, however 22% of patients were significantly sensitive to cold temperature with an estimate of -0.29 (p=0.0001) for pain and -0.21 (p=0.0005) for PGA (Figure 1). When we evaluated whether patients who demonstrate temperature-sensitivity to pain also exhibit temperature-sensitivity to PGA, we found an excellent overlap between the two patient groups (kappa: 0.81).

**Conclusions:** Our results indicate that a subgroup of patients with RA show significant sensitivity to cold temperature, and that these patients are characterized by higher pain and PGA levels at lower daily temperatures. These aspects may have to be taken into account in longitudinal analyses of disease activity of RA.

DOI: 10.1136/annrheumdis-2017-eular.2590

**THU0634** COMPARING PREFERENCES OF PATIENTS WITH RHEUMATIC DISEASES, OF RHEUMATOLOGISTS, NURSES AND PHARMACISTS TOWARDS THE TREATMENT OF RHEUMATIC DISEASES WITH BIOLOGICAL AGENTS: RESULTS FROM THE CARA STUDY

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**Background:** Electronic medical records (EMR) have emerged as a large-scale data collection option for observational studies. These huge data registries create new opportunities to study the rheumatologic phenotype and the real-life implications for these diseases. EMR usage poses new questions of quality management, such as how to reliably identify patients with the disease or phenotype of interest, as well as bioinformatic tools to handle the magnitude of data.

**Objectives:** The algorithms used to identify cases are often not validated and overly simplify by using one financial code, or they are well-validated but require very specific information which hampers the applicability to other datasets.

**Methods:** Aim I: Test the accuracy of the identification of patients with rheumatoid arthritis (RA) using the financial coding system.

Aim II: Develop a simple and precise algorithm to select patients with RA that is easy to implement at other centers.

**Results:** Aim I: Out of the 16,183 Rheumatoid arthritis patients in the Leiden out-patient EMR system 400 charts were randomly selected and reviewed for the Rheumatologist diagnosis. Next, the charts were reviewed by 200 randomly selected patients that were labeled as RA in the financial system.

Aim II: To enable generalizability, only codified data that was obtained at regular outpatient clinic visits was used. Lasso regression was applied to identify the most discriminative variables.

**Conclusions:** The vast majority of patients that are classified as having RA are registered as such in the financial system. However, a substantial number of patients are registered as RA in the financial system are not classified as RA in clinical charts. Using widely available data on anti-CCP status, MTX prescription...
and visit count improved the selection of RA patients from a 67% to 90% accuracy. The combination of these variables provides a widely applicable algorithm, as they are broadly registered in Rheumatology clinics.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4846

THU0636 INFLUENZA AND MENINGOCOCCAL C VACCINATIONS IN A COHORT OF PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: ADHERENCE, SAFETY AND IMMUNORESPONSE

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Background: The EULAR recommendations for vaccination in adult patients with autoimmune rheumatic diseases strongly recommend inactivated influenza vaccination. Insufficient data are available about safety and efficacy of meningococcal C vaccination. In 2015–2016, after an increased incidence of meningococcal C infections in our country, the health care system has promoted a free meningococcal vaccination campaign.

Objectives: To evaluate the adherence to the EULAR recommendations for influenza vaccination and to the meningococcal C vaccination campaign in a cohort of patients with autoimmune rheumatic diseases and to assess their efficacy. The safety in terms of immune response to meningococcal C vaccination has been also evaluated.

Methods: Consecutive in- and out-patients seen at our unit from February to December 2016 were enrolled in the study. A questionnaire created ad hoc the following data were collected: the percentage of patients who underwent influenza and/or meningococcal C vaccinations in the previous 12 months, the occurrence of adverse events and of disease flares after vaccinations, according with the report from the patients and with the rheumatologist clinical evaluation. Seroconversion rates in patients with previous immune control were assessed using MKBA kits for biologic anti-meningococcal ACWY IgG antibodies. Antibody titres were expressed in U/ml and according with kit reference values were classified in absent, low, medium and high titre.

Results: 286 patients (91% female) (143 SLE, 68 RA, 60 Scleroderma, 11 Sjögren Syndrome, 3 Behcet disease and 1 dermatomyositis) were included in the analysis. The mean age at evaluation was 52.9±16.1 years, mean disease duration was 15.3±10 years. The 53.1% of patients was taking steroids, at an average dose of 4.2 mg of 6-metilprednisolone/day. 124/286 (46.9%) patients were on immunosuppressive therapies, of which 49/134 (36.6%) kits for biologic agents. The 19.9% (57/286) of patients underwent influenza vaccinations and the 13.3% (38/286) meningococcal C vaccination. 8 patients underwent both vaccinations. No disease flares were observed after vaccination: seven patients reported non-specific adverse events after influenza (fever, discomfort, nausea, arthralgia) and 2 patients after meningococcal C vaccination (fever, rash at the injection site, discomfort). Seroconversion after meningococcal vaccination was analysed in 27 patients and 9 healthy subjects, no statistically significant differences in terms of antibody response to meningococcal vaccination were observed between these two groups (T-test). Treatment with steroids and immunosuppressive drugs did not influence antibody titres.

Conclusions: These data highlight the poor adherence to international recommendations on influenza vaccination in patients with autoimmune rheumatic disease at our Unit. The adherence to the meningococcal vaccination campaign conducted in our country in 2015–2016 was also low. Our data confirm the safety of these vaccinations and show that the immune response elicited by meningococcal C vaccination is comparable to healthy controls and is not influenced by therapy


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6123

THU0637 PATIENT’S AND RHEUMATOLOGIST’S PERSPECTIVES ON THE FOLLOW-UP INTERVAL AS A TOOL FOR OPTIMIZED OUTPATIENT TREATMENT

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Background: Scientific progress and better disease awareness constantly lead to increasing patient numbers in rheumatology which requires optimization of patient care.

Objectives: The aim of this study was to evaluate and to optimize the procedures of patient care in an university-based outpatient rheumatology setting in Berlin, Germany.

Methods: One hundred patients with rheumatoid arthritis (80 women, 20 men, mean age 61.2 years, mean disease duration 12.9 years) were independently assessed both by a rheumatologist and via patient-reported self-assessment questionnaires. Current follow-up interval (usually 3 months), patient’s perspective on follow-up intervals, signs of disease activity as well as individual patient concerns were recorded. Satisfaction with follow-up intervals was grouped into three categories: too early, just right/opportimal, too late.

Results: Based on the physicians perspective, 46 patients presented at the optimal time point, 51 too early, and three too late. The patients reported the category “just right” in 82 cases, too early follow-up in 10 cases and too late in 8 cases. Of note, 51% (42 individuals) of all patients with self-reported satisfactory follow-up interval were judged to visit the outpatient department too early by the expert rheumatologist. When taking into account the follow-up interval and optimal satisfactory levels, 62% of patients were concluded to visit the department too early, those who revisited anew about 12 months (n=46), and in 12% of those who were seen again after 5–6 months (n=17). 82% of patients in the latter group were judged to revisit just right by the physician.

Conclusions: There was a high proportion of overlap in the views on the satisfaction with follow-up intervals between physicians and patients, especially in patients who were seen every 3–4 months, a high proportion was deemed to could have come later to the outpatient care unit from a purely medical point of view. Here we see a way to stretch the interval to 5–6 months without risking a long-term deterioration in patient care. However, this measure should be flagged by patient education and good collaboration with the general practitioners.

Acknowledgements: We thank AbbVie for financial support in the development of measures to optimize out-patient management in patients with rheumatoid arthritis. The sponsor did not influence the scientific results.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4748

THU0638 PREVALENCE AND DIRECT HEALTHCARE COSTS OF UPPER GASTROINTESTINAL (UGI) ADVERSE EVENTS IN ASIAN RHEUMATIC PATIENTS ON LONG-TERM NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

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Background: NSAIDs are frequently used in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). NSAID-induced UGI adverse events are well described in the Western population but data is lacking in Asian patients.

Objectives: To describe the prevalence and direct healthcare costs of NSAID-induced UGI adverse events in a large cohort of RA and OA patients in Malaysia.

Methods: A retrospective cohort study of RA and/or OA patients who received long-term NSAIDs (minimum 4 weeks prescription of any NSAID) between 2010 and 2013 was conducted in 4 large tertiary care centres with rheumatology units in Malaysia. Electronic clinical records and pharmacy prescriptions were reviewed. Resource use data was collected in patients who developed UGI adverse events within the 24 months follow up period. Unit costs were estimated by combining top down (general overheads for hospital services) and bottom up (activity-based costing for clinic visits, hospitalisation, diagnostic investigations, medications) approaches.

Results: 634 patients were included in the final analysis with mean age 53.4±12.5 years, 90% female, diagnosis of RA in 60%, OA in 10% and both RA and OA in 30%. 45% and 8% of patients were on concomitant prednisone and aspirin respectively. 89% of patients had no previous upper GI disease. 59% and 41% of patients were grouped under non-selective and COX-2 inhibitor respectively. 84 (13.2%) patients developed UGI adverse events (Figure 1), consisting of 78 (12.3%) patients with dyspepsia, 5 (0.7%) with peptic ulcer disease (PUD) and 1 (0.1%) with upper GI bleeding (UGIB). The total direct cost was RM37,352 (USD 11,419) with a mean cost of RM447±535 (USD 137±163) per patient (Table 1). The largest cost components were pharmacotherapy (34%), oesophagogastroduodenoscopies (OGD) (23%) and outpatient visits (18%). The mean cost of PUD and UGIB was approximately double (RM806±579 (USD 246±177) and quadruple (RM1,602) (USD 490) of dyspepsia respectively.

<table>
<thead>
<tr>
<th>Healthcare resource</th>
<th>Mean cost per patient in RM (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspepsia (n=78)</td>
<td>PUD (n=8)</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>77 (23)</td>
</tr>
<tr>
<td>Emergency Dept visits</td>
<td>28 (9)</td>
</tr>
<tr>
<td>Inpatient stay</td>
<td>46 (14)</td>
</tr>
<tr>
<td>OGD</td>
<td>103 (28)</td>
</tr>
<tr>
<td>Blood tests</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Radiology</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>150 (46)</td>
</tr>
<tr>
<td>Mean cost per patient in RM</td>
<td>409±513</td>
</tr>
</tbody>
</table>

Conclusions: The low prevalence of UGI adverse events in Malaysian rheuma-
RHEUMATOLOGICAL MEDICATION USE IN PREGNANCY, SECOND LINE TREATMENT PERSISTENCE AND COSTS

2.

S.-N. Luong

DOI:

Disclosure of Interest:

None declared

Background:

MotherSafe is a free, statewide, phone based counselling service for the general public and healthcare professionals concerned about exposures during pregnancy, pregnancy planning and breastfeeding (1). Obstetric drug information services such as MotherSafe are important in guiding decision-making in pregnancy, breastfeeding and planning of future pregnancies, and are increasingly used worldwide by both patients and healthcare providers (1, 2). At MotherSafe, phone advice is provided by trained telephone counsellors who are generally pharmacists. Data from each phone call is entered onto an electronic document. Some patients are then referred onto the MotherSafe clinic for specialised counselling by a clinical geneticist.

Objectives: To analyse data including patient and medication characteristics and trends from phone calls made to MotherSafe regarding disease modifying antirheumatic drugs (DMARDs) and biologic DMARDs (bDMARDs) from January 2010 to December 2015 regarding conventional DMARDs and biologic DMARDs. SPSS software facilitated statistical analysis.

Results: A total of 135,115 phone calls were made to MotherSafe from January 2010 to December 2015 regarding conventional DMARDs and biologic DMARDs. Of these 2611 phone calls, 65.4% were made by patients and 13.5% by general practitioners. Most phone calls were made in metropolitan New South Wales (69.3%). 43% of phone calls were concerning exposures during breastfeeding, followed by exposures during pregnancy (32.9%), exposures whilst planning pregnancy (17.7%) and paternal exposures (2.9%). Where a specific diagnosis was given, inflammatory bowel disease was the most common indication (18.4%), followed by rheumatoid arthritis (8.2%), Corticosteroids were the most common medication exposure (37.3%), followed by azathioprine (18.8%), sulfasalazine (11.2%) and methotrexate (8.5%).

Most callers just received phone advice, especially if the call was just regarding breastfeeding exposures (73.4%). 383 callers (14.7%) were referred onto the MotherSafe clinic, which is run by a clinical geneticist. bDMARDs made up 9.5% of calls with calls trending to increase over the years, but there was a slight decrease in 2012 and 2013 albeit with small numbers. TNF inhibitors still made up the majority of calls regarding bDMARDs.

Conclusions: This study evaluated the only obstetric medicine exposure information service in New South Wales, Australia. It is the first time that DMARDs and bDMARDs have been analysed for MotherSafe. There was a trend to increasing number of calls regarding bDMARDs over 2010 to 2015, which presumably reflects change in prescribing patterns. This study highlights the need for services like MotherSafe so patients and health care professionals can receive evidence based information and make choices about treatment in pregnancy.

References:


Acknowledgements: MotherSafe staff.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5560

THU0640 SECOND LINE TREATMENT PERSISTENCE AND COSTS AMONG PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISEASES TREATED WITH SUBCUTANEOUS TNF-ALPHA INHIBITORS

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Background: For some patients with Immune Mediated Rheumatic Disease (IMRD) discontinuing 1st line treatment with a subcutaneous Tumor Necrosis Factor-alpha inhibitor (SC-TNFi), 2nd line treatment with another SC-TNFi may be appropriate.

Objectives: The primary objective of this study was to describe treatment persistence with 2nd line SC-TNFi stratified by agent in patients with IMRD in Sweden. The secondary objective was to explore the impact of non-persistence with second SC-TNFi on 12 months total healthcare costs.

Methods: We conducted a retrospective study on treatment persistence and health care costs using data from health registers. Adults (~18 years old) previously treated with one SC-TNFi and subsequently prescribed a second SC-TNFi were identified through prescriptions for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 5/6/2010 and 12/31/2012. Prescriber specialty and department were used to exclude patients treated for diseases other than IMRD. Persistence up to 3 years was estimated using non-parametric survival analysis. Given differences in baseline characteristics, analyses were conducted on propensity score matched (PSM) cohorts. Matching was based on age, gender, index diagnosis, Charslon Comorbidity Index and non-biologic DMARD use. Non-treatment health care costs were captured 12 months pre and post initiation of 2nd line SC-TNFi treatment and stratified by persistence status at 6 months.

Results: In total, 845 patients were identified (ADA: 316, ETA: 202, CZP: 140, GLM: 187). PSM cohorts were generated as GLM vs ADA, GLM vs ETA and GLM vs CZP. All patients were captured 12 months pre and post initiation of 2nd line SC-TNFi treatment.

Conclusions: In patients previously treated with a SC-TNFi, GLM exhibited significantly better persistence than ADA and numerically higher persistence than ETA and CZP at 12 and 24 months, findings that are similar to results observed in 1st line SC-TNFi patients. The lower healthcare costs for persistent patients, the choice of 2nd line SC-TNFi among eligible patients may merit careful consideration given its impact on patients and payers.

References:


DOI: 10.1136/annrheumdis-2017-eular.2554
THU0641 THE DISEASE BURDEN OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS FOR PATIENTS AND CAREGIVERS: AN INTERNATIONAL HEALTH RELATED QUALITY OF LIFE SURVEY AND RETROSPECTIVE CHART REVIEW

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Background: Systemic juvenile idiopathic arthritis (SJIA) is a severe autoinflammatory disease characterised by systemic features including high fevers, rash and arthritis. SJIA can impose a high physical, psychosocial, behavioral and financial burden on patients (pts) and their families.

Objectives: To analyse the impact of SJIA burden of disease burden utilising a SJIA-specific questionnaire combined with physician data about disease severity and treatment in an international, real-world study.

Methods: SJIA treatment centres in France, Germany, Netherland, UK and the US participated. Pts (aged 4–18 years) with confirmed SJIA received one of the following biologic treatments for ≥2 months: anakinra (ANA), canakinumab (CAN), or tocilizumab (TOC). SJIA burden in patients on biologics was assessed using a caregiver questionnaire and retrospective chart review. Validated measures included: Child Health Questionnaire Parent-Form 50 (CHO-PF50), 36-Item Short Form Health Survey (SF-36v2); and Activity and Impairment questionnaires: Specific Health Problem (WPAI:SHP). Caregivers completed function, treatment satisfaction and resource utilization questions.

Results: Sixty-one pts enrolled from June 2015–June 2016: 12 on ANA, 25 on CAN, 24 on TOC; 46% from the US; 48% female; mean age at survey was 11.2 years. Mean age at SJIA diagnosis was 6.4 years, 6 years at start of CAN, and TOC treatment was 9.9, 9.1, and 7.5 years, respectively. Caregivers were 79% female, mean age 41.2 years, 36% reduced or stopped working due to their child's SJIA. Of the pts enrolled ON CAN and TOC, 72% and 46% respectively had previously been on ANA. EQ-5D, ChAQ, CHO-PF50, and WPAI scores were worse in CAN and TOC than ANA pts. Mean (±SD) CHO-PF50 (PHS) and psychosocial (PsS) summary scores were significantly lower in SJIA patients than a normative population (PHS: 40.0±18.2 vs. 53.0±6.8, PsS: 46.2±11.3 vs. 51.2±9.1) as was caregivers’ mean SF-36v2 mental component score (46.2±10.7 vs. 50.0±10). Highest caregiver stresses were worry over long-term SJIA impact on their child (45%) and uncertainty about the future (28%).

Conclusions: Treatment sequencing and patient-reported outcome measures indicate ANA is used as 1st line for severe SJIA while CAN and TOC are used as 2nd/3rd line for severe SJIA. Caregivers expressed stress over the long-term impact of SJIA and fear for the future and had variable treatment satisfaction and resource utilisation levels.


THU0643 WHAT FACTORS RELATE TO PATIENTS CONTRIBUTE LONGITUDINAL DATA USING SMARTPHONE TECHNOLOGY? FINDINGS FROM RA PATIENTS PARTICIPATING IN ARTHRITISPOWER REGISTRY

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Background: Data capture of patient reported outcomes (PROs) is gradually shifting from data collection on paper in medical office settings to use of computer or mobile based technologies between doctor visits. Concerns have been raised that patients may have limited interest in contributing data over time or that they may only record new data when there has been a change in their clinical status.

Objectives: The objective of this study was to evaluate the patterns and factors associated with longitudinal PRO data capture among participants in the PCORI-funded Patient Powered Research Network for adult rheumatologic conditions, ArthritisPower.

Methods: Patients in the registry were asked to voluntarily complete PROs including the RAPID3 and 4 PROMIS instruments plus disease-specific information via a mobile application (App) on their smartphone or computer. We evaluated the average time it took the patient to record each of the instruments and the total number of unique days the patients recorded PROs on the smartphone. Given the newness of the registry (launched late 2015), longitudinal data was defined as contributing at least 2 sets of PROs on unique calendar days. We tested the hypothesis that patients would contribute longitudinal data only when at least one of their PROs exceeded a minimally important difference (MID) of any of the 5 PROs examined (generally 2–3 units for PROMIS instruments; 3.6 units for RAPID3). Demographic factors associated with multiple PRO data capture among participants in the PCORI-funded Patient Powered Research Network for adult rheumatologic conditions, ArthritisPower.

Results: At the time of analysis, ArthritisPower had recruited 2,103 patients, most (approximately 68%) had RA, and 20% provided their Twitter handle. Average (SD) age was 50 (12); 87% were women. The mean assessment time for each of the PROMIS instruments ranged from a low of 16 seconds (Sleep Disturbance) to a high of 155 seconds (Sleep Interference). The average score for Pain Interference was 64.3 (SD: 6.3), Physical Function 37.5 (6.5), Sleep Disturbance 59.3 (8.4), Fatigue 64.2 (8.4), and RAPID3 15.7 (5.3). Of 1,946 patients who registered the Smartphone App more than 3 months prior to analysis, 20.6% never contributed any PRO information, 53.3% answered once, and 26.1% answered at least twice. Among patients with longitudinal data (>2 assessments), the mean change score of PROs between pairwise PRO assessments was <1 point for all instruments.
Patient Decision Making in Hip and Knee Arthroplasty

Objectives

The objective of this study was to identify the decisions that are most important to patients undergoing hip and knee arthroplasty and the factors they view as important in making those decisions.

Methods

Forty-nine U.S. participants were recruited from ArthritisPower Patient-Powered Research Network and CreakyJoints arthritis patient community to participate in structured one-hour discussions held via webinar during January to April 2016 to understand patients’ experiences with joint replacement. Patient described decisions that were most important to them and the factors they used to make those decisions. Discussions were transcribed and coded to identify themes; patient decisions and factors were identified and categorized and co-occurrence of decisions and factors was tabulated. Demographic and procedure-related characteristics were captured.

Results

Eight decisions emerged that were influenced by at least ten factors (Table). The most important decisions involved whether to have surgery, selection of surgery date, surgeon, facility, implant device, and ancillary health care professionals (HCPs) and services. Factors included current situation, expectations of having or not having surgery, professional and word-of-mouth familiarity with surgeon/HCP, procedure, services, and device, and perceived value. Patients’ current situation and health status and their expectations of surgery were most commonly used to make decisions about whether and when to have surgery. Patients’ trust of and communication with doctors was the most commonly factor used when deciding on arthroplasty surgeon.

Conclusions

Arthroplasty patients are concerned about a variety of decisions. Patient-centered research should maximally address questions of importance to patients and this study is a first step in identifying and prioritizing topics that matter most to patients and the information that patients currently use to make joint replacement decisions.

Acknowledgements

This project was funded through a Patient-Centered Outcomes Research Institute (PCORI) Eugene Washington PCORI Engagement Award (2228-GHLF).
INTERCHANGEABILITY FROM INFLIXIMAB ORIGINATOR TO INFLIXIMAB BIOSIMILAR: EFFICACY AND SAFETY IN A PROSPECTIVE OBSERVATIONAL STUDY ON 89 PATIENTS

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Background: Biosimilar biologic disease modifying anti-rheumatic drug (bsDMARD) are supposed to offer a real economic advantage for these diseases for the same health benefit. While the administration of a biosimilar to a new patient is widely accepted, the switch from a biologic originator DMARD (boDMARD) to its biosimilar remained questioned.

Objectives: This study aimed to assess the safety and efficacy of switching from an IV anti-TNF boDMARD to its bsDMARD in patients with rheumatic arthritis, spondyloarthritides, juvenile arthritis and uveitis.

Methods: Prospective real-life study in the rheumatology unit of La Pitié- Salpêtrière Hospital, from February 2016 to December 2016. Patients initially treated with the boDMARD infliximab (Remicade®), all switched to infliximab bsDMARD (Inflectra®) after patient’s information by a rheumatology nurse. The dose and administration schedule remained unchanged at the switch. Our primary endpoint was infliximab maintenance rate. Secondary endpoints were evolution of disease activity, as well as evolution of both infliximab trough levels and anti-drug antibody (ADA) serum levels before and after the switch. In addition, safety events were monitored.

Results: We identified 89 patients – spondyloarthritis (61%), rheumatic arthritis (22%), psoriatic arthritis (11%), juvenile arthritis and uveitis (1%) – in rheumatology who had been switched to boDMARD infliximab to its bsDMARD. Clinical assessment was based on DAS28 (peripheral joint involvement) or BASDAI (axial involvement) scores in patients remaining treated with infliximab; 6 patients (7%) stopped the treatment due to a loss of efficacy. As shown in Figure 1, there is no significant change in disease activity before and after having switched patients to infliximab biosimilar. The ADAAdas were detected in 10 patients, 7 with high titer (>200ng/mL) and 3 with moderate titer (between 50 and 200 ng/mL). It was significantly correlated with low trough levels of IFX (<0.3 μg/mL). Among them, 6 (4 with high titer; 2 with moderate titer) also had a poor clinical response before switch (refractory patients). 4 ADA-positive patients (3 with high titer; 1 with moderate titer) were still good clinical responders.

Conclusions: The interchangeability of infliximab boDMARD to its bsDMARD does not rise any efficacy and safety concern in our experience. The role of drug and ADA monitoring during the switch remains to be further explored.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6586

INTERACTIONS BETWEEN STEPS PER DAY AND RISK FACTORS FOR OSTEOARTHRITIS IN A POPULATION BASED COHORT STUDY

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Background: It is clear that exercise helps the symptoms of osteoarthritis. However, the relationship between physical activity (PA) and progression of knee osteoarthritis (OA) remains controversial. Moreover, no guideline on the amount of PA to prevent OA progression in general older population has been recommended, and it is still uncertain whether PA should be promoted among subgroups with knee OA such as female gender, obesity, radiographic osteoarthritis (ROA) and knee injury history. Osteophyte (OP) has long been viewed as a defining structural feature of knee OA. Recently, MRI-detected OPs have been shown to be more sensitive to change than radiographs.

Objectives: The aims of this study were to describe the longitudinal association between objectively-measured PA and knee MRI-detected (OPs), and to test the interactions between PA and gender, obesity, ROA or knee injury history on the OPs.

Methods: 408 community-dwelling adults aged 51–81 were randomly selected from local community and measured at baseline and 2.6 years later. T1-weighted fat suppressed MRI was used to evaluate knee OPs at baseline and after 2.6 years. PA was assessed at baseline by pedometers (steps per day) and categorized as 3 groups: low PA (<7499 steps per day), moderate PA (7500 to 9999 steps per day) and high PA (>10000 steps per day). Radiographs were obtained and scored for individual features of radiographic osteoarthritis (ROA). Knee injury history was recorded by questionnaire and divided into body mass index (BMI) was calculated. Logistic regression and log binomial regression were used in longitudinal analyses.

Results: In total study sample, doing moderate PA was associated with reduced risk of an increase in MRI-detected OPs, compared to low PA (RR=0.73, p=0.03).

There were significant interactions between PA and gender, obesity, ROA or knee injury history (all p<0.05) for an increase in MRI-detected OPs. In stratified analyses, moderate PA was protective against an increase in MRI-detected OPs in females (OR=0.23, p<0.01), obese participants (OR=0.23, p<0.01), participants with ROA (OR=0.45, p=0.02) and participants with knee injury history (OR=0.05, p=0.02). The significant associations still existed after further adjustments for age, sex, BMI, ROA and/or knee injury history (where appropriate). High PA was not associated with an increase in MRI-detected OPs in total sample or the stratified analyses but there were relatively few in this category.

References:

Acknowledgements: The authors thank the participants who made this study possible, and acknowledge the role of the staff and volunteers in collecting the data, particularly research nurses Boon C and Boon P. Warren R assessed MRIs and Dr Srikanth V and Dr Cooley H assessed radiographs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1162

USE OF OUTPATIENT RHEUMATOLOGIC HEALTH CARE SERVICES BEFORE AND AFTER SWITCH FROM ORIGINATOR TO BIOSIMILAR INFliximab

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Background: According to Danish national guidelines issued in 2015, pts (pts) with inflammatory rheumatic diseases in routine care treatment with originator infliximab (IXN) must switch to the cheaper biosimilar infliximab (CT-P13). This switch was done for economic reasons (CT-P13 64% cheaper than IXN). Since any treatment change potentially induces additional guidance of pts and use of hospital services, it is relevant to investigate whether the switch affected use of hospital resources.

Objectives: To study difference in rates of outpatient activities and services provided 6 months before vs after the switch to CT-P13 for pts treated at rheumatologic departments which provide infliximab treatment.

Methods: The switch population and switch dates were identified in the Danish quality registry, DAnBio (1). Vital status was validated in the Central Person Registry. The Danish National Patient Registry (NPR) provided information regarding outpatient contacts and services. The use of 16 types of services relevant to the rheumatologic specialty was identified and included outpatient visits, infliximab infusion, nurse counselling, phone consultation, and rheumatologic ultrasound. Number of days with these services was counted. Services performed around the switch date were analyzed separately. Thus, for each patient the following rates were calculated 6 months before and after the switch: 1) days with at least one outpatient service provided, and 2) number of services provided. In addition, the weekly rate of days with services was calculated.

Results: Among 802 pts identified, 769 had available NPR outpatient data from hospital departments of rheumatology. The 769 pts had 1484 outpatient treatment contacts at the included rheumatology departments with a total of 9243 days with services provided (including 693 on the switch date). The mean rate of days with services provided was 5.4 before the switch and 5.7 after switch (p=0.0003).
weekly rate of days with services showed no obvious differences before and after the switch but had a clear 8-week pattern (corresponding to the average infusion interval) (Figure).

The total number of services provided was 19,752 (2,019 of these on the switch data). There were significant increases in the rates before vs after switch for 6 of the 16 service categories, although the mean rates were small: telephone consultations (mean rate 1.0 before vs 1.2 after), patient guidance (0.5 vs 0.4), intravenous medication (0.0 vs 0.1), clinical controls (2.1 vs 2.3) and clinical investigations (0.3 vs 0.5), whereas the rate of infliximab treatment decreased (3.1 vs 3.0) (all p<0.05, insignificant results not shown).

Conclusions: This analysis showed that there were only small differences in the rates of days with outpatient services and rates of services 6 months before and after the switch from original to biosimilar infliximab. Thus, it is unlikely that the switch is associated with substantially higher cost of health care resources.

References:

Disclosure of Interest:
B. Glintborg Grant/research support from: Abbvie, J. Sørensen Grant/research support from: Abbvie, M. Hetland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, MSD
DOI: 10.1136/annrheumdis-2017-eular.3008

**THU0649**

**MANDATORY CHOICE OF FIRST BDMAARD IN DENMARK – AN OPPORTUNITY TO STUDY REAL-LIFE EFFECTIVENESS? RESULTS FROM THE DANBIO REGISTRY**

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**Background:** In Denmark, biological treatments (bDMARDs) are tax paid. Since year 2013, The Danish Council for the Use of Expensive Hospital Medicines (RADS) has issued recommendations with annual updates regarding RA patients (pts) initiating biological treatment, dictating a mandatory choice of the cheapest bDMARD (1). Furthermore, the percentage of pts expected to be treated according to the RADS recommendation per year is stated. For pts treated with concomitant csDMARDs and those who were not.

**Methods:** For each of the three RADS periods bio-naive pts with RA were included. RADS guidelines and those who were not.

**Results:** More than 90% of adults with rheumatological diseases treated with bDMARDs in routine care.

**Conclusions:** To characterize Danish RA pts initiating first line, first choice treatment with a bDMARD in combination with MTX in the three RADS periods and to explore the degree of compliance to RADS recommendations. Furthermore, to investigate differences in baseline characteristics between those pts who were compliant to RADS guidelines and those who were not.

**Disclosure of Interest:** B. Glintborg Grant/research support from: Abbvie, J. Sørensen Grant/research support from: Abbvie, M. Hetland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, MSD
DOI: 10.1136/annrheumdis-2017-eular.3008

**THU0655**

**THE EFFECT OF ANTI-TNF THERAPY ON WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS OVER ONE YEAR – REAL LIFE DATA FROM THE CZECH BIOLOGICS REGISTRY ATTRA**

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**Objectives:** To assess the effect of anti-TNF therapy on work productivity using the Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP) questionnaire in patients with RA, PSA and AS in the real life setting. In the Czech Republic, anti-TNF-therapy is reimbursed for RA if DAS28<3.2 and for AS if BASDAI<4 and CRP<ESR elevated above normal.

**Methods:** WPAI-SHP scores were collected for all patients enrolled in ATTRA since 2012 at baseline and after 12 months of anti-TNF exposure. Baseline patients with RA (n=352), AS (n=442) and PSA (n=133) starting anti-TNF therapy with available baseline data on demography, disease duration and physical function, and WPAI-SHP at baseline and at 12 months were included in this analysis. Patients older than 60 years, on maternity leave or students were excluded. Only patients working for pay at baseline were assessed for WPAI-SHP summary score (mean % work time missed), and for WPAI-SHP pain (mean % productivity loss at work), overall work impairment (mean % overall work productivity loss), and activity impairment (mean % productivity loss in regular activities).

**Results:** Baseline characteristic were significantly different between diagnoses (Table 1). Working status changed significantly only in patients with RA (employed more were heterogeneous than than in clinical trials, reflecting routine care. Overall, compliance to recommendations was good. Thus, the national guidelines in Denmark with mandatory choice of the first biological drug may provide an interesting opportunity to study effectiveness of bDMARDs in routine care. This highlights observational studies as a valuable supplement to RCTs.

**References:**

**Disclosure of Interest:** K. G. Grant/research support from: BMS, B. Glintborg Grant/research support from: Abbvie, M. Nørgaard Grant/research support from: Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to (and administered by) Aarhus University, Denmark. F. Mehnter Grant/research support from: Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to (and administered by) Aarhus University, Denmark, M. Østergaard Grant/research support from: Consultation fees from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospia, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth; Research support and grants from: Abbvie, BMS, Janssen and Merck, L. Dreyer Grant/research support from: MSC, UCB, Janssen Pharmaceutical; N. Krogh: None declared, M. Hetland Grant/research support from: Abbvie, BMS, MSD, Orion, Novartis, UCB, Pfizer
Conclusions: Appropriateness criteria for BT dose reduction in three inflammatory conditions were developed and the preliminary prevalence study suggests that BTO was wisely applied. However, further research in this field is needed to determine the real prevalence of clinical profiles of patients undergoing BTO in daily clinical practice and to validate these criteria in real life.

Disclosure of Interest: I. González-Alvaro: None declared, C. Sánchez-Piedra: Grant/research support from: Unrestricted grant from Abbvie, R. Almodovar: None declared, J. Bachiller: None declared, A. Balsa: None declared, A. Blasco: None declared, R. Calzí: None declared, C. Gómez-Centeno: None declared, A. Ortiz: None declared, J. Sanz: None declared, B. Tejera: None declared, I. Notario: None declared, M. Soto: None declared, C. Plasencia: None declared, D. Vázquez: None declared, M. Espinosa: None declared, C. Ramos: None declared, P. Lazo: Grant/research support from: Unrestricted grant from Abbvie DOI: 10.1136/annrheumdis-2017-eular.3836

THU0652 ASSESSING BIOSIMILARS USING REAL WORLD DATA: THE COMPLEXITY OF CHOSING A COMPARATOR AND UNDERSTANDING UPTAKE


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The introduction of biosimilars has been linked with concerns regarding how to best monitor their similarity vs. the originator product using real world data.

Methods: Data from the Swedish Rheumatology Quality register (SRQ) was used to identify all patients with rheumatoid arthritis (RA), anklosing spondylitis (AS), psoriatic arthritis (PsA), and other spondyloarthropathy (SpA), who started a treatment with infliximab (originator Remicade or biosimilars Remsima or Inflectra) between 1st Mar 2015 and 30th Sept 2016 or with etanercept (originator Enbrel or biosimilar Benepali) between 1st April 2016 and 30th Sep 2016.

Results: During the study period, a total of 1833 patients started an infliximab treatment and 1793 started etanercept. These patients were either bDMARD-naive (patients without a history of any biological treatment), non-medical switchers (patients who switched from the originator product), or patients who had a history of a previous (but not the same) bDMARD (Table 1). These three groups were not evenly distributed across originators or biosimilars, and had different baseline demographic and disease characteristics.

The uptake in terms of treatment starts was faster for Benepali (it covered more than 90% of this part of the etanercept market after only 3 months) as compared to Remsima and Inflectra (together they accounted for 88% of this section of the infliximab market after 10 months). The uptake of biosimilars in terms of proportion of all patient on treatment was, at the end of September 2016, 27%

Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Infliximab</th>
<th>Biosimilars</th>
<th>Originator</th>
<th>Biosimilar</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016-17</td>
<td>570</td>
<td>263</td>
<td>307</td>
<td>186</td>
<td>1607</td>
</tr>
<tr>
<td>Bio-naïve</td>
<td>379 (66%)</td>
<td>508 (40%)</td>
<td>89 (48%)</td>
<td>581 (36%)</td>
<td></td>
</tr>
<tr>
<td>Non-medical switchers</td>
<td>524 (43%)</td>
<td>710 (44%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switchers from other biologics</td>
<td>191 (34%)</td>
<td>231 (18%)</td>
<td>97 (52%)</td>
<td>316 (20%)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Number of patients starting, and on, respectively, infliximab or etanercept by month. Green: total, red: biosimilar, blue: originator.
of all infliximab (after 18 months of marketing) and 16% of etanercept (after 5 months since marketing).

In contrast to the bio-naïve group and those with a history of a previous (but not the same biological), there was no readily available comparator group for the non-medical switcher group. To this end, we assessed three tentative definitions for ‘switch’, i.e. (i) patients 18–65 years old, (ii) patients who had switched within 6 months of starting their current medication, or (iii) patients who had switched within 6 months of starting their current medication. Based on these definitions, we found that 11% of infliximab patients and 37% of etanercept patients had switched within 6 months of starting their current medication. These findings suggest that infliximab patients are more likely to switch than etanercept patients.

Conclusions: This study provides evidence that infliximab patients are more likely to switch than etanercept patients within 6 months of starting their current medication. This may indicate that infliximab patients are more willing to try a different treatment, even if their current medication is effective. Further research is needed to determine the underlying reasons for this difference in switching behavior.

Disclosure of Interest: None declared


THU0653 | PREVENTING RHEUMATOID ARTHRITIS: A GENERAL POPULATION PILOT STUDY ON PERSPECTIVES OF THE RISK OF DEVELOPING THE DISEASE AND POTENTIAL PREVENTATIVE INTERVENTIONS

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Background: Evidence suggests that treatment of people at risk of rheumatoid arthritis (RA) with anti-rheumatic drugs can prevent the onset of disease. There are ongoing randomized controlled trials on the efficacy of preventing RA. However, even if these trials are successful, there will be uncertainty around the potential benefits of these programs in practice; namely, the ability to predict which patients are likely to be acceptable to pre-symptomatic people at high risk of RA. Our survey suggests that people value the potential benefits of preventative RA treatments, then between their preferred treatment and “no treatment for now”. The treatment (risk of developing RA, how treatment is taken, chance of side effects, certainty in estimates, health care provider’s opinion) and test attributes (chance test is wrong, who recommends treatment) were most influential treatment preferences, but risk reduction, how treatment is taken, and included 2 consistency checks. Responses were analyzed using a conditional logit regression model to estimate the significance and relative importance of attributes in influencing preferences.

Results: 201 respondents completed the survey. The majority of the sample was 25–54 years old (modal age category: 30–39 years (38%) and 50% were female. 23 members (11%) reported having a physician diagnosis of RA, and 91 (45%) had a family member or close friend with RA. All attributes’ levels significantly influenced treatment preferences, but risk reduction, how treatment is taken, and health care provider preference were most influential. Respondents were most willing to trade a reduction in risk of RA for a treatment preferred by their health care professional and an oral route of administration. Respondents had a similar willingness to start a medication. The medication was described using eight scenarios (manipulated using a 2x4 design). We varied the probability of an adverse event (pneumonia requiring hospitalization): 2% or 2%, and the risk presentation format: numbers, numbers + IA, numbers + balance beams (BB), or both influence willingness to start a medication.

Conclusions: SES affects how subjects respond to risk presentation formats. IA marginally increases willingness in high SES subjects, while BB increases willingness in low SES subjects; when both IA and BB are present, SES differences disappear. BB, when not accompanied by an IA, may decrease willingness in high SES subjects. These results demonstrate the differential effects of risk presentation formats, and highlight the need to identify mechanisms underlying their effects when implementing decision-support tools.

Disclosure of Interest: None declared


THU0654 | THE INFLUENCE OF RISK PRESENTATION FORMAT ON WILLINGNESS TO START A MEDICATION

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Background: Patients with rheumatoid arthritis frequently refuse to escalate care because they overweight the probability of adverse events. Effectively communicating risk information to patients is difficult. Several approaches have been developed to facilitate comparative risks; however, recent data suggest that current approaches have a limited impact on risk perceptions and willingness to take medication.

Objectives: The objective of this study was to examine whether an icon array (IA), an illustration of the gist of how medications regulate the immune system (a series of balance beams), or both influence willingness to start a medication.

Methods: Patients with a rheumatic disease were mailed a survey in which they were asked to imagine that their physician was recommending a new medication. We varied the probability of an adverse event (pneumonia requiring hospitalization): 2% or 2%, and the risk presentation format: numbers, numbers + IA, numbers + balance beams (BB), or both numbers + both. Route of administration, benefit, and cost were held constant. Each subject responded to a single, randomly-assigned scenario. We controlled for socioeconomic status (SES), using a variable including both difficulty paying for medications and as education, in a full-factorial model testing willingness to take the medication (measured on a 5-point scale).

Results: Of 1453 surveys, 465 patients completed the survey. Overall, the mean (SD) age was 59.0 (14.8); 79.7% were female; 83.2% White and 39.1% were classified as having low SES. There were no statistical differences in patient characteristics across the risk presentation formats. Willingness to start the medication was predicted by the interaction between the risk presentation format and SES (F =2.9, p=0.03). Willingness by SES status is described in the Figure 1. Among low SES subjects, addition of an IA did not affect willingness compared to the numbers-only format. In contrast, addition of BB (mean difference =0.47, p=0.07), or both IA and BB increased willingness (mean difference =0.48, p=0.04). Among high SES subjects, addition of an IA or BB or both did not influence willingness compared to the numbers only format. However, both formats including an IA increased willingness compared to the BB format among high SES subjects (mean difference IA vs BB =0.53, p<0.01; mean difference IA vs IA + BB = 0.48, p=0.02).

Conclusions: SES affects how subjects respond to risk presentation formats. IA marginally increases willingness in high SES subjects, while BB increases willingness in low SES subjects; when both IA and BB are present, SES differences disappear. BB, when not accompanied by an IA, may decrease willingness in high SES subjects. These results demonstrate the differential effects of risk presentation formats, and highlight the need to identify mechanisms underlying their effects when implementing decision-support tools.

Disclosure of Interest: None declared


THU0655 | DO VISUAL DECISION AIDS HELP PATIENTS CORRECTLY DIFFERENTIATE BETWEEN A 2% AND A 0.2% RISK?

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Background: Studies have found that patients ignore probabilities when making treatment decisions.

Objectives: The objective of this study was to examine whether addition of an icon array (IA), a series of three consecutive balance-beam (BB) illustrations depicting how medications regulate the immune system, or both resulted in improved decision-making.

Methods: Patients currently being treated for a chronic inflammatory rheumatic disease were mailed a survey in which they were asked to imagine that their symptoms had recently worsened and that their physician was recommending a new medication. The medication was described using eight scenarios (manipulated using a 2x4 design). We varied the probability of a serious AE (pneumonia...
CONCLUSIONS: Experience with etanercept biosimilar has been growing in Germany, as reflected by the growing market share. Based on the current number of patients treated with etanercept biosimilar, savings of 21.1 million EUR are projected to be returned to the health system in Germany annually. The economic burden associated with etanercept treatment is expected to decrease further with an increase in market share for the etanercept biosimilar. These savings can have a significant impact on broadening patient access to biologic treatment in Germany.

REFERENCES:
[2] INSIGHT Health GmbH & Co.KG.

Disclosure of Interest: K. Thakur Shareholder of: Biogen, Grant/research support from: Biogen, Employee of: Biogen, A. Handrich Shareholder of: Biogen, Grant/research support from: Biogen, Employee of: Biogen, E. Psachoulia Shareholder of: Biogen, Grant/research support from: Biogen, Employee of: Biogen

DOI: 10.1136/annrheumdis-2017-eular.3380

A TELE-HEALTH FOLLOW-UP STRATEGY FOR TIGHT CONTROL OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: RESULTS OF THE NON-INFERIORITY RANDOMISED CONTROLLED TRAIL (THE TERA STUDY)

A. Thurai1,2, K. Steengaard-Pedersen1,2, M. Axelsen3, U. Fredberg3,4, K. Lomborg 6,7, T. Maribo8,9.

Background: Despite the increased prevalence of rheumatoid arthritis (RA) in recent years, no studies have yet investigated the effect of monitoring disease activity through a standardized tele-health strategy in patients with RA (1).

Objectives: To test the effect of patient-reported outcome (PRO) based tele-health follow-up for tight control of disease activity in patients with RA, and the differences between tele-health follow-up performed by rheumatologists or rheumatology nurses.

Conclusions: Experience with etanercept biosimilar has been growing in Germany, as reflected by the growing market share. Based on the current number of patients treated with etanercept biosimilar, savings of 21.1 million EUR are projected to be returned to the health system in Germany annually. The economic burden associated with etanercept treatment is expected to decrease further with an increase in market share for the etanercept biosimilar. These savings can have a significant impact on broadening patient access to biologic treatment in Germany.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3380

THU0567 ETANERCEPT BIOSIMILAR USAGE AND ASSOCIATED COST SAVINGS IN GERMANY

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Background: The first etanercept biosimilar was approved by the European Commission in January 2016. Of the 27,000 patients* estimated to be treated with etanercept biosimilar in the Europe, 5,122 patients* are estimated to be treated with etanercept biosimilar in Germany at the end of the analysis period. Its usage in Europe may support healthcare sustainability by reducing costs, thereby relieving the burden associated with etanercept treatment is expected to decrease further with an increase in market share for the etanercept biosimilar. These savings can have a significant impact on broadening patient access to biologic treatment in Germany.

OBJECTIVES: To test the effect of patient-reported outcome (PRO) based tele-health follow-up for tight control of disease activity in patients with RA, and the differences between tele-health follow-up performed by rheumatologists or rheumatology nurses.

Conclusions: Experience with etanercept biosimilar has been growing in Germany, as reflected by the growing market share. Based on the current number of patients treated with etanercept biosimilar, savings of 21.1 million EUR are projected to be returned to the health system in Germany annually. The economic burden associated with etanercept treatment is expected to decrease further with an increase in market share for the etanercept biosimilar. These savings can have a significant impact on broadening patient access to biologic treatment in Germany.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3380

THU0657 A TELE-HEALTH FOLLOW-UP STRATEGY FOR TIGHT CONTROL OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: RESULTS OF THE NON-INFERIORITY RANDOMISED CONTROLLED TRAIL (THE TERA STUDY)

A. Thurai1,2, K. Steengaard-Pedersen1,2, M. Axelsen3, U. Fredberg3,4, L.M.V. Schougaard5, N.H.I. Hjøllund 5,6, M. Pfeiffer-Jensen1,2, T.B. Laurberg1, K. Lomborg 6,7, T. Maribo8,9.

Background: The first etanercept biosimilar was approved by the European Commission in January 2016. Of the 27,000 patients* estimated to be treated with etanercept biosimilar in the Europe, 5,122 patients* are estimated to be treated with etanercept biosimilar in Germany at the end of the analysis period. Its usage in Europe may support healthcare sustainability by reducing costs, thereby relieving the burden on healthcare budgets and improving patient’s ability to get the right care at the right time.

OBJECTIVES: To test the effect of patient-reported outcome (PRO) based tele-health follow-up for tight control of disease activity in patients with RA, and the differences between tele-health follow-up performed by rheumatologists or rheumatology nurses.

Conclusions: Experience with etanercept biosimilar has been growing in Germany, as reflected by the growing market share. Based on the current number of patients treated with etanercept biosimilar, savings of 21.1 million EUR are projected to be returned to the health system in Germany annually. The economic burden associated with etanercept treatment is expected to decrease further with an increase in market share for the etanercept biosimilar. These savings can have a significant impact on broadening patient access to biologic treatment in Germany.
Methods: A total of 294 patients were randomized (1:1:1) to either PRO-based tele-health follow-up carried out by a nurse (PRO-TN) or a rheumatologist (PRO-TR), or conventional out-patient follow-up by physicians. The Flare-RA (2) was used as decision aid for assessing disease activity. The primary outcome was change in DAS28 after week 52. Secondary outcomes were: physical function, quality of life and self-efficacy. The non-inferiority margin was a DAS28 change of 0.6. Mean differences were estimated following per-protocol, intention to treat (ITT) and imputation (IMP).

Results: Overall patients had low disease activity at baseline and end follow-up. Demographics and baseline characteristics were similar between groups. Non-inferiority was established for DAS28. In the ITT analysis mean difference in DAS28 between PRO-TR vs. control were -0.10 (90% CI -0.30; 0.13) and -0.19 (-0.41; 0.02) between PRO-TN vs. control. When including one yearly visit to the outpatient clinic, patients in PRO-TN had a total of 1.72 (SD 1.03) visit/year, PRO-TR 1.75 (SD 1.03) visit/year and control 4.15 (SD 1.0) visits/year. This implies that PRO-TN patients had a total of 2.47 visits/year, PRO-TR 2.55 visits/year and control 4.15 visits/year. This difference was significant in the per-protocol analysis (p=0.002). The difference in the proportion of patients with no use of prednisone was statistically significant between PRO-TN and control groups (p=0.008) but not between PRO-TR and control groups (p=0.547). Moreover, in the salivary gland tissues, the positivities of Wnt-1 (71.4% vs. 46.2%, p=0.001, r=-0.416; p=0.022) and Wnt-3a (71.4% vs. 53.8%, p=0.345) were higher in the SS group compared to the control group, respectively.

Conclusions: According to the best of our knowledge, this study is the first study evaluating the activity of Wnt/β-catenin pathway in the primary SS. The altered β-catenin pathway in the primary SS. The altered β-catenin pathway is affected in these inflammatory diseases. Salivary DKK1 level is increased in primary SS in contrast to SLE. On the other hand, Wnt-1 and Wnt-3a expressions on the salivary gland are increased in primary SS. Therefore, it may be concluded that Wnt/β-catenin pathway acts pathogenic roles on the glandular inflammation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5769

THU0659 | SKIN MICROVASCULAR FLOW ASSESSED BY DYNAMIC OPTICAL COHERENCE TOMOGRAPHY: FIRST NON-INVASIVE QUANTITATIVE OUTCOME MEASURE OF MICROVASCULAR DAMAGE IN SYSTEMIC SCLEROSIS

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Background: Reduction in capillaries number is the defining feature of microvascular disease in Systemic Sclerosis (SSc). This condition affects blood flow and function of microcirculation and is responsible for the clinical manifestations of the disease.

Aims: To determine the face and content validity of D-OCT as outcome measure of severe peripheral ischemic vasculopathy. Dynamic optical coherence tomography (D-OCT) is a recently developed imaging technique that allows non-invasive in vivo study of the microvasculature of the skin. In addition to the skin architecture and vessels morphology, it offers information about flow status, allowing the functional and quantitative evaluation of the microcirculation.1

Objectives: To determine the face and content validity of D-OCT as outcome measure of the skin microvascular disease, assuming the presence of current DU, distal to the DIP joints, as gold standard for ischemic peripheral vasculopathy in SSc.

Methods: A total of 54 patients were enrolled in this cross-sectional study, including 18 SSC patients with current DUS (DU group); 18 SSc patients without current DUS (no DU group) and 18 patients with Raynaud’s phenomenon and SSc specific AHA, who did not fulfil ACR/EULAR 2013 classification criteria (SRP group).

For each patient, we performed a D-OCT scan on both index and middle fingers, on the dorsal aspect of the second phalanx, employing VivoSight Scanner (Michelson Diagnostics). The speckle variance signal of D-OCT images within the first mm of skin depth was extracted, quantified as area under the curve (AUC) and defined as Micro Vascular Flow (MVF). MVF comparison between the groups was done using parametric or non-parametric tests as appropriate. Statistical Analysis was performed with SPSS V22.

Results: All three groups were comparable in terms of age and gender distribution (p>0.80 for both) as well as disease duration and clinical subset between the two SSc groups (p=0.839 and p=0.464, resp). With a scan time <1 minute, D-OCT allowed the visualization and quantification of capillaries within the first millimeter of skin depth (Figure 1).

The distribution of MVF was not significantly different among the four fingers within each group (DU group: p=0.459, no DU group: p=0.933 and SRP group: p=0.616). On the contrary, the distribution and median MVF for all fingers was significantly different among the 3 groups: DU group=0.134 (IQR 0.121–0.134), no DU group=0.153 (IQR 0.132–0.153) and SRP group=0.167 (IQR 0.148–0.167) (p<0.0001), as well as in the DU group vs. no DU group (p<0.001) or DU vs SRP group (p<0.001).

Further, sub analysis of the DU group showed that 10 of the total 20 DUs were on the left index finger. Within this subgroup the MVF of patients on Sildenafil (n=6) was significantly higher than the rest of the group (0.148±0.021 vs. 0.113±0.019, p=0.03).

Conclusions: MVF assessed by D-OCT is a quantitative, non-invasive surrogate outcome measure of severe peripheral ischemic vasculopathy in SSc. Longitudinal
studies assessing its sensitivity to change will inform whether MVF can be used as end point of skin microvascular involvement in SSC.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6852

THU0660 POLYMYALGIA RHEUMATICA TREATMENT SERUM BIOMARKERS VERSUS RHEUMATOID ARTHRITIS
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Background: Polymyalgia rheumatica (PMR) is a systemic inflammatory disorder with unknown etiology and overlapping symptoms with giant cell arthritis and late-onset rheumatoid arthritis (RA). To date, no proteomics studies have been performed on PMR patients, and the number of biomarker studies remain limited.

Objectives: The primary aim of this study was to thoroughly investigate the corticosteroid treatment serum proteome of PMR with a focus on acute-phase reactions, complement system, and cytokines.

Methods: Filter-aided sample preparation for mass spectrometry, cell free DNA (cfDNA) assay, and 10plex cytokine array were applied to PMR serum samples from the same patients before and after treatment, DMARD-naïve RA patients, and healthy controls.

Results: The core serum proteomes of the four groups were remarkably similar, and consisted of ~200 proteins, which included acute-phase reagents, coagulation and complement proteins (figure), immunoglobulins, and apolipoproteins, and several more. Acute Phase Serum Amyloid A (SAA1) was differentially less abundant than by PMR treatment. The individual serum proteome of each PMR patient provided more than 100 differentially abundant proteins, and highlights the heterogeneity of patients.

Conclusions: We have established the core serum proteome of PMR in response to treatment, and compared it with RA and healthy controls. The results suggest a functional role of SAA1, and increased cfDNA in the pathogenesis of PMR indicates the activation of NETs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2864

THU0661 CLINICAL RELEVANCE OF DETECTING ANTI-ADALIMUMAB ANTIBODIES WITH A DRUG-TOLERANT ASSAY
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Background: Adalimumab (Ada) has proven effective in treating rheumatoid arthritis (RA) and spondyloarthropathies (SpA), although approximately 30% of responders will present secondary clinical failure. Immunocomplex formation associated to arthritis (RA) and spondyloarthropathies (SpA), although approximately 30% of responders will present secondary clinical failure. Immunocomplex formation of ATA with the clinical status.

Methods: Filter-aided sample preparation for mass spectrometry, cell free DNA (cfDNA) assay, and 10plex cytokine array were applied to PMR serum samples from the same patients before and after treatment, DMARD-naïve RA patients, and healthy controls. Complement factors were narrowly distributed and not affected by PMR treatment. The individual serum proteome of each PMR patient provided more than 100 differentially abundant proteins, and highlights the heterogeneity of patients.

Results: Out of the 63 studied patients, 12 (19%) had RA and the rest (51, 81%) had different spondyloarthropathies (24, 38%) ankylosing spondylitis, 9 (14%) psoriatic arthritis, 14 (22%) undifferentiated spondyloarthritis and 4 (6%) spondylarthropathies associated with inflammatory bowel disease. Thirty-one patients (49%) received concomitant methotrexate. (28% RA patients and 74% SpA patients), 13 (21%) received another DMARDs associated to Ada and 19 (30%) were on monotherapy. Out of the 63 patients, 27 (43%) no ATA were detected. Thirty six patients (57%), were IDK+ and 12 patients (19%) were belISA+ (all of them IDK+). The presence of ATA by belISA was associated with absence of serum Ada levels. However, most (78%) samples with complexed ATA had low circulating Ada levels (1.65 mg/ml in ATA+ vs 6.25 mg/ml in ATA-; p<0.0001). ATA appeared by IDK at earlier treatment stages than by belISA, statistically different at all studied time points. In patients who dropped-out (30 patients, 48%) Ada concentration was frequent and significant by both methods. Ten patients (33%) belISA ATA+ was dropped-out vs 2 patients belISA ATA+ in those who continued treatment (p<0.0001). Twenty four patients (80%) IDK ATA+ dropped-out vs 12 patients (38%) who continued treatment (p<0.0001). The percentage of ATA detected by IDK was higher than by belISA, with a tendency of more IDK ATA+ among patients with less survival (24,80% IDK positive vs 10,33% belISA+; p=0.06).

Conclusions: ATA are detected by a drug-tolerant assay at earlier stages of treatment than by belISA. The antibodies formed early are associated with lower levels of circulating Ada, indicating higher drug clearance. This information might be useful to implement the Therapeutic Drug Monitoring. However, the detection of early complexed ATA has not demonstrated a significant advantage over the belISA to predict treatment survival.

Disclosure of Interest: This work has been supported by a collaboration with Leti laboratories.

Acknowledgements: This work has been supported by a collaboration with Leti laboratories.

DOI: 10.1136/annrheumdis-2017-eular.5844

THU0662 COMPARING ELECTRONIC COLLECTION OF PATIENT REPORTED OUTCOMES AT HOME VERSUS TOUCH-SCREENS IN THE WAITING AREA AMONG PATIENTS WITH ARTHRITIS IN CLINICAL PRACTICE: A RANDOMISED AGREEMENT STUDY WITH ONLINE RECRUITMENT USING DANBIO
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Background: Collection of patient-reported outcomes (PROs) is an important aspect of modern treatment strategies. Electronic capture in waiting areas by touch screens is part of routine care in the Danish DANBIO registry. It is not known whether this data collection can be replaced with electronic data entry from home.

Objectives: To test the feasibility of online patient recruitment via touch screens and to investigate if electronic reporting of PROs from home (ELECTOR IT-platform) is comparable to reporting completed at the hospital among patients with rheumatoid arthritis (RA) or axial spondyloarthritis (AS). A total of 952 patients received invitation, 45% accepted, 127 patients completed the trial. Clinicaltrials.gov identifier: NCT02818478.

Methods: Patients with RA or AS were recruited via touch screens and randomized to one of two groups by a pre-computed list generated through DANBIO; the first group completing the PROs at home and then at the hospital-site, and vice versa for the second group. All patients completed the Health Assessment Questionnaires (HAQ), the Visual Analogue Scales (VAS) for fatigue, pain and global health and the annual visit questions. Furthermore, AS patients completed the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the BAS Function Index (BASFI). Pearson’s Chi-square test, independent samples t-test and Mann-Whitney U test were calculated. Smallest detectable differences (SDDs), 95% confidence intervals (CIs) and intra-class correlation coefficients (ICCs) were calculated.

Results: A total of 952 patients received invitation, 45% accepted, 127 patients were contacted by phone, and 56 (44%) gave consent to participate. 22 patients with RA and 20 patients with AS completed the trial. All differences between scores from home vs hospital were smaller than SDD, and all were non-significant (p<0.05), except for BASFI and BASDAI item 5. ICC ranged from 0.947–0.990 (p<0.00001). Annual visit questions showed 96% concordance between the two methods. 50% of the patients preferred from home data entry over hospital and 10% vice versa.

Conclusions: Recruitment of patients for a randomized trial via touch screens was feasible. PROs collected from patients’ own devices at home generated...
results comparable to results obtained from the existing touch-screen solution and were preferred by the patients.

References:

Disclosure of Interest: None declared.

Methods: Baseline clinical and paraclinical data including disease activity and damage scores (SLICC) were obtained from 167 SLE patients. VTE (deep vein thrombosis and/or pulmonary embolism) and AT (myocardial infarction and/or cerebrovascular incident) data were available with a median follow-up period of 6 years. Baseline serum G3BP, IP-10, soluble CD163 (sCD163), TWEAK, and leptin serum levels were predictors of venous and arterial thrombotic events, damage accrual, and all-cause mortality during long-term follow-up in a large cohort of Swedish SLE patients.

Methods: Baseline clinical and paraclinical data including disease activity and damage scores (SLICC) were obtained from 167 SLE patients. VTE (deep vein thrombosis and/or pulmonary embolism) and AT (myocardial infarction and/or cerebrovascular incident) data were available with a median follow-up period of 6 years. Baseline serum G3BP, IP-10, soluble CD163 (sCD163), TWEAK, and leptin serum levels were predictors of venous and arterial thrombotic events, damage accrual, and all-cause mortality during long-term follow-up in a large cohort of Swedish SLE patients.

Results: In the follow-up period 11 (7%) VTE and 12 (7%) AT events occurred. SLICC-scores increased in 79 (47%) patients, and 19 (11%) patients died. In the univariate Cox regression analysis G3BP levels were significantly associated with an increased risk of VTE (hazard ratio [HR] 1.10, 95% confidence interval [CI]: 1.01–1.2, P=0.03). This persisted in the multivariate cox regression analyses when controlling for all-cause mortality. None of the other serum biomarkers were associated with AT and VTE. No significant associations were observed between the biomarkers and changes in SLICC-scores or all-cause mortality.

Conclusions: Our study identifies serum G3BP as a novel independent predictor of VTE in SLE. This may improve our understanding of VTE pathogenesis in SLE and aid future VTE risk stratification and prophylaxis. Further studies are needed to translate this into clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4287
as variable of high disease activity state showed the following: for ASDAS-CRP,

\[
\text{Baseline value SMD between baseline and M6 SMD between M6 and M12 SMD between M12 and M24 SMD between M24 and M36 (mean ± SD) [95% confidence interval (CI)] [95% CI] [95% CI] [95% CI]}
\]

Table 1. Sensitivity to change (SMD (95% CI)) of different outcomes in early axSpA over 3 years

**Abstract THU0667** A QUALITATIVE AND QUANTITATIVE COMPARISON OF SYNOVIAL BIOPSY TECHNIQUES DURING CLINICAL TRIALS OF INFLAMMATORY ARTHRITIS

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Background: Synovial tissue is an attractive area of research for biomarkers of disease outcome in RA. Currently acquisition of synovial tissue using an arthroscopic approach in clinical trials is recommended though two US-guided techniques have been described, a portal and forceps (P&F) approach and an adaptation using a quick core needle (NB). However before US-guided biopsy techniques are widely adopted into clinical trials validation of performance against arthroscopy is required.

Objectives: To evaluate whether there were significant differences in synovial sampling quality and quantity between arthroscopic, US-P&F and US-NB procedures within the context of clinical trials.

Methods: This was a multicentre retrospective analysis of inflammatory arthritis patients recruited to clinical trials utilizing US-guided NB (Barts Health NHS Trust), US-guided P&F (ICRSS Policlinico San Matteo and University Hospital Birmingham) and arthroscopic biopsy (Repatriation General Hospital). Paraffin embedded synovial sections from each procedure underwent H&E staining and sections examined for intact cell lining layer (graded sections). Biopsy procedures were segregated into large (knee) and small joint procedures (wrist/ MCP) for analysis. Proportion of samples yielding graded tissue per procedure was recorded. Using CellSens Dimensions software the area of synovial tissue obtained per procedure was determined. In addition the degree of synovitis was assessed using semi-quantitative scoring (0–9).

Results: 78 patient procedures were evaluated, 22 on small joints (11 US-NB, 11 US-PF) and 56 on large joints (11 US-NB, 35 US-PF, 10 arthroscopic). 47 patients had RA, 11 undifferentiated arthritis and 10 psoriatic arthritis. Arthroscopic sampling resulted in a significantly higher area of tissue retrieved per procedure than US P&F or US-NB. There were no significant differences in proportion of graded samples per procedure suggesting quality of synovial tissue was preserved between techniques. Finally no significant differences in degree of histological synovitis were demonstrated between sampling techniques.

Conclusions: The results suggest that US-guided biopsy provides a reliable method for sampling synovial tissue of comparable quality to that obtained from arthroscopy. However when sampling large joints arthroscopic techniques, and when sampling small joints US-P&F yield a significantly higher quantity, though not quality, of tissue per procedure than US-NB. These results may influence choice of biopsy technique when designing clinical trial protocols in inflammatory arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1918

**Abstract THU0666** PATIENT GLOBAL ASSESSMENT IS MORE SENSITIVE TO CHANGE THAN HEALTH-RELATED QUALITY OF LIFE INSTRUMENTS IN EARLY AXIAL SPONDYLARTHROPSIS OVER 3 YEARS: DATA FROM THE DESIR COHORT

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Background: Several questionnaires assess similar constructs of global patient-reported state or Health-Related Quality of Life (HRQoL). PGA was more sensitive to change than HRQoL measures in early spondyloarthritides (Table).

Results: In all, 442 patients were analyzed: at baseline, mean age was 34.2±8.6 years were included. A global construct of patient global state was assessed by PGA.

Objective: To evaluate sensitivity to change (ie, discriminance) of several questionnaires in early axial spondyloarthritides (axSpA) over 3 years of follow up: the SF36, axial spondyloarthritides quality of life (ASQoL), axial spondyloarthritides health assessment questionnaire (AS-HAQ) and patient global assessment (PGA).

Methods: DESIR is an ongoing prospective, multicenter, longitudinal, observational French cohort (1). Patients had inflammatory back pain of more than 3 months and less than 3 years suggestive of axSpA. For our analysis, only patients with no missing data for MCS and PCS SF36 values during the first 3 years were included. A global construct of patient global state was assessed by the SF36 questionnaire and its 2 subscales (scored 0–100 with higher scores indicating better status): the physical composite score (PCS) and the mental composite score (MCS). ASQoL, a disease-specific HRQoL scale, PGA and AS-HAQ. ASDAS-CRP was used as comparator. Each outcome was assessed at baseline, 6 months, 12 months, 24 months and 36 months. Standardized mean differences (SMD) were calculated using Cohen’s effect size with confidence intervals, between each time point for each outcome. A SMD < 0.5 is usually considered small, between 0.5 and 0.8 moderate and > 0.8 as important.

Results: In all, 442 patients were analyzed: at baseline, mean age was 34.2±8.6 years; mean disease duration was 18.6±10.7 months; 239 (54%) were females, 274 (62%) had HLAB27 and 124 (28%) had radiological sacroiliitis. At baseline, patients were not in an optimal state; improvement was clear up to month 6 then.

Conclusions: PGA showed a stronger correlation to BASDAI (r=0.912, P<0.001) than ASDAS and to acute phase reactants.

THU0668 | RELIABILITY OF PATIENT GLOBAL ASSESSMENT IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Patient’s global assessment (PtGA) is one of the most widely used patient reported outcomes in rheumatoid arthritis (RA) that reflects both disease activity and other factors. PtGA is onymous and obtained at hospital, which may cause a conscious or unconscious bias, whereas PtGA obtained anonymously may be free from any bias. The credibility of PtGA to report RA patient outcomes has been usually investigated by assessing test-retest reliability. There has been no study comparing routine PtGA and PhygA where patients and physicians assessed the same patient.

Objectives: The aim of this study was to compare routinely obtained in-hospital PtGA before clinical examination with those answered anonymously at home. Additionally, physician’s global assessment (PhygA) was compared with routine PtGA and anonymized PtGA.

Methods: We asked RA patients (n=389) to answer and mail the PtGA test anonymously. Clinical data regarding disease duration, stage, class, swollen joint counts, tender joint counts, pain visual analog scale (VAS), PhygA, Health Assessment Questionnaire (HAQ), EuroQOL five dimensions questionnaire (EQ5D), Kessler 6 scale (anxiety/depression), treatment data, laboratory data, and socioeconomic factors were collected simultaneously. We compared the PtGA that is routinely surveyed at hospital before clinical examination with those surveyed anonymously at home. We calculated a discrepancy score by subtracting anonymized PtGA from routine in-hospital PtGA. We defined (1) positive discrepancy when routine in-hospital PtGA was over-rated relative to the anonymized PtGA; (2) negative discrepancy when routine in-hospital PtGA was under-rated relative to the anonymized PtGA.

Results: The anonymized PtGA score was higher than routinely evaluated in-hospital PtGA (p<0.0001). The anonymized PtGA poorly correlated with routine PtGA (r=0.426, p<0.0001). We compared the difference between both PtGAs at 10 mm, 20 mm, or 30 mm. If we adopted 30 mm as discordance, the pain scale remained to be a risk factor of positive discrepancy (higher in-hospital PtGA than anonymized PtGA). If we adopted 20 mm or 10 mm as discordance, the pain scale remained to be a risk factor of positive discrepancy and remaining low quality of life (QOL) negative discrepancy (lower in-hospital PtGA than anonymized PtGA) after multivariate analysis. The discordance between PhygA and routine PtGA are associated with high pain VAS. The discrepancy between PhygA and anonymized PtGA is associated with tender joint counts, swollen joint counts, and low QOL.

Conclusions: Discrepancy exists between routine in-hospital PtGA and anonymized PtGA. The high pain VAS scale and low QOL are risk factors that could make the difference between routine PtGA from anonymized PtGA. There is a possibility that high pain VAS score and low QOL influence the reliability of PtGA.

Disclosures: None declared


THU0669 | THE ASSOCIATION BETWEEN HARRIS HIP SCORE AND DISEASE ACTIVITY OR HIP MRI FEATURES IN ANKYLOSING SPONDYLITIS

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Background: Hip involvement is a common clinical feature observed in ankylosing spondylitis (AS) patients and it often leads to substantial restriction of the body functions. Hip involvement in AS is mainly assessed by radiographic changes, clinical symptoms or MRI. The Harris hip score (HHS) is a valuable assessment tool to measure health status of AS patients. However, the relationship between HHS and other clinical indices is unknown.

Objectives: To evaluate relationship between HHS and other commonly used clinical indices.

Methods: In this multicentre, observational study, AS patients with hip clinical manifestations are enrolled and randomly assigned to infliximab treatment (group I), with/without DMARDs and/or NSAIDs or conventional therapy (group II, DMARDs and/or NSAIDs). Primary endpoint: to compare functional improvement of hip joint (HHS) between two treatment groups (infliximab and conventional therapy) at week 30. Secondary endpoint: to compare disease activity and functional improvement of AS and radiographic progression of hip joint between two treatment groups at week 30 and 52. Association between baseline HHS and disease activity measures such as Bath ankylosing spondylitis (BAS)-functional index (BASFI), BAS disease activity index (BASDAI), AS disease activity score (BASCR), CRP and ESR was analysed using Pearson correlation coefficient. BAS meteorology index (BASMI) and hip imaging functions (MRI of hip, BAS radiology hip index [BASI-h]) were analysed using independent two-sample t-test or ANOVA based on data characteristics.

Results: Study is ongoing; currently, only baseline information is analyzed. Baseline demographics and disease characteristics did not show any significant difference between groups. Almost all baseline disease activity measures showed significant Pearson correlation (high correlation in BASFI=0.646) with HHS, except for BASDAI (table 1). Significant association between HHS and three MRI scores (articular cartilage stripping, bone destruction under joint surface, femoral head bone marrow cavity edema) and BASRI-h were found in table 2 (appendix). Also, significant correlation was shown between BASMI and HHS (F value [degree of freedom]=4.70; p=0.0022).

Conclusions: The baseline results of HHS were found to be well associated with disease activity scores like BASFI, BASDAI and BASMI and four hip imaging features in AS patients with hip involvement.


Disclosure of Interest: Z. Wu: None declared, L. He: None declared, M. Yang: None declared, Y. Liu: None declared, D. He: None declared, Y. Zhang: None declared, C. Wang Employee of: Xi’an Janssen pharmaceuticals Ltd., H. Xu: None declared

DOI: 10.1136/annrheumdis-2017-eular.3724

THU0670 | DETECTION OF SERUM ANTI-DNASE I ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS USING IMPROVED IMMUNOSORBENT ASSAY

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Background: Diagnosis of systemic lupus erythematosus (SLE) is a sophisticated problem in most of the disease cases. The reasons of this include common diagnostic markers of SLE (ANA, anti-dDNA, anti-Sm), that are insufficiently reliable itself as well. One of possible ways to overcome these difficulties is searching for new SLE markers. These emerging diagnostic tools are not only to be valuable for diagnosis establishment, but also to provide economical efficiency and facility in common use.

Objectives: To compare diagnostic efficiency of anti-DNase I antibodies measured by conventional ELISA and by originally modified enzyme immunosorbent assay using magnetic polyacrylamide beads as an antigen carrier.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles, it was approved by the Regional Committee on Medical Ethics. All the patients signed the informed consent. We have enrolled 54 in-hospital adult patients with SLE, verified by the ACR criteria (1997). Control group (n=52) was comprised of patients with rheumatoid arthritis, systemic sclerosis, systemic vasculitis, dermatomyositis, and Sjogren’s disease. Serum
anti-DNase I concentrations were evaluated by conventional ELISA, as described elsewhere [1]. The beads were synthesized using original technique [2], modified ELISA and recovery of the beads for repeating use was performed according to the previously published protocols [2]. Antibody concentrations were expressed as relative optical density units (ODU). The cutoff values for conventional and modified ELISA were 0.068 and 0.079, respectively. All the means and operation characteristics were expressed as values (95% confidence intervals). Differences were considered significant when p < 0.05.

**Results:** Mean anti-DNase I concentrations in SLE patients (negative and positive together) were 0.088 (0.031–0.145) and 0.079 (0.033–0.125) ODU for conventional and modified ELISA, respectively; in the control group they were 0.068 (0.020–0.116) and 0.063 (0.019–0.107) ODU, respectively. Differences within these couples were not significant. Diagnostic sensitivity and specificity of modified ELISA were 64.74 (53.09–76.39) and 85.01 (72.95–97.07%), coinciding with those for conventional ELISA. LOQ for the modified ELISA was slightly lower than for the conventional one. Accuracy and repeatability of modified ELISA were also insignificantly higher than those for conventional approach. There was no substantial change in all the parameters of modified ELISA after single recovery of beads.

**Conclusions:** The newly developed ELISA for anti-DNase I antibodies was demonstrated to have equivalence or advantage in some analytical parameters over conventional ELISA. Considering some economic and maintenance benefits, our innovation can be an alternative tool to improve SLE diagnostics.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2598

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**THU0671** CAN AN INNER DISPOSABLE GLOVE BE USED UNDER AN ELECTROGONIOMETRIC GLOVE FOR MEASURING FINGER MOVEMENT WITHOUT LOSS OF ACCURACY?


**Background:** Improving joint mobility is an important outcome for patients with arthritis, but finger joint range of motion is rarely measured in clinic. Electronic gloves with movement sensors have been developed to measure joint movement accurately and it is now possible to assess dynamic mobility of the finger joints. However these gloves are expensive and it is likely that when carrying out measurements in the patient population they would be used with inner disposable gloves to avoid nonsocomical infection. Establishing accuracy and usability of electronic gloves whilst wearing disposable inner gloves is therefore an important pre-requisite for studies in patients with arthritis.

**Objectives:** To establish the accuracy and repeatability of measurements of finger movement obtained using two different electrogoniometric gloves worn with and without an inner disposable glove.

**Methods:** We used two different types of electrogoniometric glove for the purpose of this study. One is the commercially available 5DT dataglove 14 Ultra (5DT, 2011), and the other was produced to our specifications by Tyndall National Institute, University College Cork. We called this the “IMU glove”. We developed a graphical interface for both devices to facilitate detailed evaluation of joint movement in each finger. Both gloves were tested using a protocol adapted from Dipietro, Sabatini, & Dario, (2003).

**Results:** Table 1 displays comparison of Coefficient of Variation (CV) readings for both data gloves. Figure shows this information graphically.

<table>
<thead>
<tr>
<th>Sensor</th>
<th>No surgical glove</th>
<th>Surgical glove underneath</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index MCP</td>
<td>2.97</td>
<td>2.86</td>
</tr>
<tr>
<td>Middle MCP</td>
<td>7.03</td>
<td>6.77</td>
</tr>
<tr>
<td>Ring MCP</td>
<td>6.10</td>
<td>4.37</td>
</tr>
<tr>
<td>Little MCP</td>
<td>24.17</td>
<td>6.07</td>
</tr>
<tr>
<td>Index PIP</td>
<td>1.96</td>
<td>9.72</td>
</tr>
<tr>
<td>Middle PIP</td>
<td>4.40</td>
<td>10.29</td>
</tr>
<tr>
<td>Ring PIP</td>
<td>5.38</td>
<td>9.95</td>
</tr>
<tr>
<td>Little PIP</td>
<td>9.11</td>
<td>3.71</td>
</tr>
</tbody>
</table>

Results show no significant change for SDT angular readings with and without a surgical glove worn underneath the data glove. Results for PIP sensors show an improvement in repeatability with a surgical glove. CV variance was smaller for MCP sensors with a surgical glove worn underneath the data glove compared with no surgical glove. CV for the IMU data glove show negligible changes in MCP readings when a surgical glove is worn underneath. PIP readings show small changes when using a surgical glove.

**Conclusions:** Inner disposable gloves can be worn when using electrogoniometric gloves for testing finger movement without loss of accuracy or any significant discomfort in patients with arthritis.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4429

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**THU0672** REAL WORLD EVIDENCE COMPARING THE PATIENT REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM TO THE CDAI IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Patient (Pt) reported outcomes (PROs) play a role in overall disease evaluation, therapeutic response assessment and care of rheumatoid arthritis (RA) patients (Pts). The Pt Reported Outcomes Measurement Information System (PROMIS [P]) questionnaires developed by the NIH have been validated and are a feasible assessment tool in RA (Bartlett 2015). Outcomes: AWARE (Comparative and Pragmatic Study of Golimumab Intravenous (IV) Versus Infliximab in RA) is a real-world study of golimumab IV (G-IV) vs. infliximab (IFX) in RA and will assess infusion reactions, disease activity and multiple PROs as outcomes measures.

**Methods:** AWARE is a prospective, noninterventional, ongoing US-based study in which 1,200 adult Pts will be enrolled on initiation of treatment with G-IV or IFX. Objectives include PRO assessments of Pt response to treatment using the PROMIS-29 Profile v2.0 (P29v2), P Pain Interference Short Form-6b (PISF) and P Fatigue Short Form-7a (FSF), 36-Item Short Form Health Survey (SF-36v2) and the Clinical Disease Activity Index (CDAI). We report an interim analysis from the first 353 Pts of baseline PROMIS questionnaire and CDAI scores, and their inter-relationships. PROMIS questionnaire results are scored on a 0 to 100 scale, normed to the US population and reported as a “T-Score” (mean of 50 and standard deviation (SD) of 10). PROMIS T scores were compared across CDAI disease activity (DA) categories.

**Results:** Baseline mean (SD) CDAI score was 33.46 (±15.79), with 73.4% of pts with high DA (HDA), 22.1% with moderate disease activity (MDA), 3.7% with low disease activity (LDA) and 0.8% pts in remission. PROMIS scores are shown below. All P29v2 domains, PISF and FSF scores were significantly worse in pts with CDAI≥22 vs. CDAI<22 (p<0.05). The same was true for SF-36 domains (data not shown). PROMIS scores are shown below for all pts, and also based on CDAI DA category. PROMIS T scores across all domains (P29v2 domains, PISF and FSF) were compared to CDAI disease activity category (below). As shown, PROMIS T scores correlated with CDAI disease category, with HDA Pt T scores significantly (*, p<0.05) greater than those of MDA, LDA and Remission pts (excepting the Sleep Disturbance domain).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4429
Conclusions: These interim data further support the viability of using PROMIS questionnaires to evaluate RA pts, and indicate in this predominantly HDA population of RA pts correlations between PROMIS and CDAI disease activity category. Confirmation of the baseline interim analysis findings with the fully enrolled AWARE study, as well as inclusion of longitudinal and subset analyses based on disease activity levels, will further define the role of PROMIS relative to CDAI in RA pts in a real-world setting.

Disclosure of Interest: J. Curtis Consultant for: Janssen, AbbVie, Roche/Genentech, BMS, UCB, Myriad, Lilly, Amgen, Pfizer, Corrona, S. Kalka Employee of: Janssen Scientific Affairs, LLC, D. Parenti Employee of: Janssen Scientific Affairs, LLC, B. Krumeich Employee of: Janssen Scientific Affairs, LLC, V. Haiduc Employee of: Janssen Research & Development, LLC, C. Bingham Grant/research support from: Janssen, PCORI, NIH, Pfizer, Consultant for: Janssen, AbbVie, Amgen, BMS, Celgene, Genentech/Roche, Lilly, Macrogenics, Mboebast, Novartis, NovoNordisk, Pfizer, Regeneron, UCB


THU0673 THE EUROPEAN CONSENSUS FINDING STUDY GROUP (ECFSG) HELPS CHARACTERIZING NEW TENTATIVE REFERENCE STANDARDS FOR AUTOANTIBODY MEASUREMENT
J. Rönnel1, C. Dahle2, M. Blüthner3, E. Feist4, C. Dolman5, S.J. Thorpe6, E. Monogioudi7, I. Zegers8, D. Hamann9 on behalf of ECFSG.

Methods: Four autoimmune diseases (EULAR autoantibody study group, also known as the EULAR autoantibody study group, has been distributing sera with unspecified antibodies to align test results by adopting internationally used measurement units, but reference materials are missing for many autoantibody specificities.

Objectives: Recently the scope for ECFSG was expanded to also include unbiased autoantibody characterization of serum/plasma specimens planned to constitute raw material for production of future autoantibody reference materials. Materials: Four autoimmune diseases (EULAR autoantibody study group, also known as the EULAR autoantibody study group, has been distributing sera with unspecified antibodies to align test results by adopting internationally used measurement units, but reference materials are missing for many autoantibody specificities. Results: All or almost all participating laboratories detected the target specificities, and all four samples showed restricted autoantibody specificities related to the target specificity. Anti-dsDNA was detected by all laboratories using Chithraud IgG ELISA/EIA, FARR assay or ALBIA and all labs reported a homogenous ANA pattern. Other specificities were restricted to histones, nucleosomes and anti-Ku. All laboratories but one detected IgG anti-b2GPI and IgG anti-cardiolipin, mostly in high levels, in the tentative IgG anti-b2GPI reference standard, whereas corresponding IgA and IgM antibodies were absent. All laboratories detected anti-PR3, mostly monospecific and in high levels together with P-ANCA pattern in the anti-PR3 reagent, irrespective of method used. Conclusions: The expanded scope of ECFSG has enabled broad characterization of new tentative autoantibody reference standards. The anti-dsDNA specimen has been processed by the National Institute for Biologic Standards and Control (NIBSC) for consideration as the 2nd WHO anti-dsDNA reference standard. The other materials are basis for certified reference material for IgG anti-myeloperoxidase (ERM-DA476/IFCC), and the candidate reference materials for IgG anti-proteinase 3 (in certification) and for IgG anti-b2PG1 (in evaluation) from the Joint Research Centre.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1743

THU0674 ANTI-DFS70 ANTIBODY – A BIOMARKER THAT AID IN THE EXCLUSION OF ANA ASSOCIATED RHEUMATIC DISEASES
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Background: Positive ANA may lead to additional testing and potentially even inappropriate treatment in patients with rheumatic symptoms not caused by ANA associated rheumatic diseases (AARDs).

Objectives: It has been shown that autoantibodies directed against lens epithelial derived growth factor (LEDFG), also named DFS70 according to the staining pattern (dense fine speckled) and molecular weight of the target antigen (70 kDa), are common among ANA positive individuals with no evidence of AARD [1,2]. The aim of the current study was to evaluate the autoantibodies directed against DFS70 can be used to exclude AARD in ANA positive patients.

Methods: Anti-DFS70 antibody were determined by chemoluminescence assay (CLIA) in sera of 352 apparently healthy controls (AHI), 1048 patients of an ANA positive routine cohort, 579 patients with AARD (300 SLE, 76 idiopathic inflammatory myopathies, 167 systemic sclerosis, 36 Sjögren's syndrome), 56 patients with undifferentiated connective tissue disease (UCTD), and 660 non-AARD patients (302 rheumatoid arthritis, 94 ANCA-associated vasculitis, 87 atopnic rhinitis, 135 pediatric patients with celiac disease, and 42 autoimmune liver diseases.

Results: In AHI and in the non-AARD cohort, anti-DFS70 antibodies occur with a prevalence of 5.1% and 2%, respectively. Of the 1048 selected routine sera, 205 (19.6%) were positive for anti-DFS70 antibodies. Up to now, clinical reports are available for 116 of anti-DFS70 positive patients in this group. The diagnoses were widely scattered (nonspecific rheumatic symptoms, arthritis, thyroiditis, asthma, psoriasis, tumor, infections, inflammatory bowel disease), but no definite AARD could be diagnosed. In the AARD group, only 6 of 579 patients (1.2%) were positive for anti-DFS70 antibodies, all of them also showed disease specific autoantibodies (two anti-Scl70 antibody positive SSc, one anti-RA33/anti-RA22 antibody positive SSC, one Ro-52 positive SSC, one anti-Mi-2 antibody positive IIM, one SLE patient with multiple autoantibodies including dsDNA antibodies). In patients with UCTD, 6 (10.7%) were anti-DFS70 antibody positive in the absence of disease specific autoantibodies. Up to now, no development of an AARD was observed in these patients.

Conclusions: Anti-DFS70 antibodies are frequently observed in sera with chromatin binding antibodies in the absence of disease specific autoantibodies. If anti-DFS70 antibodies are positive in the absence of AARD specific autoantibodies, an AARD can be excluded with high certainty.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5915

THU0675 DEVELOPMENT AND PSYCHOMETRIC VALIDATION OF A TOOL TO ASSESS THE FEARS OF PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: THE FAIR SCALE

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Background: Patients (pts) with chronic inflammatory rheumatic diseases (CIRDs) such as rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) have fears related to their disease that can negatively impact health-related quality of life and compromise treatment adherence.

Objectives: To develop and validate a patient-reported outcome (PRO) ques-
tionnaire to explore fears related to CIRDs using the Fears Assessment in Inflammatory Rheumatic Diseases (FAIR) Scale.

Methods: The preliminary questionnaire included 44 items (23 related to fears) most frequently cited by pts in a qualitative study of 50 French pts. Each item was formulated as an affirmative sentence and scored from 0 (completely disagree) to 10 (totally agree). Item scores were summed to provide a total score. The questionnaire was finalised and validated. Pts diagnosed with RA (EULAR/ACR criteria) or axSpA (ASAS criteria), recruited during routine visits by 100 participating rheumatologists across France, completed the preliminary questionnaire, HAD (Hospital Anxiety and Depression) and AHI (Arthritis Helplessness Index) scores. Redundant items (inter-item correlation coefficient < 0.65) were eliminated. For the others, internal consistency (Cronbach alpha) and the factorial structure of the scale (principal component analysis) were assessed. Pts were classified according to their level of fears (cluster analysis) and corresponding score thresholds were determined (ROC analysis). The final questionnaire was independently translated into English and back into French twice, with reconciliation of the translated texts.

Results: 672 pts were included: 432 RA pts (mean±SD disease duration was 13.1±11.4 years, DAS28[ESR] was 2.6±1.2, 77.3% were taking biologics) and 240 axSpA pts (disease duration was 13.8±10.6 years, BASDAI was 3.5±2.2, 72.7% were taking biologics). The final FAIR Scale included 10 (Table) with total scores ranging 0–100. Mean±SD scores were 51.2±25.4 in RA and 60.5±22.9 in axSpA. Three pt groups were identified, characterised by high, moderate and low level of fears (cluster analysis) and corresponding score thresholds were determined (ROC analysis). The final questionnaire was independently translated into English and back into French twice, with reconciliation of the translated texts.

Table: FAIR Scale – 10 items [3]

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-1</td>
<td>1</td>
<td>I am afraid that my disease is getting worse.</td>
</tr>
<tr>
<td>I-2</td>
<td>2</td>
<td>I am afraid that my joint will hurt me.</td>
</tr>
<tr>
<td>I-3</td>
<td>3</td>
<td>I am afraid that my joint will weaken.</td>
</tr>
<tr>
<td>I-4</td>
<td>4</td>
<td>I am afraid that my joint will become rigid.</td>
</tr>
<tr>
<td>I-5</td>
<td>5</td>
<td>I am afraid that my joint will dislocate.</td>
</tr>
<tr>
<td>I-6</td>
<td>6</td>
<td>I am afraid that my joint will become immobile.</td>
</tr>
<tr>
<td>I-7</td>
<td>7</td>
<td>I am afraid that my joint will become sensitive to cold.</td>
</tr>
<tr>
<td>I-8</td>
<td>8</td>
<td>I am afraid that my joint will become painful.</td>
</tr>
<tr>
<td>I-9</td>
<td>9</td>
<td>I am afraid that my joint will become swollen.</td>
</tr>
<tr>
<td>I-10</td>
<td>10</td>
<td>I am afraid that my joint will become red.</td>
</tr>
</tbody>
</table>

Conclusions: The FAIR Scale is a 10-question PRO to evaluate disease-related fears in CIRD pts. In this pt population, 17.2% had high fear scores, contrasting with a disease that is often well-controlled. The FAIR Scale was associated with psychological distress. This psychometrically-validated and easy to use questionnaire could be used to improve physician dialogue in CIRDs and also be of value in clinical studies. Further validation in other populations is needed.

References:

Acknowledgements: The authors acknowledge Costello Medical Consulting, funded by UCB Pharma, for editorial assistance. This study was funded by UCB Pharma and Arthritis Foundation Olivier Courtin.

Disclosure of Interest: L. Gossec Grant/research support from: UCB Pharma, Lilly, Consultant for: AbbVie, BMS, Celgene, Janssen, Novartis, MSD, UCB, P. Chauvin: None declared, C. Hudry: None declared, G. Quikerman Employee of: UCB Pharma, V. Saulot: None declared, F. Russo-Marie: None declared, T. de Chalus Employee of: UCB Pharma, J. M. Joubert Employee of: UCB Pharma, A. Saraux Consultant for: UCB Pharma, F. Berenbaum: None declared


THU0676 ANTI-RO/SS-A 52-KDA ANTIBODIES: A MARKER FOR LUNG FIBROSIS IN RHEUMATIC DISEASES


Background: Lung fibrosis (LF) is a type of interstitial disease that leads to lung scarring, respiratory failure and later on, death. There are 2 main types of LF: idiopathic and secondary; and the prognosis is very different. LF becomes relevant in connective tissue diseases (CTD) and some studies have suggested that there could be an association between anti-Ro/TRIM21 antibodies and the development of interstitial lung disease in these patients.

Objectives: The aim of this study was to assess if the presence of anti-Ro52/TRIM21 antibodies is an independent risk factor for developing CTD-associated LF. We also aimed to evaluate the initial manifestations of systemic diseases and clinical characteristics linked to certain antibodies.

Methods: It is a prospective, observational, longitudinal, single-center study conducted among unselected patients with CTD (rheumatoid arthritis, systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis (PM), overlap CTD syndrome (OCTD), MCTD, primary Sjögren’s sd (PSS), primary antiphospholipid syndromes, and undifferentiated connective tissue disease). We analysed data from 1,432 caucasian patients included in the “Systemic Autoimmune Diseases (SAD) Registry” from 1988 to 2014. They were all checked at least biannually and blood samples were taken according to clinical practice. Exclusion criteria were LF as the initial manifestation of the SAD, LF already diagnosed at the first visit and also LF secondary to drugs or a specific environment.

Results: 10% of patients included in the study developed LF. The OR for LF in patients with anti-Ro52/TRIM21 antibodies was 1.757 (95% CI=1.1–2.7). The OR for LF increased with every year of age (OR=1.03, 95% CI=1.02–1.04). Only 9 out of 146 patients with LF were positive for Anti-La-SS-B antibodies, and the OR for males was 8.6 compared to women (95% CI=1.8–39.5). Patients with SSc and PM showed a higher OR for the development of LF (6.9 95% CI=4.6–10.4 and 2.0, 95% CI=1.2–2.8 respectively) compared to those diagnosed with other CTD. The time passed from the first symptoms to the diagnosis of LF was inversely associated LF. We also aimed to evaluate the initial manifestations of systemic diseases and clinical characteristics linked to certain antibodies.

Conclusions: Anti-Ro52/TRIM21 antibodies have been proved to be a risk factor for developing LF. The earlier the age of onset, the slower the progression to fibrosis. However, patients with anti-Ro52/TRIM21 antibodies tend to have a faster development, independent of the age of onset. Anti-La-SS-B antibodies seem to be a protective factor for the development of LF in both genders; but the association is stronger in women. 

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2890
Background: International scientific networks have raised concerns about inadequate reporting of safety outcomes in randomised trials and systematic reviews. Outcome Measures in Rheumatology (OMERACT) has previously developed an adaptation of the US National Cancer Institute (US NCI) Common Terminology Criteria for Adverse Events (CTCAE), the RCT (Rheumatology Common Toxicity Criteria) to collect adverse events in rheumatology clinical trials. To respond to this need to also report safety outcomes from the patient perspective, the Safety Working Group is developing a core outcome set, followed by a core outcome measurement set. A scoping review of available instruments for measuring safety outcomes is needed to inform this work.

Objectives: To identify candidate measurement instruments for safety outcomes in rheumatology clinical trials.

Methods: A systematic search was performed in the MEDLINE database (via PubMed) in January 2017 using MeSH terms covering synonyms for adverse events, rheumatology and measurement instruments and the Boolean operator OR to combine them. Full-text articles about the development or evaluation of instruments identified were then screened for eligibility based on title and abstracts. Two reviewers (LK and RC) screened the full text articles.

Results: Of 434 unique references identified, 19 were read in full-text, and 8 were included (see figure). The instruments identified were: Glucocorticoid Toxicity Index (GTI), Patient Reported Experiences and Outcomes of Safety in Primary Care (PRESOS-PC), Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI flare index (cSFI), the BioSecure questionnaire, Rheumatology Common Toxicity Criteria (RCTC), OMERACT 3x3, and the Stanford Toxicity Index (STI). These instruments were specific for substance (GTI), BioSecure questionnaire, setting (PRESOS-PC), condition (cSFI), or not fully validated (RCTC, OMERACT 3x3, STI).

Conclusions: The instruments identified are either too specific, or require further development/evaluation, for the purpose of standardizing measurement of safety in rheumatology clinical trials. Thus, we will proceed to gain consensus on the domains that must be measured to develop a core outcome set.

Disclosure of Interest: None declared


Figure 1

Conclusions: Our study confirms previous evidences suggesting a higher expression of CD44v3 and v6 on T cells from SLE patients compared to HS. Higher expression of CD44v3 and v6 on patients with active disease suggests their possible use as biomarkers of disease activity. The good specificity and sensitivity of CD44v6 on CD4+ T cells, and the shift of the ratio towards this...
CAN THE USE OF NEW TECHNOLOGIES IMPROVE THE USE OF PATIENT REPORTED OUTCOMES (PROs) AND PATIENT PARTICIPATION IN A NATIONAL REGISTRY?

Background: PROs are especially useful in the management of rheumatic diseases in complement to physician evaluation. However they are time consuming and used in a limited manner in the daily clinical practice. Reuma.pt is the Portuguese national rheumatic diseases register and one of the few registries in Europe that allows the patient to do at home the PROs before the appointment. In our institute we have complemented that with the creation of a paper free day hospital with the use of touchscreen computers that also allows the patient to do the PROs before the clinical evaluation by the rheumatologist.

Objectives: To compare the impact of the use off Reuma.pt at home PROs completion platform before and after the utilization of touch screen computers in the day hospital.

Methods: We determined the number of patients and appointments with the use at home of the PROs platform one year prior to the introduction of the touch screen computer at our day hospital (October 2014 –October 2015) and one year after the paper free day hospital was installed (November 2015-November 2016).

To determine any change of pattern of the use at home of the platform and the relations between that and patients characteristics.

Results:

| Table 1. Differences between previous use of touchscreen computers in the use at home PROs |
|-----------------|-----------------|-----------------|-----------------|
| Date            | Number of appointments | Number of patients | Age (SD) |
| October 2014    | 93/419 (22.1%)       | 57/106            |
| October 2015    | 1,264/48/48.2%       | 106               |
| November 2015   | 410±17M              | 75F+31M           |
| November 2016   | 11,793±96 (N=29)     | 10,351±43 (N=68)  |
| Under biology   | 53 appointments (56.99%) | 162 appointments (75%) |
| Diagnosis       | 43±3 11 RA e 3 PSA   | 61±5 33 RA e 12 PSA |

When we analyse the available variables between the patients that performed the PROs at home we found for both periods considered that they were younger (45.2±49.8 vs 53.4/55.1 p < 0.001) they have more education (11.8/10.35 vs 8.2/7.8) no differences were found regarding gender. There is a tendency that with the continuous use of touchscreen computers at the day hospital less educated patients are using more at home platform of Reuma.pt. The use of technology could have a considerable impact on the way we collect data from our patients. With the use of a touchscreen computer we have improved not only the overall completion of PROs but also increased the frequency of patient to the online questionnaires. Number of appointments with previous at home completion of the questionnaires more than double. This has a clear impact on patient participation, quality of data in the registry but even more important a change in the use of resources at a day hospital.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7001

VALIDATION OF EQ-SD, RAPID-3 AND HADS QUESTIONNAIRES FOR THE ASSESSMENT OF THERAPY EFFICACY IN PANCREATITIS PATIENTS

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Background: Pan is a group of heterogeneous inflammatory diseases characterized by involvement of the subcutaneous fat (SF), locomotor system and visera, and the number of pancreatitis (Pn) cases is increasing in everyday practice of a rheumatologists. There are no specific scales available to assess efficacy of Pn therapy. EQ-SD, RAPID-3 and HADS validity, sensitivity and specificity were proven for some rheumatic diseases. Thus, evaluation of EQ-SD, RAPID-3 and HADS psychometric properties in Pn patients has become the objective of this study.

Objectives: Evaluate psychometric properties of questionnaires EQ-SD, RAPID-3 and HADS in Pn patients.

Methods: The study group included 83 Pn pts (80 females, 3 males) aged 43.4±13.9 years with median disease duration of 5 [2;24] months who were at the record of V. A. Nasonova Research Institute of Rheumatology during 2009–2015 yrs. EQ-SD, RAPID-3 and HADS were filled in at the first and the control visits at 12 months. Questionnaires’ sensitivity was assessed by comparing patient’s answers and objective response to therapy measured by achievement of complete resolution of the nodules on the control visit. The construct validity was measured based on correlation with ‘external criteria’, including presence of arthritis and arthralgias, tenderness of nodules at palpation measured by VAS, ESR and CRP values.

Results: Positive dynamics (nodule regression) correlated with improved EQ-SD (EQ-SD-scale - p=0.005, EQ-SD-VAS - p=0.004) and RAPID-3 (p<0.001). Median ± EQ-SD and HADS-depression after therapy were 0.27 [0.12; 0.45] (p=0.005), and 2 [1.5] (p=0.13) scores, respectively, while average decline in RAPID-3 and HADS- anxiety scores after therapy was 9.2±5.2 (p=0.001) and 4±3 (p=0.15), respectively. EQ-SD showed the greatest power in Pn patients’ quality of life assessment. EQ-SD-scale and VAS “thermothermometer” showed moderate correlation with nodule tenderness at baseline (r= -0.23, p=0.036) & (r=-0.45, p=0.003), and control visits (12 months) (r= -0.38, p=0.002) & (r=-0.41, p=0.002); EQ-SD scale showed moderate correlation with ESR and CRP values at the control visit (r=-0.23, p=0.03) & (r=-0.25, p=0.005), and EQ-VAS – with CRP value at 12 months (r= -0.33, p=0.002), demonstrating clear correlation with patient’s objective health status and lab parameters values. Moderate correlation between functional RAPID-3 values and nodule tenderness at baseline (r=0.34, p=0.0015) and after 12 months (r= 0.5, p=0.0001) are also indicative of close links between the questionnaire data and pts’ objective health status. As for the HADS assessment, moderate correlation was found only between HADS-depression and nodule tenderness at baseline (r=-0.24, p=0.026) and 12 months (r=0.28, p=0.014) visits. There were no other significant correlations identified.

Conclusions: EQ-SD and RAPID-3 questionnaires should be considered as valid and sensitive instruments for the assessment of the quality of life and efficacy of therapy in Pn pts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2518

BASAL ESSDAI/DAS SCORES IN 8061 PATIENTS WITH PRIMARY SJÖGREN SYNDROME: CHARACTERIZATION OF SYSTEMIC DISEASE

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Objectives: To characterize and quantify systemic involvement at diagnosis in a large international cohort of patients with primary Sjögren’s syndrome (SS).

Methods: The Big Data Sjögren Project was formed in 2014 to take a “high-definition” picture of primary SS at diagnosis by merging international databases (9302 consecutive patients from 21 countries of the 5 continents). The main features including ESSDAI/DAS scores were analysed.

Results: Baseline ESSDAI was available in 8061 patients (93% female, mean age 53yrs). The mean ESSDAI score at diagnosis of the entire cohort was 6.4±7.9. In 1488 patients (19%), score at diagnosis was 0, while 681 (8%) presented with high activity in at least one domain. The main systemic features at diagnosis were
biological (51%), articular (38%), haemato logical (24%) and glandular (22%). Low
DAS was reported in 4483 (56%) patients, moderate DAS in 2483 (31%) and high
DAS in 1098 (14%) patients. The mean baseline ESSDAI was higher for younger
the patient was (p < 0.001), higher in White patients (6.9 vs 5.1, p < 0.001), males
(8.4 vs 6.2, p < 0.001), those with positive ocular (6.7 vs 4.9, p < 0.001) or oral (6.8
vs 5.7, p < 0.001) vs those with non-ocular (6.7 vs 5.7, p < 0.001) and anti-Ro/La antibodies (7.2 vs 4.4, p < 0.001). Logistic regression identified
as independent variables White ethnicity (OR 3.07), abnormal ocular
AUCs of 63.5% and 73.4% based on patient’s and physician’s OSSA,
predicting main diagnoses were constructed and estimated to perform with
the point of care. This rapid test shows excellent agreement to a corresponding
laboratory assay based on 178 serum samples from RA and PsA patients
was performed against the BÜHLMANN sCAL (MRP8/14) reference ELISA.
ifar, the patient was asked twice (1 to 2 year interval) to answer questionnaires evaluating: disease
and 571 patients (54%) showed an ESSDAI score at the time of diagnosis, with nearly 80% of patients showing an ESSDAI score > 0.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4472

THU0683 RAPID DETERMINATION OF THE INFLAMMATION MARKER CALPROTECTIN IN SERUM FROM PATIENTS WITH INFLAMMATORY ARTHRITIS AT THE POINT OF CARE
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Background: A Treat-to-Target (T2T) strategy for inflammatory arthritis, targeting remission or minimal disease activity, is the recommended treatment approach by EULAR and ACR. This strategy relies on “tight monitoring” which necessitates regular
clinical examination and measuring acute-phase reactants such as C-reactive protein. Calprotectin (MRP8/14; SI00A/9), a relatively novel inflammation and disease activity marker in the arthritis field, exhibits several features which fit the “theranostic needs” for accurate therapy monitoring. Those features include dis-
correlation between responders and non-responders [1], determination of disease activity [2] and prediction of relapse or radiographic progression [3]. The classical method to determine calprotectin in serum (sCAL) is ELISA which is
used in service or central laboratories. A rapid and simple determination of sCAL at the point of care is a substantial step forward in supporting clinicians to deliver an efficient T2T strategy. Here, we report on the validation of a quantitative, rapid
assay for calprotectin.

THU0062 POPGEN-OSSA: DEVELOPMENT OF AN ORGAN SPECIFIC SELF ASSESSMENT (OSSA) FOR INTERDISCIPLINARY DOCUMENTATION OF PATIENT REPORTED CLINICAL OUTCOMES
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Background: Patient reported outcome measures are comprised of either sets of questions which are applied on a global scale or assessment based on visual analogue scale (VAS). These patient-reported outcome measures lack accuracy and/or clinical feasibility when comparing heterogeneous patient groups with different diseases, or when characterizing patients with systemic disease involving different organ systems.
Objectives: Developing a clinical feasible patient-reported outcome measure based on VAS assessment of different organ systems.
Methods: Patients were asked to rate their health status in a 10cm VAS (0–100%) concerning their global health as well as of different organ systems, namely heart, lung, muscle and joints, gastro-intestinal, metabolic, uro-genital, skin, neuro-psychiatric, eyes and ears. All VA-scales were “anchored”. Patients were asked to rate their health status below 75% if they felt “medical action is needed”, they should rate the health status > 50% in case of a “strong need for medical action” and > 25% in case of a “medical emergency”.
336 patients from different outpatient clinics (cardiologic, pneumologic, gastro-intestinal, nephrologic, neuropsychologic, dermatologic, rheumatologic, ophthalmologic and obesity outpatient clinic) as well as patients from internal emergency clinics and a general practitioner clinic were evaluated. Both, patients and the attending physicians completed the Popgen-OSSA. In addition the attending physician was asked to document ranking of the 5 most important diagnoses of the patient. Statistical analysis was carried out using non-parametric testing. Furthermore,
to predict main diagnoses based on patients’s as well as physician’s OSSA

References:

THU0684 WORK IMPACT IN AXIAL SPONDYLOARTHRITIS: THE AS-WIS QUESTIONNAIRE PREDICTS THE RISK OF WORK IMPACT: A LONGITUDINAL STUDY OF 101 PATIENTS
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Background: Axial spondyloarthritis (axSpA) mainly affects the working-age
subject and can have a moderate (short-term sick leave) or significant (long-term
sick leave, disability status, unemployment) work impact.
Objectives: To evaluate the value of a simple and short (2 minutes) questionnaire, the AS-Work instability scale (AS-WIS) to predict the work impact of axSpA after 1–2 years.
Methods: Longitudinal study in 3 centers in Paris, France. Patients with axSpA according to the rheumatologist and the ASAS criteria were included. Patients were asked twice (1 to 2 year interval) to answer questionnaires evaluating: disease activity, demographic characteristics, impact on work (short-term and long-term sick leave, disability, unemployment), and the ASWIS questionnaire (1): a 20 item, simple screening tool for Work Instability (the consequence of interaction between an individual’s functional ability and their work tasks). The risk of disability is assessed as low if the score is <11, medium between 11–18 and high–18. Only patients who answered both questionnaires were included for analyses. Statistical analyses included descriptive analyses and univariate/multivariate

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4472
analyses to search for baseline factors of work impact at 1–2 years (including a medium/high ASWIS score, gender, age, schooling level, BASDAI, BASFI).

Results: Among the 188 patients who answered the first questionnaire, 144 were currently working and were asked to answer the second questionnaire. A total of 101 patients answered both questionnaires. Mean age at inclusion was 45 (SD 9) years, 52% were male, disease duration was 14 (SD 8) years and 62% had an education level equivalent to more than high school. The BASDAI and the BASFI were respectively 34 (SD 21) and 23 (SD 23). At baseline, median ASWIS was 10, a low-risk score was found in 55 patients (54%), and a medium/high risk score in 46 (46%). 1–2 years later, 37 patients (36%) had work impact: 25 patients (25%) a short-term sick leave, and 12 patients (12%) a significant work impact (long-term disability or unemployment due to AxSpA).

Among patients with a low ASWIS score at baseline (n=55), only 13 (24%) had a work impact (including only 2 with a significant impact). Among patients with a medium/high ASWIS score (n=46), 24 (52%) had a work impact (including 10 patients of a significant impact).

In univariate analysis, baseline factors associated with work impact (moderate or significant) were a medium/high ASWIS score, a high BASFI and a shorter disease duration. In multivariate analysis, medium/high ASWIS (odds ratio, OR 2.71 (1.04–7.22)) and a lower disease duration (0.94 (0.89–0.99)) were independent predictive factors of work impact.

Conclusions: In patients with AxSpA, a medium/high ASWIS score was followed by a work impact in 50% of cases within 2 years in this well-controlled population. This short questionnaire can be helpful to screen for future difficulties at work, whatever the stage of disease.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3280

THU0685 ASAS HEALTH INDEX FOR PATIENTS WITH SPONDYLOARTHRITIS: TRANSLATION INTO PORTUGUESE, VALIDATION, AND RELIABILITY

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Background: The Assessment of SpondyloArthritis international Society Health Index (ASAS HI), is a unidimensional questionnaire, that includes 17 items, measuring functioning and health in patients with spondyloarthritis (SpA) (1). At the beginning of this project, only an English version of the instrument existed.

Objectives: The aim of this study was to conduct the cross-cultural adaptation of the ASAS HI into European Portuguese language and investigate its reliability and validity in a sample of Portuguese patients with SpA.

Methods: The ASAS HI has a range from 0 (best health state) to 17 (worst health state). The questionnaire was first translated and then back translated following published guidelines. Patients fulfilling ASAS classification criteria for either axial (axSpA) or peripheral SpA (pSpA) were included. Reliability was assessed through internal consistency coefficient, and internal consistency was assessed using Cronbach’s alpha.

Concluding remarks: The findings of this study showed that the Portuguese version of the ASAS HI is a comprehensive questionnaire that is reliable and valid. Therefore, its use can be recommended, both for clinical practice and research purposes, to assess the state of health and functioning in Portuguese SpA patients. Future research is needed to evaluate the responsiveness of the ASAS HI in SpA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3927

THU0686 HEART RATE VARIABILITY IN INFLAMMATORY JOINT DISEASE. A META-ANALYSIS

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Background: Autonomic dysfunction is an established predictor of all-cause mortality and post-myocardial infarction mortality. It has been suggested to be a pathogenic factor for the development of cardiovascular disease (CVD) in the general population, possibly acting through the impact of the autonomic nervous system on inflammation (1). Heart rate variability (HRV) is a marker of cardiac autonomic function and is increased in many conditions including chronic widespread pain. HRV is responsive to physical exercise. Inflammatory joint diseases (IJD) are characterized by joint inflammation and symptoms include pain, functional decline and restricted movement. Patients with IJD have an increased risk of premature death due to CVD.

Objectives: To compare HRV between adult patients with IJD and healthy controls, using the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses” (PRISMA) methodology, and to describe the associations between IJD disease activity, pain and physical activity, and HRV.

Table 1 – Correlation between ASAS-HI at baseline and other health outcomes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>R</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI</td>
<td>0.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASFI</td>
<td>0.63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASAS-CRP</td>
<td>0.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-36 (functional)</td>
<td>-0.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-36 (mental)</td>
<td>0.44</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2 - Discriminant ability of ASAS-HI (at baseline) stratified by disease activity (mean±SD)

<table>
<thead>
<tr>
<th>Disease Activity</th>
<th>ASAS-HI (mean±SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive</td>
<td>1.6 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>2.3 (2.2)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>6.2 (4.1)</td>
<td></td>
</tr>
<tr>
<td>Very high</td>
<td>8.1 (3.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Methods: A research librarian conducted systematic searches in Medline, Embase and Amed from earliest date until August 2016. Inclusion criteria were adult human case-control studies published in English or a Scandinavian language, presenting data on HRV in patients with JD (Rheumatoid Arthritis (RA) or Spondyloarthritis (SpA)). Included under the SpA diagnosis were patients with psoriatic arthritis or ankylosing spondylitis. Six established measures of HRV were selected: the Square root of mean squared difference of successive R-R interval (rMSSD), high frequency (HF), total power (TP), Ewing protocol standing (E-S), breathing (E-B) and Valsalva (E-V). Patients with RA, SpA and healthy controls were compared separately using random-effects meta-analyses of standardized mean differences (SMD).

Results: 847 titles and abstracts were reviewed, 36 papers were eligible for inclusion (Figure 1). For rMSSD the pooled SMD (95% CI) RA vs. controls was -0.90 (-1.35 to -0.44), for SpA vs. controls -0.34 (-0.73 to 0.06). For HF, the pooled SMD RA vs. controls was -0.78 (-0.99 to -0.57), for SpA vs. controls -0.04 (-0.22 to 0.13). For TP the pooled SMD RA vs. controls was -0.60 (1.26 to 0.06), SpA vs. controls -0.27 (-0.51 to 0.03). All pooled Ewing parameters were significantly lower in cases compared to controls, except for E-V which was comparable between cases and controls in patients with RA. 18/36 papers examined the relationship of JD disease activity to HRV, of which the majority, 13, describe an inverse association between the parameters. The impact of pain on HRV was not explored in any study, and only one study explored the impact of physical activity on HRV, finding no cross-sectional association. Conclusions: Patients with JD have lower cardiac parasympathetic modulation compared to healthy controls and this may be a risk factor for CVD. There is an inverse relationship between JD disease activity and HRV. The relationship between pain, physical activity and HRV should be further explored.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2897
the worker's performance whilst at work due to ill health (i.e. presenteeism). A number of global measures have been developed to assess presenteeism in clinical studies. However, limited information is available on the correlation between these measures and the construct validity of these measures.

**Objectives:** To determine the correlation between four global measures of presenteeism and to evaluate the construct validity of these measures.

**Methods:** The main aim of this international observational study (7 countries in Europe and Canada), recruiting patients with IA (RA, PsA or AS) or OA in paid employment, was to investigate content and construct validity of global presenteeism measures. Patients completed 4 global measures (Work Productivity Scale – Arthritis (WPS-A), Work Productivity and Activity Impairment Questionnaire (WPAI), Work Ability Index (WAI), and both the Quality and Quantity scales of the QQ questionnaire) (see table legend for descriptions individual scales). Spearman correlations were applied to test the correlation between individual presenteeism scales and to test construct validity with the 11-item Workplace Activity Limitation presenteeism Scale (WALS) and several health related patient reported outcome measures. Interpretation of correlation coefficients: (very) weak (r range=0.0–0.39), moderate (r range=0.40–0.59) to strong (r range=0.60–1.0).

**Results:** 468 patients with a median disease duration of 10 [IQR 5–18] yrs were included; 62% were female. Median [IQR] presenteeism scores were, respectively: 2 [0.5–5] for WPS-A, 3 [1–5] for WPAI, 8 [6–9] for WAI, 81 [49–100] QQ-total, with WAI and QQ having reversed scales (Legend table). Correlations between the 4 global measures were moderate to strong, ranging from 0.49 for the correlation between WPS-RPA and QQ-Quality to 0.83 between WPS-RPA and WPS-RPA. The multi-item presenteeism scales WALS, measuring difficulty at work, strongly correlated with both WPSI (r=0.65, p<0.05) and WPS-RPA (r=0.64, p<0.05), both measures capturing the affect of interference of illness on work productivity. Moderate correlations were achieved between all six global presenteeism measures and health outcomes (r range=0.36–0.54; 0.37 to 0.54; and 0.40 to 0.58).

**Conclusions:** Global measures of presenteeism show good to moderate construct validity, with the WAI and WPS-IA/OA showing slightly better construct validity compared to the WAI and QQ. The information obtained in this study will further tailor the treatment strategy of various rheumatic diseases. Traditionally used measures to assess disease activity and treatment response in spondyloarthritis (SpA) are ESR, CRP and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Serum amyloid A (SAA) is an acute-phase reactant predominantly synthesized in the liver by hepatocytes in response to proinflammatory cytokines. Some studies have shown that SAA can be a valuable indicator of disease activity, damage and functional impairment, however it has not been extensively used in clinical practice.

**Objectives:** To study the association between SAA levels and its variation with other biomarkers and disease activity/functional parameters in a cohort of PsA patients under biologic therapy.

**Methods:** Observational retrospective study was conducted including PsA patients (according to CASPAP criteria) followed at our Rheumatology department with at least one measurement of SAA levels from January 2015 until December 2016. Demographic and clinical data were obtained by consulting the national database (Reuma.pt). The disease activity/functional scores from at least one visit and corresponding measurements of SAA, ESR and CRP levels were collected. The difference (Δ) between 2 evaluations separated by a median time of 6 months [5–18] was calculated for all variables. Agreement between biomarkers was calculated using kappa coefficients. Correlations were studied using Pearson and Spearman coefficient analysis. Significance level was set as 0.05.

**Results:** 53 PsA patients were included. 31 (58%) patients were females with a mean (SD) age of 50 (11.2) years and a median disease duration of 9 years [1–43]. 28% had axial involvement, 34% peripheral involvement and 38% had both types. All patients were under biologic DMARD. 100 SAA measurements were collected. Median SAA and ESR levels were significantly superior in female patients (23 vs 6mm/1st and 8.6 vs 4.4mg/l, respectively, p<0.05) and only ESR levels correlated with age (r=0.20, p<0.05). The three biomarkers showed a weak association with serum creatinine levels, with greater correlation for SAA (r=0.46, p<0.001) and SAA had a stronger correlation with CRP (r=0.75, p<0.001) than with ESR levels (r=0.26, p<0.01). SAA and CRP (dichotomized as negative/positive) had a greater level of agreement (k=0.40) compared to ESR (k=0.26 and k=0.32, respectively). No significant correlations were found between the biomarkers and the tender/swollen joint count or the pain/global disease activity VAS. SAA levels correlated with ASDAS CRP (r=0.43, p<0.001) and no significant associations between SAA and ESR or DAS28 CRP (r=0.20 and r=0.24, respectively, p>0.05). Only ESR had a very weak correlation with both ASDAI, MASES and SPARCRC scores (r=0.25, r=0.21, r=0.35; p<0.05). All the biomarkers had weak correlations with BASFI and HAQ scores. SAA levels had a weak correlation with ΔCRP (r=0.32, p=0.03; n=47) and no significant association was found with ESR, SAA correlated significantly with ASDAS CRP and ΔBASMI (r=0.32, r=0.39; p<0.05).

**Conclusions:** This study showed that SAA levels and its variation had a significant correlation with CRP levels and its variation, respectively. Significant association with ASDAS CRP variations suggests that serial measurements of SAA may represent an additional marker for monitoring disease activity over time in PsA patients.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5466

**THU0691** IS SERUM AMYLOID A PROTEIN AN USEFUL BIOMARKER TO MONITOR TREATMENT WITH ANTI-TUMOUR NECROSIS FACTOR-ALPHA AGENTS IN SPONDYLOARTHROPATHIES PATIENTS?


**Background:** Quantitating the degree of inflammation has become essential to tailor the treatment strategy of various rheumatic diseases. Traditionally used measures to assess disease activity and treatment response in spondyloarthritides (SpA) are ESR, CRP and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Serum amyloid A (SAA) is an acute-phase reactant predominantly synthesized in the liver by hepatocytes in response to proinflammatory cytokines. Some studies have shown that SAA can be a valuable indicator of disease activity, damage and functional impairment, however it has not been extensively used in clinical practice.

**Objectives:** To determine if SAA levels have better correlation with conventional biomarkers than CRP and ESR.

**Methods:** Prospective study, including SpA patients under anti-TNFα treatment at a Rheumatology Department of a Portuguese University Hospital. The following parameters were collected and registered in two different evaluations 6 months apart from each other: SAA, CRP and ESR levels, BASDAI, ASDAS-PCR, ASDAS-VA, BASFI, BASMI, swollen and tender joints counts (SJC and TJC), MASES, SPARCRC, and patient global assessment (PGA); physician global assessment (PGA), full back pain (TBP), nocturnal back pain (NBP) measured in a visual analogue scale (VAS). The variation of each parameter was calculated as the difference between the levels registered at each evaluation (baseline and 6 months) and presented as Δ (parameter). We compared the correlation between ΔSAA, ΔCRP and ΔESR levels with ΔBASDAI, ΔASDAS-PCR, ΔASDAS-VA, ΔBASFI, ΔBASMI, ΔSJC, ΔTJC, ΔMASES, ΔSPARCRC, ΔPGA-VA, ΔPGA-VAS, ΔTBP-VAS, ΔNBP-VAS. The statistical analysis was performed using SPSS 21.0 software, and p<0.05 was taken to indicate statistical significance. Correlation was calculated using the Spearman rank correlation (r).

**Results:** 89 patients were included, 58.4% (n=52) were male. On baseline the median age was 44.0 years (range 21.0–74.6) and median disease duration was 18.8 years (2–51.6). ΔSAA was moderately correlated with ΔCRP (r=0.65, p<0.05), both measures
p < 0.001) and had lower correlation with ΔESR (r = 0.28, p = 0.009). ΔSAA correlated with ΔNBV-VAS (r = 0.260, p = 0.016), but ESR and CRP did not correlate with this parameter. We also found statistically significant correlation between ΔSAA and ΔASDAS-VS (r = 0.257, p = 0.017), ΔASDAS-CRP (r = 0.387, p < 0.001), ΔBASFI (r = 0.301, p < 0.005). ΔCRP also showed significant correlation with ΔNBV-VAS, but it was lower than the observed with ΔSAA (r = 0.230, p = 0.033). There was no statistically significant correlation between ΔSAA levels and ΔMASES, although ΔCRP had a weak correlation (r = 0.217, p = 0.041). There was no significant correlation between either ΔSAA, ΔCRP or ΔESR and the following parameters: ΔTP-VAS, ΔPICA-VAS, ΔPQGA-VAS ΔBASDAl, ΔBASMI. ΔSPARCC, ΔTJC or ΔJJC.

Conclusions: This study suggests that SAA can be a useful tool in monitoring treatment with anti-TNFα and that could be introduced in clinical practice. However more studies, with larger sample sizes, should be undertaken to better assess this subject.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5492

THU0692 THE TURKISH VALIDATION AND RELIABILITY OF DISEASE-SPECIFIC, PATIENT REPORTED OUTCOME MEASURE IN RHEUMATOID ARTHRITIS: TR AIMS2-SF
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Background: Rheumatoid arthritis (RA) can have a major impact on health related quality of life (HRQoL). The revised AIMS-2 is the main outcome measure that has been used for measuring HRQoL in patients with rheumatic diseases. Guillen et al. developed a short form of AIMS-2 (AIMS-2 SF) (1) which is more practical and less time consuming compared to AIMS-2.

Objectives: The purpose of this study was to investigate validity and reliability of the Turkish version of AIMS2-SF (TR AIMS2-SF).

Methods: Turkish AIMS2-SF was developed after translation and back-translation method. Culturally adapted version preserved 5 component-structure (upper limb function, lower limb function, affect, pain and social interaction) with 26 items according to the original article (1). Subjects fulfilling ACR/EULAR 2010 classification criteria for RA were consecutively enrolled into the study. Patients with malignancy, fibromyalgia syndrome and other systemic inflammatory diseases were excluded. Demographic data, the body mass index (BMI), severity of pain (VAS), disease duration (month) and other clinical features was evaluated. Reliability was investigated with test-retest reliability (intra-class correlation coefficient-ICC) and internal consistency (Cronbach’s alpha). Spearman’s rank correlation coefficient was used to evaluate the relation between quantitative parameters and the validity. Construct validity was assessed by the correlation of TR AIMS2-SF with other clinical parameters (age, disease duration, VAS pain, DAS-28) and functional parameters such as Nottingham Health Profile (NHP), Health Assessment Questionnaire (HAQ), Beck Depression Inventory (BDI), Duruoz Hand Index (DHI).

Results: Sixty patients (6 males) were recruited into the study. The mean ± standard deviation (SD) of age (years) and disease duration (months) were 51.8±12.5 and 71.4±69.3, respectively. Mean scores of TR AIMS2-SF were; upper limb function 7.3±6.9, lower limb function 7.7±4.7, affect 7.4±3.2, pain 6.3±1.1, social interaction 4±2.3 and total score 35.5±16.6. The floor and ceiling effects were 0% and 0% with mean scores 3.5±0.3 and 35.5±16.6, respectively. Both Cronbach’s alpha and ICC were 0.83 indicating good reliability. There was significant correlation (rho, p value) with parameters that were directly related to HRQol which were NHP subscales (energy level: 0.46, pain: 0.63, emotional reaction: 0.55, sleep 0.33, social interaction: 0.60, physical activity: 0.63, p < 0.001), HAQ (0.30, p < 0.0001), BDI (0.54, p < 0.0001), DHI (0.60, p < 0.0001). Poor or no significant correlation was found with parameters that were not directly related to HRQol such as age (r = 0.04, p = 0.97), disease duration (0.21, p = 0.09), pain (0.37, p = 0.05); on the other hand, disease activity (DAS-28) correlated moderate (0.49, p < 0.0001).

Conclusions: Turkish version of AIMS2-SF is a reliable and valid tool that can be used to evaluate the quality of life in RA. This is a feasible measure that can be used in daily practice easily.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6351

THU0694 EFFECTS OF ANTI-TNF THERAPY ON SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR (sPAR) LEVELS IN ARTHRITIS
Department of Rheumatology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary

Background: The urokinase plasminogen activator receptor (uPAR) is expressed mainly on immune cells, smooth muscle cells and endothelial cells, favoring extracellular matrix degradation, cell adhesion, cell proliferation and regulates cell migration. The suPAR is the soluble form of the cell membrane-bound protein...
uPAR, elevated levels may reflect increased activation of immune system which observed in the autoimmune diseases.

**Objectives:** The aim of this study was to assess the effects of anti-TNF therapy on uPAR production in rheumatoid arthritis (RA) and ankylosing spondylitis (AS). We also wished to correlate uPAR levels with various autoimmune-inflammatory biomarkers.

**Methods:** Altogether 33 arthritis patients including 22 RA patients treated with either etanercept (ETN) or certolizumab pegol (CZP) and 11 AS patients treated with ETN were included in a 12- month follow-up study. Circulating suPAR levels were assessed by suPARnostic Quick Test Reader. In addition, disease activity (DAS28 or BASDAI), CRP for inflammatory biomarker at V2 were measured. Assessment were performed at baseline, as well as 6 and 12 months after treatment initiation.

**Results:** Anti-TNF treatment was highly effective in both disease, as the mean DAS28 decreased from 3.25 to 2.5 at V1, mean BASDAI decreased in AS. There was no significant change in the suPAR levels after 12 months of anti-TNF therapy, although resulted non-significant decrease (p=0.18) in RA patients with critical suPAR levels (>9ng/ml). Baseline suPAR levels positively correlated with anti-CCP (p=0.001) and rheumatoid factor (p=0.024) in RA patients. Circulating suPAR levels did not correlate with DAS28, BASDAI or CRP.

**Conclusions:** In a mixed cohort of RA and AS patients, anti-TNF therapy did not affect the suPAR levels after 12 months. suPAR levels correlated with rheumatoid factor and anti-CCP. Based on these results suPAR may be a marker of autoimmunity rather than that of disease activity.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3428
Background: Clinical trials in juvenile spondylarthropathy (JSpA) and axial disease are lacking. To assess the effectiveness of medications, we need measures to evaluate structural progression in the pediatric sacroiliac joint (SIJ).

Objectives: To evaluate the reliability of the SPARCC sacroiliac joint structural score (SSS) in children with suspected or confirmed JSpA.

Methods: The SSS assesses a spectrum of structural lesions of the SIJ on MRI including fat metaplasia, erosion, backfill, and ankylosis on 5 consecutive slices through the cartilaginous part of the joint. These components are scored 0–20 (backfill and ankylosis) or 0–40 (fat metaplasia, erosion). We developed a pediatric training module that included a detailed description of each SSS component plus sclerosis (0–40), scoring methodology, and numerous examples.

Poster 2

Results: Correlation (ICC).

A second training module based on DICOM images and scored an additional component plus sclerosis (0–40), scoring methodology, and numerous examples. A pediatric training module that included a detailed description of each SSS component plus sclerosis (0–40), scoring methodology, and numerous examples.

Poster 3

Analysis of the item level revealed a strong floor effect (WALS: 16% ± 56%; WLQ: 27% ± 81% of answers for all items except one) but no ceiling effect, likely reflecting the relatively low limitation expected in a working sample. Correlations with disease (fatigue, pain, physical function, depression) and job characteristics (job demand, autonomy, social support at work, commuting difficulty) with time, difficulty, or combined scores of the WALS and WLQ met the a priori hypothesized correlation levels.

Disclosure of Interest: None declared

THU0698 MEASUREMENT PROPERTIES OF PRESENTEEISM MEASURES WITH DUAL ANSWER KEYS IN INFLAMMATORY ARTHRITIS

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Background: Employment studies in arthritis have emphasised the importance of decreased productivity at work, or presenteeism. Yet, how to best measure presenteeism remains challenging. The “Work Limitations Questionnaire” (WLQ) is frequently used. A drawback is that it measures the amount of time people are limited, but not the degree to which they are limited. In contrast, the “Workplace Activity Limitations Scale” (WALS) measures the degree of limitation, but not the time it modifies the response key. We compared the WLQ and WALS to measure both degree of productivity and amount of time with productivity suffering.

Objectives: Our objective was to evaluate measurement properties, i.e. internal consistency and construct validity, of the WLQ and WALS with combined scores from dual answer keys.

Methods: A cross-sectional study used baseline data from the RCT of an employment intervention, the “Making It Work” Program. Participants were recruited from BC, Alberta and Ontario. Inclusion criteria included: having inflammatory arthritis, currently employed, age 19–59, and having concerns about work productivity. Participants were included (RA:195, PsA:54, SLE:46, AS:69; 77% female, mean (SD) age: 45.9 (9.8) yrs). Combined scores were obtained by i) multiplying, and ii) adding, the scores of difficulty and time answer keys at the item level. No significant differences were observed between the additive and multiplicative models. Hence, we report on the multiplicative model, which reflects consumers’ preference. Internal consistency was analyzed using Cronbach’s alphas; construct validity by measuring correlation (Spearman coefficients) between WALS or WLQ subscales and constructs such as work productivity activity impairment (WPAI), risk of impending work loss (work instability, RA-WIS), disease measures, and job characteristics.

Results: Analyses at the item level revealed a strong floor effect (WALS: 16% ± 56%; WLQ: 27% ± 81% of answers for all items except one) but no ceiling effect, likely reflecting the relatively low limitation expected in a working sample. Correlations with disease (fatigue, pain, physical function, depression) and job characteristics (job demand, autonomy, social support at work, commuting difficulty) with time, difficulty, or combined scores of the WALS and WLQ met the a priori hypothesized correlation levels.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6146
among participants using observed variables, was used to differentiate "pain phenotypes" considering sex, body mass index (BMI), emotional problems, comorbidities, number of painful sites and knee structural damage on MRI.

**Results:** Three pain phenotypes were identified: Class 1: high levels of emotional problems and low levels of structural damage (24%); Class 2: high levels of structural damage and low levels of emotional problems (20%); Class 3: relatively low levels of emotional problems and low levels of structural damage (56%). People within Class 1 were more likely to be female, had greater BMI, lower education level, more comorbidities, more severe knee pain and more painful sites as compared to Class 2 and Class 3. Furthermore, WOMAC pain scores and number of pain sites were consistently greater at baseline, 2.6, 5.1 and 10.7 years in Class 1 than Class 2 and Class 3 (all P < 0.05).

**Conclusions:** Psychological and structural factors interact with each other to influence pain perception.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3033

**THU0700 IMMUNOGENICITY IN PATIENTS SWITCHING FROM STABLE ORIGINATOR INFLIXIMAB TREATMENT TO CT-P13: ANALYSES ACROSS SIX DISEASES FROM THE 52-WEEK RANDOMIZED NOR-SWITCH STUDY**

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**Background:** TNF-inhibitors (TNFi) have improved treatment of Crohn’s disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and chronic plaque psoriasis (Ps). The NOR-SWITCH study was funded by the Norwegian government to investigate if switching from originator infliximab (Remicade®, INX) to biosimilar CT-P13 (Remsimä®), is safe. Previously, the primary analyses of the pooled indications have been published. Immunoegenicity is associated with treatment failure and has been of particular concern in switching.

**Objectives:** The NOR-SWITCH study aimed to assess if immunogenicity to infliximab differed between patients treated with continuous INX vs patients switched to CT-P13.

**Methods:** The study was designed as a 52-week randomized, double-blind, non-inferiority phase IV trial. Adult patients with a diagnosis of CD, UC, SpA, RA, PsA or Ps on stable treatment with the originator infliximab were eligible. Patients were randomized 1:1 to either continued INX or switch to CT-P13 treatment, using an unchanged dosing regimen. Trough drug levels and neutralizing anti-drug antibodies (ADAb) measurements were done prior to every infusion, but results were not reported during the study. Assays for drug serum levels and ADAb are fully automated on the AutoDELFI® (PerkinElmer, Waltham, MA) immunoassay platform.

**Results:** Twenty patients entered the study with detectable ADAb (9 in INX arm, 11 in CT-P13 arm). 36 additional patients developed detectable ADAb during the 52-week study period (17 in INX arm, 19 in CT-P13 arm). Incident ADAb in each disease are shown in the table. Patients with detectable ADAb at any time during the study period were more likely to discontinue study drug treatment (7/26 (26.9%) in INX arm, 5/30 (16.7%) in CT-P13 arm) than patients without detectable ADAb (17/214 (7.9%) in INX arm, 13/210 (6.2%) in CT-P13 arm) (p<0.001).

**Conclusions:** The NOR-SWITCH study demonstrated similar immunogenicity in patients switched to CT-P13 vs those who continued INX treatment, supporting that switch does not influence ADAb formation. Presence of ADAb was associated with termination of study treatment.

**References:**
1. Jørgensen KK, Olsen IC, Goll GL et al. Switching from originator infliximab to biosimilar CT-P13 compared to maintained treatment with originator infliximab (NOR-SWITCH); a 52-week randomised double-blind non-inferiority trial. The Lancet, in press.

**Disclosure of Interest:** G. Goll Consultant for: Novartis, Pfizer, Orion Pharma, AbbVie, I. Olsen: None declared, K. Lundin Consultant for: Orion Pharma, MSD, Takeda, K. Jørgensen Consultant for: Orion Pharma, AbbVie, Tillott, Intercept, M. Lorentzen: None declared, R. Klaassen: None declared, D. Warren: None declared, C. Mark Consultant for: Novartis, LeoPharma, ACHUd, AbbVie, Galdenra Nordic, Celltrion, J. Jahnsson Consultant for: Orion Pharma, Celltrion, Pfizer, MSD, AbbVie, Takeda, Napp Pharm, AstroPharma, E. Haavardsholm Consultant for: AbbVie, UCB, Pfizer, MSD, Roche, T. Kvien Consultant for: Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Hospira, Merck-Serono, Novartis, Orion Pharma, Pfizer, Sandoz, UCB, N. Bolstad: None declared

DOI: 10.1136/annrheumdis-2017-eular.4112

**THU0701 THE EFFECTS OF STRUCTURAL DAMAGE ON FUNCTIONAL DISABILITY IN PSORIATIC ARTHRITIS**

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**Background:** Functional outcomes are central in patients with chronic inflammatory musculoskeletal diseases. It has been shown in rheumatoid arthritis that functional outcomes are impaired in the presence of structural damage, a finding that has not yet been investigated in psoriatic arthritis (PsA), which has a more complex phenotype than rheumatoid arthritis (RA).

**Objectives:** To quantify the association of radiographic damage with physical function in PsA patients.

**Methods:** We analysed patients enrolled in the GO-REVEAL study 1 who had received golimumab. We obtained modified Sharp-van-der-Heijde scores (mSvDHS) from X-rays, performed at week 0, 24, 52 and week 104 (n=262). In longitudinal data analysis, we then used generalized estimating equations (GEE) on all patients in DAPSA remission (n=96), utilising all their remission visits, whereby the health assessment questionnaire (HAQ) disability index of each patients visit was used as dependent variable and mSvDHS, joint space narrowing (JSN) and erosion (ERO) scores, respectively, were used as independent variables in separate models. To analyse effects of structural damage on changeability of functional limitations, we identified a subgroup of patients who had functional limitations at baseline (HAQ≥1) and who showed a major response of DAPSA (improvement of ≥85% from baseline). In this model we assess the effect of mSvDHS on changes in HAQ, while adjusting for HAQ at baseline (n=54).

As validation cohort, we analysed a routine clinic PsA cohort with complete HAQ, while adjusting for HAQ at baseline (n=32).

**Results:** As shown in table 1 and visualised in figure 1A, for patients in DAPSA remission, significant effects were seen for both DAPSA and mSvDHS, whereas no effects were seen for either for patients in DAPSA major response (n=96) and in patients with limited/intermediate activity (n=96).

In the second analysis, looking at patients achieving DAPSA major response, again, results were significant for the association total mSvDHS and JSN. Additionally, higher estimates of JSN, compared to mSvDHS could be observed, with relative HAQ change as outcome parameter (see table 1 and figure 1B).

Table 1. Association of radiographic damage and HAQ in separate GEE models

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>DAPSA remission (n=96)</th>
<th>DAPSA Major Response (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mSvDHS</td>
<td>0.0037 (0.0018 to 0.0055)</td>
<td>0.0020 (0.0007 to 0.0032)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0.0054 (0.0021 to 0.0086)</td>
<td>0.0030 (0.0013 to 0.0047)</td>
</tr>
<tr>
<td>JSN</td>
<td>0.0095 (0.0057 to 0.013)</td>
<td>0.0011 (0.0008 to 0.0012)</td>
</tr>
</tbody>
</table>

*Adjusted for HAQ at baseline.

**Conclusion:** Our results suggest that in JSN is functionally more important than...
erations. Functional outcomes have an irreversible component that is strongly related to the amount of structural damage. This needs to be considered when targeting functional outcomes in clinical practice.

References:

Acknowledgements: We thank Janssen for provision of an 80% random data cut of patients in the GO-REVEAL trial for our analyses.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2835

THU0702 ARE MRI-DETECTED EROSIONS SPECIFIC FOR RA? A LARGE EXPLORATIVE CROSS-SECTIONAL STUDY
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Background: Magnetic resonance imaging (MRI) is recommended in the diagnostic process of rheumatoid arthritis (RA), as it can detect damage at an earlier time point than conventional radiographs. However, MRI-detected erosions as defined by EULAR and included in RAMRIS are also observed in symptom-free controls, especially at older age. It is unclear how RA-specific erosions on MRI can be distinguished from physiological erosions in symptom-free individuals. Therefore this study compared MRI-detected erosions between RA-patients and healthy controls, including evaluation of the effect of age.

Objectives: To compare characteristics of MRI-detected erosions (total erosion score, location and severity of erosions and simultaneous presence of MRI-detected edema) found in metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints between RA-patients and healthy controls.

Methods: 422 subjects (229 newly presenting patients with a clinical diagnosis of RA and fulfilling the 2010-criteria and 193 symptom-free controls) underwent contrast enhanced 1.5T MRI of unilateral MCP and MTP joints. The readers were blind to the clinical information. Total erosion score according to the RAMRIS method (hence a combination of number and severity), location and severity of erosions and simultaneous presence of MRI-detected inflammation (synovitis and/or bone marrow edema) were compared between groups, also in relation to age.

Results: First total erosion scores were analyzed. Both in RA-patients and in controls this score was associated with age (p<0.001 in both groups). In addition, at all ages and on group level, RA-patients had 1.2 (95% CI 1.1–1.3) times higher erosion scores than controls. Despite this difference, total erosion scores could not differentiate RA-patients from controls on the individual level, as there was large overlap (Figure). Next different characteristics of erosions were explored within age groups (<40, 40–59, ≥60) to search for RA-specific features. With respect to location, erosions found in MTP5 were specific for RA (spec 90–98% for different age groups). Erosions found in MTP1 were specific for RA if subjects were aged <40 (spec 98%), but specificity decreased by increasing age (spec 86% if aged 40–59 and 63% if aged ≥60). Evaluating the severity revealed that “severe erosions” (scores ≥2) were infrequent in all subjects, but almost exclusively present in RA (spec 98–100%). Finally the simultaneous presence of erosions with inflammation was studied. In the age group <40 years, the simultaneous presence was exclusively observed in RA-patients (specificity 100%); but specificity decreased by age since the combined presence was also seen in symptom-free controls (spec 91% if aged 40–59 and 71% if aged ≥60 years).

Conclusions: Whilst the group of RA-patients at disease presentation had significantly higher erosion-scores than healthy controls, scores of individuals subjects were largely overlapping. Some erosion characteristics were specific for RA, but these were present in only a minority of all RA-patients (22%).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4026

THU0703 SYSTEMATIC REVIEW OF RHEUMATOID ARTHRITIS CLINICAL STUDIES: SUBOPTIMAL STATISTICAL ANALYSIS OF RADIOLOGICAL DATA
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Background: Radiography is an inexpensive, reliable and reproducible method to detect and quantify progression of damage, an important outcome in rheumatoid arthritis (RA) trials and observational studies. However, the distribution of progression scores is skewed with many low or small readings. Analysis of such data is challenging, and the choice of analysis technique may influence the result. Current analysis practice is unknown.

Objectives: We systematically searched the literature to identify current practice for the analysis of radiographic progression in clinical trials and observational studies of RA.

Methods: PubMed Embase and Cochrane databases were searched (2006–2016) to identify studies that described analysis techniques to compare radiographic progression in at least two groups. Studies in animals, children as well as conference abstracts and studies not written in English were excluded. Titles and abstracts were screened by one researcher (SM); a second investigator (LvT) evaluated the included cases, doubtful cases and a random sample of the excluded cases.

Results: On study design, sample size, assessment methods and analysis technique was extracted by one researcher (SM), in consultation with 3 others (LvT; MB and JT).

Results: Of 5980 identified papers, 252 were eligible. 228 of these reports were on a single study while 26 were on multiple studies in one paper. Of the 226 eligible studies, 75 studies used parametric techniques (hence a combination of number and severity), location and severity of erosions and simultaneous presence of MRI-detected edema were compared between groups, also in relation to age.

Results: First total erosion scores were analyzed. Both in RA-patients and in controls this score was associated with age (p<0.001 in both groups). In addition, at all ages and on group level, RA-patients had 1.2 (95% CI 1.1–1.3) times higher erosion scores than controls. Despite this difference, total erosion scores could not differentiate RA-patients from controls on the individual level, as there was large overlap (Figure). Next different characteristics of erosions were explored within age groups (<40, 40–59, ≥60) to search for RA-specific features. With respect to location, erosions found in MTP5 were specific for RA (spec 90–98% for different age groups). Erosions found in MTP1 were specific for RA if subjects were aged <40 (spec 98%), but specificity decreased by increasing age (spec 86% if aged 40–59 and 63% if aged ≥60). Evaluating the severity revealed that “severe erosions” (scores ≥2) were infrequent in all subjects, but almost exclusively present in RA (spec 98–100%). Finally the simultaneous presence of erosions with inflammation was studied. In the age group <40 years, the simultaneous presence was exclusively observed in RA-patients (specificity 100%); but specificity decreased by age since the combined presence was also seen in symptom-free controls (spec 91% if aged 40–59 and 71% if aged ≥60 years).

Conclusions: Whilst the group of RA-patients at disease presentation had significantly higher erosion-scores than healthy controls, scores of individuals subjects were largely overlapping. Some erosion characteristics were specific for RA, but these were present in only a minority of all RA-patients (22%).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1829

THU0704 EVALUATION OF THE ACCURACY OF HAND AND FOOT MRI IN THE EARLY IDENTIFICATION OF RA: USING THE PREVALENCE OF LOW-GRADED INFLAMMATION IN THE SYMPTOM-FREE POPULATION AS REFERENCE REDUCES FALSE-POSITIVE MRI RESULTS
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Background: Early identification of rheumatoid arthritis (RA) is important, because it allows early treatment initiation and is associated with better disease outcomes. In this perspective, the use of hand and foot MRI in the diagnostic process of rheumatoid arthritis (RA) has been advocated. Recent studies showed that MRI is helpful in predicting progression from clinically apparent arthritis (CAA) to clinical arthritis, and from undifferentiated arthritis (UA) to RA. However, the diagnostic value of MRI is still undetermined. Most studies focussed on the sensitivity rather than the specificity of inflammation detected on MRI. It is known that symptom-free persons can also show inflammation on MRI. Consequently, it has been questioned if MRI-findings in symptom-free volunteers are relevant to consider as a reference when defining a “positive MRI”.

Objectives: To determine the value of considering MRI-findings in a control group for the predictive accuracy of MRI when defining a positive MRI.

Methods: 225 patients with CSA and 201 patients with UA underwent MRI of MCP-, wrist- and MTP-joints at baseline and were followed for 1 year on progression to arthritis and RA respectively. MRI was considered positive either if ≥1 joint showed inflammation (called “uncorrected definition”), or if ≥1 joint had inflammation that was present in <5% of persons of the same age-category and location in a symptom-free reference population (called “5% corrected definition”). MRI scans were scored according to RAMRIS method. Test characteristics were compared for both definitions, hence with and without the incorporation of a reference population when defining a “positive MRI”.

Results: By using MRI-data of symptom-free volunteers as reference, the
specificity of MRI-detected inflammation increased from 22% to 56% in CSA-patients, and from 10% to 36% in UA-patients. The sensitivity was not affected; it was 88% and 85% in CSA-patients and 93% and 93% in UA-patients. The accuracy also increased, from 32% to 60% in CSA-patients and 22% to 44% in UA-patients.

Conclusions: The use of a reference population resulted in a substantial reduction of false-positive results, without affecting the sensitivity. This is of high importance because of the potential risks of false-positive MRI-results, for example in the setting of UA as a positive MRI-result may influence the decision to initiate disease modifying medication. Although a reference population is generally used in medicine for other tests to derive a definition of a positive test result, this is the first study demonstrating the value of a reference population to define a “positive MRI”.

Disclosure of Interest: None declared

THURSDAY, 15 JUNE 2017
Rehabilitation

**THU0705 EXPERIMENTAL USE OF 3D PRINTING TECHNOLOGY FOR THE CONSTRUCTION OF DEVICES AS INTEGRATION OF OCCUPATIONAL THERAPY INTERVENTION WITH RHEUMATOID ARTHRITIS PATIENTS (RA)**

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Background: RA is a chronic inflammatory disease that can interfere with the ability to perform activities of daily living. The adoption of aid devices allows to maintain and/or improve employment performance, reducing the pain preventing further joint damage. However, it is known that the abandonment rate of such devices is quite high, resulting in failure of the rehabilitation project, and waste of resources. The reasons people give for abandoning support technology are that they have not been involved in the process of provision, and that the devices do not have the intended effect (1).

Objectives: technology may allow customization of 3D printing devices agreed together with patients, utilizing materials which are cheap, fast and easily adjustable.

Methods: The study was organized into the following phases: recruitment of RA patients for the “joint protection laboratories”; sessions of the “joint protection laboratories”; recruitment of patients for the identification of needs for customized aid devices; co-design of customized aid devices; printing of customized aid devices; delivery of customized aid devices; detection using customized aid devices. We have collected a list of needs to be able to develop such customized aid devices at the end of a course to educate on joint protection covering: ergonomic gestures, management of fatigue and pain, environmental adaptations and aid devices.

18 patients (17 women and 1 man), age between 30 and 75 years old, were organized into small groups for the “joint protection laboratories”. 9 patients expressed their specific needs regarding the aid devices and therefore subsequent meetings were organized that have allowed us to produce and deliver customized objects. Autodesk® Fusion360 for object modeling; Ultimaker Care for slicing; 3D printing laboratories”; recruitment of patients for the identification of needs for customized aid devices; co-design of customized aid devices; printing of customized aid devices; delivery of customized aid devices; detection using customized aid devices. We have collected a list of needs to be able to develop such customized aid devices at the end of a course to educate on joint protection covering: ergonomic gestures, management of fatigue and pain, environmental adaptations and aid devices.

Results: 6 aid devices were customized: hand grip holder for chalk, toothbrush, ignition key, tablespoon, iron, as well as a handle to open the moka coffee machine.

The psychosocial assessment of 6 delivered aid devices, collected through PIADS, showed an overall positive outcome (mean competence +1,488; adaptability: +1,690; self-esteem: +1,375). The assessment of patient satisfaction through QUEST, was good overall (scale 1–5: satisfaction aid: 4,75; service satisfaction: 4,68).

Conclusions: This work also demonstrated, over a range of small numbers, that the path of co-design and production of customized aid devices via rapid manufacturing with 3D printing technology is feasible and fulfilling.

References:

Disclosure of Interest: None declared

**THU0706 LOW DISEASE ACTIVITY AFTER A SHORT COURSE OF DRUG THERAPY AND REHABILITATION IS ASSOCIATED TO A GREATER IMPROVEMENT IN FUNCTIONAL CAPACITY IN RHEUMATOID ARTHRITIS**

B. Cunha, B. Ferreira, L. Moreira, C. Barros, A. Gushikem, J. Kauer, T. Ferreira on behalf of SARAR 2 cohort. Rheumatology, SARAF Network of Rehabilitation Hospitals, Brusia, Brazil

Background: Patients with rheumatoid arthritis (RA) have lower functional capacity than general population (1). Studies have shown that patients are able to improve their functional capacity after adequate treatment with disease-modifying antirheumatic drugs (DMARDs) (1–2), but it is unclear which other factors are involved in rehabilitation settings.

Objectives: To investigate which clinical factors are associated to improvement in functional capacity in patients with RA in the context of DMARD therapy and rehabilitation.

Methods: It was a case-control study. Patients with RA admitted between June 2014 and July 2016 were included. Assessments were carried out just before and after completion of rehabilitation program. Functional capacity was assessed with Health Assessment Questionnaire-Disability Index (HAQ-DI). Disease activity was evaluated with Clinical Disease Activity Index (CDAI). It was allowed to change DMARD treatment or dose during the follow-up period. Interventions were carried out at the discretion of the rehabilitation team and could include joint injections, exercises, orthoses, insoles, educational interventions and assistive devices. Patients that were operated in the follow-up period were excluded. An improvement in HAQ-DI was defined as a difference of -0,22. Patients that improved after treatment were compared with those who did not, regarding clinical characteristics and modalities of treatment that were employed. Chi-square or Fisher exact test analyses were employed.

Results: Forty-six women and two men were included, with average age of 56 (11) years old and 10,8 years of diagnosis, Rheumatoid factor was positive in 58% (mean title 2423 U/L); anti-CCP was positive in 48% (mean title 283,8 U/L). Patients were followed for 6–12 months.

HAQ-DI improved 0,51 (0,3–0,71; p<0,001) and CDAI improved 12,8 (7,6–17,9). Patients that were able to improve HAQ-DI had a better average CDAI in the second assessment (16 vs. 7; p<0,011). There was no association between improvement of HAQ-DI and other clinical and laboratory variables, including drug and rehabilitation modalities.

Conclusions: Low disease activity after a short course of drug therapy and rehabilitation is related to a greater improvement of functional capacity in patients with RA. Therefore, patients with RA may have better outcomes in rehabilitation if disease activity is controlled.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1670

**THU0707 RACE & REHABILITATION DESTINATION AFTER TOTAL HIP REPLACEMENT**

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Background: There are marked racial/ethnic disparities in the utilization of hip joint replacement in the US. Differences in post-surgical rehabilitation care may influence this disparity. There is relatively little research on racial variations in post-hip joint replacement surgery care processes.

Objectives: The main objective of this analysis was to examine racial differences in where patients go for post-acute care rehabilitation after elective hip replacement surgery. We also assessed whether or not where patients go for post-surgery rehabilitation care impacts quality of care markers such as 90-day hospital readmission.

Methods: A retrospective, large regional dataset analysis using the Pennsylvania Health Care Cost Containment Council database was performed. Patients who underwent elective hip replacement surgery and discharged from Pennsylvania hospitals between fiscal years 2008–2012 were selected. Post-surgery rehabilitation destination options included: home with self-care, home with health (HH) care; skilled nursing facility (SNF) and in-patient rehab facility (IRF).

We used multinomial logistic regression models to estimate unadjusted and adjusted relative risk ratios (aRRRs) of being discharged home with HH care, to a SNF or to an IRF (vs. home with self-care) after surgery, comparing African-American (AA) to white patients. Multivariable models adjusted for patient-level and facility-level variables associated (p<0,10) with post-surgical discharge destination based on bivariate analyses. Unadjusted and adjusted odds ratios (aORs) of 90-day hospital readmission were estimated using binary logistic regression models. Multivariable models adjusted for patient-level and facility-level variables associated
Among patients <65 years of age, compared to whites, AAs had higher risk of discharge to an IRF (aRRR 1.96, 95% CI, 1.39–2.76) and a SNF (aRRR 1.60, 95% CI, 1.15–2.23). Among those ≥65 years of age, compared to whites, AA patients who underwent hip replacement were more likely to rely on Medicare or Medicaid (47.5% vs. 17.3%) (both p<0.001), compared to whites (p<0.001, all comparisons, both age groups).

The Figure summarizes the unadjusted (UN) and adjusted (ADJ) RRRs of referral within 90 days.

Comparing to whites, AA patients who underwent hip replacement were more likely to receive total knee arthroplasty (3).


Background: Knee osteoarthritis affects mobility leading to substantial loss of perceived health and quality of life. Our previous study showed that aged persons with various comorbidities may profit from comprehensive rehabilitation in the short-term by corrected effect sizes up to 0.62 in pain, 0.51 in physical function, and 0.32 in psychosocial health (1).

Objectives: To follow-up those patients to 5 years by 1) quantifying observed effects in pain, function, and psychosocial health and 2) associating risk factors to total knee arthroplasty during the observation period.

Conclusions: Compared to whites, AA patients who underwent hip replacement were more likely to be discharged to an IRF or SNF. Furthermore, discharge to either IRF or SNF was associated with higher risk of hospital readmission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2168

THU0708 LONG-TERM OUTCOME AND RISK FOR TOTAL ARTHROPLASTY OF KNEE OSTEOARTHRITIS AFTER COMPREHENSIVE REHABILITATION

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Background: Knee osteoarthritis affects mobility leading to substantial loss of perceived health and quality of life. Our previous study showed that aged persons with various comorbidities may profit from comprehensive rehabilitation in the short-term by corrected effect sizes up to 0.62 in pain, 0.51 in physical function, and 0.32 in psychosocial health (1).

Objectives: To follow-up those patients to 5 years by 1) quantifying observed effects in pain, function, and psychosocial health and 2) associating risk factors to total knee arthroplasty during the observation period.

Methods: Prospective cohort study with assessments at baseline (start of rehabilitation) and 1, 2, 3, 4, 5 years after. Comprehensive rehabilitation lasted 2–3 weeks for inpatients and 6 weeks for outpatients. Changes between baseline and the follow-ups were measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Short Form 36 Health Survey (SF-36). They were expressed as raw scores (RS) according to Kazis (2). Multivariate logistic regression included various sociodemographic and disease-modifying confounders and provided adjusted odds ratios (OR) for the risk of getting total knee arthroplasty.

Results: At baseline, n=205 knee osteoarthritis patients were included: 77.1% were women; mean age 65.7 years (sd=10.3y), 81.5% having 3 or more comorbidities. Up to the 5 year follow-up, n=83 (40.5%) remained with complete data, 48 (23.4%) received arthroplasty. At 5 years, ES were 0.13 to 0.79 for pain, −0.12 (worsening) to 0.42 (improvement) for function, and −0.25 to 0.21 for psychosocial health. At the last follow-up before surgery, WOMAC pain had worsened by ES=−0.42 (p<0.001) and WOMAC function by ES=−0.54 (p=0.002) in the total knee arthroplasty group. Getting total knee arthroplasty was statistically significantly associated with female sex (OR=3.30), educated at university (OR=3.54), minus 1 commodity less (OR=1.14), and 10 (of 100 possible) points worsening on the WOMAC factor ascending-descending (OR=1.60).

Conclusions: Moderate to small improvements on pain, function, and psychosocial health were observed up to 5 years after comprehensive rehabilitation of knee osteoarthritis. Nevertheless, almost one quarter of the participants were referred to total knee arthroplasty suffering from significant deterioration in pain and function. The WOMAC seems to be sensitive to predict the need for arthroplasty. Highly educated women with low number of comorbidities and high disability to manage stairs were more likely to receive total knee arthroplasty (3).

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1822

THU0709 DOES THE USE OF ANALGESIC CURRENT THERAPIES INCREASE THE EFFECTIVENESS OF NECK STABILIZATION EXERCISES FOR IMPROVING PAIN, DISABILITY, MOOD, AND QUALITY OF LIFE IN CHRONIC NECK PAIN? A RANDOMIZED, CONTROLLED, SINGLE-BLIND STUDY (A PILOT STUDY)

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Background: Analogics; such as intercurrent pain (IFC) and transcutaneous electrical nerve stimulation (TENS) have been applied solo or combined with exercise for management of neck pain (NP), however, the efficacy of these combinations are unclear.

Objectives: To determine if TENS or IFC increase the effectiveness of neck stabilization exercises on pain, disability, mood, and quality of life for chronic NP.

Methods: 60 patients with chronic NP were included in the study. Patients were randomly assigned into 3 groups; Group I: neck stabilization exercise, Group II: TENS+ neck stabilization exercise and Group III: IFC+ neck stabilization exercise. Patients’ pain levels (visual analogue scale (VAS)), quality of life (short form-36), mood (Beck depression inventory (BDI)), levels of disability (Neck Pain and Disability Index) and the need for analgesics were evaluated prior to treatment, at 6th and 12th week follow-up. All participants had group exercise accompanied by a physiotherapist for 3 weeks and an additional 3 weeks of home exercise program.

Results: All three groups had statistically significant improvement regarding their VAS, neck disability index and most sub-scores of short form-36 (p<0.05). At 12th-week follow-up, no difference was found between groups regarding pain, disability, and quality of life (p>0.05). On the other hand, analyses indicated significantly lower scores of neck disability index (p=0.004) and less need for paracetamol (p=0.036) in TENS group 6th-week follow-up when compared to exercise and IFC groups.

Conclusions: All treatment modalities improved pain, disability, mood and quality of life in patients with chronic NP. Besides, results suggest TENS enhanced the efficacy of exercise therapy on pain, disability and need for analgesics in acute phase but not in long term, since there was no difference at 12th week follow-up. To conclude, we think exercise protocols can be of choice since they are inexpensive, easy and effective in the management of chronic NP.

References:


Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5843

Variable 2009 (n=7,189) 2014 (n=13,459) P value

<table>
<thead>
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<th>Variable</th>
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<th>2014</th>
<th>P value</th>
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<tbody>
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<td>64.1±12.8</td>
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<tr>
<td>Duration of disease (mean ± SE, years)</td>
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<td>13.0±12.9</td>
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<td>MHAQ score (median)</td>
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<td>0.13</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DAS28 CRP (median)</td>
<td>2.9</td>
<td>2.4</td>
<td>&lt;0.05</td>
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<tr>
<td>DAS28 ESR (median)</td>
<td>3.6</td>
<td>3.0</td>
<td>&lt;0.05</td>
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<tr>
<td>Total joint score (median)</td>
<td>3.4</td>
<td>2.4</td>
<td>&lt;0.05</td>
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<tr>
<td>Joint score: ROC analysis cut-off value</td>
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<td>3.0</td>
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<tr>
<td>AUC</td>
<td>0.72</td>
<td>0.68</td>
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</table>

Conclusions: Disease activity changed from moderate to low in the NinJa cohorts and the scoring system was validated for the years 2009 and 2014. The weighted scoring system appears useful to predict functional disability in a simpler way by examining each joint rather than changes in disease activity among patients with RA.

References:

DISCLOSURE OF INTEREST: None declared DOI: 10.1136/annrheumdis-2017-eular.4968

THU0712 DUTCH NORM SCORES FOR FOUR DUTCH-FLEMISH PROMIS ITEM BANKS IMPORTANT FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In the assessment of patients with rheumatoid arthritis (RA), it is important to measure physical function, fatigue, pain behavior and pain interference. The Patient-Reported Outcomes Measurement Information System (PROMIS) initiative developed item banks for measuring these concepts. These item banks were translated into Dutch-Flemish language.

Objectives: To facilitate interpretation and implementation of PROMIS in the Netherlands, we aimed to calibrate and validate the Dutch-Flemish PROMIS Physical Function (DF-PROMIS-PF), Fatigue (DF-PROMIS-PA), Pain Behavior (DF-PROMIS-PBP) and Pain Interference (DF-PROMIS-PI) Item Banks in the general Dutch population, to obtain Dutch norm scores for these item banks.

Methods: 3568 persons of the general Dutch population completed a web-based survey, of which 1309 persons completed the full DF-PROMIS-PF (121 items), 1007 persons completed the full DF-PROMIS-PA (95 items), and 1049 persons completed the full DF-PROMIS-PBP (39 items) and the full DF-PROMIS-PI (40 items). The sample was stratified for gender, age, education, and ethnicity according to the distribution of the Dutch census of the 2015 census of the general Dutch population. A one-factor confirmatory factor analysis (CFA) was performed per item bank to assess unidimensionality. A graded item response model (GRM) was fitted per item bank to evaluate the item characteristics of the item banks and to facilitate future development of computer adaptive tests (CATs). Ordinal regression models were used to evaluate Differential Item Functioning (DIF) for language (Dutch vs. English) as a measure of cross-cultural validity.

Results: All four item banks showed good fit to the GRM: they showed good fit indices for CFA and high percentages of explained variance by first factor. The item banks showed only little local dependency and the scalability coefficients suggested strong scalability for all four item banks. The item characteristics
HOW THE VARIATION IN THE LUMBOPELVIC PATTERNS OF MOVEMENT AFFECTS THE NEUROMOTOR CONTROL OF THE BICEPS FEMORIS DURING TRUNK FORWARD BENDING

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Background: Trunk forward bending is one of the most common activities in daily living; it is a two-part movement involving the lumbar spine flexion and pelvis rotation at hip joint. The pattern of movement during forward bending was defined as the relative contribution of the lumbar spine to pelvis motion, and was expressed as the ratio between the ranges of lumbar spine motion to pelvis motion (L/P), which, calculated at certain degrees of trunk flexion during the entire movement, provides the lumbo-pelvic rhythm. This is associated with a specific pattern of activation for back and hip extensor muscles which was coined as flexion relaxation phenomenon, observed either in the erector spinae and biceps femoris. This paper aims to have described the whole lumbo-pelvic pattern of movement for entire flexion range, showing both lumbar spine dominant and pelvis dominant-patterns of movement.

Objectives: To find out whether the variation in the lumbo-pelvic pattern of movement (lumbar spine or pelvis dominant) affects the appearance of the respective “range of motion” of trunk forward bending.

Methods: Surface electrodes were applied to the skin on right BF, midway between ischial tuberosity and head of fibula to record EMG during trunk flexion (from the upright position). Trunk flexion EMG signal was full-wave rectified and averaged (40ms) to produce a linear envelope. An electrogoniometer measured the differential lumbar spine - pelvis sagittal angular displacement during trunk flexion in asymptomatic subjects. Both signals (EMG and degrees) were synchronized and continuously captured during the movement. Ranges of flexion (RF) for the lumbar spine, pelvis and trunk motion were calculated for the entire movement. The subjects (both sexes) were assigned to group-L (n=11) and group-P (n=15) according to exhibiting lumbar spine and pelvis dominant-patterns of movement (average age, 24.5±3.3 years).

The mean age was found 21.69±2.13 years old for the control group and 20.09±2.85 years old for the HMG group. Body Mass Index was found 22.13±2.54 kg/m² in the control group and 21.54±3.50 kg/m² in the HMG group. HMG group showed significantly wider step width in tandem walking (p=0.001), significantly longer reaction time (p=0.23, p=0.030), significantly higher end-point excursion (p=0.003, p=0.026, p=0.049), significant higher maximum mean excursions (p=0.018) (Table 1).

Table 1. Comparison of Groups About Balance Variables

Conclusions: In this study it was found that hypermobility has significant effects on the stability limits test and tandem walking. In previous studies it was found that hypermobility affects the static balance assessment variables (1, 2), but in this study dynamic balance assessment variables were affected.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6256

ESTIMATION OF THE EFFECT OF FOOT ORTHOTICS ON HIP JOINT LOADING FOR RHEUMATOID ARTHRITIS PATIENTS USING MRI-BASED MUSCULOSKELETAL MODELS: A PILOT STUDY

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M.B. People1, 1 Department of Mechanical and Manufacturing Engineering, Aalborg University, Aalborg; 2 Bandagist-Centret A/S, Haderslev; 3 Department of Rheumatology, Hjørring Hospital, Hjørring; 4 King Christian 10th Hospital for Rheumatic Diseases, Gråsten, Denmark

Background: Over 85% of rheumatoid arthritis (RA) patients experience foot and ankle problems during the course of the disease. Persistent foot and ankle problems still occur even after clinical remission is reached [1]. In RA, synovitis, effusion, and eventually erosive arthritis are thought to cause clinically recognized planovalgus or valgus heel [1]. With the intention to stabilize and align the foot, patient-specific foot orthotics (FO) are commonly prescribed to this patient group. A limitation of the previous literature on FO to treat RA and related diseases is that it has focused on clinical outcomes of FO such as pain and physical function, while overlooking the biomechanical principles on which the rationales for FO is based [2].

Objectives: The aim of this study was to investigate the effect of patient-specific FO on hip loading during gait. This was accomplished by developing patient-specific (PS) musculoskeletal models (MS) capable of estimating joint mechanics with and without the FO.

Methods: Four early stage RA patients were recruited for this study. A pair of FO was developed for each patient using a weight bearing casting technique. PS bone geometry was obtained from magnetic resonance imaging (MRI) images and segmented in an image analysis package (Mimics 19, Materialise, Belgium). Motion capture was performed with an eight-camera setup (Qualysis, Sweden) with reflective markers together with three force plates (AMTI, USA) sampling at 100 and 1000 Hz, respectively. The gait trials consisted of two conditions: one with PS FO and one with control insole (C). Three force plates of each patient were developed using the AnyBody Modeling System (AnyBody Technology, Denmark), Figure 1A. Muscle attachments were made PS based on the Twente Lower Extremity Model version 2.0 dataset using advanced morphing to customize a generic cadaver-based model with respect to PS morphology.
acquired from MRI [3]. Accurate joint centers and axes were calculated with analytical surface fits to the segmented MRI bones for the hip, knee and ankle. **Results:** Peak hip force for medio-lateral (ML) proximo-distal (PD) and antero-posterior (AP) is presented in Figure 1B for the C and FO with values for each subject. **Conclusions:** The results of this study indicate that FO can change the load distribution in the hip joint. A reduction or similar values for ML, DP and AP force was found for all but one participant. These changes may potentially contribute to the reduction in pain. Further studies are needed to investigate if there is a relationship between changed loading and pain for RA patients. This knowledge can potentially be used for design of better FO and clinical guidelines for use of FO. **References:** [1] Hennessy K. et al, Arthritis Care Res, 64: 311–320, 2012. [2] Lewinson R. et al, Ann Biomed Eng, 44: 3173–3185, 2016. [3] Maria M. et al, J Biomech Eng. 137: B10–14, 2015. **Acknowledgements:** The study is financially supported by The Danish Rheumatism Association [R142-A4113]. **Disclosure of Interest:** None declared DOI: 10.1136/annrheumdis-2017-eular.2169

**THU0716** Longitudinal outcome of aerobic fitness in adolescents and young adults with JIA

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**Background:** Aerobic fitness may serve as an important health-related outcome measure in JIA. A reduced aerobic fitness is associated with cardiovascular morbidity, mortality and osteoporosis in adult patients with chronic diseases. However, in adolescents and young adults, long-term outcome data of aerobic fitness are unknown. Reduced aerobic fitness was described in cross-sectional studies in children and adolescents with JIA, and was more impaired in active disease.

**Objectives:** Our objectives are to describe course of the aerobic fitness in a longitudinal cohort of adolescents and young adult JIA-patients who are intensively treated including the possibility of biologics and to identify the association of clinical variables with aerobic fitness.

**Methods:** In a longitudinal cohort, all consecutive JIA patients aged 10–24 years were included after informed consent. Annual examinations were obtained from demographic and disease-related items. At baseline and end of the study, aerobic fitness (VO2peak) test was assessed using a graded cardiological exercise test (CPET) to volitional exhaustion performed on an electronically braked cycle ergometer. Absolute and relative VO2peak values were measured and related to healthy controls (Z-scores), using one-sample T-tests. Non-parametric tests were used to evaluate results.

**Results:** Paired Z-scores were available from 27 patients. 44% were male, median age at baseline was 13.0yrs (IQR 4.3), disease duration 7.6yrs (6.7), JADAS27 4.0 (5.9), DAS28 2.2 (1.2). 76% of the patients were in DAS28-remission. 11% had systemic JIA. 7% persistent oligoarticular and 82% had a polyarticular course. Baseline and end Z-scores were reduced compared to healthy controls (ZAbs_base -0.68, IQR2.3 p<0.01; Zrel_base -1.33, IQR 2.0, p<0.01; Zabs_end -0.23, IQR 1.7, p<0.06; Zrel_end -0.87, IQR 2.2, p<0.01) and did not change significantly over time (change Zabs_change 0.45, p=0.34; Zrel_change 0.46, p=0.31). At baseline, MTX-use (p<0.04) and a higher DAS28 (p<0.015) and ESR (p<0.013) are associated with a worse outcome of aerobic fitness. The greatest improvement of aerobic fitness over time was seen in patients with a higher ESR (p<0.01) and thrombocytes (p=0.01) at baseline. Multivariate analysis showed that a higher DAS28 and male gender were the most important variables for worse aerobic fitness at baseline, a higher ESR at baseline was the most important predictor for improving aerobic fitness over time.

**Conclusions:** Aerobic fitness is significantly reduced in adolescents and young adults with JIA and does not improve over time, despite intensive treatment. Be aware of a reduced quality of life due to a persistent reduced aerobic fitness during disease course of JIA, despite low disease activity.


**Disclosure of Interest:** None declared DOI: 10.1136/annrheumdis-2017-eular.4756

**THU0717** Mirror visual feedback therapy improves clinical outcomes and the activity of daily living in patients with hand complex regional pain syndrome

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**Background:** Wrist osteoporotic fractures may be as disabling as vertebral or hip fractures and the functional decline attributed to them is similar to that seen for arthritis and diabetes mellitus. Sometimes these fractures will lead to a painful, debilitating condition with sensory and motor disturbances, changes in vascular tone, temperature and edema complex regional pain syndrome (CRPS). We found in clinical trials and case reports which conclude that mirror visual feedback therapy (MVFT) improves clinical outcomes and the activity of daily living to patients with hand neurological disorders, including CRPS.

**Objectives:** In this controlled randomized clinical study we tried to investigate the effects of (MVFT) in CRPS type I following osteoporotic wrist fracture.

**Methods:** We included 21 subjects with osteoporotic wrist fracture and early CRPS (duration of 3–4 weeks), with a single hand affected by aloldynia, stiffness and vasomotor disturbances, from Physical Medicine and Rehabilitation outpatient clinic. They are randomly assigned into two groups: MVFT group (n=11), simply place a mirror between their two hands and train the patient by asking them to move both hands while watching the reflection of the non-affected hand in the mirror, 10 minutes for each session, four times a day) and Control group (n=10, moved both hands separated by an opaque partition between the arms). All subjects also received conventional therapy. On presentation and after 4 weeks of rehabilitation programme we assessed the wrist flexion and extension with a goniometer and the Patient-Rated Wrist Evaluation (PRWE) a 15-items questionnaire designed to measure wrist pain and disability in activities of daily living.

**Results:** Subjects in the mirror therapy group showed significant improvement in range of motion: extension increased with 50.4% vs. 41.7% and for flexion MVFT achieved 33.2% and Control group 16.8% (P<0.001). The rehabilitation programme also increased hand function with better results to 4 weeks PRWE for MVFT group (40.4 vs. 51.8, P=0.003).

**Conclusions:** MVF is a simple, inexpensive, without adverse events treatment option that significantly reduces pain and stiffness and improves hand mobility in early CRPS after osteoporotic wrist fracture.


**Disclosure of Interest:** None declared DOI: 10.1136/annrheumdis-2017-eular.2339

**THU0718** Differences in the course of Italian- and German-speaking patients’ outcome after interdisciplinary pain program

T. Benz 1,2, S. Lehmann 2, R. Brioschi 2, A. Effering 1, A. Aeschlimann 2, F. Angst 3. 1Institute of Psychology, University of Bern, Bern; 2Research Department, RehaClinic, Bad Zurzach, Switzerland

**Background:** Available evidence shows that the experience and perception of pain varies among different populations. Further, inequalities are reported in pain treatment across various types of pain and in different settings (1). In particular, it is unknown how much immigrants in Western European countries profit from pain management programs.

**Objectives:** The aim of this study was to detect differences in the course of Italian- and German-speaking patient’s state of health and quality of life after a 4-week interdisciplinary pain management program for chronic pain patients in Italian.

**Methods:** The prospective cohort study with 61 Italian-speaking and 63 German-speaking patients with fibromyalgia or chronic back pain measured health-related quality of life, pain, anxiety and depression comparing at baseline, after 4 weeks of pain program and at 1 year follow-up. Differences between the two groups...
were tested on significance by generalized estimation equations (GEE) (2). This method modeled changes of health by multivariate logistic regression adjusting for sex, education, number of comorbidities and the baseline score over both follow-ups for each scale.

Results: Italian-speaking patients (n=61) showed higher proportions of males, lower educated and less burdened by comorbidities than German-speaking patients (n=63). At baseline, physical and psychosocial health, depression and anxiety of the Italian-speaking patients were worse than German-speaking patients, with the exception of less pain in the Italian-speaking patients on the SF-36. Changes of health showed more improvement in German- than in Italian-speaking patients on all scales and at both follow-ups. In GEE, the highest differences were observed in SF-36 physical functioning (p<0.035), HADS anxiety (p<0.038) and HADS depression (p<0.023). On SF-36 bodily pain, the difference was not significant (p=0.166).

Conclusions: This study detected that short- and mid-term outcome of Italian-speaking patients was worse than that of German-speaking patients, even after adjustment for baseline differences. The reasons for this study’s results remain unclear, but may have consequences for future management of Italian-speaking patients in interdisciplinary pain management programs. Considering language as a proxy for acculturation, this supports the hypothesis that patients with lower level of acculturation may have special needs in therapeutic management. A cultural sensitive approach in a multidisciplinary pain program might enhance the positive outcome in the short- and mid-term (3).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5888

**Table 1**

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<th>Effect sizes (ES)</th>
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<td>SF-36 Physical functioning</td>
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<td>SF-36 Role physical</td>
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<tr>
<td>SF-36 Bodily pain</td>
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<tr>
<td>SF-36 Vitality</td>
<td>0.89</td>
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<td>SF-36 Social functioning</td>
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<tr>
<td>SF-36 Mental health</td>
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<td>NASS Pain</td>
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<td>CSQ Catastrophizing</td>
<td>1.03</td>
<td>0.62</td>
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Median working capacity improved from 0 at entry to 21 at 6 months and to 30 hours/week at 5 years.

Conclusions: Moderate to large long-term effects were observed. Substantial improvements still occurred between 6 and 60 months after start of the pain program, especially in pain, catastrophizing, and physical role performance. Improvements observed after the inpatient pain program can be maintained and expanded in the long-term at home (3).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6178
ALL STAGES OF SYNOVIAL MESENCHYMAL STEM CELL (SF-MSC) FCS expanded cells (p=0.3429, n=4). Interestingly, replacing TGF
staining Ca++ assay and Nile Red showed no significant difference compared to
FCS-expanded cells (n=4). In osteogenic and adipogenic induction, Alizarin red
up to 21 days on p-TCP. Osteogenic differentiation was performed in the presence of
osteogenic supplements under normoxic conditions (37 °C, 18% O2). Adhesion
and proliferation of hMSCs on p-TCP were evaluated by immunofluorescence and histochemical
analysis. To confirm cell attachment and biocompatibility of p-TCP
particles cellular release of LDH was assessed. Osteogenic differentiation was
analyzed on gene expression level using qRT-PCR. The chondrogenic model, a
scaffold-free 3D cartilage construct (Fitz & Breyer) was generated using hMSCs.
Chondrogenic differentiation was performed under hypoxia (37 °C, 1% O2) with
intermittent mechanical stimulation and analyzed by histology.

Results: We developed an in vitro 3D trabecular bone model by seeding hMSCs
on p-TCP scaffold after pre-incubation for 24 hours. The analysis of cell viability
via LDH detection showed no toxic effects on the cells seeded as compared to
the corresponding control. Furthermore, we assessed cell attachment and
proliferation by measurement of LDH activity after scaffold crushing. As a result,
samples showed higher LDH activity compared to the controls. Histological and
immunofluorescence analysis based on DNA and actin staining demonstrated
cell attachment until day 21. After 21 days, cells were located more inside the
scaffold compared to day 1. qRT-PCR expression of bone-related genes such as
RUNX2, SPPI and COL1A1 confirmed the phenotypic change during osteogenic
differentiation on the scaffold. Furthermore, the scaffold-free 3D chondrogenic
structure was confirmed by HE staining representing the different zones. Cartilage
phenotype was confirmed by the reduced expression of Col1A1, an abundant
expression of Col1A1 and Aggrecan.

Conclusions: The initial results from our in vitro 3D osteogenic and chondrogenic
model confirm good cell vitality which indicates successful progression. To confirm
the exchange of p-TCP through cellular matrix, we will now extend the assay
co-culture time for up to 6 weeks. This 3D multi-component joint model enabled us
to simulate arthritis and to study the efficacy of drug treatment in vitro.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5898
and PRO-C2), aggrecanase degraded aggrecan (AGNvi) and MMP degraded aggrecan (exFFGV). C1M and C3M are synovial membrane biomarkers and C2M, AGNvi and exFFGV are cartilage biomarkers.

**Results:** Explants were viable throughout the experiments, albeit the bSME lost some viability with time. bSME treated with O+T showed increased C1M and C3M (450% 0 day 10, compared to w/o), whereas in bCC O+T increased C1M from day 21 and C3M from day 14 (>400%, >1900%), O+T treatment increased C2M was increased from day 21 (>400% and >1000%) in both BEX and BC. The release was blocked by the generic MMP inhibitor GM6001 which also decreased the C1M and C3M compared to w/o. O+T treatment increased AGNvi at day 7 and 10 (>600%) and exFFGV from day 21 (>650%) in both BEX and BCC. In bSME, TGF-b1 continuously and dose-dependently increased P1NP from day 7 compared to w/o (250%). O+T pre-treatment for 10 days followed by TGF-b1 stimulation increased P1NP after 7 days of TNF-b1 treatment (150%, figure). IGF-1 did not affect the P1NP level at any time point in bSME. In bCC both TGF-b1 (dose-dependently) and IGF-1 sustained the PRO-C2 level at the level of baseline throughout the study periods (figure), whereas O+T decreased PRO-C2 compared to w/o. The PRO-C2 level in BEX with TGF-b1 was unaltered compared to w/o.

**Conclusions:** We here show that bovine synovium can be anabolic and catabolic stimulated, both alone and in co-culture with cartilage. Anabolic stimulation was achieved with TGF-b1 in both bSME and bCC, while IGF-1 only showed an anabolic effect in the bCC. Previous human explant models using human tissue have lacked the anabolic capacity. These translational explant models may be applied in the early development of anabolic drugs for cartilage degenerative diseases.

**Disclosure of Interest:** A. S. Siebuhr Employee of: Nordic Bioscience, C. Cabanes: None declared, S. Dahab: None declared, M. KarsdalShareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Employee of: Nordic Bioscience, A.-C. Bay-Jensen Employee of: Nordic Bioscience, C. Dubois: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5737

**FRI0004 14-3-3 ETA AS A NOVEL INVADOSOME REGULATORY MOLECULE IN RHEUMATOID ARTHRITIS**

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1University of Sherbrooke, Sherbrooke; 2Augurex Life Sciences Corp., Vancouver, Canada

**Background:** Progressive cartilage destruction, mostly mediated by invasive fibroblast-like synoviocytes (FLS), is a central feature in the pathogenesis of rheumatoid arthritis (RA). We have reported that the ability of arthritic FLS to degrade the extracellular matrix depends on the formation of actin-rich plasma membrane invadosomal structures detected in cells strategically located at the cartilage-synovial membrane interface. Interference with the formation of invadosomes in RA FLS impeded matrix degradation in vitro and cartilage at the cartilage-synovial membrane interface. Interference with the formation of invadosomal structures detected in cells strategically located fibroblast-like synoviocytes (FLS), is a central feature in the pathogenesis of patients (N=5) was extracted and the relative level of 14–3-3 isoforms and MMP degrade the ECM.

**Objectives:** To evaluate the role of 14–3-3η in inflammatory processes and the ability of synoviocyte cell lines to form invadosomes was observed (r=2.8299). Knockdown of 14–3–3η decreased the ability of arthritic synoviocytes to form invadosomes indicating a role of 14–3–3η in extracellular matrix degrading ability. Confocal microscopy revealed that 14–3–3η staining was mostly found in small punctated structures in the cytoplasm and at the cell periphery of arthritic synoviocytes where they colocalized with leading edge F-actin and discrete patches of the exocyst component, Exo70.

**Conclusions:** The findings propose that the role of 14–3–3η in invadosome formation points to a previously unappreciated facet of how 14–3–3η influences joint ECM remodelling and reinforces its role as a marker of RA progression and joint damage. How 14–3–3η is involved in the regulation of MMP production/secretion and the possible role it plays in remodelling of actin-rich subcellular structures is the subject of ongoing studies.

**Disclosure of Interest:** C. Lalanne: None declared, R. Laviole: None declared, M. Charbonneau: None declared, J. Savill Employee of: Augurex Life Sciences Corp., A. Marotta Employee of: Augurex Life Sciences Corp., C. Dubois: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5737

**FRI0005 TARGETING CARTILAGE AGING AS OSTEOARTHRITIS THERAPEUTICS BY DRUG REPURPOSING**

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**Background:** Effective treatments for Osteoarthritis (OA) are not available. In aging-related diseases, including OA, failure of cellular homeostasis mechanisms, such as autophagy can cause extracellular matrix destruction and cell death (1). With aging, chondrocyte function is diminished, contributing to a cellular senescence phenotype often observed in OA chondrocytes. In addition, a defect in autophagy is observed in both aging and cartilage degeneration (2,3).

**Objectives:** The objective of this study was to identify anti-senescence and pro-autophagy molecules by a cell-based high-throughput screening (HTS) in human chondrocytes.

**Methods:** To induce cellular senescence or reduced autophagy, immortalized human chondrocytes (TC28a2) were seeded (2500 cells/well) in 384 well plates, and treated with IL-6 (20 ng/ml) for 72 hours or 18 hours, respectively. Then, chondrocytes were incubated with Prestwick Chemical Library (1120 approved drugs with chemical and pharmaceutical diversity, as well as bioavailability and safety in humans) at 10 μM for 72 hours. To identify anti-senescence hits, nuclei were stained with Hoechst 33342 (2.5μg/ml), while β-galactosidase subcellular structure was stained by using Imagene Green C12FDG substrate (30 μM). To evaluate autophagic flux, a reporter cell line was generated by retrovirus transfection of pBABE-mCherry-EGFP-LC3 plasmid in TC28a2 chondrocytes. Plates were imaged by using Operetta® High Content Screening (HCS) system in non-continuous mode using the 20x WD objective. For each well, 4 fields and 4 planes of bright field, Hoechst and fluorescein channels were obtained. Relative intensity of C12FDG in cytoplasm and number of autophagosomes/autolysosomes per area of cytoplasm were determined to quantify β-galactosidase activity and autophagy flux respectively. Compound validation was performed in TC28a2 chondrocytes and in primary human chondrocytes by evaluating cell senescence, autophagy pathway and cell death by apoptosis.

**Results:** A primary screening was performed to identify anti-senescence compounds by measurement of senescence-associated β-galactosidase activity. 283 compounds with both anti-senescence and anti-autophagy effects were identified. The anti-senescence hits were analyzed by monitoring autophagic flux. 29 compounds with both anti-senescence and pro-autophagy effects were selected. Then, one compound was selected for further validation. The compound reduced chondrocyte senescence, increased autophagy (p<0.0001) and protected against inflammation and cell death by apoptosis in human chondrocytes (p<0.05) in response to IL-6. Interestingly, this protective effect was partially mediated by mTOR inhibition, a proposed mechanism to prevent cartilage aging.

**Conclusions:** Our screening methodology provides a unique opportunity to use drugs and mechanisms to prevent cartilage aging. Autophagy activation and protection against senescence by 14-3-3η may be potential targets for delaying cartilage degeneration.

**References:**


**Acknowledgements:** This study was supported by Instituto de Salud Carlos III-Ministerio de Economía y Competitividad, Spain;PI14/01324 and Fondo Europeo de Desarrollo Regional (FEDER).
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3658

**PROTEIN CITRULLINATIONS BY PAD ENZYMES PROMOTE DENDRITIC CELL TRANS-DIFFERENTIATION INTO OSTEOCLAST AND GENERATE TARGETS FOR RA-SPECIFIC ANTIBODIES**

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**Objectives:** Immature dendritic cells (DCs) are able to trans-differentiate into osteoclasts (OCs) although the mechanisms regulating this process are little understood. We have recently described an important role for protein citrullination and peptidylarginine deiminase (PAD) enzyme activity in the regulation of OC development (1).

**Background:** Immature dendritic cells (DCs) are able to trans-differentiate into osteoclasts (OCs) although the mechanisms regulating this process are little understood. We have recently described an important role for protein citrullination and peptidylarginine deiminase (PAD) enzyme activity in the regulation of OC development (1).

**Methods:** We studied the molecular bases of DC-OC trans-differentiation and aimed at understanding the role of protein citrullination in this process.

**Dosage:** Three groups of mice were treated with either hIL4–10FP (n=3), PBS (n=3) or LPS (n=3).

Conclusions: Therefore, we confirmed that protein citrullination, most likely through a PAD enzyme mechanism, was important for OC development. In conclusion, our results strongly indicate that the regulation of protein citrullination could be a potential therapeutic target for the treatment of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2141

**EFFECTS OF THE HUMAN IL4-10 FUSION PROTEIN IN THE CANINE GROOVE MODEL OF OSTEOARTHRITIS**

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**Objectives:** Ideally a disease modifying osteoarthritis drug (DMOAD) combines treatment for pain, tissue damage and inflammation, all in one molecule. Intra-articular application of a DMOAD brings additional value to treatment for two reasons, (i) lower risk of systemic side effects and (ii) higher drug concentration and potentially improved penetration of non-vascularized articular cartilage. Interleukin-4 (IL-4) and Interleukin-10 (IL-10) have been shown to prevent joint degeneration and can work synergistically. The aim of this study was to evaluate whether hIL4–10FP could be a useful substance for development of plant-based anti-inflammatory and anti-arthritic therapies.

**Background:** hIL4–10FP was approved for treatment of RA patients and was shown to be efficacious in two studies. We further demonstrated that hIL4–10FP can prevent bone loss in vivo. The objectives of this study were to evaluate the effects of hIL4–10FP on osteoarthritis in a canine model.

**Methods:** Through surgical procedures we treated dogs with either hIL4–10FP or PBS. The treated and control dogs were sacrificed after 6 weeks and their tibiae were harvested. Tissue samples were analyzed for bone mineral density (BMD), histology, and quantitative RT-PCR.

Conclusions: Consequently, the overall data strongly indicated that methyl gallate could be a useful substance for development of plant-based anti-osteoarthritic therapies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5971

**METHYL GALLATE INHIBITS OSTEOCLAST FORMATION AND FUNCTION THROUGH SUPPPRESSING THE AKT AND BTK-PLCγ2-Ca2+ SIGNALING, AND PREVENTS LPS-INDUCED BONE LOSS**


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**Background:** Methyl gallate, a plant-derived phenolic constituent has been known to possess numerous pharmacological features against inflammation, oxidation, and cancer. But so far, there have been no evidences to describe relationship between methyl gallate and bone metabolism.

**Objective:** In order to propose a promising candidate for osteoporosis, we performed experiments in this study by using methyl gallate.

**Methods:** We performed screening of methyl gallate utilizing TRAP staining and revealed intracellular mechanisms responsible for methyl gallate-mediated regulation of osteoclastogenesis through western blotting and quantitative RT-PCR. Also, we assessed the role of methyl gallate on characteristics of mature osteoclasts. We used LPS-induced bone loss mice as a model of osteoporosis and analyzed using micro-CT system and the right femurs were stained with TRAP and H&E.

**Results:** We observed that methyl gallate significantly suppressed osteoclast formation through Akt and BTK-PLCγ2-Ca2+ signaling. The blockade of these pathways was reconfirmed through transduction of CA-Akt retrovirus and evaluation of Ca2+ influx intensity stained with Fluor-3/AM. Indeed, methyl gallate down-regulated the formation of actin ring-positive osteoclasts and resorption pit areas. In agreement with in vitro results, we found that the administration of methyl gallate restored osteoporotic phenotype stimulated by acute systemic injection of LPS in vivo through micro-CT and histology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2141
in hIL4–10FP group there was no enhanced cartilage degeneration detected compared to the PBS group (fig 3).

Conclusions: Repetitive intra-articular injection of human IL4–10FP led to antibody formation in a non-inflammatory canine model of OA. Despite the immune response, proteoglycan turnover parameters were comparable between the two treatment groups, suggesting a beneficial effect of hIL4–10FP. This study also shows that it is not evident to use a human protein in a (canine) animal model, although this is often done. Instead, a species specific protein is warranted. Therefore a canine version of IL4–10FP will be developed to study its DMOAD activity in this model.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1498

FR0009 ACCELERATED DEVELOPMENT OF AGING-ASSOCIATED AND INSTABILITY-INDUCED OSTEOARTHRITIS IN 12/15-LIPOXYGENASE DEFICIENT MICE

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Background: 12/15-Lipoxygenase (12/15-LOX) catalyzes the generation of various anti-inflammatory lipid mediators, and has been implicated in several inflammatory and degenerative diseases. However, there is currently no evidence that 12/15-LOX has a role in osteoarthritis (OA).

Objectives: The aim of this study was to investigate the role of 12/15-LOX in the pathogenesis of OA.

Methods: The development of aging-associated and destabilization of the medial meniscus (DMM)-induced OA were compared in 12/15-LOX-deficient (12/15-LOX-/-) and wild-type (WT) mice. The extent of cartilage damage was evaluated by histology. The expression of OA markers was evaluated by immunohistochemistry and RT-PCR. Cartilage explants were stimulated with IL-1β in the absence or presence of the 12/15-LOX metabolites, 15-HETE, 13-HODE or LXA4, and the levels of MMP-13, NO and PGE2 were determined. The effect of LXA4 on the progression of OA was evaluated in WT mice.

Results: The expression of 12/15-LOX in cartilage increased during the progression of DMM-induced OA and with aging in WT mice. Cartilage degeneration was more severe in 12/15-LOX-/- mice compared to WT mice in both models of OA, and this was associated with increased expression of MMP-13, ADAMTSS, INOS, and mPGES-1. Treatment of cartilage explants with 12/15-LOX metabolites, suppressed IL-1β-induced production of MMP-13, NO and PGE2, with LXA4 being the most potent. Intra-peritoneal injection of LXA4 reduced the severity of DMM-induced cartilage degradation.

Conclusions: These data demonstrate an important role of 12/15-LOX in OA and suggest that activation of this pathway may provide a novel strategy for prevention and treatment of OA.

Acknowledgements: This work was supported by the Canadian Institutes of Health Research (CIHR) Grant MOP-130293, the Arthritis Society, and the Fonds de la Recherche du Centre de Recherche du Centre Hospitalier de l’Université de Montréal (CRCHUM).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6184

FR0010 METABOLIC DYSREGULATION ACCELERATES JOINT DEGENERATION UPON MECHANICALLY INDUCED CARTILAGE DAMAGE, DRIVEN BY LOCAL INFLAMMATION; AN IN VIVO RAT STUDY

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Background: Obesity is a well-known and important risk factor for osteoarthritis (OA). Moreover, obesity is highly associated with the metabolic syndrome (MetS). Growing evidence indicates that both OA and MetS are low-grade inflammatory conditions with elevation in systemic inflammatory markers. Nonetheless, it is unclear whether MetS low-grade inflammation induces OA, or contributes to the disease.

Objectives: To determine the contribution of metabolic alterations, induced by a High-Fat Diet (HFD), on the onset or progression of OA in a rat model of local cartilage damage.

Methods: Forty Wistar rats (12 weeks old, male), were randomly divided over two groups: twenty rats were fed a HFD (60% of the kcal contained fat; D12492i, Research Diets Inc.) while the other animals received a standard diet. After 12 weeks, local articular cartilage damage was induced on the femoral condyles, in one knee joint according to the groove model in 14 rats of each diet group. Remaining animals served as a control group in each arm. At week 24, serum was collected, subchondral bone was assessed by μCT scan (Quantum FX, PerkinElmer,USA), OA severity was evaluated by rat OARSI histopathology score and macrophage presence with CD68 immunostaining from histological sections was assessed.

Results: HFD feeding resulted in metabolic dysregulation as indicated by significantly increased metabolic parameters (weight, fasting insulin and total cholesterol) compared to the standard fed rats. HFD feeding alone resulted in mild cartilage degeneration (2±1.1 vs 0.58 ±0.7; p=0.06) and synovial membrane inflammation (1.0±0.6 vs 0.3±0.3; p=0.07) but both subscores of the rat OARSI histopathology score. However, when HFD feeding is combined with the surgical model of local cartilage damage, OA severity is statistically significant increased compared to the local cartilage damage group on a standard diet (6.2±2.1 vs 3.4±1.4; p=0.001). Synovial membrane inflammation (1.3±2.9 vs 0.5±0.5; p=0.011) and multiple large osteophyte formation, demonstrated by histology (0.9±1 vs 0.2±0.4; p=0.04) and quantified on μCT (328±349 μm3 vs 7±14 μm3; p=0.0001), contributes most to this increased OA severity. Immunohistochemical CD68 expression as observed on both the synovial membrane as well as in the subchondral bone and around the formed osteophytes can explain the increase in selected inflammatory parameters when groove surgery is combined with a HFD (Figure 1).

Conclusions: This study shows that a HFD induces metabolic alterations and increases the inflammatory state of the joint. This by itself does not result in severe OA. However, when adding a HFD to a mild cartilage damage model of OA, joint degeneration is significantly increased. This progression of joint degeneration appears to be driven mainly by inflammatory responses as demonstrated by an increased CD68 expression in both the subchondral bone and synovium membrane with increased osteophytosis. Hence, our findings indicate that systemic metabolic and subsequent inflammatory factors need an additional trigger to contribute to the progression of the OA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1639

FR0011 TARGETING NEUTROPHIL MICROVESICLES TO DAMAGED CARTILAGE USING ANTIBODIES TO POST TRANSLATIONALLY MODIFIED COLLAGEN II

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Background: Microvesicles (MV) are double membrane-bound extracellular vesicles released from the plasma membrane of cells. MV derived from polymorphonuclear neutrophils (PMN) promote tissue protection, and have been demonstrated to penetrate cartilage during inflammatory arthritis and provide protection to the tissue.}

Figure 1: Immunohistochemical CD68 expression in subchondral bone, synovium, and cartilage. The red staining represents CD68 expression. (A) CD68 expression in the subchondral bone and synovium membrane of control animals fed a standard diet. (B) CD68 expression in the subchondral bone and synovium membrane of control animals fed a high-fat diet. (C) CD68 expression in the subchondral bone and synovium membrane of OA animals fed a standard diet. (D) CD68 expression in the subchondral bone and synovium membrane of OA animals fed a high-fat diet.
Collagen type II (CII) is the most abundant protein found in cartilage. We have produced a single chain variable fragment (scFv) antibodies specific to CII modified by reactive oxygen species (ROS), namely anti-ROS-CII-scFv. Previously, we have demonstrated the ability of anti-ROS-CII-scFv to localise exclusively and deliver payload drugs to the arthritic joint in mice models of rheumatoid arthritis.

Objectives: To test a new association technology: i) target delivery of MV to inflamed joint and/or ii) enhance the avidity of the scFv (several scFv can be loaded in each MV) and may thus increase localisation and enhance therapeutic efficacy.

Methods: Cy5.5 labeled Anti-ROS-CII-scFv were loaded on fluorescently labelled microvesicles (MV) and delivered to arthritic joints using a biocompatible matrix. MV loaded with Cy5.5 Anti-ROS-CII-scFv were observed by flow cytometry analysis.

Results: Positive incorporation of Anti-ROS-CII-scFv upon MV was observed by flow cytometry analysis. ELISA demonstrated the ability of the anti-ROS-CII scFv loaded MV to bind strongly to ROS-CII following incorporation into MV.

Conclusions: In this study, we have demonstrated a simple, efficient and cost effective way of antibody targeting that retains antibody function. Such technology has the potential to improve efficacy of existing therapies by ensuring specific targeting. Future in vivo studies will assess the ability of the Anti-ROS-CII-scFv MV to localise to arthritic joints.

References:

Acknowledgements: The authors would like to acknowledge Timothy Harrison and Amit Gupta for their contributions to preliminary results. The authors would also like to acknowledge Dr Jesmond Dalli for his guidance on methodology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4842

FRI0012 ROLE OF VOLATILE COMPOUNDS RELEASED BY SYNOVIAL FLUID IN THE DIAGNOSIS OF OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS OF THE KNEE JOINT

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Background: Synovial fluid (SF) receives protein contribution from the tissue around; cartilages, synovial membranes and bones. The presence of inflammation and oxidative stress alters the its chemical composition. In particular, inflammation modulates the release of volatile organic compounds (VOCs) that are the product of reactive oxygen species and free radicals excreted by mithocondria during oxidative stress (1). Articular inflammation plays a major role both in Osteoarthritis (OA) and Rheumatoid arthritis (RA), thus, the identification of specifics VOCs associated with inflammation in the SF may represent a suitable procedure to facilitate a diagnosis and a better characterization of these diseases. E-noses are versatile instruments based on arrays of partially selective gas sensors system that do not provide specific information about the individual molecules but can detect a large spectrum of VOCs to provide a discrimination among samples classified according to their chemical composition (VOC pattern) (2).

Objectives: Aim of this study was to prospectively investigate whether analysis of VOCs profile emitted from SFs can identify differences between osteoarthritis (OA) and rheumatoid arthritis (RA).

Methods: VOCs Profile emitted from SFs was performed using a gas sensor array (electronic nose). The results were evaluated using statistical analyses.

Results: The analysis of the relative abundance indicated five VOCs significantly different between OA and RA. The abundance of five compounds allowed to identify OA with respect to RA with an accuracy of 82% (sensitivity: 0.90, specificity: 0.80, AUROC=0.92, 99.7% CI). The signals of the electronic nose sensors allowed to classify the studied subjects in OA or RA. In particular, OA patients could be distinguished from that of RA patients with an accuracy of 100% (sensitivity: 1, specificity: 1, AUROC=1, 99.9% CI) (Figure 1). However, no single VOC was specific for OA or RA.

Conclusions: This study shows that OA and RA patients exhibit qualitative and quantitative differences in the chemical compositions of knee synovial fluid. These differences may be attributed to five volatile compounds and can be detected by an electronic nose which may represent a suitable diagnostic tool for diagnosis and characterization of OA vs. RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3695

FRI0013 ACFA-INDUCED MOBILITY OF PRIMED SYNOVIAL FIBROBLASTS: THE MISSING LINK BETWEEN ACFA-INDUCED BONE LOSS AND SYNOVIAL CHANGES

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Background: Anti-citrullinated proteins antibodies (ACPAs) injected in mice induce IL-8 dependent bone loss and arthralgia, but no synovial changes. We hypothesized that additional stimuli, sensitizing the synovial compartment to ACPA effects, is needed for the transition from bone to synovial pathology.

Methods: Synovial fibroblasts (SFs) were isolated from synovial tissue of RA patients by enzymatic digestion. Polyclonal ACPAs and other non-ACPA IgGs were separated from peripheral blood of RA patients by affinity purification on a fibrinogen-Sepharose column. Polyclonal ACPA and other non-ACPA IgGs were mixed with SFs and incubated for 72 hours in the absence or presence of IL-8. The results were evaluated by NIH ImageJ software.

Results: Serum starvation of SFs increased citrullinated proteins and PAD expression and protein citrullination were evaluated by immunohistochemistry. The role of signaling pathways in the ACPA-mediated SF modulation was analyzed by using specific signal inhibitors and by monitoring protein phosphorylations using western blot.

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Results: Serum starvation of SFs increased citrullinated proteins and PAD expression and protein citrullination were evaluated by immunohistochemistry. The role of signaling pathways in the ACPA-mediated SF modulation was analyzed by using specific signal inhibitors and by monitoring protein phosphorylations using western blot.
in starved SF indicated an important role for PI3K-mediated signals in the ACAP-induced increase of SF mobility.

Conclusions: We demonstrated that additional stimuli (such as stress-induced citrullination and cytokine priming) were needed for SF to react upon ACAP stimulation. This is an indirect proof supporting the idea that a synovial insult that would normally resolve unobserved, might be essential for the transition towards chronic synovial changes in the presence of ACAP.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6448

FR00104 ANTIOXIDANT ROLE OF MICROVESICLES FROM ADIPOSE TISSUE-DERIVED MESENCHYLMAL STEM CELLS IN HUMAN OSTEARTHRITIC CHONDROCYTES

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Background: Oxidative stress results in the disruption of normal physiological signaling leading to inflammatory changes, cartilage degradation and osteoarthritis (OA) progression (1). Recent advances have revealed the role of cell-derived microvesicles (MV) as a new mechanism of cell-to-cell communication with paracrine therapy potential (2). We have shown previously the antiinflammatory effects of human adipose tissue-derived mesenchymal stem cells (AD-MSC) conditioned medium in OA chondrocytes (2).

Objectives: We have isolated the MV fraction from the secretome of AD-MSC to conditioned medium in OA chondrocytes (2).

Methods: We isolated the MV fraction from the secretome of AD-MSC to conditioned medium by differential centrifugation with size filtration. MV size and concentration were determined by resistive pulse sensing. Proteomic analysis was performed by LC-MS/MS, with ProteinPilot and PeakView software and the bioinformatic tools UNIPROT and PANTHER. OA chondrocytes were isolated from knee specimens of advanced OA patients, stimulated with IL-1β (10 ng/mL) and treated with MV (3.6x10⁵ particles/mL) for 24h. Accumulation of 4-hydroxy-2-nonenal (HNE)-modified proteins and cytokines were measured by ELISA, NO production and MMP activity by fluorometry. Expression of specific proteins was evaluated by confocal microscopy or immunostaining. The data were analysed by ANOVA followed by Dunnett’s test.

Results: MV reduced the accumulation of HNE-modified proteins, a biomarker of oxidative stress in these cells. Moreover, we analysed the induction by two inflammatory mediators in vitro. These results are also supported by positive of vanox staining. Additionally, qRT-PCR results yielded higher expression of RUNX2, SP1, RANKL and DLx5. Furthermore, immunohistochemistry showed high ALP-activity and Coll-expression.

Conclusions: Preliminary results of our study focusing at developing a 3D bone-like model displayed a promising trend towards modelling endochondral ossification in vitro by increased mineralization (in vitro μCT analysis and vanox staining), and upregulation of osteogenic-relevant RUNX2 and SP1 expression as well as ALP-activity and Coll-expression. High expression of SP1 and RANKL could refer to osteoblast-like activities, which will be in the focus of further investigations. Finally, the complete 3D model will leave us the opportunity for studying the first phase of fracture healing under in vitro conditions.

Disclosure of Interest: None declared


FR0016 INVOLVEMENT OF RUNX2 AND β-CATENIN SIGNALING IN THE PRODUCTION OF ADAMTS-7 AND ADAMTS-12 IN OSTEARTHRITIC SYNOVIAL FIBROBLASTS

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Background: Proteinsases released from synovial membrane of osteoarthritic (OA) patients contribute to cartilage damage. We recently reported in synovial fibroblasts (SF) the expression of ADAMTS (a disintegrin and metalloproteinsase domain with thrombospondin motifs)-7 and -12, involved in the destruction of the cartilage oligomeric matrix protein (COMP) (1). Signaling pathways regulating these ADAMTS are poorly understood. As Runx2 and β-catenin are two transcription factors involved in chondrocytes metabolism and OA pathiology (2-5), we studied whether these factors are implicated in the expression of ADAMTS-7 and 12 in SF. Moreover, we analyzed the induction by two inflammatory mediators present in OA joints: interleukin-1β (IL-1β), and fibronectin fragments (Fn-fs), previously described in ADAMTS expression (1).

Objectives: To elucidate the effects of Runx2/β-catenin pathways involved in the production of ADAMTS-7 and -12 in healthy donors (HD) - and OA-SF.

Methods: ADAMTS-7 and -12 were detected in HD- and OA-SF protein extracts by Western blot. Blockade experiments were performed after stimulation with IL-1β or 45-kDa Fn-fs. We used inhibitors for two mitogen-activated protein kinases (MAPKs), ERK and p38, implicated in the activation of Runx2/β-catenin signaling.

Results: Intra cellular precipitation with ADAMTS-7 and -12 was confirmed in HD- and OA-SF, with higher levels of ADAMTS-7 in OA. After IL-1β or Fn-fs stimulation, DDK decreased ADAMTS-7 transcript in HD and OA-SF that was translated to a protein reduction in OA. Besides, ERK inhibitor decreased ADAMTS-12 mRNA and protein exclusively in OA-SF.

Conclusions: We reported that ADAMTS-7 protein expression is higher in OA-SF compared to HD confirming previous data at mRNA level (1). As DDK decreased ADAMTS-7, Wnt-β-catenin signaling seems to be implicated in its expression. By contrast, the expression of ADAMTS-12 is regulated by ERK, pointing to a possible implication of ERK-Runx2 axis, exclusively in OA-SF.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3682

FR0015 MODELING THE INITIAL PHASE OF FRACTURE HEALING IN VITRO: 3D BONE-LIKE MODELS OF ENDOCHONDAL OSSIFICATION

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Background: Intra cellular precipitation with ADAMTS-7 and -12 was confirmed in HD- and OA-SF protein extracts by Western blot. Blockade experiments were performed after stimulation with IL-1β or 45-kDa Fn-fs. We used inhibitors for two mitogen-activated protein kinases (MAPKs), ERK and p38, implicated in the activation of Runx2/β-catenin signaling.

Results: Intra cellular precipitation with ADAMTS-7 and -12 was confirmed in HD- and OA-SF, with higher levels of ADAMTS-7 in OA. After IL-1β or Fn-fs stimulation, DDK decreased ADAMTS-7 transcript in HD and OA-SF that was translated to a protein reduction in OA. Besides, ERK inhibitor decreased ADAMTS-12 mRNA and protein exclusively in OA-SF.

Conclusions: We reported that ADAMTS-7 protein expression is higher in OA-SF compared to HD confirming previous data at mRNA level (1). As DDK decreased ADAMTS-7, Wnt-β-catenin signaling seems to be implicated in its expression. By contrast, the expression of ADAMTS-12 is regulated by ERK, pointing to a possible implication of ERK-Runx2 axis, exclusively in OA-SF.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3682

FR00105 MODELLING THE INITIAL PHASE OF FRACTURE HEALING IN VITRO: 3D BONE-LIKE MODELS OF ENDOCHONDAL OSSIFICATION

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Background: Intra cellular precipitation with ADAMTS-7 and -12 was confirmed in HD- and OA-SF protein extracts by Western blot. Blockade experiments were performed after stimulation with IL-1β or 45-kDaFn-fs. We used inhibitors for two mitogen-activated protein kinases (MAPKs), ERK and p38, implicated in the activation of Runx2/β-catenin signaling.

Results: Intra cellular precipitation with ADAMTS-7 and -12 was confirmed in HD- and OA-SF, with higher levels of ADAMTS-7 in OA. After IL-1β or Fn-fs stimulation, DDK decreased ADAMTS-7 transcript in HD and OA-SF that was translated to a protein reduction in OA. Besides, ERK inhibitor decreased ADAMTS-12 mRNA and protein exclusively in OA-SF.

Conclusions: We reported that ADAMTS-7 protein expression is higher in OA-SF compared to HD confirming previous data at mRNA level (1). As DDK decreased ADAMTS-7, Wnt-β-catenin signaling seems to be implicated in its expression. By contrast, the expression of ADAMTS-12 is regulated by ERK, pointing to a possible implication of ERK-Runx2 axis, exclusively in OA-SF.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3682

Friday, 16 June 2017 485

Sci ence Abstracts
A NOVEL CONCEPT OF M1 AND M2 MONOCYTES IN RHEUMATOID ARTHRITIS: PRO-INFLAMMATORY MONOCYTE POLARIZATION IMBALANCE, ANTI-CITRULLINATED PROTEIN ANTIBODY AND OSTEOCLASTOGENESIS

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Background: Monocytes can differentiate into either proinflammatory, microbiocidal M1 macrophage or anti-inflammatory M2 macrophage subtypes. In addition to macrophages, regarding monocyte subsets, M1 monocytes and M2 monocytes mirroring the M1/M2 macrophage polarization concept were suggested. Little is known regarding the relationships between osteoclastogenesis and M1/M2 monocyte subsets.

Objectives: We investigated the relationships among M1 monocytes, M2 monocytes, osteoclast differentiation ability and clinical characteristics in patients with rheumatoid arthritis (RA).

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from RA patients and healthy donors, and then we investigated the number of M1 monocytes or M2 monocytes by fluorescence-activated cell sorting. We defined positive CD14, CD68 and CCR2 monocytes as M1 monocytes, and in separate tubes, we defined positive CD14, CX3CR1 and CD163 or CD206 monocytes as M2 monocytes. We also obtained and cultured CD14-positive cells from PBMCs from RA patients and healthy donors, and we then investigated the number of M1 monocytes or M2 monocytes by fluorescence-activated cell sorting. We defined positive CD14, CX3CR1 and CD163 or CD206 monocytes as M2 monocytes.

Results: Forty RA patients and 20 healthy donors were included. Twenty-two patients (55%) were ACPA-positive. The ACPA-positive patients had significantly higher M1/M2 ratio in vivo (p<0.028) (E) and significantly greater numbers of osteoclasts in vitro (p<0.01) (F) than the ACPA-negative patients. We show an ACPA-negative patient’s osteoclasts in vitro (G) and those of an ACPA-positive patient (H).

Conclusions: The M1/M2 ratio is strongly correlated with the in vitro differentiation of osteoclasts in patients with RA. The RA patients with positive ACPA had higher M1/M2 ratio and higher numbers of osteoclasts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5808
ditions, respectively. CTLA-4 expression in MSC was co-cultured with peripheral blood mononuclear cells (PBMC) isolated by density gradient centrifugation from venous blood of healthy donors. The cells were stimulated by anti-CD3 and anti-CD28 (1 μg/ml) and were challenged using IFN-γ (~18% O2) or hypoxic (~1.5% O2) conditions and analyzed by TNFα secretion by suspension assay. Results: The MSC phenotype of bone-marrow derived cells could be verified according to their surface marker expression and their osteogenic and adipogenic differentiation capacity. On transcriptional level, MSC possessed both full-length and - to a higher extent - the soluble CTLA-4 isoforms with a higher mRNA abundance under normoxic as compared to hypoxic conditions. Extra- and intracellular analysis of CTLA-4 expression on protein level, demonstrated a significant decrease of phospho-CTLA-4 (p<0.01) in the soluble CTLA-4 isoforms in MSC from bone marrow. This decrease in CTLA-4 expression by suspension assay. Disclosure of Interest: None declared

Conclusions: We have demonstrated that co-culture of MSC with PBMC significantly reduced the amount of secreted TNFα (p<0.05) which could be reversed by anti-CTLA-4-antibody (p<0.05), under both normoxic and compared to hypoxic conditions, respectively. Conclusions: We clearly demonstrate the existence of CTLA-4 on hMSC and its functionality with regard to the inhibition of PHA-induced TNFα secretion by PBMC. We also demonstrate that the expression of CTLA-4 (l) contributes to the immunomodulatory capacity of hMSC and (ii) supports the ‘immune privileged’ status of these cells.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4078
Objectives: We evaluated the role of these metabolic pathways in RA-FLS proliferation and autoimmune arthritis in SKG mice.

Methods: The expression of glycolysis- or glutaminolysis-related enzymes was evaluated by real-time PCR and Western blotting, and the intracellular metabolites were evaluated by metabolic analyses. The effects of glucose or glutamine on RA-FLS proliferation were investigated in glucose- or glutamine-deprived conditions. The growth of RA-FLS was inhibited by GLS1 siRNA transfection or GLS1 inhibitor treatment. Silencing of GLS1 in RA-FLS did not affect IL-6 or MMP-3 production in supernatants. GLS1 expression in RA-FLS was not affected by pro-inflammatory cytokine stimulation. Compound 968 ameliorated the autoimmune arthritis and decreased the number of Ki-67-positive synovial cells in SKG mice.

Conclusions: Our findings suggested that glutamine metabolism plays an important role in regulating RA-FLS proliferation, without being affected by pro-inflammatory cytokine stimulation or affecting cytokine production, and may be a novel therapeutic target for RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2804

FR0023 ARTESANTE CAN INHIBIT MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES VIA SUPPRESSION OF MATRIX METALLOPROTEINASE 9 IN RHEUMATOID ARTHRITIS PATIENTS

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Methods: Synovial tissues were obtained from active RA patients as well as osteoarthritis (OA) and noninflammatory orthopedic arthropathies (Orth.A) patients and immunohistochemical (IHC) staining were performed for MMP9 expression. FLS isolated from these patients were analyzed for MMP9 expression by western blot (WB) and incubated with artesunate at different concentrations (0, 5, 10, and 20 μM) and methotrexate (MTX, 10 nmol/L) or hydroxychloroquine (HCQ, 20 μM) for 24 hours. Effects of artesunate on migration and invasion capacity were detected by transwell and wound healing assays. MMP9 and PI3K/Akt signal transduction protein expression after artesunate treatment was measured by WB. Serum cytokine levels were measured by Elisa.

Results: (1) IHC staining showed that synovial MMP9 expressed in lining and sublining area with intense nuclear and endochylema staining in RA synovium and the percentage of MMP9+ cells was significantly higher in RA (n=32) than that in OA (n=6) or Orth.A (n=6), Figure 1A, B.

(2) Migration and wound healing assays for 12 hours and invasion assay for 24 hours showed that RA-FLS possessed stronger capacity in migration and invasion than OA-FLS or Orth.A-FLS (Figure 1E, F). Artesunate inhibits the migration and invasion capacity of RA-FLS in a dose-dependent manner. MTX also has an inhibition effect on the migration and invasion of RA-FLS, but not HCQ (Figure 2A).

(3) MMP9 expression in RA-FLS was significantly higher than that in OA-FLS or Orth.A-FLS (Figure 1C, D). 40 μM or 60 μM artesunate markedly inhibited the expression of MMP9 in RA-FLS by WB (Figure 2B).

(4) WB analysis showed artesunate suppressed generation of pphospho-Akt in a dose-dependent manner which indicated that Akt activity (phospho-Akt/Akt) in RA was significantly lower than that in untreated group (Figure 1C).

Conclusions: Artesunate could inhibit the migration and invasion capacity of RA-FLS and the expression of MMP9 through suppressing Akt activity.

Acknowledgements: This work was supported by National Natural Science Foundation of China (81671612 and 81471597), Research Project of Traditional Chinese Medicine Bureau of Guangdong Province (20161058) and Guangdong Natural Science Foundation (2014A030313074).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2039

FR0024 MICRONNA-146A CONTROLS LOCAL BONE DESTRUCTION BY REGULATING FIBROBLAST INDUCED OSTEOCLASTOGENESIS IN INFLAMMATORY ARTHRITIS

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Background: MicroRNA (MiR-) 146a plays an important role in the regulation of the innate immune response and has also been shown to suppress cancer development in myeloid cells. Although in late stages of arthritis elevated expression of miR-146a in synovial tissue of rheumatoid arthritis patients was detected, the level of this miRNA was found to be down regulated in early disease, but its role in the development of inflammatory arthritis is still elusive.

Objectives: The objective of this study is to analyse the role of miR-146a in arthritis by the use of a chronic arthritis disease model. We aim to investigate the regulatory function of this miRNA in the pathogenic stroma, therefore in fibroblasts but also in immune cells.

Methods: To induce arthritis we used the chronic inflammatory hTNFtg disease model, therefore we crossed miR-146a deficient into hTNFtg mice. Disease severity was assessed clinically and histologically. Blood of arthritis animals was analysed by flow cytometry. Serum cytokine levels were measured by ELISA. Synovial fibroblasts were isolated from metatarsal bones and their proliferation
was analysed histologically and by 3[H]thymidine incorporation. RNA expression levels were measured by qPCR.

**Results:** When we crossed mir-146a RANKL−/− onto TNFtg mice, histological examination revealed a significant increase in synovial inflammation and even more striking a more than twofold increase in local bone destruction, due to increased generation of osteoclasts. Moreover, the levels of mir-146a−/−TNFtg mice compared to TNFtg mice. Interestingly, systemic bone loss was comparable in TNFtg compared to mir-146a−/−TNFtg mice, suggesting an important local role of mir-146a. Indeed, we detected increased levels of IL-1, TRAF6, a major target of mir-146a and RANKL, in addition the expression level of OPG was decreased locally in the paws of TNFtg−/− compared to TNFtg mice. By performing bone marrow transplants we could indeed show a pivotal role for mir-146a in mesenchymal cells in controlling local osteoclast generation and bone destruction. Analysis of important mesenchymal cells in arthritis, the synovial fibroblasts exhibited enhanced proliferation if mir-146a was missing, in vitro and in vivo. Moreover, stimulation of these cells with IL-1β, a prominent cytokine in arthritis which was also shown to be negatively regulated by mir-146a, led to increased expression of RANKL and TRAF6 in mir-146a deficient synovial fibroblasts.

**Conclusions:** These data demonstrate an important protecting role of the mir-146a in inflammatory arthritis, most importantly in local bone destruction, by controlling mesenchymal expression of osteoclastogenic factors. This shows an important anti-inflammatory role of mir-146a, which might possibly be exploited for therapeutic purposes.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3384

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**FR10026**  IDENTIFICATION OF MICRORNAS CANDIDATES SPECIFICALLY EXRESSED IN MONOCYTES OF UNDIFFERENTIATED ARTHRITIS PATIENTS WHO PROGRESSED TO RHEUMATOID ARTHRITIS

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**Background:** Monocytes are central to the initiation of inflammation and bone erosion in the development of Th17 and T(H)17 arthritis. Therefore, understanding of molecular pathways regulating monocytes, especially at the early stages of RA development, is of crucial importance as it may help to predict the progression to the full-blown disease. However, mechanisms of gene regulation in monocytes, particularly the role of microRNA (miRNA) expression, which can be involved in regulation of several cellular inflammatory pathways, in early phases of RA (i.e. at undifferentiated arthritis-UA stage) are not fully characterized.

**Objectives:** To investigate the pattern of miRNAs expression in monocytes that could serve as new biomarkers for RA development.

**Methods:** Magnetically sorted monocytes from peripheral blood of 19 patients with UA served for total RNA isolation. Total RNA from both sample and reference was labelled with Hy3 and Hy5 fluorescent label, respectively, using the miRCURY LNA microRNA H-Prime Labeling Kit (Exiqon, Denmark). Fluorescent labelled samples and a reference RNA sample were hybridized to the miRCURY LNA microRNA Array Microarray Scanner (Agilent Technologies, USA). The image analysis was carried out using ImageGene 9 Software (Exiqon).

**Results:** Out of 19 patients with UA enrolled in the study, 12 were verified for diagnosis after 4 years of follow-up (7 patients did not respond to the call for re-evaluation). Four patients developed full-blown RA (UA→RA patients), 6 patients remained still in UA phase (UA→UA patients), 1 patient was diagnosed as having Sjögren’s Syndrome, and 1 undifferentiated connective tissue disease. Baseline characteristics of UA→RA vs UA→UA patients were as follows: age (median: 50, range 37–59 years), sex (52.5, range 32–74 years), CRP (median: 9.0, range 1–22 mg/l vs 8.0, range 1–21 mg/l), ESR (median: 37.0, range 4–47 mm/h vs 34.0, range 15–44 mm/h) and swollen joints count (median: 3.0, range 1–9 vs 2.5, range 1–4). Following computational unsupervised analysis we identified 50 miRNAs in monocytes that have the largest variation across all patients samples. From these 50 miRNAs we selected several specific miRNA candidates on the basis of significantly changed expression in monocytes of UA→RA vs UA→UA patients. Predicted specific miRNAs targeting inflammatory genes in monocytes of UA→RA patients are: mir-483–3p (2.7-fold increased, p=0.009), mir-376d (4.1-fold decreased, p=0.0059), mir-3718–5p (52.8-fold increased, p=0.0381) miR-6422b–5p (13.7-fold increased, p=0.0380), and miR-25–3p (1.8-fold decreased, p=0.0317). Additional validation of selected miRNAs candidates will be further performed using qPCR analysis.

**Conclusions:** Our results indicate new miRNA candidates differentially expressed in peripheral blood monocytes from patients with UA who subsequently developed RA, in comparison to patients with UA who did not progress to RA after 4 years follow-up.

**Acknowledgements:** Supported by NCN Poland (grant 2012/06/A/NZ5/00059).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5703

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**FR10027**  TNF EXPRESSION ON MICROPARTICLES FROM RHEUMATOID ARTHRITIS PATIENTS MEDIATES ENDOTHELIAL CELL FATE IN VITRO

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**Background:** Microparticles (MPs) are small membrane vesicles released by activated platelets or monocytes under physiological and pathological conditions. MPs have increased levels of MPs have been reported in patients with autoimmune diseases, such as Rheumatoid Arthritis (RA) which is characterized by an accelerated atherosclerosis. TNF, a key cytokine involved in the pathogenesis of RA, has been associated to RA atherosclerosis (2). Moreover, MPs could also have a role in endothelial dysfunction contributing to atherosclerosis in RA patients.

**Objectives:** The aim of this study was: 1) to evaluate TNF expression on RA-MPs. 2) to estimate the effects of serum RA-MPs on endothelial apoptosis and 3) to evaluate the effects of TNF on endothelial cell apoptosis in vitro and in vivo treatment with Etanercept.

**Methods:** 15 RA patients were recruited from the Department of Rheumatology Sapienza University of Rome at baseline (T0) and after three months of therapy (T3) with Etanercept. A fasting blood sample was collected and centrifuged twice to obtain platelet-poor plasma rich in MPs. The resulting plasma was stained with anti-TNF and analysed by flow cytometry. In vivo, MP samples from RA patients on endothelium were evaluated using human umbilical vein cell line EA.hy926. Cells were treated with RA-MPs purified at T0 and T3 and with RA-MPs in vitro treated with Etanercept. At the end of experiments apoptosis and autophagy were evaluated. Apoptosis was analyzed by flow cytometry using a FITC-conjugated
annexin V and propidium iodide apoptosis detection kit; autophagy was analyzed by western blot for the expression level of the autophagic marker LC3-II.

**Results:** Our results showed that MPs purified from RA patients at T0 expressed TNF on their surface and this expression decreased after three months of treatment with Etanercept (p<0.04). Moreover, serum RA-MPs at T0 significantly increased, in a dose-dependent manner, both apoptosis and autophagy levels in the human umbilical vein cell line EA.hy926 (p<0.005 and p<0.02, respectively versus untreated cells). After three months of treatment with Etanercept, RA-MPs were not able to significantly change these parameters. Finally, in vitro studies showed that RA-MPs treated with Etanercept significantly decreased surface expression of TNF and were no longer able to modulate apoptosis and autophagy in EA.hy926 cells.

**Conclusions:** Our data demonstrate that serum RA-MPs express TNF on their surface. Moreover, both in vivo and in vitro treatment with Etanercept interfere with the ability of MPs to significantly modulate apoptosis and autophagy of endothelial cells by decreasing surface expression of TNF.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3434

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**FR0028 IN VITRO INHIBITORY EFFECT OF ETANERCEPT ON AUTOPHAGY: A NEW MECHANISM OF ACTION OF TNF INHIBITORS IN RHEUMATOID ARTHRITIS**

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**Background:** Autophagy has emerged as a key mechanism in the development, survival and function of immune cells and dysregulation of autophagic pathway has been implicated in the pathogenesis of several autoimmune diseases including Rheumatoid Arthritis (RA) (1). In fact, autophagy seems to be involved in the generation of citrullinated peptides, with consequent breakdown of tolerance in RA (2). Moreover, increased autophagy levels and a reduction of apoptosis-related molecules have been found in RA synovial tissues and a role of TNF-induced autophagy in RA development has been proposed (3).

**Objectives:** The aim of the study was to analysed the effect of TNF and anti-TNF inhibitor etanercept on autophagy and apoptosis in cells involved in RA pathogenesis.

**Methods:** Peripheral blood mononuclear cells (PBMCs) and fibroblast-like synoviocytes (FLS) isolated from RA patients were cultured in presence of TNF and in serum deprivation state (starvation) for 4 hours and then etanercept, at concentration of 15 ug/mL, were added to the culture. After 24h cells were analyzed for levels of autophagy marker LC3-II by western blot and for percentage of annexin V-positive apoptotic cells by flow cytometry.

**Results:** As expected, TNF and starvation induced autophagy on RA PBMC and FLS in dose-dependent manner after 24h of culture (p<0.05 in all experimental conditions). Moreover, the adding of etanercept caused a significant reduction of LC3-II levels (p<0.004) and an increase of apoptosis rate (p=0.002) after both pro-autophagic stimuli (p<0.05).

**Conclusions:** We demonstrated for the first time an inhibitory effect of etanercept on autophagy activation of cells involved in RA pathogenesis. In addition, our findings suggest a crucial role of autophagy in RA cells survival.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5194

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**FR0029 THE OXYGEN SENSOR PHD1 IS AN INDISPENSABLE REGULATOR OF ARTHRITIS DEVELOPMENT**

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**Background:** Oxygen supply is a fundamental requirement for all living tissues. Some tissues such as articular joints are characterized by a physiological state of hypoxia. Interestingly, under conditions of inflammation such as in arthritic disease, this level of hypoxia is even further enhanced. However, the functional significance of these observations and the molecular mechanisms involved remain poorly characterized to date. Our goal was therefore to examine the role of 3 hypoxia-sensing receptors, particularly PHDs, in inflammation.

**Objectives:** Our goal was to examine the role of oxygen sensors PHD1, PHD2 and PHD3 in preclinical models of rheumatoid arthritis, and to delineate the cellular source involved.

**Methods:** We subjected the collagen antibody induced arthritis (CAIA) model (resembling rheumatoid arthritis) to hypoxic (10% O2) and normoxic conditions (21% O2). Furthermore, the CAIA-model was induced in mice with germeline deficiency of the specific PHD’s and in mice with a myeloid cell-specific PHD1 deficiency versus controls. Arthritis development was assessed by clinical scoring of paw swelling, histopathology of knee joints and μCT.

**Results:** Mice kept in hypoxic conditions during CAIA experiments showed markedly less arthritis (both by clinical and histopathological assessment) compared to mice in normoxic conditions. Furthermore, we demonstrated that PHD1 knockout (KO) mice had significantly less joint inflammation compared to wildtype mice. PHD1 KO mice were also protected against inflammation induced bone loss as evidenced by μCT. By contrast, no difference was found in between PHD2 heterozygous (PHD2 KO mice are not viable) or PHD3 KO mice and littermate controls. Because myeloid cells are considered critical effector cells upon passive transfer of arthrogenic antibodies in the CAIA model we also generated myeloid cell specific ko mice (PHD(−/−)M). Of interest, PHD(−/−)M mice developed less arthritis compared to wildtype mice and were protected against inflammation induced bone loss.

**Conclusions:** Our data are consistent with a new paradigm that the oxygen sensor PHD1 is a critical regulator of myeloid cell function in arthritic disease. Overall, the data suggest that PHD1 is a potential target in the treatment of arthritis.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5194
progression, our work suggests that the analysis of synovial MCs could help to identify patients at high risk of progression in radiographic damage, warranting further investigations to confirm the association of MCs with the development of joint damage and their direct contribution to bone erosion, possibly via a RANKL-mediated activation of osteoclasts.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6393

Abstract FR00032 – Table 1. Effect of Cs on oxidative stress markers

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<th>S. No</th>
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<th>Cs</th>
<th>CIA (Arthritic)</th>
<th>CIA+Cs (Treatment)</th>
<th>CIA (Infected)</th>
<th>CIA+I+Cs (Treatment)</th>
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<td>Glutathione (μmoles of GSH/tissue)</td>
<td>1.29±0.042</td>
<td>1.69±0.02</td>
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<td>Lipid peroxidation (μmoles of TBARS formed/hr/tissue)</td>
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<td>Antioxidant activity (mg/g tissue)</td>
<td>1.35±0.00</td>
<td>250±0.13</td>
<td>182±1.00</td>
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<td>193±2.50</td>
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<td>Superoxide dismutase (nmole of epinephrine protected from oxidation/min/mg protein)</td>
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<td>2.21±0.082</td>
<td>1.84±0.135</td>
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<td>Nitric oxide (μmoles nitrite/mg wet tissue)</td>
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<td>0.39±0.065</td>
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<td>Catalase (μmoles of H2O2 consumed/min/mg protein)</td>
<td>161±2.94</td>
<td>144±3.10</td>
<td>390±0.055</td>
<td>106±1.00</td>
<td>37±0.00</td>
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All the values expressed in Mean ± SD (n=6). Significant differences indicated by *p<0.05 and **p<0.01 as compared to CIA and CIA-I group and ***p<0.001 as compared to control group.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1057
**FR0033 IMPORTANT ROLE OF CD11C+ DENDRITIC CELLS IN INFLAMMATORY ARTHRITIS**

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**Background:** Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different subsets with specific functions. A powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the actual role of DCs in joint inflammation is not known yet.

**Methods:** We analyzed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We also performed synovial biopsies and analyzed the cellular composition of the inflammatory infiltrate with respect to DCs. We used CD11c-diphtheria toxin receptor (DTR) transgenic mice, which express the human diphtheria-toxin receptor under the CD11c promoter, allowing for specific depletion of CD11c+ cells by administration of diphtheria toxin (DT). K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.

**Results:** We show that CD11c+ cells are present in significant numbers in the synovia of K/BxN and TNF driven arthritis. Both CD8+CD11c+ and CD11b+CD11c+, can be found in synovial tissue. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthrits were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. Analysis of K/BxN arthritis in wt mice and BATF3-/- mice, which lack a subset of DCs, namely CD8+CD11c+ DCs, revealed no difference in arthritis severity between the two groups. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.

**Conclusions:** These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived dendritic cell intermediate phenotype, play an important role in inflammatory arthritis, suggesting that they could be an important therapeutic target for patients suffering from inflammatory arthritis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6625

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**FR0034 ADALIMUMAB REDUCES CXCR4 EXPRESSION DURING INFLAMMATORY ARTHRITIS AND IN FIBROBLAST-LIKE SYNOVOCYTES AND OSTEOCLASTS UNDER CHRONIC TNF EXPOSURE**

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**Background:** The CXCL12/CXCR4 chemokine axis has been implicated in the pathogenesis of RA. The expression of this chemokine and receptor has been shown to be increased in RA synovium, and moreover, CXCR4 levels in synovium have been correlated with joint destruction in RA patients.

**Objectives:** Given that high levels of CXCR4 are associated with RA pathogenesis, we sought to determine whether CXCR4 levels are altered by adalimumab (a) both in RA patients, and in the human TNF transgenic mouse model (huTNF Tg197) of arthritis, as well as in vitro with RA fibroblast-like synoviocytes (RA-FLS) and human osteoclast precursors (OCP) following TNF exposure. In addition, we investigated the role of CXCR4 in human osteoclastogenesis (OCogenesis) under chronic TNF exposure.

**Methods:** Public DNA microarray data of synovial tissue from ADA treated RA patients was analyzed for changes in the expression level of various chemokines and their cognate receptors. PBMC populations from ADA treated RA patients taken at baseline, wks. 4 & 12 were assessed by CyTOF for CXCR4. IHC staining was performed on formalin paw sections from wk. 13 placebo control and ADA treated (1 mg/kg i.p.) huTNF Tg197 mice to evaluate CXCR4 expression in various pannus-associated cells. To assess the role of TNF and concomitant ADA treatment on human cultures in vitro, CXCR4 RNA expression was evaluated in RA-FLS stimulated with conditioned media from PBMCs +/-ADA for 6 hrs., and CXCR4 protein on OCP by flow cytometry in response to 72 hr. M-CSF+RANKL +/-TNF +/-ADA. To demonstrate the role of CXCR4 in OCgenesis, OCP were cultured for 6 d. in M-CSF+RANKL+/-TNF+/-ADA. Pretreatment with CXCR4 neutralizing antibody. CC maturation and activity were assessed by measuring TRAP5b activity in the conditioned media of OCP. Additionally, OCP were treated with conditioned media from PBMCs +/-ADA for 6 hrs., and CXCR4 protein on OCP by flow cytometry in response to 72 hr. M-CSF+RANKL+/-TNF+/-ADA. To demonstrate the role of CXCR4 in OCgenesis, OCP were cultured for 6 d. in M-CSF+RANKL+/-TNF+/-ADA. Pretreatment with CXCR4 neutralizing antibody. CC maturation and activity were assessed by measuring TRAP5b activity in the conditioned media of OCP.

**Results:** Preliminary microarray data analysis of synovial tissue demonstrated that active RA patients over-expressed CXCR4 while CXCR4 was significantly normalized (two-fold reduction) in the responders to ADA therapy. In addition, CyTOF analysis of PBMC from ADA treated RA patients indicated a significant 2-fold reduction from baseline in CXCR4 expression on B cells with a modest trend of reduction on CD4+ T cells by wk. 4. In huTNF Tg197 mice, CXCR4 expression in the inflamed pannus (most notably in FLs, lymphocytes and OC) was also decreased by ADA therapy. In vitro human cultures of similar cell types including RA-FLS and OCP were subjected to conditioned media or TNF, respectively, and found to express lower levels of CXCR4 that were reduced with concomitant ADA treatment. Finally, antibody-mediated blockade of CXCR4 on human OCP decreased both TNF-enhanced OC maturation and activity.

**Conclusions:** Our findings demonstrate that ADA therapy reduces CXCR4 expression in vivo both in RA patient PBMCs and in the pannus of huTNF Tg mice with inflammatory arthritis expression in FLs, lymphocytes, OCPs and OC. Similar results were also observed with our in vitro human cultures of equivalent cell types. More importantly, we’ve shown that inhibition of CXCR4 can reduce TNF-enhanced OCgenesis in vitro, suggesting that CXCR4 may be a contributing factor to TNF-enhanced osteolysis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2982

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**FR0035 SPECIFIC MONOCYTE SUBSETS IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH THE PROGRESSION OF CARDIOVASCULAR DISEASE AND AUTOIMMUNE AND PRO-ATHEROMATOUS PROFILES**

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**Background:** We show that Cd11c+ cells are present in significant numbers in the synovia of K/BxN and TNF driven arthritis. Both CD8+CD11c+ and CD11b+CD11c+, can be found in synovial tissue. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. Analysis of K/BxN arthritis in wt mice and BATF3-/- mice, which lack a subset of DCs, namely CD8+CD11c+ DCs, revealed no difference in arthritis severity between the two groups. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.

**Conclusions:** These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived dendritic cell intermediate phenotype, play an important role in inflammatory arthritis, suggesting that they could be an important therapeutic target for patients suffering from inflammatory arthritis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4918
FRI0036  ASSOCIATION BETWEEN THE 18FDG-PET IMAGING AND THE PATHOLOGICAL FINDINGS OF RHEUMATOID SYNOVITIS

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Background: It has been reported that 18FDG-PET (PET) is useful in the evaluation of RA and for monitoring the effects of treatment on the disease activity, so its utility for the evaluation of arthritis is expected. However, the mechanism underlying the uptake of FDG into the inflamed joint is still unclear.

Objectives: The aim of this study was to investigate the associations among the amount of FDG uptake in RA joints, the inflammatory findings with regard to the pathology of the synovium and the clinical findings.

Methods: We performed PET in 18 RA patients who underwent Total Kne Pisaoplasty surgery in our hospital just prior to surgery. We calculated the FDG uptake as the standardized uptake value (SUVmax) and scored it using the Rooney score, with the degree of inflammation of the synovial tissues used for the pathological evaluation. We evaluated the associations among the SUVmax, Rooney score, CRP level, ESR and MMP-3 level just before surgery.

Results: The subjects were 18 cases with 20 joints, which were in four females and 14 males. At the time of surgery, the average age of the patients was 66.7±7.9 years old, and the mean disease duration was 20.8±14.0 years. Significant correlation was not observed between SUVmax and total Rooney score (r=0.056, p=0.814). But there were strong correlations between SUVmax and some of the individual items in Rooney score, including the “Synoviocyte hyperplasia”, and also between SUV max and “Diffuse infiltrates of lymphocytes” (r=0.512, p=0.021 and r=0.581, p=0.007, respectively).

Conclusions: The accumulation of FDG was associated with the extent of “synoviocyte hyperplasia” and “diffuse infiltrates of lymphocytes”. It is estimated that accumulation of FDG is associated with relatively early stage of active inflammation of RA.

References:

FRI0037  MER-MEDIATED EFFECOTOMY TEMPS ARTHRITIS BY PREVENTING NEUTROPHILS TO GO INTO SECONDARY NECROSIS AND SPILL THEIR INFLAMMATORY CONTENT IN THE JOINT


Background: Rheumatoid arthritis is characterized by an inflammatory response in synovial joints, showing a predominant influx of neutrophils. These cells are cytotoxic and contribute to matrix degradation. In addition, they are implicated as a source of citrullinated auto-antigens, leading to the production of anti-citrullinated protein antibodies (Acpa). Neutrophils have a relative short life span and many of them undergo apoptosis. If they are not cleared, they undergo secondary necrosis and release their cell content. A key mediator in the resolution of inflammation and the uptake of apoptotic cells, or efferocytosis, is the receptor tyrosine kinase Mer.

Objectives: To elucidate the local role of Mer during gonarthritis.

Methods: Macrophages were transduced by adenoviruses encoding the Mer ligand Pros1 or Luciferase. One day after the collagen booster injection in mice, Mer-specific antibodies or IgG antibodies, or adenoviruses overexpressing Pros1 or Luciferase were injected intravenously. Mice were euthanized at day 30 and joint homogenates were assessed.

Results: Adenoviral overexpression of the Mer ligand Pros1 resulted in reduced production of pro-inflammatory cytokines and chemokines by macrophages, compared to Luciferase. In addition, local Pros1 overexpression resulted in reduced expression of pro-inflammatory and pro-destructive mediators by synovial cells of arthritic mice. Systemic and local Pros1 overexpression diminished joint pathology, reduced the number of cleaved Caspase 3-positive apoptotic cells and secondary necrotic neutrophils. Conversely, inhibiting Mer-mediated efferocytosis by Mer-specific antibodies or Merther gene ablation resulted in aggravation of arthritis compared to controls, as evidenced by increased inflammation and tissue destruction. Additionally, Mer-inhibited mice had increased numbers of apoptotic cells in their knee joints, and higher serum levels of IL-16C, a cytokine released by secondary necrotic neutrophils.

Conclusions: Together, these results demonstrate that Mur locally plays a unique protective role in knee joint disease by enhancing resolution of arthritis. Our data suggest that promoting and/or restoring Mer-mediated uptake of apoptotic cells in the arthritic joint might be therapeutically beneficial.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7021

FRI0038  RELEASE OF PEPTIDYLARGININE DEIMINASE 2 FROM ACTIVATED NEUTROPHILS

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Background: Extracellular citrullination catalyzed by peptidylarginine deiminase (PAD) is thought to play a central role in the pathogenesis of rheumatoid arthritis. Neutrophils are a major reservoir of PAD2 and PAD4. Cellular release of PAD2 and PAD4 is usually considered a consequence of cell death.

Objectives: We aimed to determine if PAD2 can be released from live, activated neutrophils as an active process.

Methods: Whole blood cells were purified from healthy blood were stimulated with phorbol 12-myristate 13-acetate (PMA). To capture PAD2 released from neutrophils and detect it by flow cytometry, we used biotinylated anti-CD15 and anti-PAD2 antibody (mAb D59). In addition, intracellular PAD2 was quantified by intracellular staining with PE-anti-PAD2. PAD2 released from leucocytes and subcellular fractions of human granulocytes were assessed for content of PAD2 using an in-house lumixen-based assay.

Results: On incubation of whole blood cells with PMA, PAD2 was detectable in the supernatant 30 minutes, and levels increased thereafter in parallel with increasing cell death. However, using PAD2 catch reagent, we found that live neutrophils released PAD2 in the 30 minutes after stimulation. Intracellular staining for PAD2 showed that the content of PAD2 in live neutrophils decreased correspondingly. Upon subcellular fractioning of granulocytes, the majority of PAD2 was found in cytosol and, in 25 times lower quantities, in the fraction containing plasma membranes and secretory vesicles. Sparse amounts of PAD2 were also observed in gelatinase granules.

Conclusions: In conclusion, PAD2 can be released from live, activated neutrophils, which may contribute to extracellular citrullination and thereby play a role in driving inflammatory processes in RA patients with immune responses to citrullinated proteins.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4902

FRI0039  ENDOTHELIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS: WHICH EFFECT OF METHOTREXATE? A STUDY IN ADJUVANT INDUCED ARTHRITIS MODEL

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Background: Rheumatoid arthritis (RA) is associated with increased cardio-vascular risk [1]. The mechanism of this increased CV risk [1] seems to be endothelial dysfunction (EDHF). EDHF is involved in the regulation of peripheral resistance arterioles. EDHF is mainly generated by NO, produced by nitric oxide synthase (NOS) [2]. Inhibition of NOS reduces the production of EDHF [3]. This supports the hypothesis that RA is associated with increased CV risk due to impaired EDHF generation. In this study we aimed to investigate the effect of MTX on EDHF generation in the RA model.

Objectives: The aim of this study was to determine the effect of MTX on endothelial function in arthritis and to investigate its effect on endothelial pathway.

Methods: Experiments were conducted in the adjuvant-induced arthritis (AIA) model in Lewis rat. At onset of arthritis, rats were treated by a sub-cutaneous injection of MTX (1 mg/kg/wk) or phosphate buffer saline (vehicle) for 3 weeks. Arterial score was daily recorded. At the end of treatment, thoracic aorta was harvested to measure the relaxation to acetylcholine on pre-constricted aortic rings in the presence or not of inhibitor of nitric oxide (NO) synthase (L-NAME), arginine (nor-NOHA), EDHF (Apamin/Charybdotoxin), or a superoxide dismutase analog (Tempol). The effect of norepinephrine (NE) and sodium nitroprusside (SNP) was also measured. We used an in-house luminex-based assay.

Results: MTX treatment induced a marked impairment of EDHF generation in AIA-induced arthritis. The effect of MTX on EDHF generation was significantly different between the two treatment conditions.

Conclusions: The results of this study suggest that MTX treatment may reduce the severity of EDHF generation in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5964
CHARACTERIZATION OF ANTI-CARBAMYLATED SYNOVIAL IN VIVO MONITORING OF ANTI-FOLATE THERAPY IN ARTHRITIC RATS USING [18F]FLUORO-PEG-FOLATE AND PET


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Background: Macrophages play a key role in the pathophysiology of rheumatoid arthritis (RA). The folate receptor (FR) is expressed on these macrophages and [18F]fluoro-PEG-folate PET can be used to visualize arthritis in vivo. In addition, [18F]fluoro-PEG-folate PET could be a highly interesting tool for therapeutic monitoring of MTX therapy, the corner stone for RA therapy.

Objectives: To study the potential of [18F]fluoro-PEG-folate PET for monitoring response to MTX in a rat model of RA.

Methods: Arthritic rats [3] (n=3–6 per group) received interventions with either MTX (1 mg/kg; 2 times [group A] or 4 times [group B]) or PBS (control group) with a time interval of 3–4 days. Healthy rats didn’t receive any arthritic induction or therapy. [18F]fluoro-PEG-folate PET-CT were acquired for one hour after tracer injection [2]. Scans were analysed using the region of interest method and standardized uptake values (SUVs) were determined (50–60 min time frame). Sixty minutes after the PET scan, ex-vivo tissue distribution was performed and the amount of radioactivity measured in a gamma counter (expressed as percentage of the injected dose/gram tissue (%ID/g)) [2]. For histopathology (Hematoxylin-Eosin (HE) and immunohistochemistry with macrophage specific antibodies ED1 and ED2) were applied. Synovial macrophages were counted in predefined areas of the knees [3].

Results: PET scans clearly visualized significantly lower SUVs (1.5-fold, p<0.01) in arthritic knees of both MTX-treated groups, approximating the levels observed in healthy rats. Corroborating [18F]fluoro-PEG-folate PET, ex vivo tissue distribution ([18F]fluoro-PEG-folate demonstrating a 2- and 4-fold decrease (group A and B, respectively) in tracer uptake in arthritic knees after MTX therapy (0.12 and 0.06 for groups A and B, and 0.22 and 0.14 for controls, respectively) (Figure). This reduction in uptake of [18F]fluoro-PEG-folate in arthritic knees was also associated with a significant decrease in ED1 and ED2 positive synovial macrophages in arthritic knees (4-fold) for both treated groups compared with control rats knees (p<0.01).

Conclusions: This study in arthritic rats underscores the potential and usefulness of [18F]fluoro-PEG-folate PET as tool to monitor of MTX therapy and potentially other anti-folate treatments of RA.

References:

Disclosure of Interest: None declared
BAFF-R EXPRESSION IN NAIVE CD5+IGM+ B CELLS IN RHEUMATOID ARTHRITIS PATIENTS REPOPULATING AFTER RITUXIMAB

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Background: Serum levels of B cell activating factor (BAFF) rise following Rituximab (RTX) therapy in patients with Rheumatoid arthritis (RA). CD5+IgM+B cells are present within transitional and naïve B cell subsets and their increased production or accumulation is associated with some autoimmune diseases. Previous studies have shown that BAFF does not enhance their survival compared with CD5- naïve B cells, suggesting that signalling pathways are important in promoting their survival.

Objectives: To determine serum BAFF levels and BAFF-receptor (BAFF-R) expression in CD5+IgM+B cells in healthy controls (HC), RTX-naïve RA patients (pre-RTX), and relapsing at different time points after peripheral B cell repopulation post-RTX treatment, divided into 2 groups: early relapsers (0–3 months post-B cell return) and later relapers (~4 months post-B cell return).

Methods: Immunophenotyping of peripheral blood mononuclear cells was used to determine %CD5+IgM+B cells and BAFF-R (% and expression, mean fluorescence intensity (MFI)) in 5 HC, 13 pre-RTX and 12 post-RTX RA patients. Results were analyzed with respect to timing of relapse after peripheral B cell return

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>%BAFF-R+ve</th>
<th>BAFF-R MFI</th>
<th>BAFF levels (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-RTX</td>
<td>98.7 (97.9–99.5)</td>
<td>62.5 (50.5–82.4)</td>
<td>1.1 (0.9–1.2)</td>
</tr>
<tr>
<td>Post-RTX early</td>
<td>97.3 (85.8–100)</td>
<td>58 (34.3–129)</td>
<td>1.4 (0.9–1.7)</td>
</tr>
<tr>
<td>Post-RTX late</td>
<td>60.6 (12.9–71.2)</td>
<td>15.6 (11.8–17.5)</td>
<td>2.4 (2–6.4)</td>
</tr>
</tbody>
</table>

Results: %CD5+IgM+B cells, but not absolute numbers, were significantly higher in post-RTX early relapers compared to HC (p<0.01), pre-RTX patients (p<0.001) and post-RTX later relapers (p<0.01). There was a strong inverse correlation between %CD5+IgM+B cells and time after B cell return (r²=0.88, p<0.0001). BAFF-R expression was significantly lower in both post-RTX groups compared to HC and pre-RTX patients; early relapers showed the lowest % and MFI BAFF-R+ expression, compared with later relapers (p<0.01). BAFF-R+ expression increased with time after B cell return, both % (r²=0.47, p=0.002) and MFI (r²=0.76, p=0.0004). BAFF levels were significantly higher in both post-RTX groups compared to HC and pre-RTX patients, with the highest BAFF levels in early relapers (p<0.05 compared to later relapers). There was a significant inverse correlation between BAFF levels and % (r²=0.51, p<0.01) and MFI (r²=0.4, p<0.05) BAFF-R+ expression.

Conclusions: Early relapers show increased %CD5+IgM+ naïve B cells, and decreased BAFF-R expression, similar to ontogeny and what is seen in cord blood B cells. Whether the increased numbers of CD5+ naïve cells were contributing to relapse was not determined but they have the capacity to rapidly mature into autoantibody producing plasma cells, independent of the BAFF/BAFFR system. The aim of this study was to evaluate the radiological outcomes after an early treatment during 21 days by Etanercept, or Naproxene, or Celecoxib, or Prednisone, or Diclofenac or Methotrexate in adjuvant induced arthritis in rats.

Methods: Adjuvant-induced arthritis (AIA) was induced in 6 weeks old male Lewis rats by injection of Mycobacterium butyricum in adjuvant at the basis of the tail. At the onset of arthritis, rats were daily treated with Naproxene (10 mg/kg/d), or Diclofenac (5mg/kg/d), or Celecoxib (3 mg/kg/d), or Prednisone (10 mg/kg/d), or Etanercept (10 mg/kg/3 days, s.c.), or Methotrexate (1mg/kg/3 days, s.c.), or saline solution (Vehicle), for 21 days. Arthritic score was daily monitored. At the end of treatment, paws’ radiological exam was performed with a BMA High Resolution Digital X Ray (40mV, 10mA). A score of 0 to 20 was determined for each paw using a grading scale modified from Ackerman et al (1979).

Abstract FRI0043 – Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>%CD5+IgM+ (median/range)</th>
<th>%BAFF-R+ve</th>
<th>BAFF-R MFI</th>
<th>BAFF levels (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC</td>
<td>18.5 (9.1–26.8)</td>
<td>98.7</td>
<td>62.5</td>
<td>1.1 (0.9–1.2)</td>
</tr>
<tr>
<td>Pre-RTX</td>
<td>5.4 (1.9–21.4)</td>
<td>97.3</td>
<td>58</td>
<td>1.4 (0.9–1.7)</td>
</tr>
<tr>
<td>Post-RTX early</td>
<td>44.4 (39.6–55.8) ***</td>
<td>60.6</td>
<td>15.6</td>
<td>2.4 (2–6.4) ***</td>
</tr>
<tr>
<td>Post-RTX late</td>
<td>12.7 (2.3–27.9) ***</td>
<td>93.1</td>
<td>30.2</td>
<td>1.7 (1.3–2.4) ***</td>
</tr>
</tbody>
</table>

*** p<0.0001 compared with HC, ** p<0.01, * p<0.05 compared with pre-RTX.
Results: Compared to the Vehicle, all treatments significantly reduced (p < 0.001) arthritic score with a reduction of the arthritic score evaluated between 40% (for methotrexate) and 70% (for diconfexan) (figure 1. Compared to the vehicle, the radiographic score was improved by Naproxene, Diconfexan, Celcoxib, Glucocorticoids, Etanercept (p < 0.001) but not by methotrexate. Compared to Etanercept, Naproxene and diconfexan showed less radiological structural changes (p < 0.01) (figure 2).

Conclusions: Our study demonstrates for the first time that an early treatment with NSAIDs, excluding COX2 selective inhibitor, is more beneficial than Etanercept on the radiological damages in adjuvant induced arthritis. The close efficiency of all drugs on the arthritis suggests that the beneficial impact of NSAIDs is not only driven by their impact on the systemic inflammation. NSAIDs should be used during the window of opportunity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2611
Conclusions: The persistence of 14–3-3-η levels ≥0.50 ng/ml appears to be associated with a lower probability of reaching remission in polyarthritis patients. 14–3-3-η levels >0.50 ng/ml in patients in clinical remission appear to be associated with more rapid radiographic (especially erosive) progression over the following year. A larger study is required to validate these findings, especially with the most stringent criterion of Boolean remission.

Disclosure of Interest: N. Carrier: None declared, M.-P. Garant: None declared, A. Marotta Employee of: Augurex Life Sciences Corp., A. De Brum Fernandes Grant/research support from: AJDBF is part of the Centre de Recherche Clinique from the CHUS, which received a team grant from the Fonds de Recherche en Santé-Québec, P. Liang: None declared, A. Masetto: None declared, Y. Gui Employee of: Augurex Life Sciences Corp., J. Savill Employee of: Augurex Life Sciences Corp., S. Michienzi Employee of: Augurex Life Sciences Corp., W. Maksymowych Consultant for: Augurex Life Sciences Corp., G. Boire Grant/research support from: GB is part of the Centre de Recherche Clinique from the CHUS, which received a team grant from the FRSQ. GB is the recipient of CHF Grant MCP-110889. Since 2007, the Sherbrooke EUPA cohort has also received financial support from the Canadian Arthritis TiCS CORT (CATCH), a study designed and implemented by investigators and financially supported via unrestricted research grants initially by Amgen Canada Inc. DOI: 10.1136/annrheumdis-2017-eular.4085

THE ANTI-CD20 ANTIBODY RITUXIMAB REDUCES THE INFLAMMATORY AND PROTHROMBOTIC PROFILE OF LEUKOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS AND MODULATES THE ACTIVITY OF ENDOTHELIAL CELLS
I. Cecchi 1, C. Perez-Sanchez 2, P. Ruiz-Limon 2, I. Arias de la Rosa 2, M.C. Abalos-Aguilera 2, Y. Jimenez-Gomez 2, R. Ortega 2, E. Collantes-Estevez 2, A. Escudero 2, N. Barbarosa 2, S. Sciascia 2, C. Lopez-Pedrera 2. 1 Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rheumatic Diseases · Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Turin, Italy; 2 GC-5/Rheumatology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain

Background: Rituximab (RTX) has been shown to be successful in the treatment of rheumatoid arthritis (RA), indicating that B cells have an important role in this disease.

Objectives: The present study was undertaken to investigate the mechanisms of action of RTX on the immune and endothelial cells (EC) of the vascular system in the setting of RA.

Methods: Purified lymphocytes from five RA patients with high disease activity were treated with RTX (1μg/mL) for 24 hours. Then, the depletion of B cells was assessed by flow cytometry, and the changes occurred in the inflammatory profile of T-lymphocytes was analysed by RT-PCR. In a second set of experiments, to evaluate the influence of B-cell depletion on the inflammatory/prothrombotic profile of cells belonging to the vascular system, supernatants from cultured lymphocytes of RA patients in the presence or in the absence of RTX were added to isolated monocytes from AR patients and to cultured endothelial cells. The response to RTX was then examined.

Results: As expected, RTX promoted a significant depletion of B-cells. In parallel, the inflammatory profile of T lymphocytes from RA patients was downregulated, as shown by a significant drop of IL-1, IL-6, IL-17, IFN and TNF expression levels, thus suggesting that the anti-inflammatory effects of RTX might be related to B cell depletion. Supernatants from RTX-treated lymphocytes further abridged the prothrombotic profile of RA-monocytes, promoting a significant inhibition of TF, MASP-1 and VEGF-A gene expression. Moreover, endothelial cells, activated after treatment with supernatants from cultured RA-lymphocytes, showed reduced expression of cell-adhesion molecules (i.e. VCAM, ICAM, E-Selectin) and pro-thrombotic factors (i.e. TF, VEGF, IL-8) after treatment with supernatants from cultured RA-lymphocytes in the presence of RTX.

Conclusions: Overall, these results reveal that depletion of B-cells by RTX in RA influences the inflammatory profile of T lymphocytes, as well as their interaction with monocytes and ECs, thus modulating the inflammatory and prothrombotic shape of vascular cells in the setting of RA.

Acknowledgements: Supported by CTS-794, ISCIII (P11/01333; RIER RD16/0012/0015).

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4916

FRI0048 | THE ANTI-CD20 ANTIBODY RITUXIMAB REDUCES THE INFLAMMATORY AND PROTHROMBOTIC PROFILE OF LEUKOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS AND MODULATES THE ACTIVITY OF ENDOTHELIAL CELLS
I. Cecchi 1, C. Perez-Sanchez 2, P. Ruiz-Limon 2, I. Arias de la Rosa 2, M.C. Abalos-Aguilera 2, Y. Jimenez-Gomez 2, R. Ortega 2, E. Collantes-Estevez 2, A. Escudero 2, N. Barbarosa 2, S. Sciascia 2, C. Lopez-Pedrera 2. 1 Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rheumatic Diseases · Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Turin, Italy; 2 GC-5/Rheumatology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain

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Objectives: The present study was undertaken to investigate the mechanisms of action of RTX on the immune and endothelial cells (EC) of the vascular system in the setting of RA.

Methods: Purified lymphocytes from five RA patients with high disease activity were treated with RTX (1μg/mL) for 24 hours. Then, the depletion of B cells was assessed by flow cytometry, and the changes occurred in the inflammatory profile of T-lymphocytes was analysed by RT-PCR. In a second set of experiments, to evaluate the influence of B-cell depletion on the inflammatory/prothrombotic profile of cells belonging to the vascular system, supernatants from cultured lymphocytes of RA patients in the presence or in the absence of RTX were added to isolated monocytes from AR patients and to cultured endothelial cells. The response to RTX was then examined.

Results: As expected, RTX promoted a significant depletion of B-cells. In parallel, the inflammatory profile of T lymphocytes from RA patients was downregulated, as shown by a significant drop of IL-1, IL-6, IL-17, IFN and TNF expression levels, thus suggesting that the anti-inflammatory effects of RTX might be related to B cell depletion. Supernatants from RTX-treated lymphocytes further abridged the prothrombotic profile of RA-monocytes, promoting a significant inhibition of TF, MASP-1 and VEGF-A gene expression. Moreover, endothelial cells, activated after treatment with supernatants from cultured RA-lymphocytes, showed reduced expression of cell-adhesion molecules (i.e. VCAM, ICAM, E-Selectin) and pro-thrombotic factors (i.e. TF, VEGF, IL-8) after treatment with supernatants from cultured RA-lymphocytes in the presence of RTX.

Conclusions: Overall, these results reveal that depletion of B-cells by RTX in RA influences the inflammatory profile of T lymphocytes, as well as their interaction with monocytes and ECs, thus modulating the inflammatory and prothrombotic shape of vascular cells in the setting of RA.

Acknowledgements: Supported by CTS-794, ISCIII (P11/01333; RIER RD16/0012/0015).

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4916

FRI0049 | FC GAMMA RECEPTOR IV ENHANCES BONE EROSION IN EXPERIMENTAL ARTHRITIS BY PROMOTING INFUX OF PMNS
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Background: FCγ-Rs are involved in regulation of synovial activation and bone destruction during immune complex (IC)-mediated arthritis. The balance between activating FCγ-Rs (FCγRII,III and IV) and inhibiting FCγ-Rs determines synovial activation. Here we investigated the particular role of activating FCγ-RIV in bone erosion in IC-mediated osteoarthritis (OA) by comparing FCγRI,II,III,IV-/- mice with their WT controls. This observation suggests that the anti-inflammatory effects of RTX might be related to bone erosion in the knee joints of FcγRI,II,III,IV-/- mice to differentiate into osteoclasts in vitro was comparable to the one of WT controls. Moreover, we observed comparable numbers of TRAP+ osteoclasts on the bone surface of FCγRII/III,IV-/- and WT arthritic mice, suggesting that the observed decrease in bone erosion is mainly caused by a reduced osteoclast activity, rather than decreased osteoclast number. However, in contrast to FCγRII/III,IV-/-, AIA induction in knee joints of FCγRII/III,IV-/- resulted in increased bone erosion and inflammatory cytokines compared to WT mice. AIA induction in knee joints of FCγRII/III,IV-/- resulted increased, whereas it was decreased in the knee joints of FCγRII/III,IV-/- compared to their WT controls. This observation suggests that particularly FCγ-RIV is involved in regulating influx of PMNs. PMNs are potent producers of alarmins S100A8/A9 which are described to promote osteoclast activity. In line the number of S100A8/A9 positive cells in synovium was increased in FCγRII/III,IV-/- while decreased in FCγRII/III,IV-/-, compared to their WT control.

Conclusions: FCγ-RIV promotes bone erosion in AIA by enhancing influx of PMNs within the synovium. PMNs are potent producers of S100A8/A9 which has been described to induce osteoclast activity.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5386

FRI0050 | TYPE II COLLAGEN SECRETED FROM ARTICULAR CHONDROCYTES IS MAINLY DESTROYED BY CATHEPSIN S IN RA MICE
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Background: Mast cells have long been recognized to increase strikingly in number in the synovial membrane of rheumatoid arthritis (RA), accounting for 5% of the surface synovial membrane cells. Type II collagen has the longest half-life in cartilage matrix. The main cells which might affect articular cartilage in RA are synovial fibroblasts, synovial macrophages and mast cells. The latter two could express cathepsin S.

Objectives: We aimed to find the cells which have the biggest influence on type II collagen secreted from articular chondrocytes and the possible mechanisms in RA mice.

Methods: Four types of cells from collagen-induced arthritis model-established C57BL/6 mice were primary cultured, including synovial fibroblasts, peritoneal...
macrophages, bone marrow-derived mast cells and articular chondrocytes. The first three were co-cultured with articular chondrocytes separately. LHV5, a specific inhibitor of caspase 8 and 9, a broad-spectrum inhibitor of cytotoxic proteins, were added into the cocultures of macrophages and articular chondrocytes separately. Also, C48/80, an activator of mast cells, LHV5, and E64 were added into the cocultures of articular chondrocytes. When articular chondrocytes were co-cultured with mast cells, the type II collagen could be restrained by C48/80 (9.82±0.42ng/ml), compared with the control group (17.75±7.84ng/ml). The secretion of type II collagen could return to normal by the inhibitors of caspase 8, both LHV5 (16.15±5.05 ng/ml) and E64 (12.55±6.64 ng/ml). When articular chondrocytes were co-cultured with mast cells, the type II collagen could be restrained by C48/80 (9.82±0.42ng/ml), compared with the control group (26.09±5.34ng/ml). Similarly, the secretion of type II collagen could return to normal by the inhibitors of caspase 8, both LHV5 (16.15±5.05 ng/ml) and E64 (12.55±6.64 ng/ml), respectively. There was no significant difference in the expression of type II collagen mRNA between different groups. It showed that the type II collagen was not suppressed at the transcription level, but was mainly destroyed by cathepsin S and cathepsin K.

Conclusions: Macrophages and mast cells are the major sources of caspase 8, which might be the main factor that destroys type II collagen secreted from articular chondrocytes in RA mice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5664

FRI0051 EARLY ARTHRITIS INDUCES DISTURBANCES AT BONE NANOARCHITECTURAL LEVEL REFLECTED IN DECREASED TISSUE HARDNESS

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Background: Arthritis induces joint erosions and skeletal bone fragility.

Objectives: The main goal of this work was to analyze the early arthritis induced events at bone tissue level.

Methods: Eighty-eight female-type Cotswold rats were randomly housed in experimental groups, as follows: adjuvant induced arthritis (N=47) and a control healthy group (N=41). Rats were monitored during 22 days for the inflammatory score, ankle perimeter and body weight and sacrificed at different time points (11 and 22 days post disease induction). Bone samples were collected for histology, micro-CT, 3-point bending, nanointerdenraland and Fourier transformed infrared spectroscopy (FTIR) analysis. Blood samples were also collected for bone turnover markers and systemic cytokine quantification.

Results: At bone tissue level, measured by FTIR analysis and nanointerdenraland, there was a reduction of the mineral and collagen content and of hardness in the arthritic group, associated with an increase of the ratio of bone concentric to parallel lamellae and of the area of the osteocyte lacuna. In addition, increased bone turnover and changes in the microstructure and mechanical properties were observed in articularhritis, since the early phase of arthritis, when compared with healthy controls.

Conclusions: Arthritis induces very early changes at bone tissue level characterized by decreased tissue hardness and of collagen and mineral content. These results highlight the pertinence of immediate control of inflammation in the initial stages of arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5664

FRI0053 ANTIBODIES TO A SUBSET OF CITRULLINATED PEPTIDE ANTIGENS CORRELATE WITH NEUTROPHEL EXTRACELLULAR TRAP LEVELS IN THE SPUTUM OF SUBJECTS AT-RISK FOR FUTURE RA

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Background: Prior data suggest that anti-citrullinated protein/peptide antibodies (ACPA) may originate in the lung prior to the onset of synovitis in rheumatoid arthritis (RA) (1). Neutrophil extracellular trap (NET) formation is one potential mechanism that could trigger or be associated with local ACPA generation because NETs externalize citrullinated proteins and release peptidylarginine deiminase that could citrullinate nearby proteins (2-4).

Objectives: Using induced sputum, we recently identified a significant correlation between NETs and anti-cyclic citrullinated peptide antibodies (CCP) antibodies in subjects at-risk for future RA. Herein, we sought to explore associations of individual ACPAs and NETs in these subjects.

Methods: From the Studies of the Etiology of RA (SERA) cohort, we included 24 RA-free subjects at-risk for future RA based on familial (i.e. first-degree relative of RA patient) or serologic (i.e. serum anti-CCP positive identified at health fairs) risk. Induced sputum was tested using a bead-based ACPA array for IgG and IgA titters. Levels of NET complexes in sputum were measured using a deoxyribonucleic acid (DNA)-myeloperoxidase (MPO) and DNA-neutrophil elastase (NE) sandwich ELISA. Analyses included Spearman’s correlation and linear regression. Using Bonferroni’s correction, results were considered significant if both DNA-MPO and DNA-NE assays had a p<0.05.

Results: Subjects had a median age of 51 years, were 67% female and 38% ever-smokers. Increasing sputum NET levels significantly correlated with increasing ACPA levels for 27/29 ACPAs, including proteins/peptides of cit-vimentin, cit-fibrogen, cit-fibroactin, cit-apolipoproteins and cit-alpha-enolase. After adjusting for ever-smoking, sputum NET levels remained significantly associated with 17/29 ACPAs. The strongest associations (p<0.001 and 4.4 (1.2–10.9), p<0.05). Comparing PAD activity in saliva samples of RA patients we found significant differences between the low (2.3±0.5), moderate (3.4±0.8) and high (4.3±0.3) disease activity subgroups (p<0.01%), whereas patients in remission demonstrated a PAD activity similar to the low disease activity group (1.9±0.39). Additionally, we found a significant correlation between oral PAD activity and RA activity, but not with autoantibody titers.

Conclusions: These results show that RA activity is associated with severe periodontitis, high oral PAD activity and the presence of T. forsythia and P. gingivalis, suggesting that both bacteria equally participate in PAD activity present in the oral microenvironment.

Acknowledgements: Disclosure: This work was supported by a grant from SEP/CONACYT CB-2010 (#155392).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3894
A NOVEL PHARMACOLOGICAL ACTION OF MTX THROUGH CIRCADIAN CLOCK GENES IN RA FIBROBLAST-LIKE SYNOVIAL CELLS

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Background: Methotrexate inhibits the proliferation of RA fibroblast-like synovial cells (RA-FLS) by folic acid metabolism. We previously reported that disruption of circadian clock genes was involved in the pathogenesis of inflammatory arthritis (1,2).

Objectives: To explore pharmacological effects of MTX on circadian clock genes of RA-FLS.

Methods: Under treatments of MTX on RA-FLS, cell viabilities were determined of RA-FLS.

Results: MTX (1,10 nM) treatment significantly decreased the cell viabilities. MTX (10nM) increased mRNA expression of Per2, BIK and CYTOCHROME C and morphological changes of the nucleus were observed by fluorescent immunostaining. RA-FLS were transfected with Per2 and BIK siRNAs and successively treated with MTX to determine cell viabilities.

Conclusions: The transcriptional factor PAR bZip binds to the D-box elements of Per2 and BIK promoters (3,4). Here, we propose a novel action of MTX that up-regulates the expressions of Per2 and BIK via PAR bZip to induce apoptosis in RA-FLS.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6757

FRIO0554

INCREASED EXPRESSION OF THE COLLAGEN INTERNALIZATION RECEPTOR ENDO180 IN FIBROBLAST-LIKE SYNOVIOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Hyperproliferative and invasion are the characteristics of fibroblast-like synoviocytes in rheumatoid arthritis (RA-FLSs), which contribute mainly to RA disease progression and ultimately to joint destruction. Endo180 is a recycling endocytic receptor that has functions to regulate cell migration and bind and internalize collagen. However, the expression of Endo180 in RA-FLSs and its underlying mechanisms remain unclear.

Objectives: To examine the expression of Endo180 in RA-FLSs and the role it played in RA.

Methods: Tissues were collected from RA patients with joint replacement surgery or arthroscopy and RA-FLSs were obtained by tissue culture; Western blot was used to measure the expression of Endo180 in RA-FLSs. Chemically synthesized small interference RNA (siRNA) specifically targeting Endo180 gene was transfected into RA-FLSs by cationic liposome; The interference efficiency of Endo180-siRNA on the production of Endo180 mRNA and protein was determined by RT-qPCR and Western blot respectively; The proliferative inhibition rate was examined by CCK8 assay and the migration of RA-FLSs were examined by Transwell assay.

Results: Expression of Endo180 was obviously higher in fibroblast-like synoviocytes in RA than OA and the traumatic patients. And its expression level has positive correlation with disease activity. The proliferative inhibition rate was obviously higher in the Endo180-siRNA group than the control groups (P<0.05) after transfection for 48h (83.11±1.17%), 72h (15.93±2.12%), 96h (18.01%±2.78%); Transwell migration assay demonstrated the RA-FLSs through the transwell membrane in Endo180-siRNA group (21.27±6.35) were lesser than the NC-siRNA group (80.20±11.12) (P<0.05) and the blank control group (82.17±10.36) (P<0.05).

Conclusions: Endo180 may play a role in the regulation of proliferation and migration of RA-FLSs, which may provide beneficial therapeutic effects in RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5162

FRIO0555

HISTONE DEACETYLASE 1 (HDAC1): A NOVEL THERAPEUTIC TARGET IN RHEUMATOID ARTHRITIS

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Background: Autoactive T cells have been shown to play a major role in Rheumatoid Arthritis, which drive the inflammatory process leading to an important destruction of the joints. Gene transcription and regulation of proinflammatory cytokone production in T cells is regulated by epigenetic mechanisms. Histone deacetylases (HDACs) modify the epigenetic landscape by removing acetyl groups of lysine residues of histones, resulting in chromatin condensation and repression of transcription. The application of pan-HDAC inhibitors has been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underline the need of more specific HDAC inhibitors.

Objectives: Our aim was to to investigate whether HDAC1 is linked with the development of autoimmune diseases. Therefore we were using the collagen-induced arthritis model (CIA) and the experimental autoimmune encephalomyelitis model (EAE).

Methods: Mice with a T cell specific deletion of HDAC1 (HDAC1cKO) were generated by using the CD4Cre/LoxP system. The clinical and the histological phenotype were assessed in the CIA and the EAE. Anti-collagen antibody levels were determined by ELISA. Qualitative and quantitative analysis of T cell subsets of the spleen and draining LN were assessed using flow cytometry. Additionally comparative RNA-sequencing of CD4+ T cells from wild type (WT) and HDAC1cKO mice was performed.

Results: To address whether HDAC1 is involved in the pathogenesis of autoimmune diseases we induced the CIA and the EAE in WT and HDAC1cKO mice. Unexpectedly, HDAC1cKO mice did not develop any clinical or histological signs of inflammation, despite the presence of serum anti-CII antibodies. A similar protection against disease development was also observed in the context of EAE. A molecular analysis of HDAC1cKO CD4+ T cells revealed increased STAT1 phosphorylation in activated HDAC1cKO CD4+ T cells in comparison to WT cells. This was accompanied with an impaired expression of CCR6 in activated HDAC1cKO CD4+ T cells, which is an essential chemokine receptor for the development of arthritids and EAE. In line with this finding we observed increased expression of CCR6 in STAT1−/− CD4+ T cells. This indicates a negative role of STAT1 in the regulation of CCR6 expression.

Conclusions: Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of collagen induced arthritis. Therefore it might be considered as an interesting novel therapeutic target in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3351
**FR10057** EVALUATION OF THE IMMUNODOMINANCE OF A HISTONE H4 PEPTIDE IN ANTI-CCP ANTIBODIES FROM RHEUMATOID ARTHRITIS PATIENTS

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**Background:** The anti-CCP assay identifies antibodies against endogenous citrullinated proteins that are not completely characterized. The histone H4 seems to be a prominent one according to a recent study (1), which found this protein specifically in the immune complexes from synovial fluid of anti-CCP positive RA patients. Only vimentin, among the previously proposed autoantigens, was present in those immune complexes, but its abundance was much lower than that of histone H4. Consequently, a citrullinated H4-derived peptide, H4-c39/40, showed marked immunodominance since antibodies directed against this peptide were present in 100% of synovial fluid samples and in 92–94% of anti-CCP positive sera. These frequencies are much larger than the reported with other autoantigens.

**Objectives:** To confirm the immunodominance of the H4-c39/40 peptide in anti-CCP antibodies from RA patients by direct comparison with citrullinated peptides of two other potential autoantigens.

**Methods:** Five hundred and thirteen patients with established RA and 273 healthy controls were included. Antibodies against H4-c39/40, rFibB36–52 and rMIF 7C were evaluated using indirect ELISA. Concordance between positives and negatives was analyzed with the Goodman and Kruskal’s gamma coefficient (γ).

**Results:** In contrast to the previous report (1), only 68.5% of the anti-CCP positive patients carried anti-H4-c39/40 antibodies. However, this frequency was higher than the observed with the other two peptides, 50.5% of anti-FibB36–52 and 28.8% of anti-rMIF60–75 positive patients. Consequently, a high concordance was found between anti-CCP and anti-H4-c39/40 antibodies (γ = 0.95), which was moderately larger than that observed between anti-CCP and anti-rFibB36–52 antibodies (γ = 0.86). In addition, anti-H4-c39/40 antibody titers were correlated with anti-CCP titers, but this correlation was similar to the observed between anti-rFibB36–52 and anti-CCP titers (r = 0.34 and 0.33, respectively). The anti-rMIF60–75 antibodies, in turn, showed notably low concordance and low correlation with the anti-CCP antibodies.

**Conclusions:** Our results confirm that anti-H4-c39/40 antibodies are a significant component of the antibodies detected with the anti-CCP assay. However, immunodominance of this peptide was not as marked in our patients as the described in the original study.

**References:**
2. This study was supported by funding from the National Council of Science and Technology (CONACYT) Grant #161749 assigned to JFMV.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4566

**FR10058** EFFECT OF MIF GENE HAPLOTYPES ON RHTNF-A AND RHMIH RESPONSE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine that plays important role in the development and pathogenesis of rheumatoid arthritis (RA). MIF promotes the expression of cytokines related to RA development, as tumor necrosis factor alpha (TNF-α) and interleukin (IL)-6 and IL-17. Two polymorphisms in the promoter of the MIF gene have been associated with increased production of protein and it has been shown that TNF-α is involved in the regulation of MIF mRNA expression and protein secretion in a dose-dependent manner.

**Objectives:** To evaluate the effect of MIF gene haplotypes on rHTNF-α and rHMIH response in peripheral blood mononuclear cells (PBMC) of RA patients.

**Methods:** Genotyping was performed for MIF gene haplotypes in 230 RA patients. Cell culture of PBMC from two patients per homozygous haplotype (5G, 6G and 7C) was performed and stimulated with rHTNF-α and rHMIH. Cytokine levels were analyzed by a microsphere-based ELISA method (Bio-Plex® MAGPIX™).

**Results:** rHTNF-α and rMIF-induced IL-6, IL-17A and IL-17F secretion in PBMC of RA patients. We observed that PBMC extracted from patients with MIF 7C haplotypes stimulated with rHTNF showed higher secretion of IL-17A and IL-17F than patients with 5G and 6G haplotypes. IL-6 production with rMIF stimulation was more pronounced in the 5G haplotype group than 6G or 7C haplotype groups. Conversely, in a MIF responsive model, rhTNF promote chronic inflammatory joint and intestinal diseases.

**Conclusions:** Similarly to human RA patients, TNF-driven arthritis models develop multiple RA-associated comorbidities, offering novel insights into potential molecular and cellular mechanisms commonly underlying these complex pathologies.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5142
MONOCYTE-DERIVED MICROPARTICLES IN CIRCULATION OF PATIENTS WITH RHEUMATOID ARTHRITIS: A NOVEL BIOMARKER FOR THE DISEASE ACTIVITY

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Background: Rheumatoid arthritis (RA) is a systemic connective tissue disease and characterized by inflammation of synovium of multiple joints, however, its pathogenesis is still unclear (1). Physiologically, microparticle (MP) is categorized as a membrane microvesicle which contains various humoral factors such as cytokines or growth factors and 0.1–1 μm in size (2). And MPs can distribute systemically through circulation. MP is released from almost all cell types and induced by stimulation, stress or apoptosis (3). Thus, we hypothesized that MPs derived from various cells contribute to the lesion of RA and be associated with systemic disease process of RA.

Objectives: To clarify the source of MPs in circulation of RA and elucidate their role in the pathogenesis and the possibility for application as a novel disease marker.

Methods: Twenty patients with RA and 13 healthy controls were involved. Using gradient centrifugation, platelet-rich plasma was isolated from whole blood and applied to flow cytometry. MP is defined as a vesicle less than 1 mm in diameter and Megamix® was used to set a gating condition to detect microparticles (4). Subsequently, MPs were identified by the expression of cell-specific markers using flow cytometry with fluorescently labeled antibodies as follows: platelets: CD41+CD62P+; monocytes MP: CD45+CD41- MP, MP derived from other cells: CD41-CD31-CD45- MP. U-test with Bonferroni correction. Significant difference was defined as corrected p-value ≤ 0.01

Results: Mean age of 20 patients with RA was 56±14 years, 95% was female, disease duration was 6.5±3.0 years, and DAS28-ESR was 2.0±1.1. Methotrexate was administered to 15 patients, average dose was 8.0±2.4 mg/week. Platelet-derived MP covered the largest proportion in all groups. Interestingly, proportion of immune-cell-derived MP was higher (P<0.001) in patients with RA compared to controls. Proportion of immune-cell-derived MP was positively correlated with inflammatory markers such as CRP and composite disease activity markers such as DAS28-ESR. Furthermore, when stratified by monocyte fraction and non-monocyte fraction based on CD14 expression, proportion of immune-derived MP showed higher (P<0.01) in patients with RA compared to controls, but non-monocytes MP did not, and that of monocyte-derived MPs was also correlated with disease markers for activity of RA.

Conclusions: Proportion of circulating immune-cell-derived MPs, especially monocyte-derived MPs, increased in RA and correlate with disease activity. These results suggest that monocyte-derived MPs can be measured as a novel biomarker and involved in the disease process of RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4599

FRI0060 SYNIOVAL FLUID TREG CELLS SECRETE IL-17 AND AT THE SAME TIME ARE POTENT SUPPRESSORS OF TRESP CELL PROLIFERATION. TNF ALPHA AND IFN GAMMA PRODUCTION

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Background: IL-17-expressing FoxP3 regulatory T cells have been described, and their suppressive capacity has been questioned. An inflammatory environment seems to favor IL-17 secretion by regulatory CD4+CD25+FoxP3+ T cells. However, other cytokines or growth factors and 0.1–1 μm in size (2). And MPs can distribute systemically through circulation. MP is released from almost all cell types and induced by stimulation, stress or apoptosis (3). Thus, we hypothesized that MPs derived from various cells contribute to the lesion of RA and be associated with systemic disease process of RA.

Objectives: To clarify the source of MPs in circulation of RA and elucidate their role in the pathogenesis and the possibility for application as a novel disease marker.

Methods: Twenty patients with RA and 13 healthy controls were involved. Using gradient centrifugation, platelet-rich plasma was isolated from whole blood and applied to flow cytometry. MP is defined as a vesicle less than 1 mm in diameter and Megamix® was used to set a gating condition to detect microparticles (4). Subsequently, MPs were identified by the expression of cell-specific markers using flow cytometry with fluorescently labeled antibodies as follows: platelets: CD41+CD62P+; monocytes MP: CD45+CD41- MP, MP derived from other cells: CD41-CD31-CD45- MP. U-test with Bonferroni correction. Significant difference was defined as corrected p-value ≤ 0.01

Results: Mean age of 20 patients with RA was 56±14 years, 95% was female, disease duration was 6.5±3.0 years, and DAS28-ESR was 2.0±1.1. Methotrexate was administered to 15 patients, average dose was 8.0±2.4 mg/week. Platelet-derived MP covered the largest proportion in all groups. Interestingly, proportion of immune-cell-derived MP was higher (P<0.001) in patients with RA compared to controls. Proportion of immune-cell-derived MP was positively correlated with inflammatory markers such as CRP and composite disease activity markers such as DAS28-ESR. Furthermore, when stratified by monocyte fraction and non-monocyte fraction based on CD14 expression, proportion of immune-derived MP showed higher (P<0.01) in patients with RA compared to controls, but non-monocytes MP did not, and that of monocyte-derived MPs was also correlated with disease markers for activity of RA.

Conclusions: Proportion of circulating immune-cell-derived MPs, especially monocyte-derived MPs, increased in RA and correlate with disease activity. These results suggest that monocyte-derived MPs can be measured as a novel biomarker and involved in the disease process of RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4599
RESVERATROL ATTENUATES SYNOVIAL HYPERPLASIA IN AN ACUTE ANTIGEN-INDUCED ARTHRITIS MODEL BY AUGMENTING AUTOAPOTHEXY AND DECREASING ANGIGENESIS

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Background: Previously, we have demonstrated that dietary supplementation with resveratrol lowers synovial hyperplasia, inflammatory markers and oxidative damage in an acute antigen-induced arthritis (AIA) model.

Objectives: In this work, we investigated whether resveratrol can also regulate this abnormal proliferation of synovial tissue in an acute AIA model by inducing cell death pathways and by modifying angiogenesis in the synovial membrane.

Methods: Animals were randomly divided into 3 groups: control, AIA, and resveratrol-treated AIA group. Resveratrol (12.5 mg/kg/day) was given orally 8 weeks before AIA induction until sacrifice day (48 h after intra-articular injection). Control and AIA animals were administered 100 μl of water. Resveratrol effects on apoptosis and angiogenesis were evaluated by LC3 and active caspase-3 expression (confocal and immunohistochemistry, respectively). Angiopoietin 1 (Ang-1) and vascular endothelial growth factor (VEGF), and the mouse factor NF-kappa-B p65 subunit (p65) were also determined by immunohistochemistry and cartilage degradation with Safranin-O.

Results: Resveratrol significantly reduced the histological score of synovial tissue. Results showed a significant higher expression of LC3 signals in the synovial membranes, compared with control samples, in which the presence of vesicles was easily observed. Interestingly, the synovial tissues from the resveratrol group showed a significantly higher signal for LC3, compared with the AIA samples. Active caspase-3 expression was up-regulated at the same level in the synovial membranes of AIA group than in resveratrol-treated AIA group; however, in resveratrol-treated AIA group active caspase-3 signal was mainly located in the inflammatory cells. Resveratrol consumption significantly attenuated Ang-1 signal, whereas expression of VEGF showed a non significant reduction. Resveratrol administration also mitigated, even not significantly, p65 expression that was significantly higher in the AIA animals than those from the control animals. In addition, resveratrol decreased articular cartilage degradation.

Conclusions: These data suggest that resveratrol is able to modulate synovial hyperplasia by increasing apoptotic cell death and limiting angiogenic response in an acute AIA model, which could also modulate the inflammatory and destructive processes for rheumatoid arthritis.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6270

CHEMOKINE RECEPTOR 6 MODULATES ARTHRITIS IN A T CELL DEPENDENT MANNER

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Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease, characterized by synovial infiltration of various cells. Chemokines are involved in the recruitment of different cell types into the synovial membrane. Accumulation of CCR6 expressing mononuclear cells can be found in joints of RA patients. CCR6 expression has also been reported on CD4+ T cells, in particular regulatory as well as Th17 cells. In addition, a subset of regulatory T cells, namely CD25+Foxp3+ T cells, can upregulate CCR6 and RANKL and thereby can promote osteoclastogenesis.

Objectives: In this study, we investigated the role of CCR6 in the pathogenesis of arthritis using different arthritis models.

Methods: Clinical as well as histological signs of arthritis were investigated in the collagen-induced arthritis (CIA), K/BxN serum transfer arthritis and in the human tumor necrosis factor (TNFα-)/- mice model. We analyzed the phenotype of lymph node cells by flow cytometry and cytokine concentrations in serum. Anti-collagen antibodies and cytokines were measured by enzyme-linked immunosorbent assay.

Results: The K/BxN serum transfer arthritis and hTNFtg arthritis model are known to be T cell independent. Since CCR6 is an important component of the innate immune system we compared the development of arthritis in both models. We did not detect any significant differences in clinical signs of inflammation or histological severity of arthritis between wt and CCR6-/-mice. In addition, bone volume was similar between wt and CCR6-/- mice. To investigate the role of CCR6 as part of the adaptive immune system in the development of arthritis we induced CIA in wt and CCR6-/- mice, which is known to be T cell dependent. CCR6-/- mice were almost completely protected from CIA. Indeed, analyses of T cell subsets by flow cytometry revealed a significant reduction of CD25 Foxp3+ T cells in CCR6-/- mice.

Conclusions: CCR6 is necessary for the generation of pathogenic CD25 Foxp3+ T cells in CIA, suggesting an important function of CCR6 on T cells in the development of autoimmune arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3065
Conclusions: Our group demonstrated for the first time GRP expression in FLS and that GRP are able to activate FLS invasion through AKT pathway. Finally, our results suggest that GRP/GRPR pathway could be relevant in the development of FLS-targeted therapy for RA.

References:

Acknowledgements: FIEP-HCPA, CAPES, CNPq.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-early.2484

MICRONA PROFILING OF MTX-TREATED FIBROBLAST-LIKE SYNOVIAL CELLS IN RHEUMATOID ARTHRITIS REVEALED A POSSIBILITY OF MICRONA-887-3P AS NOVEL THERAPEUTIC TARGET OF RA

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Background: The hallmarks of rheumatoid arthritis (RA) is the expansive of fibroblast-like synovial cells (FLS) in affected joints, causing joint destruction. FLSs are resistant to programmed cell death resulting in aggressive, invasive phenotype like a cancer invades and the hyperplastic synovial tissue destroys cartilage and bone. Therefore inhibition of FLS proliferation is one of the therapeutic targets of RA. MicroRNAs (miRNAs), a group of small non-coding RNAs, have been shown to regulate cell differentiation through regulation of gene expression post-transcriptionally. Recently, several studies reported anti-cancer drugs modulate miRNA expression and that have been considered as one of important mechanism of cellular action to drug.

Objectives: To investigate the changes in microRNA expression profiles in response to MTX.

Methods: RA-FLS were treated with MTX with 1nM 48 hours, that could inhibit IL-6 production from RA-FLS. To investigate differentially expressed miRNAs in response to MTX, we performed miRNA array analysis. Expression of miR-887–3p in response to MTX of RA-FLS was analyzed by quantitative real-time PCR. To investigate the functional role of miR-887–3p, RA-FLS was transfected with synthetic precursor miR8–3p (anti-miR) of miR-887–3p using Lipofectamine and then gene expression microarray was performed. The cytokine/chemokine production was screened by Multiplex cytokine/chemokine bead assays and confirmed by ELISA. Finally, we analysed migratory activities of RA-FLS by scratch assay.

Results: After 48 h of treatment with MTX, 7 miRNAs were up-regulated and 6 miRNAs were down-regulated as compared with that of untreated control. Among them quantitative real-time PCR with additional samples confirmed that miR-887–3p was up-regulated in response to MTX treatment of RA-FLS. 1.7±0.46-fold, p<0.05, n=7). To elucidate the functional consequence of the deregulation of miR-887–3p of RA-FLS, we performed gain-and-loss of function assays with miR-887–3p. Microarray analysis with gene ontology analysis revealed several genes correlated with cell signalling was modulated by miR-887–3p. Multiplex bead assay showed that overexpression of miR-887–3p decreased cytokine/chemokine production of RA-FLS such as TNF-a, GM-CSF, CCL4. Among these candidates, the secretion of GM-CSF was consistently and strongly decreased from RA-FLS transfected with pre-miR-887–3p. Furthermore overexpression of miR-887–3p reduced migratory activity of RA-FLS in scratch assay.

Conclusions: Our result revealed that miRNA expression profiles in RA-FLS. MiR-887–3p might be downstream effector of MTX in suppression of its cytokine production and invasive phenotype. This knowledge may also be useful for the development of novel therapeutic strategies for RA based on other treatments able to boost the cellular reservoir of miR-887–3p.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-early.3327

REDUCTION OF PROLIFERATION, MIGRATION AND INVASION OF RHEUMATOID SYNOVIOCYTES BY ALL-TRANS RETINOIC ACID

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Background: Fibroblast-like synovial cells (FLS) are pivotal in inflammatory and joint destruction of rheumatoid arthritis (RA). These cells proliferate, become resistant to apoptosis, migrate and invade, contributing to perpetuate synovial inflammation and destruction of cartilage and bone. Current treatments of RA are focused against inflammatory factors and immune cells, however, a significant percentage of patients do not successfully respond. Combined treatments with drugs that control inflammation and with others that reverse the pathogenic phenotype of FLS could improve the prognosis of these patients. An unexplored area includes vitamin A and its metabolites. These compounds modulate differentiation, development, apoptosis and proliferation. Indeed, retinoids are being successfully used in the treatment of several cancers for their anti-proliferative and pro-differentiative actions. In addition, several studies have shown a notable reduction of cell migration and invasion in different cell types after treatment with all-trans retinoic acid (ATRA). However, it is not known if ATRA could modify the migratory and invasive ability of rheumatoid synoviocytes.

Objectives: To analyse the effect of treatment with the retinoid all-trans retinoic acid in proliferation, migration and invasion of rheumatoid synoviocytes.

Methods: FLS were obtained from 8 RA patients. Cellular proliferation was determined using the CellTiter-Blue luminescent viability assay (Promega). Migration was analysed by wound healing assay, using ibidi inserts. Percentage of migrating cells was determined by Image J. Invasion was tested by the Boyden chamber method using inserts (Millicell) coated with Matrigel (BD Biosciences). Invasion was determined by quantification of Giemsa stained cells on the bottom side of the inserts under the microscope. Proteome analysis was performed using LC-MALDI-TOF/TOF and 1D- and 2D-gels. MS and MS/MS data was searched against the UniProt/Swiss-Prot database of protein sequences.

Results: We analysed the effect of ATRA in the spontaneous proliferation of FLS from 8 RA patients. ATRA treatment significantly inhibited proliferation at 48, 72 and 96 h (p<0.005; p<0.002; p<0.04; respectively). Next, we analysed the effect of ATRA on RA FLS migration and invasion. Migration of RA FLS treated with ATRA for 96 h was reduced by 46% when compared with cells treated with vehicle control (p<0.002). In addition, in wound healing assay showed that ATRA treatment, as the invaded area was 31% lower than in controls (p=0.018). To elucidate the mechanisms underlying the effects of ATRA on RA FLS a proteomic analysis was performed. We compared the proteome of FLS from 5 RA patients treated with ATRA or with vehicle using LC-MALDI analysis. The differentially identified proteins in ATRA-treated FLS vs control FLS were Septin, Rho GTPase activating protein (ARHGAP1) and actin related protein 2 (ARPP2). Validation experiments using 1-DE and 2-DE gels were performed.

Conclusions: Overall these results reveal that retinoid treatment reduces the proliferative, migratory and invasive capacity of RA FLS, indicating that this treatment could decrease joint damage and loss of function in RA patients.

Acknowledgements: Supported by grant PI14/1153 of the ISCIII (Spain), partially financed by FEDER.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3327
Background: MicroRNAs (miRNA) are a new class of modulators of gene expression, regulating inflammation, degradation of extracellular matrix and invasive behavior of the resident cells in rheumatoid arthritis (RA).

Objectives: 1) To investigate the miRNA expression profile in synovial and blood neutrophils in RA and its role in the pathogenesis of this disorder. 2) To study the effects of biological therapies on the miRNA profile in neutrophils.

Methods: Neutrophils were isolated from peripheral blood (PB) of 25 healthy donors (HD) and 25 RA patients. Neutrophils were isolated from paired synovial fluid (SF) of 15 RA patients. nCounter miRNA Assay was used to detect 800 human microRNAs simultaneously. Altered miRNAs were analyzed for potential miRNA targets using Ingenuity pathways analysis (IPA) software. miRNA targets and genes involved in miRNA biogenesis were evaluated. RA neutrophils were treated in vitro with tocilizumab and infliximab. Healthy neutrophils were treated in vitro with anti-CCPs isolated from RA patients alone or combined with tocilizumab or infliximab. RA neutrophils were cotransfected with the pre-miRNA 126 and 148.

Results: 94 miRNAs were downregulated and 3 upregulated in PB neutrophils from RA patients compared to HD. Among the miRNAs deregulated in blood, 34 miRNAs were also downregulated in SF neutrophils from RA patients. Accordingly, RA neutrophils showed a downregulation of the proteins participating in miRNA biogenesis and upregulation of its mRNA targets. Altered miRNAs were mainly involved in immunological disease and inflammatory response, suggesting the abnormal activation of this cell subtype in RA. In vitro treatment of RA neutrophils with tocilizumab and infliximab increased the expression of miRNAs, genes involved in their biogenesis and reduced the inflammatory profile in these cells. In addition, treatment of healthy neutrophils with IgG anti-CCPs isolated from RA patients decreased the expression of the miRNAs proteins, involved in the biogenesis machinery and increased its inflammatory targets. Finally, cotransfection of RA neutrophils with the pre-miRNAs 126 and 148 reduced the levels of their target proteins.

Conclusions: 1) RA neutrophils exhibit a defect in the miRNAs processing, showed by a decrease in most of the detected miRNAs and the downregulation of proteins involved in their biogenesis. This defect seems to be modulated by anti-CCPs antibodies. 2) miRNA downregulation is even more pronounced in synovial neutrophils isolated from RA patients compared to HD. Among the miRNAs deregulated in blood, 34 miRNAs were also downregulated in SF neutrophils from RA patients. Accordingly, RA neutrophils showed a downregulation of the proteins participating in miRNA biogenesis and upregulation of its mRNA targets. Altered miRNAs were mainly involved in immunological disease and inflammatory response, suggesting the abnormal activation of this cell subtype in RA. In vitro treatment of RA neutrophils with tocilizumab and infliximab increased the expression of miRNAs, genes involved in their biogenesis and reduced the inflammatory profile in these cells. In addition, treatment of healthy neutrophils with IgG anti-CCPs isolated from RA patients decreased the expression of the miRNAs proteins, involved in the biogenesis machinery and increased its inflammatory targets. Finally, cotransfection of RA neutrophils with the pre-miRNAs 126 and 148 reduced the levels of their target proteins.
the development of arthritis or are rather a consequence of the inflammatory processes. Furthermore, while both germ-free condition and administration of oral antibiotics prevent arthritis in mice, it is unclear whether modulation of the intestinal microbiota after the onset of arthritis may still suppress the disease.

Objectives: We aimed to assess potential alterations of the intestinal microbiome in the preclinical phase of inflammatory arthritis in mice, and to determine the efficacy of microbiota modulations in the treatment of established disease in mice.

Methods: We sequenced fecal bacterial 16S rRNA to define the intestinal microbiome in mice before immunization with collagen and 21 days later before the booster injection for the induction of collagen-induced arthritis (CIA). To assess the efficacy of microbiota modulation during arthritis, mice with ongoing CIA were treated orally by a broad-spectrum antibiotic cocktail for one week to partially eliminate the intestinal microbiota. T cell differentiation and production of cytokines in intestinal lamina propria and joint-draining lymph nodes were assessed by flow cytometry. Immunohistochemistry and confocal microscopy were used to assess macroscopically and by histology. Serum-transfer arthritis induced by intraperitoneal injections of arthrogenic K/BxN mouse serum was used as a control. T cell-independent, model.

Results: The preclinical phase of inflammatory arthritis in mice was characterized by marked changes in the intestinal microbiome, represented by a significant increase of the phylum Bacteroidetes and a decrease of Firmicutes and Proteobacteria. Among the most abundant bacterial families, S24–7 and Staphylococcaceae were expanded, whereas Lachnospiraceae were reduced during the immune priming phase of CIA. Several operational taxonomic units associated with CIA were expanded, whereas those assigned to Lachnospiraceae and Ruminococcaceae were expanded in the intestinal microbiota before the clinical onset of arthritis. The abundance of intestinal lamina propria Th1 cells significantly correlated with the severity of CIA; however, intestinal Th1 cells were not correlated with the disease. Elimination of intestinal microbiota in mice with ongoing CIA significantly reduced intestinal Th1 cell differentiation without affecting Th1 and Treg cells. Importantly, elimination of intestinal microbiota suppressed Th1 cell differentiation and IL-17 production in joint-draining lymph nodes, and reduced the severity of established CIA. In contrast, the T cell-independent serum-transfer arthritis induced by T cell-independent arthritis (T CIA) was not affected by this strategy.

Conclusions: These observations suggest that perturbations of the intestinal microbiome may precede the development of inflammatory arthritis. Similar studies are warranted in human pre-RA or at-risk individuals to shed light on the functional role of the microbiome in the development of RA. Our studies also suggest that modulation of the intestinal microbiota after the onset arthritis may still provide opportunities to treat inflammatory arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5533

FR0074 | ANTI-INFLAMMATORY EFFECT OF RESVERATROL IN VITRO; POTENTIAL ROLE IN MANAGING LOW DISEASE ACTIVITY IN ARTHRITIS?
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Background: Resveratrol (RSV), a non-toxic polyphenol found in grapes, certain nuts, roots etc., has received increased attention in the last decade due to its anti-inflammatory potential. Perturbations of the intestinal microbiota may precede the development of inflammatory arthritis. Similar studies are warranted in human pre-RA or at-risk individuals to shed light on the functional role of the microbiome in the development of RA. Our studies also suggest that modulation of the intestinal microbiota after the onset arthritis may still provide opportunities to treat inflammatory arthritis. The preclinical phase of inflammatory arthritis in mice was characterized by marked changes in the intestinal microbiome, represented by a significant increase of the phylum Bacteroidetes and a decrease of Firmicutes and Proteobacteria. Among the most abundant bacterial families, S24–7 and Staphylococcaceae were expanded, whereas Lachnospiraceae were reduced during the immune priming phase of CIA. Several operational taxonomic units associated with CIA were expanded, whereas those assigned to Lachnospiraceae and Ruminococcaceae were expanded in the intestinal microbiota before the clinical onset of arthritis. The abundance of intestinal lamina propria Th1 cells significantly correlated with the severity of CIA; however, intestinal Th1 cells were not correlated with the disease. Elimination of intestinal microbiota in mice with ongoing CIA significantly reduced intestinal Th1 cell differentiation without affecting Th1 and Treg cells. Importantly, elimination of intestinal microbiota suppressed Th1 cell differentiation and IL-17 production in joint-draining lymph nodes, and reduced the severity of established CIA. In contrast, the T cell-independent serum-transfer arthritis induced by T cell-independent arthritis (T CIA) was not affected by this strategy.

Results: The preclinical phase of inflammatory arthritis in mice was characterized by marked changes in the intestinal microbiome, represented by a significant increase of the phylum Bacteroidetes and a decrease of Firmicutes and Proteobacteria. Among the most abundant bacterial families, S24–7 and Staphylococcaceae were expanded, whereas Lachnospiraceae were reduced during the immune priming phase of CIA. Several operational taxonomic units associated with CIA were expanded, whereas those assigned to Lachnospiraceae and Ruminococcaceae were expanded in the intestinal microbiota before the clinical onset of arthritis. The abundance of intestinal lamina propria Th1 cells significantly correlated with the severity of CIA; however, intestinal Th1 cells were not correlated with the disease. Elimination of intestinal microbiota in mice with ongoing CIA significantly reduced intestinal Th1 cell differentiation without affecting Th1 and Treg cells. Importantly, elimination of intestinal microbiota suppressed Th1 cell differentiation and IL-17 production in joint-draining lymph nodes, and reduced the severity of established CIA. In contrast, the T cell-independent serum-transfer arthritis induced by T cell-independent arthritis (T CIA) was not affected by this strategy.

Conclusions: These observations suggest that perturbations of the intestinal microbiome may precede the development of inflammatory arthritis. Similar studies are warranted in human pre-RA or at-risk individuals to shed light on the functional role of the microbiome in the development of RA. Our studies also suggest that modulation of the intestinal microbiota after the onset arthritis may still provide opportunities to treat inflammatory arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1701
RA group exhibited significant bone quality abnormalities including deterioration of the bone microstructure, decreased calcification of the bone matrix, increased osteocyte atrophy and empty lacunae (Figure), and an impairment bone material strength properties.

<table>
<thead>
<tr>
<th>Control</th>
<th>RA</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>FRAX score (%)</td>
<td>Mean</td>
<td>Mean</td>
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<tr>
<td>Major osteoporosis fx.</td>
<td>10.7±4.8</td>
<td>33.5±8.9</td>
</tr>
<tr>
<td>Femoral neck fx.</td>
<td>2.8±2.2</td>
<td>9.9±1.2</td>
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<td>Severity (# x grade)</td>
<td>4</td>
<td>29</td>
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<tr>
<td>Mechanical strength (N/mm)</td>
<td>218.8±24.6</td>
<td>164.9±36.5</td>
</tr>
</tbody>
</table>

Figure: Histological morphological deterioration of bone quality in RA patients receiving GCCs. (A-D) Representative photomicrographs of H&E stained sections of the specimens. Images show sections from Control (A, C) and RA groups (B, D). Boxed areas in B and D are shown at higher magnification in the indicated images. (E, F) Representative micrographs focused on osteoclasts of Control (E) and RA groups (F) with toluidine blue staining. Osteoclastic lacunae (red arrows) are out of shape and eminuous in RA patients. (G) Representative micrographs of Control (H) and RA groups (I) with immunostaining of sclerostin (black arrow). (J, K) Representative micrographs of Control (J) and RA group (K) with von Kossa staining. (L) Representative micrographs of Control (L) and RA groups (M) with immunostaining of sclerostin. (N) Representative micrographs of Control (P) and RA group (Q) with TRAP staining. Osteoclasts are stained red. Values shown are means ± SD (p < 0.05).

Conclusions: Our findings showed that RA patients receiving glucocorticoid treatment have severe bone fragility regardless of increased bone quantity by using bisphosphonate. The functional deteriorations of the osteocyte system and the abnormalities of bone quality might induce bone fragility fracture. Therefore, management of osteoporosis associated with RA should be targeted about bone quality as well as bone quantity.

References:

Acknowledgements: This project was supported in part by a Grant-in-Aid for Scientific Research (C) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan 25462357 (M. Takahata).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3514
aeroaciens had a complete opposite effect. Suppression of arthritis by P. histiola was dependent on an increase in the numbers of CD103+ dendritic cells, myeloid suppressors, CD11b+Gr-1, and T regulatory cells, CD4+CD25+FoxP3+, in the gut as well as systemically. This led to reduction in TH17 response while increasing IL-10. On the other hand, C. aeroaciens gavage increased expression of IL-17 and regulatory chemokines as compared to controls. DO11.10 mice gavaged with intestinal microbes of arthritis-resistant mice developed arthritis with lower incidence and had skewed Th17/Th2 response.

**Conclusions:** Our studies suggest that gut commensals influence immune response in and away from the gut. Commensals and their products may provide novel targets for therapeutic strategies in arthritis.

**Acknowledgements:** Funds were provided by the Department of Defense and Mayo Center of Individualized Medicine

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2307

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**FR10078** ADENOSINMONOFOSFAT-AKTIVATING PROTEIN KINASE (AMFK) – THE BIOPOWER REGULATOR OF AN AUTOPHAGY IN RHEUMATOID ARTHRITIS (RA)

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**Background:** Rheumatoid arthritis is an autoimmune disease characterized by altered cellular homeostasis. A great role of an autophagy is expected in the pathogenesis of these changes.

**Objectives:** To assess the functional activity of AMFK as a strategic biower regulator of an autophagy and specific indicator of red-ox potential of cells in the synovial fluid (SF) of patients with rheumatoid arthritis (RA)

**Methods:** SF of knee joints of 7 RA patients with active synovitis and 5 donors were investigated. Activity of enzymes was measured in cytosol of SF cells after ultracentrifugation. Activity of AMFK was estimated with the Western blotting method. The consumption speed of oxygen by SF cells was recorded polarographically using as the substrate glumatic acid (5 μmol/ml in incubation fluid). Registration of the active forms of oxygen was carried out by EPR (electron paramagnetic resonance). Levels of adenyl nucleotides were determined chromatographically.

**Results:** In RA SF we noted activation of AMFK (on average by 2.5 times) at the considerable increase of the AMP level and decrease in ADP and ATP.

**Conclusions:** These data demonstrate transition of cells of SF in RA to the energy saving mode of functioning that is followed by strengthening of oxidizing processes, deep dissociation of respiration with oxidizing phosphorylation and sharp increase of oxygen consumption spectated by SF cells glucose acid (5 μmol/ml in incubation fluid). Registration of the active forms of oxygen was carried out by EPR (electronic paramagnetic resonance). Levels of adenyl nucleotides were determined chromatographically.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5025

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**FR10079** TASS315, A NOVEL BRUTON’S TYROSINE KINASE INHIBITOR, IMPROVE BONE MINERAL DENSITY (BMD) AND BONE EROSION VIA INHIBITION OF OSTEOCLAST ACTIVATION IN MURINE MODEL FOR RHEUMATOID ARTHRITIS


**Background:** The erosions of bone and cartilage are a cardinal feature of rheumatoid arthritis (RA) and associated with disease severity and poor functional outcome. Although several anti-inflammatory drugs improve symptoms of articular inflammation, they are less effective against bone erosion. The bone erosions in RA are associated with aberrant activations of osteoclasts induced by pro-inflammatory cytokines and receptor activator of nuclear factor-κ B ligand (RANKL). Bruton’s tyrosine kinase (BTK), which is expressed in immune cells and mature osteoclast, is reported to be a key molecule in inflammatory response and bone resorption. Thus, targeting BTK may be efficacious against not only inflammation but also bone erosion through direct regulation of activation of effectors such as B cells, macrophages and osteoclasts in RA.

**Objectives:** In this study, we evaluated the effect of TASS315, a novel BTK inhibitor, on in vitro and in vivo bone erosion in mouse collagen-induced arthritis

**Methods:** Kinase selectivity of TASS315 was assessed by available kinase assay panels. The effects of TASS315 on macrophages and osteoclasts were assessed by examining phosphorylation of BTK, cytokine productions, osteoclast differentiation and bone resorptions. The effects of TASS315 were investigated in mouse collagen-induced arthritis (CIA). Disease severity was evaluated by clinical score of paw swelling. Changes in bone mineral density (BMD) and bone erosion were assessed using microCT. TNF blocker was used as a control drug.

**Results:** TASS315 selectively inhibited the enzyme activity of BTK and had less off target inhibition against other kinases. TASS315 dose-dependently inhibited cytokine productions by macrophages, phosphorylation of BTK, osteoclastogenesis and bone resorbing activity in osteoclasts. In established mouse CIA, TASS315 significantly ameliorated paw swelling in a dose dependent manner and the anti-inflammatory effect of TASS315 (0.3 mg/kg, once daily) was comparable to that of TNF blocker. Most importantly, improvement of BMD and bone erosion were observed in TASS315 treated mice at a doses of higher than 0.1 mg/kg within 13 days from treatment initiation, but not in TNF blocker-treated mice. The onset of action of TASS315 on BMD and bone erosion was earlier and stronger compared with that of TNF blocker. These data suggest that TASS315 had direct effect against osteoclasts function and led to improvement of bone erosion in murine model for RA.

**Conclusions:** Our study demonstrates that TASS315, a novel BTK inhibitor, would be an ideal RA therapeutic agent that could inhibit bone destruction as well as inflammation.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1761

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**FR10080** CD11b+Gr1dim TOLEROGENIC DENDRITIC CELL-LIKE CELLS ARE EXPANDED IN INTERSTITIAL LUNG DISEASE IN SKG MICE

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**Background:** SKG mice develop interstitial lung disease (ILD) resembling human rheumatoid arthritis (RA)–associated ILD. We identified a unique cell population of CD11b+Gr1dim cells in the severely inflamed lungs in SKG mice.

**Objectives:** The aims of this study is to clarify the mechanism behind the ILD pathology, and to elucidate the phenotype and function of CD11b+Gr1dim cells in ILD-induced SKG mice.

**Methods:** We assessed the severity of zymosan A-induced ILD in SKG mice histologically, and examined lung-infiltrating cells by Giemsa stain and flow cytometry. Total lung cells and isolated monocytic myeloid-derived suppressor cells (M-MDSCs) were cultured in vitro with GM-CSF (and IL-4). The proliferation of CSFE-labeled naïve T cells co-cultured with isolated CD11b+Gr1dim cells and M-MDSCs was evaluated by flow cytometry.

**Results:** MDSCs, Th17 cells, and group 1 and 3 innate lymphoid cells (ILC1s and ILC3s) were increased in the lungs; the proportion of these cells varied with ILD severity. In this process, we found that a unique cell population, CD11b+Gr1dim cells, were expanded in the severely inflamed lungs (Figure). About half of the CD11b+Gr1dim cells expressed CD11c and Giemsa stain revealed that they were morphologically dendritic cell (DC)-like. The CD11b+Gr1dim cells were induced from M-MDSCs with GM-CSF in vitro and were considered tolerogenic because they expressed high levels of PD-L1 and suppressed T-cell proliferation. The CD11b+Gr1dim cells have never described previously and termed CD11b+Gr1dim tolerogenic DC-like cells. (CD11b+Gr1dimDC-LCs). Th17 cells, ILC1s and ILC3s in the inflamed lung produced GM-CSF, which in turn could induce CD11b+Gr1dimDC-LCs to reduce inflammation.

**Conclusions:** We identified a unique cell population, termed CD11b+Gr1dimDC-LCs, in ILD-induced lungs in SKG mice.

**References:**

[1] Nishimura K, Saegusa J, Matsuki F, Akashi K, Kageyama G, Morinobu A. The authors thank Shino Tanaka (Department Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine) for providing technical assistance.
A MACAQUE MODEL OF RHEUMATOID ARTHRITIS BY IMMUNIZATION WITH CITRULLINATED PEPTIDES: LESSONS FOR THE HUMAN DISEASE

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Background: Recent evolution in the understanding of rheumatoid arthritis (RA) mechanisms is the role of antibodies directed against citrullinated (cit) proteins (ACPAs). The shared epitope (SE) on the MHC class II is the main genetic risk factor of RA and favors presence of ACPAs. Mouse models dependent on cit peptides immunization require transgenic expression of the SE and are controversial. Non-human primates are ideal to study the interaction between ACPA and RA since 8% carry, similarly to humans, the SE called the H6 haplotype.

Objectives: The goal of this study was to develop a new animal model of RA based on immunization of genetically predisposed macaques against cit peptides to generate an ACPA-mediated model of arthritis.

Methods: Six macaques were intra dermally (ID) immunized with 4 peptides: vimentin (59–71) and (66–78), α-lilogenin (79–91) and aggrecan (89–103). H6 animals were immunized with either cit (n=2) or arginine (arg) (n=2) containing peptides. Two non H6 animals were immunized with cit peptides. These peptides are known to induce a T cell response in RA patients carrying the SE. T-cell response was assessed with Interferon γ ELISPOT and B-cell response by ELISA. An intra articular (IA) boost was done 30 weeks after initial immunization with either incomplete Freund’s adjuvant (IFA) alone, IFA and cit peptides and IFA plus non relevant peptides.

Results: In the macaques, the T-cell response was specific to cit or arg peptides (depending on the peptides used for immunization). Surprisingly, the presence of the H6 epitope did not influence the response. Conversely the antibodies generated in response to the peptides were cross-reactive between the cit and arg peptides. Since no clinical response was observed, an IA boost was performed with the same 4 cit peptides and IFA adjuvant. This led to a prolonged neutrophil-rich mono-arthritis preferentially in H6 animals (Figure). Conversely, animals boosted with IFA alone only or with IFA plus myelin oligodendrocyte glycoprotein (MOG) peptides and previously immunized with MOG peptides presented with a transient mono-arthritis. Histological analysis revealed a local mononuclear infiltrate in one of the two animals that had prolonged knee monoarthritis. There was no clinical polyarthritis but 2 animals displayed synovial proliferation in 1 MCP and 1 MTP, respectively.

Conclusions: Immunization of macaques with cit peptides, then IA boost with the same cit peptides plus IFA, induced a prolonged monoarthritis. Shared epitope bearing did not restrict the T-cell response but seemed to favor the prolonged swelling after the IA boost. Neutrophil infiltration of the joint occurred similarly to what is seen in RA. Further use of neutrophil chemo-attractant might lead to a poly-articular disease. This macaque model of RA appears unique to study the events occurring during the pre-clinical phase of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2843

FR0082 RAS SIGNALING INHIBITORS ATTENUATE ARTHRITIS IN ANIMAL MODELS OF RHEUMATOID ARTHRITIS BY DOWN MODULATING THE PATHOGENIC TH17 CELL RESPONSE

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Background: Ras-GTPases are vital for normal T cell activation, and downstream effectors of Ras include the MEK/ERK, PI3 kinase/AKT, mTOR/p70S6-kinase, and NF-kB pathways. Somatic mutations in NRAS cause an autoimmune lymphoproliferative disorder and T cells from Rheumatoid Arthritis (RA) patients exhibit perturbation of the Ras/MEK/ERK pathway. The small molecule Farne-synthiosalicylic acid (FTS) inhibits the interaction between Ras-GTPases and prenyl-binding chaperones vital for proper plasma membrane localization and downstream signaling [1]. Previous pre-clinical studies suggested that FTS has an immunomodulatory effect in various animal models of autoimmunity [2].

Objectives: To test in the Lewis rat adjuvant induced arthritis (AIA) and in the DBA/1 mouse collagen type-II induced arthritis (CIA) models the therapeutic immunomodulatory effect of FTS alone or combined with methotrexate (MTX).

Methods: Arthritis was induced in 8–12 week old male Lewis rats by complete Freund’s adjuvant (CFA) injection and in male DBA/1 mice by collagen type-II (CII) immunization. Animals were treated prophylactically with once daily oral FTS (100 mg/kg); weekly i.p injection of MTX (0.5 mg/kg), oral FTS combined with MTX, or daily oral vehicle solution (0.5% carboxy methyl cellulose: CMC). Arthritis severity was scored daily from disease onset until study termination. In addition, we measured multiple disease- and drug-related immunological/molecular biomarkers.

Results: AIA severity was significantly reduced by FTS treatment compared to CMC controls (Figure 1A, P<0.001). Combining FTS and low dose MTX significantly increased its therapeutic efficacy compared to each drug alone (Figure 1A, P<0.05). FTS or FTS+MTX treatment also suppressed the upsurge in serum IL-17 and CRP compared to ailing controls. Global gene expression analysis of relevant splenic CD4+ T cells revealed that FTS is a potent inhibitor of pro-inflammatory and TH17 related gene networks. Next, our data from the mouse CIA model show that the therapeutic efficacy of FTS was non inferior to MTX and it significantly reduced arthritis severity compared to controls (Figure 2, P<0.001). Importantly, FTS significantly inhibited the production of pathogenic anti-IgG autoantibodies and upregulation of serum IL-6 and IL-17A compared to control arthritic mice. The in depth, multiplex, analysis of the effect of FTS on the T cell cytokine response to CII, revealed strong suppression of IL-22, IL-17, IL-9, GM-CSF and TNF production. Noteworthy, FTS therapy positively correlated with reduced Ras-GTP, p-ERK and p-AKT levels in splenic lymphocytes (drug related biomarkers).

Conclusion: FTS, a first-in-class oral selective Ras-GTPases inhibitor, exhibits a potent immunomodulatory effect in two classical murine model of arthritis, coupled with the inhibition of the TH17 response to relevant arthritogenic-antigens. Thus, Ras-signaling-blockade is a promising novel therapeutic approach for RA.

References:
REDUCED INCREASE OF ACPA IGG-FC GALACTOSYLATION DURING PREGNANCY IN COMPARISON TO TOTAL IGG: AN EXPLANATION WHY AUTOANTIBODY POSITIVE RA-PATIENTS IMPROVE LESS DURING PREGNANCY?

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Background: Rheumatoid arthritis (RA) disease activity (DAS28- CRP) improves less during pregnancy in autoantibody positive patients.1 The most specific autoantibodies for RA are anti-citrullinated protein antibodies (ACPA), which mainly occur as the immunoglobulin (Ig) G isotype. An association with DAS28- CRP and the pregnancy-associated improvement is well established for the Fc glycosylation of total IgG, in particular for galactosylation (Gal) and sialylation (SA).2 The Fc glycosylation of ACPAs – mainly present as IgG – has been reported to be different from the total IgG Fc glycosylation.3

Methods: ACPA positive patient sera (n=152) were obtained within the framework of the PARA cohort, a prospective study designed to investigate pregnancy-associated improvement of RA. ACPA IgG was isolated using microscale affinity chromatography. Trypsin digested ACPA IgG was measured using nano-liquid chromatography mass spectrometry, and compared to total IgG.

Results: Pregnancy-associated changes in the levels of glycosylation were observed for all ACPA IgG subclasses. Pregnancy-associated glycosylation changes were less pronounced during pregnancy and after delivery in ACPA IgG (Gal +5%; SA +0.5%) compared to total IgG (Gal +11%; SA +2.5%; Figure 1), but – for total IgG – not different between ACPA+ and ACPA- patients. No association of the change in DAS28-CRP with the change in ACPA IgG or total IgG galactosylation was observed for ACPA- patients, whereas a strong association of total IgG galactosylation was observed for ACPA+ patients.

Conclusions: During pregnancy the increase in galactosylation of ACPA IgG was less pronounced than that of total IgG, whereas the increase in the galactosylation of total IgG was not different between ACPA+ and ACPA- patients. Since it is known that changes in IgG galactosylation are associated with improvement of RA during pregnancy and since ACPA is thought to be of pathogenic significance in RA, our data might provide an explanation why ACPA+ RA patients are less likely to improve during pregnancy.

References:

Acknowledgements: This project is funded by the Dutch Arthritis Foundation (NR 10–1411) and by the European Union’s Seventh Framework Program (FP7- Health-F5–2011) under grant agreement no 278535 (HighGlycan). We thank Dr Jan Wouter Drijfhout (LUMC, Leiden) for providing the CCP2 peptide.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6229
of antibodies against individual citrullinated peptides (ACPAs; Hansson M et al. Arthritis Res Ther 2012;14:R201). We have also developed a method for the quantification of autoantibodies in immune complexes (IC; Sobhian et al. Ann Rheum Dis 2015;74(Suppl 1):A74). Here we have combined these techniques to determine ACPA profiles in RA IC.

Objectives: To investigate measurement of specific ACPA in synovial fluids (SF) and in IC from sera and SF can provide more prognostic information than conventional measurement of total ACPA and rheumatoid factor (RF) in serum.

Methods: Seventy-seven RA patients with knee synovitis were treated with intra-articular trimethiconel hexaconeotide, and followed until relapse. DAS28 and radiographic joint damage according to Larson-Dale were recorded. Anti-CCP2, IgM and IgA RF and circulating C1q-binding immune complexes (CIC) were determined in paired sera and SF. IC were purified from sera and SF by binding to C1q-coated beads, and thereafter eluted with a procedure developed in our laboratory. Antibodies against 19 citrullinated peptides were investigated with a custom-made microarray assay based on the ImmunoCAP ISAC system (Phadia AB, Sweden) in sera and SF as well as in IC from sera and SF. The target peptides were filaggrin 307–324 (CCP1), vimentin peptides 60–75 and 2–17, fibrinogen β563–583, α563–583, α560–600, δ21–75, δ26–74, δ26–81 (with citrullination in positions 72 and 74, respectively), ε-enolase 5–21 (CEP-1), peptides 1, 5, 21, 22 and Bla26 from hnRNPs, and histone 4 peptides 31–34 and 31–50. Cutoffs were established in relation to healthy controls. Backward stepwise regression was used to investigate what factors determined Larsen Dale index, DAS28, and steroid treatment. Independent factors with anti-CCP2-CPCP, IgM RF, IgA RF, CIC, number of ACPA peptide reactivities, and number of ACPA reactivities in IC, all measured both in serum and paired SF.

Results: A considerable proportion of anti-CCP2 negative patients had multiple ACPA in SF, and in IC fractions. High DAS28 associated with reactivity against 7/19 peptides in serum and 9/19 in SF. High Larsen score associated with number of specific ACPA in SF and IC with CIC in SF, DAS28 levels associated with IgM RF in SF and with CIC in SF, and steroid response duration with number of specific ACPA in serum and in IC.

Conclusions: We found that reactivity to ACPAs in SF, and especially in the IC fraction of SF, offers additional information beyond anti-CCP2 levels and allows radiological destruction and length of remission after intra-articular steroid therapy. Our data do not support a role for any unique ACPA specificity in RA pathogenesis. Instead, the number of individual ACPA specificities may be important.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3222

FR00086] EFFICACY AND SAFETY DATA BASED ON HISTORICAL OR PRE-EXISTING CONDITIONS AT BASELINE FOR PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WHO WERE TREATED WITH BARICITINIB

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Background: Patients (pts) with rheumatoid arthritis (RA) often experience comorbidities that may affect efficacy and safety when treated with different drugs. Baricitinib (BARI) is a selective inhibitor of Janus kinase 1 and 2 that improves disease activity in pts with RA with an acceptable safety profile.1-4,6 Objectives: To investigate the effect of selected comorbidities on safety and efficacy outcomes in pts treated with BARI.

Methods: Pts were selected for this post hoc analysis on the basis of historical or ongoing conditions defined by Medical Dictionary for Regulatory Activities and divided by the following comorbidity subgroups: depression, osteoporosis, hepatic disorders, and previous cardiovascular events. Efficacy outcomes included 20% disease activity score for 28 joints improvement (DAS28, ≤3.2) at 12 weeks, and ≥50% improvement in American College of Rheumatology 20 Response (ACR20) and American College of Rheumatology 50 Response (ACR50) criteria, respectively; the proportion of pts who achieved a Disease Activity Score for 28 joints (DAS28) ≤3.2; and change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 12. Pts who had an inadequate response (IR) to conventional disease-modifying antirheumatic drugs (cDMARDs) from 5 studies with BARI 4 mg and placebo (PBO) were included in efficacy analyses (N=1684) and safety analyses (N=1684). The interaction of comorbidity by treatment was analysed using logistic regression or analysis of variance modelling. Interaction tests were performed within each comorbidity subgroup for increased risk of events after treatment with BARI 4 mg compared with PBO.

References:


DOI: 10.1136/annrheumdis-2017-eular.2227

FR00087] LOW RATES OF RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE OVER 2 YEARS OF BARICITINIB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In p3 studies, baricitinib (bari) inhibited progression of radiographic joint damage up to 1 year in pts with active rheumatoid arthritis (RA) who were DMARD-naïve or who had an inadequate response to conventional synthetic DMARDs (csDMARD-IR).

Objectives: To evaluate radiographic progression of structural joint damage in pts with RA over 2 years of treatment.

Methods: Upon completion of a bari p3 study, pts could enter a long-term extension (LTE) study, in which they continued to receive the same bari dose as in the original p3 study. At 52 wks, DMARD-naïve pts receiving methotrexate (MTX) or combination therapy (bari 4 mg + MTX) were switched to bari 4 mg monotherapy; LTE-IR pts receiving adalimumab (ADA) were switched to bari monotherapy subgroup for ACR20, ACR50, DAS28-50CRP ≤3.2, response, and HAQ-DI was higher for BARI 4 mg compared with PBO. Within each comorbidity subgroup, BARI responses compared with PBO were similar (interaction P ≥ 0.1) (Table 2).

Table 1: Adverse Events Reported by Selected Comorbidity up to Week 10

Table 2: Effect of comorbidity subgroup for increased risk of events after treatment with BARI 4 mg compared with PBO.
4mg on background MTX. At 24 wks, csDMARD-IR pts receiving placebo (PBO) were switched to 4mg on background csDMARD. Radiographs at baseline, year 1 and year 2 were scored using the van der Heijde modified total sharp score (mTSS). Data are least squares mean change from baseline using mixed model repeated measures on observed data.

Results: Of all pts randomised, 82.6% entered the LTE, and 87.6% of those could be entered in this analysis. At year 2, progression was significantly lower with initial bari (including monotherapy) vs. initital MTX in DMARD-naive pts. In MTX/csDMARD-IR pts, progression with initial bari was significantly lower than initial PBO, and similar to initial ADA.

Conclusions: Treatment with once-daily oral bari resulted in low rates of radiographic progression for up to 2 years. Pts starting with bari showed progression that was significantly less than those starting with PBO or MTX, and comparable to those starting with ADA. The most robust benefit was seen with the 4mg dose.


DOI: 10.1136/annrheumdis-2017-eular.1324

FR0089 | EFFECT OF STARTING DOSE OF BARICITINIB IN ACHIEVING SUSTAINED LOW DISEASE ACTIVITY

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Background: In Phase 3 studies, baricitinib (bari) treatment with 2 different doses (2 mg and 4 mg once daily) demonstrated significant improvements across multiple measures of disease activity in patients (pts) with active RA and an inadequate response (IR) to conventional synthetic (cs) DMARDs (RA-BUILD1) or biologic (b) DMARDs (RA-BEACON2).

Objectives: To determine the effect of starting dose of bari on achieving and sustaining low disease activity (LDA).

Methods: RA-BUILD and RA-BEACON trials were 24 week (wk), placebo (PBO) controlled studies. Pts completing the studies on bari treatment could enter a long-term extension (LTE) study, RA-BEYOND, continuing blinded treatment with the same dose, while pts on PBO switched to bari 2 mg. This post hoc analysis assessed disease activity in pts who achieved CDAI ≤10 at ≥1 visit (LDA) or at ≥2 consecutive visits (sustained LDA) within the originating study (24 wks) and continued into the LTE. The length of time required by pts to achieve LDA was determined by the incidence rate (percent pts responding per month) for each group.

Results: Treatment with bari 2 mg and 4 mg, when compared to PBO, resulted in higher rates of LDA and sustained LDA, as well as higher incidence rates (shorter time to achieve LDA/sustained LDA) within 24 wks of each originating study. Analysis of treatment with bari 4 mg demonstrated higher incidence rates when compared to bari 2 mg, both in achieving LDA and sustained LDA, indicating that these pts reached the desired LDA state faster. Incidence rates were lower in all treatment groups in bDMARD-IR pts compared with csDMARD-IR pts.

Conclusions: The most robust benefit in terms of achieving LDA and sustained LDA was observed with bari 4 mg treatment, which required shorter time to response, than treatment with 2 mg. This was observed in both the short (24 wks) and in the long-term in pts with IR to csDMARDs or bDMARDs.

References:
ANALYSIS OF NEUTROPHILS, LYMPHOCYTES, AND PATIENT-PROVIDER DISCORDANCE MAY BE ASSOCIATED WITH SLIGHTLY HIGHER RATE OF INFECTIONS (Table 1).

Mean platelet counts increased to peak at wk 2, returned towards baseline, stabilized over time, and returned to baseline after treatment discontinuation (Figure 1). Permanent study drug discontinuations from thrombocytosis occurred in 2 bari-treated pts (0.1%). No clear association between platelet increase and thromboembolic events was observed.

Conclusions: Treatment with bari was associated with a decrease in ANC and an increase in ALC and platelets, which stabilized over time and returned to baseline with prolonged treatment (ALC) or treatment discontinuation (ANC and platelets). No associations between ANC decrease and infections or between thrombocytosis and thromboembolic events were observed.

References:


DOI: 10.1136/annrheumdis-2017-eular.1339
Objectives: We aimed to assess the occurrence and severity of patient-reported flares of RA in patients who had discordant estimates of RA disease activity with their provider at baseline compared to those who had concordant estimates.

Methods: Patients with RA (age ≥18 years; 2010 ACR criteria) participating in an ongoing prospective study underwent clinical evaluation by a rheumatologist (MD/NI/PD) at baseline with assessment of tender (TJC28) and swollen joint counts (SJOC28), C-reactive protein (CRP), patient and provider GA of RA disease activity, disease activity score (DAS28-CRP), clinical disease activity index (CDAI), completion of Health Assessment Questionnaire-II (HAQ-II), visual analogue scales (0–100 mm) for pain (VAS-pain) and the flare-assessment in RA (FLARE) questionnaire. Patient-provider discordance was defined as ≥25 mm difference in GA between the patient and provider. Occurrence of patient-reported RA flares was compared between patients with and without discordance in GA. Flare was defined based on patient report when answered “Yes” to the question “Are you having a flare of your RA at this time?” or a predefined cut-off ≥2.5 on FLARE questionnaire (1,2).

Results: The study included 55 patients with RA (mean age 60.7 years; 65% female), of whom 40 had GA concordant with their provider and 15 had higher GA than their provider. Table 1 summarizes patient characteristics depending on GA discordance at baseline. Patients with discordance were similar in age, sex, duration of follow-up, had similar TJC28 and SJOC28, but had significantly higher HAQ-II, VAS-pain, CRP, DAS28, CDAI, provider GA and FLARE scores at baseline vs patients with concordant GA. During the follow up, patients with discordance had significantly higher number of visits and number of flares, and tended to have more visits with discordant GA compared to patients who had concordant GA with their provider at baseline.

Conclusions: Patients with patient-provider discordance at baseline were more likely to report flares of RA during follow-up. Patient-provider discordance tended to persist at follow-up visits. Disease activity assessments with patient-reported component (i.e., HAQ-II, VAS-pain, DAS28, CDAI, FLARE score), as well as CRP and provider GA, but not joint counts, were higher at baseline in patients with discordance. Consideration of the results of clinical and laboratory assessment in combination with patient-reported measures of RA disease activity may be important to inform future risk of flares in patients with RA and help improve patient-provider communication and shared decision making.

References:

Disclosure of Interest: None declared
CAROTID ATHEROSCLEROSIS IS ASSOCIATED WITH DISEASE ACTIVITY AND BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which causes joint-articular and generalized bone loss. Several studies revealed that bone mineral density (BMD) is associated with atherosclerosis.

Objectives: In the present study, we investigated the association between BMD and RA disease activity and the carotid atherosclerosis in RA patients based on Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) cohort study.

Methods: A total of 323 patients with RA, who performed dual-photon x-ray absorptiometry and carotid ultrasound, were included. We assessed RA disease activity, risk factors for atherosclerosis including hypertension, diabetes mellitus and dyslipidemia, presence of carotid plaque, carotid intima-media thickness (IMT), and BMD. BMD was measured at the lumbar spine (L-spine, L1-L4), femur (total femur neck) and distal forearm (total radius), and low BMD was defined as a T score of -1.0 or less.

Results: The BMD in the L-spine, femur, and radius was significantly lower in patients with carotid plaques (n=152) compared to patients without plaques (n=171) (1.014 g/cm² ± 0.21 vs. 1.066 g/cm² ± 0.18, p < 0.001 for L-spine; 0.816 g/cm² ± 0.16 vs. 0.863 g/cm² ± 0.13, p < 0.001 for femur; 0.542 g/cm² ± 0.13 vs. 0.603 g/cm² ± 0.12, p < 0.001 for radius). The frequency of low BMD in these areas was also higher in patients with carotid plaques, compared to patients without plaques (52.7% vs. 47.5%, p = 0.045 for L-spine; 56.0% vs. 44.0%, p = 0.003 for femur; and 59.5% vs. 57.9%, p = 0.036 for radius). In subgroup analysis, patients with the highest IMT quartile had a significantly lower BMD in all the regions than those with the lowest IMT quartile (61.2% vs. 37.7%, p = 0.004 for L-spine; 59.5% vs. 35.1%, p = 0.003 for femur; and 71.4% vs. 28.6%, p = 0.004 for radius). Multivariate logistic regression analysis demonstrated that BMD at radius (OR 1.906, 95% CI [1.067–10.276], p < 0.001), DAS28-ESR (OR 2.334, 95% CI [1.164–4.730], p < 0.02) and dyslipidemia (OR 4.995, 95% CI [1.067–10.276], p < 0.001) were risk factors for presence of carotid plaques.

Conclusions: The present study showed that carotid atherosclerosis was influenced by both disease activity and impaired bone health.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6387

TIME TO AND FACTORS ASSOCIATED WITH INITIATION OF BIOLOGICAL THERAPY WITH DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN COLOMBIA

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Background: Rheumatoid arthritis (RA) treatment is usually done with non-biological disease-modifying antirheumatic drugs (DMARDs), but the addition of a biological DMARD can be necessary. Biological drug therapy is usually prescribed following failure to achieve remission of the morbidity with one or more non-biological DMARDs. However, there is the possibility of using them as a first line in the initial phase, which there is the possibility of potentially altering its course or even reverting it to normality.

Objectives: To determine the time Colombian patients with rheumatoid arthritis (RA) are treated with non-biological disease-modifying antirheumatic drugs (DMARDs) before changing to biological therapy.

Methods: A retrospective cohort study that collected information about the start of antirheumatic treatment in patients of all ages with a diagnosis of RA until the change to biological DMARD therapy. Survival analysis using Kaplan–Meier curves, from 1 January 2007 until 31 December 2013 by SPSS 23.0 for Windows, was made.

Results: A total of 3880 patients (75.3%) women with a mean age of 51.3 years started non-biological DMARDs. After 5 years, 234 patients (6.0%) initiated biological DMARD therapy in 17.5±13.9 months. Differences in the socio-demographic and pharmacological characteristics between the two groups of treatment are shown in the table. The use of glucocorticoids was associated with a greater risk of biological DMARD initiation (OR: 2.49; 95% CI: 1.658–3.732; p < 0.001), while the use of methotrexate (OR: 0.04; 95% CI: 0.014–0.108; p < 0.001) and chloroquine (OR: 0.13; 95% CI: 0.092–0.187; p < 0.001) reduced the risk of initiation.

Conclusions: After 5 years of non-biological DMARD therapy, 6.0% of people with RA started biological DMARDs. Receiving glucocorticoids, having any comedication, being treated in Bogota City or cities of the Colombian Atlantic coast affected the probability of switching to biological therapy in these patients.

References:

Acknowledgements: To Universidad Tecnológica de Pereira y Audifarma S.A.

Disclosure of Interest: None declared

**PILOT STUDY OF THE EARLY RHEUMATOID ARTHRITIS DIAGNOSIS PROGRAM WITH A STRUCTURED REFERRAL FORMAT**


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**Background:** The delay in referral of patients with suspicion of Undifferentiated Inflammatory Arthritis (UIA) is especially the Rheumatoid Arthritis (RA), from the primary care physician (PCP) to the Rheumatologist prevents diagnosing and treatment in a timely manner. Early diagnosis and treatment decreases progression and permanent joint damage. Several strategies have been proposed to improve the time to referral of patients with UIA, however there is none for early RA in specific.

**Objectives:** We present a pilot study for the use of a weighted construct format for the improvement of the time to referral of patients with suspicion of early RA.

**Methods:** Since June 2005, in clinics and hospitals, PCPs were trained for the use of the weighted construct format tool. Adult patients with less than 1 year of symptoms were considered for the referral. The criteria for reference of suspicion of early RA are shown in Table 1. The patient referral was made through the counter-reference system, including the complete format and laboratory results. The patient’s appointment was given within 15 business days. Once the patients were evaluated and studied in the Department of Rheumatology, they were classified with RA according to 2010 ACR/EULAR criteria when was available this criteria classification. For the demographic variables, we used descriptive and inferential statistics and for the format validation we verified the reliability, and validity of the construct and criterion tool.

**Results:** Between July 2005 and July 2015, 298 patients were referred to our clinic. The average referral time in the first year (2005–2006) was 34.3±20.4 days, maintaining an average of 32.1±16.8 days until 2015. There was a reduction of 74% of referral time compared to a historical reference (mean time of referral was 127.4±51.8 days; in 122 patients). 182 (62%) patients filled out the 2010 ACR/EULAR criteria classification. For the demographic variables, we used descriptive and inferential statistics and for the format validation we verified the reliability, and validity of the construct and criterion tool.

**Conclusions:** In this pilot study, we observed that the construct had a suitable sensitivity, specificity and PPV for a referral format. Therefore, on suspicion of early RA the referral format could be used as a simple clinical tool for the timely referral to the Rheumatologist. On the other hand, the program implementation allowed the reduction in the referral time substantially. To implement the use of this tool in the daily clinical practice it needs to be validated with an open population and an adequate sample size.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2561

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**DURABILITY AND MAINTENANCE OF EFFICACY FOLLOWING PROLONGED TREATMENT WITH BARICITINIB**


**Background:** Baricitinib (bari) demonstrated clinical efficacy in Phase 3 trials in RA patients (pts) naïve to DMARDs (RA-BEIGIN1); and in RA pts with inadequate response to conventional synthetic DMARDs (RA-BEAM2 and RA-BUILD3) or biologic DMARDs (RA-BEACON4).

**Objectives:** To evaluate durability and maintenance of efficacy over an additional 96 weeks (wks) of bari treatment.

**Methods:** Pts included were those randomised to bari in an originating study (OS), completed that study without rescue (52 wks in RA-BEigin or RA-BEAM; 24 wks in RA-BUILD or RA-BEACON), and entered the long-term extension (LTE) study ≥96 wks prior to data cut-off. Durability of response was evaluated as pts achieving low disease activity (LDA) of SDAI ≤11 and minimal clinically important difference (MCID) of HAQ-DI improvement ≥0.22. Maintenance of response was evaluated as proportion of pts who had responded to bari at entry into LTE and maintained response at wk 96. Data are also provided for pts who had not responded to bari at entry into LTE who achieved response.

**Results:** Approximately half the pts in the durability analyses were categorised as LDA by wk 24 and the proportion of pts in the LDA category were similar or higher at wk 96. Three quarters of pts across groups demonstrated HAQ-DI improvement by wk 12 and more than half achieved MCID at wk 96. Most responders at entry into LTE maintained their response through wk 96. More than 25% of SDAI and HAQ-DI nonresponders at entry into LTE achieved response after 96 wks of treatment.

**Conclusions:** These data provide further evidence of the effectiveness of bari treatment in achievement of meaningful clinical control of disease activity long term.

**References:**


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**Table 1**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymyalgia rheumatica: ≥5 joints</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Small joints: proximal interphalangeal, metacarpophalangeal, wrist, elbow, knee, ankle</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Morning stiffness greater than 30 minutes (&gt;30)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Oligoarthritis: &lt;5 joints (small and large joints)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rheumatoid factor (RF): &gt;11 or 20 U/l for seropositivity or turbidity</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP): positive (&gt; normal reference parameter)</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>RA-BEIGIN</th>
<th>RA-BEAM</th>
<th>RA-BUILD</th>
<th>RA-BEACON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bari 4mg</td>
<td>Bari 4mg</td>
<td>Bari 2mg</td>
<td>Bari 4mg</td>
</tr>
<tr>
<td>Bari 2mg</td>
<td>Bari 4mg</td>
<td>Bari 2mg</td>
<td>Bari 4mg</td>
</tr>
</tbody>
</table>

**Durability of Response, n (%)**

<table>
<thead>
<tr>
<th>SDAI ≤11</th>
<th>Wk12 OS</th>
<th>Wk24 OS</th>
<th>Wk48 LTE</th>
<th>Wk96 LTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>69 (41.2)</td>
<td>70 (46.2)</td>
<td>87 (56.5)</td>
<td>98 (63.6)</td>
<td>86 (55.8)</td>
</tr>
</tbody>
</table>

**Maintenance of Response at 96 wks, % (n/N)**

<table>
<thead>
<tr>
<th>SDAI ≤11</th>
<th>Wk12</th>
<th>Wk24</th>
<th>Wk48</th>
<th>Wk96</th>
</tr>
</thead>
<tbody>
<tr>
<td>70.9 (61.96)</td>
<td>66.7 (68/102)</td>
<td>77.5 (31/40)</td>
<td>77.8 (42/54)</td>
<td></td>
</tr>
</tbody>
</table>

Data were analysed using nonresponder imputation without considering rescue status in LTE. N = number of MITT pts; N = number of responders (R) or nonresponders (NR) at entry into LTE; n = number of pts in the specific category.
**FR0097 REPAIR OF JOINT DAMAGE IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS OCCURS BUT DOES NOT RELATE TO PREVIOUS SUPPRESSION OF INFLAMMATION; AN 8-YEARS SUB ANALYSIS IN THE BEST-COHORT**

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**Background:** Joint damage in rheumatoid arthritis (RA) is thought to be irreparable. We hypothesized that in patients where inflammation is well suppressed for a long time, repair may be possible.

**Objectives:** To investigate whether reversal of erosions and joint space narrowing (JSN) in RA occurs and whether clinical variables predict repair.

**Methods:** In the BeSt study, patients with active early RA (ACR 1987 criteria, and symptoms <2 years) were randomized to 4 treatment strategies, each with the aim to ensure and maintain suppression of disease activity by adjusting medication based on three-monthly calculations of the 44-joint Disease Activity Score (DAS), target ≤24. Radiographic joint damage was assessed yearly, using the Sharp/van der Heijde score (SHS). In this analysis, 8-years data of the study were used. Repair of erosions or JSN was defined as the individual joint level as a reduction of ≥3 SHS point compared to the previous available X-ray, present in ≥2 consecutive visits and with ≥3 out of 4 independent scorers agreeing. Radiographs were scored in random order per patient, blind for patient identity and treatment arm. Multiple logistic regressions were applied at the patient level for associations between achieving repair and maximum duration of previous remission, mean DAS until repair, gender, presence of ACPA, or previous exposure to prednisone or infliximab use, anti-citrullinated protein antibody (ACPA), age, and randomization arm. All models were adjusted for mean joint damage over time in the group with repair. In the group without repair, the models were corrected for mean damage over time until mean time point of repair in the group with repair.

**Results:** Seven out of 508 patients did not have any X-ray images taken in the study. Of the remaining 501 patients, 329 had damage in at least 1 joint and thus could potentially show repair. In total, 2385 X-ray images were available, on average 7.5 per patient (range 2–9). Median SHS after 8 years in these patients was 10 (IQR 4–21, range 0–234), and mean (SD) DAS from month 3 was 2.00 (0.67). In 3 patients repair was seen in 2 joints (same time point). Mean (SD) time to repair was 44.1 (20.1) months. Ten of 17 patients (59%) had previously achieved DAS-remission, compared to 100% of the patients who at a matching time point showed no repair. Adjusted for mean SHS until repair, we found no associations with remission for duration of remission, mean DAS until repair, gender, age, presence of ACPA, or previous exposure to prednisone or infliximab (table 1). Apart from a trend towards fewer patients with repair in the initial infliximab study arm, there were no differences in any of the groups in any of the regression analyses.

**Conclusions:** In this early RA cohort, during 8 years treated to target DAS ≤2.4, repair of JSN and erosions was seen in 17 patients (3.3%), which supports that repair occurs in early RA. However, repair is a rare phenomenon, and does not seem to relate to previous inflammation or other predictors in this cohort.


DOI: 10.1136/annrheumdis-2017-eular.1311
RA patients with low MBDA scores (N=6 of 16; 37%) but high in those with moderate/high scores (N=10 of 13; 77%) (chi square p=0.015) (Figure; right graph).

**Conclusions:** These data show that the majority of RA patients in sustained clinical remission with low MBDA scores can successfully taper TNFi. In contrast, tapering cannot be recommended in patients with moderate to high MBDA scores, as relapse rates are high in these patients.

**References:**

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.4787

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**FR00100**

**DETERMINING MINIMUM CLINICALLY IMPORTANT CHANGE IN MULTI BIOMARKER DISEASE ACTIVITY SCORE ASSOCIATED WITH CLINICAL IMPROVEMENT IN METHOTREXATE NAIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

K. Chatzidionysiou 1, A.H. Hensvold 1, S. Saevarsdottir 1, R.J. Boice 2, D. Chernoff 2, C.C. Hwang 2, X. Wang 2, A.I. Catrina 1.

1Karolinska University and Institute, Stockholm, Sweden; 2Crescendo Bioscience Inc., South San Francisco, United States.

**Background:** The Multi-Biomarker Disease Activity (MBDA) score is a validated tool that quantifies 12 biomarkers to assess disease activity in rheumatoid arthritis (RA) patients. Many studies have demonstrated usefulness of the score for assessing RA disease activity.

**Objectives:** To determine minimum clinically important change in MBDA score (ΔMBDA) from baseline (BL) to Month 3 (M3) associated with clinical improvement (decrease in DAS-ESR >1.2) in early RA patients after initiating methotrexate (MTX).

**Methods:** We evaluated the MBDA test in patients from one of the sites participating in the Solna Epidemiological Investigation of RA (EIRA) cohort. EIRA patients were eligible if they were ≥18 years; RA diagnosis within 12 months of symptom duration; had serum and clinical assessments at BL and M3; and clinical follow-up data in the Swedish Rheumatology Quality Register. Patients naïve to disease modifying anti-arthritic drugs who received MTX were included. Krukas-Wallis was used to test the null hypothesis that medians of ΔMBDA scores of 3 EULAR response groups are equal. Receiver operating characteristic (ROC) analysis was performed. The optimal threshold of ΔMBDA associated with DAS28-ESR improvement (decrease in DAS-ESR >1.2 at M3) was determined by Youden criterion maximizing sum of sensitivity and specificity.

**Results:** 176 patients were included: 72% women, mean age 51 (SD: 11.7) years, mean DAS28-ESR score 5.6 (SD: 0.99); 51% had ESR ≤28 mm/hr, 66% were anti-CCP2+; and 22% received prednisone. Mean BL MBDA score was 56.8 (SD: 14.7) with 8 (5%) patients in low (<30), 29 (16%) patients in moderate (30–44) and 179 (79%) patients in high MBDA disease activity categories. Median MBDA scores for patients with no EULAR response worsened by 2 points and for patients with moderate and good response improved by 12 and 16 points, respectively (p<0.0001 across groups, Fig 1A). Median MBDA scores improved by 10 points for all patients and 15 points in patients with a DAS28-ESR decrease >1.2. The best combination of sensitivity and specificity to achieve a DAS28-ESR decrease >1.2 was provided by a >8 point MBDA score improvement (Fig 1B). A similar result was obtained using the bootstrap method. AUROC was 0.77 (95% CI: 0.71, 0.84). 125 patients (71%) had concordance between DAS28-ESR improvement and ΔMBDA improvement at the optimal threshold (Table 1).

**Conclusions:** The optimal threshold of ΔMBDA score associated with a clinically relevant decrease of DAS28 was 8 points. Using this threshold, the MBDA test is informative to detect clinical improvement. Thus, based on these results improvement in MBDA score >8 points at M3 after initiating MTX is indicative of meaningful clinical improvement.

**Table 1. Performance Measures (95% CI) Based on Optimal Threshold of ΔMBDA Score from BL to M3 Associated with DAS28-ESR Improvement**

<table>
<thead>
<tr>
<th>MBDA (optimal threshold: improvement &gt;8 points)</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement</td>
<td>75</td>
<td>27</td>
<td>102</td>
</tr>
<tr>
<td>DAS28-ESR (decrease &gt;1.2)</td>
<td>24</td>
<td>50</td>
<td>74</td>
</tr>
</tbody>
</table>

Sensitivity: 0.76 (0.66, 0.83); Positive predictive value: 0.74 (0.64, 0.81); Specificity: 0.65 (0.54, 0.75); Negative predictive value: 0.68 (0.56, 0.77); Concordance rate: 71%.

**Figure A** Median change in MBDA score by EULAR response; **B** Receiver Operating Curve (ROC) to determine the Optimal Threshold of Change in the MBDA Score Associated with Clinical Improvement (ΔDAS28-ESR Decrease >1.2).

**Figure B** Median change in MBDA score by EULAR response; **B** Receiver Operating Curve (ROC) to determine the Optimal Threshold of Change in the MBDA Score Associated with Clinical Improvement (ΔDAS28-ESR Decrease >1.2).
RA IN MALE CARPENTERS: OCCUPATIONAL WOOD DUST EXPOSURE INCREASES ACPA AND RF SEROPOSITIVITY AND SIGNIFICANTLY RAISES RF TITRES

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Background: Wood dust has been hypothesised as a trigger in RA. Exposure may activate peptidyl arginine deaminase through exposure to silica and carbon nanoparticles, stimulating RF autoantibody production. Though non-silica dusts have shown increased RA risk in construction workers, wood dust exposed individuals were excluded from analysis in a recent large registry study.

Objectives: To analyse the autoantibody status of male RA woodworkers in Cornwall, UK, compared to matched RA controls with no occupational dust or fume exposure.

Methods: All male RA patients were sent an occupational questionnaire, detailing current occupation, last occupation (if retired) and other occupations for >1 year. A control cohort was recruited using local employment data. Each patient was matched to 102 RA controls with no dust or fume exposure for age ±/– 5 years, sex and index date. RF and ACPA seropositivity was compared using a Z test of 2 proportions. Mann Whitney U test, and ACPA seropositivity was compared using a Z test of 2 proportions.

Results: No significant differences were seen in median age between woodworker cases (median 59 years IQR 50–63), and controls (median 58 years IQR 48–65).

Conclusions: Wood dust exposed RA patients are more likely to be seropositive. Sequential environmental insults of smoking and wood dust exposure have an additive effect on rheumatoid factor levels, conferring increased disease severity. Further studies are needed to determine if occupational wood dust exposure causes RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5534

Table 1: Seropositivity rates and RF levels for woodworkers vs. controls

<table>
<thead>
<tr>
<th></th>
<th>Median RF (IQR)</th>
<th>ACPA+ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control ever smokers (n=40)</td>
<td>16 (IQR 6.7–47.2)*</td>
<td>19/40 (48%)**</td>
</tr>
<tr>
<td>Control ever smokers (n=62)</td>
<td>68.9 (IQR 20.65–167.58)**</td>
<td>46/62 (74%)****</td>
</tr>
<tr>
<td>Wood worker never smokers (n=8)</td>
<td>84.4 (IQR 19.5–230.3)***</td>
<td>7/8 (88%)****</td>
</tr>
<tr>
<td>Wood worker ever smokers (n=36)</td>
<td>156.1 (IQR 54–321.1)**</td>
<td>15/36 (36%)****</td>
</tr>
</tbody>
</table>

p<0.04; *p<0.01; **p<0.004; ***p<0.0004; ****p<0.00004

Conclusions: Wood dust exposed RA patients are more likely to be seropositive. Sequential environmental insults of smoking and wood dust exposure have an additive effect on rheumatoid factor levels, conferring increased disease severity. Further studies are needed to determine if occupational wood dust exposure causes RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3733

FRI0103

ULTRASOUND AND MRI DURING FLARES OF PALINDROMIC RHEUMATISM REVEAL A DISTINCT PHENOTYPE EVEN IN IMPIMIENT RA

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Background: Palindromic rheumatism (PR) is a recurrent, self-abORTive arthritis and peri-arthritis which progresses to RA in up to 50% of patients, especially those that are anti-CCP positive (1). Whether PR is truly a prodrome of RA or a distinct syndrome is unclear; the pathological phenotype of PR flare, and whether this changes when RA is imminent, remains unknown

Objectives: To describe the clinical and imaging (US and MRI) phenotype during PR flares and to determine whether this changes in PR patients with imminent RA. We hypothesised PR patients with imminent RA would have a RA phenotype during flare.

Methods: Patients were recruited from a prospective PR cohort. PR flares were defined as ≥ 2 of pain, swelling, erythema or in around ≥ 1 joint, that joint was later normalised. Clinical details were recorded during flares. Blinded US assessment (wrists, MCPs, PIPs, elbows, knees, MTPs, ECUs and 2nd-5th finger flexor tendons) was performed during and between flares. Synovitis, tenosynovitis, subcutaneous oedema, peri-articular inflammation and peri-tendinous oedema were reported at each joint. Where possible, MRI was also performed on the most symptomatic region during flare. Patients were followed for progression to RA.

Results: US was performed in 22 patients during flare. 19 patients also had non-flare US. Mean age was 49 yrs. 16/22 (73%) were anti-CCP+ and 6/22 (27%) anti-CCP-. Six (27%) patients developed RA (mean 23 weeks post flare); these patients had higher frequencies of flares and absence of flare trigger (figure) but no difference in distribution of flaring joints. The flare US showed grey scale (GS) synovitis in 13/22 (59%) patients, power Doppler (PD) synovitis in 4/22 (18%) and no erosions. 12/22 (55%) patients had peri-articular inflammation and/or subcutaneous oedema; in 6 patients this was without synovitis/tenosynovitis. Tenosynovitis and/or peri-tendinous oedema were present in 6/22 (27%) patients. Non-flare US demonstrated fewer erosions with improvement post flare. In 6 patients multiple flares were imaged with variable US abnormalities identified. The US flare phenotype did not differ (from non-progressors) in patients who progressed to RA, with PD synovitis present in only 17% (table 1) contrasting with our early RA cohort where PD synovitis occurred in 73% of patients (2). MRI was performed on 8 patients (2 flares imaged in 1 patient) and detected more pathology than US. Bone marrow oedema (BME) was found in only 1 patient. No erosions were seen.

Table 1: Proportion of flares with US abnormalities

<table>
<thead>
<tr>
<th>US abnormality</th>
<th>Progressed to RA (n=6)</th>
<th>Not progressed to RA (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD synovitis</td>
<td>3 (50%)</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>GS synovitis</td>
<td>3 (50%)</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>Tenosynovitis</td>
<td>1 (17%)</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>Peri-tendinous oedema</td>
<td>1 (17%)</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Peri-articular inflammation</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Subcutaneous oedema</td>
<td>3 (50%)</td>
<td>4 (25%)</td>
</tr>
</tbody>
</table>

Conclusions: PR flares have a distinct imaging phenotype characterised by peri-articular inflammation and subcutaneous oedema, often without synovitis. The low prevalence of PD synovitis, BME and erosions distinguishes PR from RA. PR patients with imminent RA have no triggers and more frequent flares, but retain the distinct PR phenotype. This suggests distinct pathological mechanisms in PR and should be of value for potential therapeutic interventions.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6237
Methods: A total of 426 newly diagnosed RA patients treated from August 2011 to December 2014 were included. The DAS28-P score (the subjective components of the DAS28 relative to the total components) was calculated as DAS28-P = 0.56*sqrt(TJC28) + 0.014*(VAS-GH) / 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.78*(ESR) + 0.014*(VAS-GH). The EULAR response was assessed after 6 months of treatment. Of those who failed to attain good EULAR responses, those for whom the objective measures (the ESR, the CRP peak, and swollen joints) were normalized were defined as having failed treatment because of subjective measures.

Results: The mean age of all patients was 54 years and 79% were female. The median (IQR) DAS28 score at baseline was 4.8 (4.0–5.4) and that after 6 months of treatment 3.21 (2.4–3.95). Good responders (according to the EULAR criteria) numbered 180 (38.9%), moderate responders 150 (32.4%), and non-responders 96 (20.7%). The DAS28-P score fell significantly from baseline to 6 months in good (0.43 versus 0.28, p<0.001) and moderate responders (0.44 versus 0.4, p=0.003), but not in non-responders (0.43 versus 0.45, p=0.727). Younger age, a lower DAS28 score, and a lower DAS28-P score at baseline were related to a good EULAR response. Subjects who failed to respond because of subjective measures tended to have higher DAS28-P scores at baseline.

Conclusions: We found that RA patients with high DAS28-P scores, reflecting subjective measures, were less likely to achieve good EULAR responses 6 months after treatment initiation and tended not to be classified as good responders despite normalization of objective measures.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.1588

References:

FRIO105 FFLUCTUATING, UNPREDICTABLE AND CHALLENGING: HOW PAIN, FATIGUE AND SLEEP DISTURBANCE IMPACT QUALITY OF LIFE IN PEOPLE WITH RHEUMATOID ARTHRITIS

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Background: Qualitative studies of patient experiences have provided useful insights into how rheumatoid arthritis (RA) affects quality of life (QoL). RA threatens self-image and feelings of independence, reduces personal control, and is associated with difficulty in juggling self-management alongside pre-existing demands of work, home and family life. Pain, fatigue, sleep problems and low mood are commonly reported by patients and perceived as particularly troublesome aspects of RA. We wanted to know whether these symptoms of RA were viewed as the key drivers of reported changes to QoL.

Objectives: To explore RA patients’ perceptions of RA-related pain, fatigue, sleep problems and mood, and their impact on QoL.

Methods: Participants, recruited through RA charities across England, were purposively sampled to include a broad range of current ages and ages at onset of RA. Eleven individuals with RA were interviewed either in a group interview (three participants) or individual semi-structured interviews (eight participants). The interview topic guide was developed in consultation with patient representatives. Interviews were audio-recorded and transcribed in full. Interview data were analysed using inductive latent thematic analysis.

Results: All participants were female, aged 36–75 years. Disease duration ranged from five months to 31 years. Pain, fatigue, poor sleep and low mood were all attributed to RA, and viewed as having wide-ranging impacts on QoL. Participants saw the bidirectional nature of relationships between these four symptoms as particularly challenging. For example, reduced sleep led to increased pain and vice versa. Themes included: “Fluctuating symptoms” referring to the impact of the significant changes in mood, fatigue or pain which can occur within a single 24 hour period “an RA flare”; “The unpredictability of symptoms” was viewed as emotionally draining, anxiety-provoking and undermined both short and long-term plans; “Challenging” described both the symptoms and the need to anticipate potential daily challenges in the context of current levels of symptoms. Most were able to articulate the attitudinal, practical and emotional strategies which could facilitate adaptation to living with RA such as the need to maintain focus on what could realistically be achieved, day-to-day cognitive flexibility and practical support. Pain, fatigue and changes to sleep patterns were viewed as affecting the following aspects of QoL; ability to work effectively, family and social relationships, self-worth, ability to feel “in control”, threats to future plans and appearance. The appearance theme included a desire not to be viewed as ill or “disabled”, weight-gain and self-consciousness.

Conclusions: Daily and hourly variations in pain, fatigue and low mood are challenging for individuals with RA. The unpredictable nature of RA often was associated with anticipatory anxiety and mood fluctuations within the day. However, despite this the importance of positivity and acceptance were identified as mitigating some of the impact RA was having on QoL.

Acknowledgements: This study was funded by an Arthritis Research UK project grant (Project number 21188).

RESULTS OF A SYSTEMATIC LITERATURE REVIEW OF PROGNOSTIC FACTORS IN RHEUMATOID ARTHRITIS AS A BASIS FOR A PROSPECTIVE RHEUMATOLOGISTS SURVEY

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Background: Selecting the most appropriate therapy for each patient with rheumatoid arthritis (RA) is crucial in order to prevent joint damage, particularly in patients with rapidly progressing disease. The literature on prognostic factors is tremendous, being practical to summarize which factors are most strongly associated with a particular outcome and what is the utility that rheumatologists assign to these factors.

Objectives: To identify well established factors predicting long-term outcomes in RA, as the basis for a survey.

Methods: The identification of the factors was performed via an overview of systematic reviews studying prognostic factors in RA, followed by scoping reviews for individual factors. All searches were conducted in PubMed. In order to be included in the overview, the study had to have a systematic review of prognostic factors of any of the following outcomes: disability, mortality, remission, response to treatment, or radiological damage. All factors identified, in positive or negative association with the selected outcomes, were compiled in a matrix of factors * outcomes. Subsequent scoping literature reviews were performed for each combination of the matrix.

Results: The overview of systematic reviews allowed the identification of 36 prognostic factors (see Table 1).

Table 1. Prognostic factors identified in the overview of systematic reviews

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability</td>
<td>Genetic markers, Genetic polymorphisms</td>
</tr>
<tr>
<td>Mortality</td>
<td>Quality of life index, HAQ, Shared epitope, Lung disease, Clinical Presentation, Advanced age, Age at disease onset, Duration of disease, Tobacco, Obesity, Comorbidities, Disease activity, Monotherapy, Biological treatment, Response to treatment</td>
</tr>
<tr>
<td>No remission</td>
<td>Medical history, Clinical Presentation, Advanced age, Age at disease onset, Duration of disease, Tobacco, Obesity, Comorbidities, Disease activity, Monotherapy, Biological treatment, Response to treatment</td>
</tr>
<tr>
<td>Radiological data</td>
<td>Residual synovitis by US, MRI, Scintigraphy</td>
</tr>
<tr>
<td>No response to treatment</td>
<td>Biomarkers, Calprotectin, C-reactive protein, IL-6, CRP, ESR, RF, CRP, IL-12, TNF, IL-6</td>
</tr>
<tr>
<td>Structural damage</td>
<td>Genetic markers, Shared epitope, Polymorphisms, Biomarkers, RA, SLE, MCH, RF</td>
</tr>
<tr>
<td>Treatment</td>
<td>Treatment Failure, Treatment</td>
</tr>
<tr>
<td>Biomarkers</td>
<td>Treatment Failure, Treatment</td>
</tr>
<tr>
<td>Radiological data</td>
<td>Treatment Failure, Treatment</td>
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<tr>
<td>Treatment</td>
<td>Treatment Failure, Treatment</td>
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<tr>
<td>Biomarkers</td>
<td>Treatment Failure, Treatment</td>
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<tr>
<td>Treatment</td>
<td>Treatment Failure, Treatment</td>
</tr>
</tbody>
</table>

Conclusions: We have analyzed and compiled a summary of prognostic factors published in RA and their predictability of long-term outcomes. This may act as a reference for cross-factor comparison and evidence-based risk assimilation and serve as a basis of surveying the value of such factors.

Acknowledgements: This study was funded by Bristol-Myers Squibb.

Disclosure of Interest: L. Carmona Grant/research support from: BMS, T. Otón Grant/research support from: BMS, A. Royo Employee of: BMS, J.L. Baquero Grant/research support from: BMS, S. Luján: None declared, S. Muñoz-Fernández Grant/research support from: BMS

DOI: 10.1136/annrheumdis-2017-eular.4765

DEVELOPMENT OF A PREDICTIVE MODEL FOR RHEUMATOID ARTHRITIS MORTALITY USING RANDOM SURVIVAL FOREST

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Background: Different machine learning methods have been used to develop predictive models of high quality and precision [1]. Among them, Random Survival Forests (RSF) has been proposed as an alternative to traditional survival models [2], being able to overcome most of the limitation of traditional survival techniques, such as Cox proportional hazards models.

Objectives: Our objective was to develop and internally validate a predictive model for rheumatoid arthritis (RA) mortality using Random Survival Forests (RSF).

Methods: Retrospective longitudinal study involving 1,461 patients diagnosed with RA between January 1994 and August 2011, and followed at the outpatient clinic of the Rheumatology Department of the Hospital Clínico San Carlos (Madrid, Spain) until death or September 2013. Demographic and clinical-related variables collected during the first two years after disease diagnosis were used. RSF models were developed, based on 1,000 trees. 100 iterations of each model were performed to measure the mean and standard deviation (SD) of the predictive error and the integrated Brier score (IBS). Missing values were imputed using the function implemented by the randomForestSRC package [3]. The predictive capacity of the variables was assessed using the “variable importance” (VIMP).

Results: 148 patients died (10.1%). M LG showed the lowest prediction error. All variables exhibited a positive VIMP. Final model showed a mean (SD) prediction error and IBS of 0.187 (0.002) and 0.150 (0.003) respectively. The most important predictor variables were age at diagnosis, median erythrocyte sedimentation rate and number of hospital admissions in the first 2 years after RA diagnosis.

Conclusions: We developed an accurate and precise model for RA mortality using RSF. Age and disease activity showed the highest influence in mortality.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5139

TIME TO FIRST TREATMENT IS ASSOCIATED WITH A REFRACtORY COURSE OF RHEUMATOID ARTHRITIS

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Background: It is an ongoing matter of research, whether the natural course of rheumatoid arthritis (RA) can be altered by an early intervention, a concept historically referred to as the “window of opportunity” [1]. So far, only short-term disease activity outcomes have been investigated, which are, however, inherently affected by the unknown rate of underlying rate self-limiting disease. It is unclear, whether among those, who eventually develop RA, the disease course is really affected by the timing of their initial treatment.

Objectives: To explore whether the long-term course of RA is different according to the delay of initial treatment.

Methods: Based on a longitudinal observational dataset, we initially identified a group of patients with an observed refractory disease, we defined presenting with ongoing moderate or high disease activity (by the Simplified Disease Activity Index, SDAI), despite at least three courses of DMARDs, of which at least on course was a biological compound. To ensure that sufficient time had been allowed for the previous treatments to be exert their non-effects, we also required these patients to have total treatment time of at least 18 months in accordance with treat to target strategy (3 x 6 months). We identified 399 patients with a treatment time of at least 18 months. 48 patients were excluded despite fulfilling the disease activity criteria, because they haven’t experienced enough treatment courses, or had received a biological compound yet, to claim refractory disease as per our criteria above. We could include 69 refractory and 262 non-refractory patients in our analyses and then performed
logistic regression analysis to assess the effects of different characteristics at baseline, including disease duration, on becoming refractory.

Results: By comparing patient characteristics (Table 1), more of the patients, who later will become refractory, are female (94.2% vs 73.4%, p<0.001), have higher baseline disease activity (SDAI of 25.5 vs 17.7, p<0.001), and longer delay of the initial treatment from symptom onset (3.17 vs 1.34 years, p<0.001). The multivariable logistic regression model confirmed that a longer delay of first treatment is independently affiliated with a higher probability of a refractory disease course at a later stage. This model was adjusted for disease activity at baseline, including disease duration, on becoming refractory.

The multivariable logistic regression model confirmed that a longer delay of first treatment from symptom onset (3.17 vs 1.34 years, p=0.001).

Our data suggest that delay to initial treatment in RA affects the chance of a dire disease course rises by approximately 1% every 6 months.

Table 1. Baseline characteristics in refractory and non-refractory patients

<table>
<thead>
<tr>
<th>Baseline Descriptive</th>
<th>ReRA (n=69)</th>
<th>non-ReRA (n=282)</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Female</td>
<td>94.2</td>
<td>73.4</td>
<td>-0.001</td>
</tr>
<tr>
<td>% RF</td>
<td>56.5</td>
<td>62.1</td>
<td>0.398</td>
</tr>
<tr>
<td>% ACPA</td>
<td>60.9</td>
<td>61.0</td>
<td>0.985</td>
</tr>
<tr>
<td>Time to Treatment*</td>
<td>3.17 (4.10)</td>
<td>1.34 (2.70)</td>
<td>0.001</td>
</tr>
<tr>
<td>SDAI</td>
<td>25.54 (12.24)</td>
<td>17.70 (12.17)</td>
<td>-0.001</td>
</tr>
<tr>
<td>CRP†</td>
<td>2.02 (2.30)</td>
<td>1.80 (2.02)</td>
<td>0.435</td>
</tr>
<tr>
<td>SJIC</td>
<td>6.42 (0.35)</td>
<td>4.64 (4.72)</td>
<td>0.009</td>
</tr>
<tr>
<td>TJC28</td>
<td>9.22 (5.98)</td>
<td>4.35 (5.40)</td>
<td>-0.001</td>
</tr>
<tr>
<td>PGA†</td>
<td>37.70 (20.49)</td>
<td>28.77 (21.40)</td>
<td>0.002</td>
</tr>
<tr>
<td>PGA†</td>
<td>55.19 (26.67)</td>
<td>41.42 (26.67)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*years; †mg/dl; ‡100mm VAS scale.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3537

**FR01010 METHOTREXATE MONOTHERAPY IN REAL LIFE: A DRUG SURVIVAL ANALYSIS INCLUDING VERY EARLY ARTHRITIS AND EARLY ARTHRITIS COHORTS**

M.G. Anelli 1, C. Rotondo 2, G. Righetti 3, A. Rinaldi 2, S. Perniola 2, M. Nivuori 2, C. Scioscia 1, F. Cacciapaglia 2, C. Scioscia 3

Background: Methotrexate (MTX) is the first line drug suggested in the ACR/EULAR guidelines to treat the rheumatoid arthritis (RA) (1) and spondyloarthritides (SpA). Although MTX efficacy is demonstrated by high levels of evidences, maximum benefit might require interventions even earlier. For this reason, it is suggested to identify the patients (pts) with symptom onset of less than 12 weeks, that is very early arthritis, to obtain better outcomes. Few data are available by the clinical practice on MTX monotherapy (MTXm) survival in very early or early arthritis pts.

Objectives: We aim to evaluate the presence of different outcomes in MTXm drug survival and MTXm efficacy between Very Early Arthritis (VEA) pts (less than 12 weeks from symptom onset) and Early Arthritis (EA) pts (12–52 weeks from symptom onset), and between early RA pts and early SpA pts.

Methods: On 305 pts, we selected 219 pts (30 pts diagnosed as VEA (4.2 (4) weeks from symptom onset) and 185 pts as EA (25.7 (25) wks from symptoms onset) in which MTXm could be started. The RA pts were 93 and SpA pts were 126. To assess the MTXm survival we used the Kaplan-Meier survival curve analysis. Although MTX efficacy is demonstrated by high levels of evidences, maximum benefit might require interventions even earlier. For this reason, it is suggested to identify the patients (pts) with symptom onset of less than 12 weeks, that is very early arthritis, to obtain better outcomes. Few data are available by the clinical practice on MTX monotherapy (MTXm) survival in very early or early arthritis pts.

Conclusions: A single intra-articular corticosteroid injection, performed under US guidance, is a very fast treatment to reduce synovitis of the injected joint. In the hours next to the injection is common to reveal a rise of joint space enlargement together with that of PD signal score.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3537
earlier diagnosis from symptom onset (p<0.0001), higher tier of rheumatoid factor (p=0.037) and female gender (p=0.019). In early SpA pts the only predictor of shorter MTXm survival was younger age at diagnosis (p=0.037). VEA and EA diagnosis did not influence the MTXm survival.

Conclusions: The MTXm survival is not influenced by VEA or EA diagnosis. The presence of ACPA is associated with radiographic progression in RA, and it has been suggested that ACPAs with different reactivities may be associated with different phenotypes of RA.

Objectives: To assess the prevalence of baseline ACPA reactivities in an inception cohort of early RA patients, including subgroups based on anti-CCP/RF status, and to compare the findings to healthy controls.

Methods: 217 DMARD-naïve early RA patients from the ARCTIC trial (1) were analysed. Radiographs were scored according to van der Heijde Sharp (vdHS) score. Anti-CCP status was analysed by FEIA (pos. if ≥10 U/mL) and RF by ELISA (pos. if ≥25 U/mL). ACPA titres (AU/ml) were considered positive if above the 98-thec. of values in 619 non-RA subjects. Analysis of 13 ACPA reactivities targeting citrullinated peptides from fibrinogen, alpha-1 enolase, vimentin, fillagrin and above the histone were performed at baseline in patients and 94 controls (blood donors matched for age/gender/smoking), using a multiplex chip-based assay (2).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4237

### Table 1

<table>
<thead>
<tr>
<th>Anti-CCP</th>
<th>Anti-CCP-</th>
<th>RF+</th>
<th>RF-</th>
<th>All RA</th>
<th>Controls</th>
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</thead>
<tbody>
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<td>Age, years</td>
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<td>51.9 (13.3)</td>
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<td>Female</td>
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<td>22 (56)</td>
<td>91 (59)</td>
<td>40 (64)</td>
<td>131 (60)</td>
</tr>
<tr>
<td>Ever-smoker</td>
<td>122 (69)</td>
<td>26 (67)</td>
<td>71 (59)</td>
<td>39 (69)</td>
<td>148 (68)</td>
</tr>
<tr>
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<td>3.5 (1.2)</td>
<td>3.5 (1.2)</td>
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<tr>
<td>vDHS score</td>
<td>4.0 (1.5–8.0)</td>
<td>4.5 (2.0–10.0)</td>
<td>4.5 (2.0–8.0)</td>
<td>3.5 (1.5–10.0)</td>
<td>4.0 (1.5–8.0)</td>
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<tr>
<td>Vim2–17 cit4</td>
<td>87 (49)</td>
<td>1 (3)</td>
<td>80 (52)</td>
<td>8 (13)</td>
<td>88 (41)</td>
</tr>
<tr>
<td>Fib591 cit4</td>
<td>66 (37)</td>
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<td>56 (36)</td>
<td>13 (21)</td>
<td>69 (32)</td>
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<tr>
<td>Fib72 cit4</td>
<td>24 (14)</td>
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<td>27 (12)</td>
</tr>
<tr>
<td>Fib74 cit4</td>
<td>60 (34)</td>
<td>6 (15)</td>
<td>54 (35)</td>
<td>12 (19)</td>
<td>66 (30)</td>
</tr>
</tbody>
</table>

### Figure

**Fig. 1a** Ankle Function Score and **Fig. 1b** Knee Function Score in SpA patients with different levels of serum IL-33 and sST2.

**Table 2**

<table>
<thead>
<tr>
<th>Anticyclic C-19 Peptides</th>
<th>Anti-CCP</th>
<th>Anti-CCP-</th>
<th>RF+</th>
<th>RF-</th>
<th>All RA</th>
<th>Controls</th>
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>50.8 (13.2)</td>
<td>55.0 (14.9)</td>
<td>51.9 (13.3)</td>
<td>50.8 (14.2)</td>
<td>51 (14)</td>
<td>52 (9.4)</td>
</tr>
<tr>
<td>Female</td>
<td>109 (61)</td>
<td>22 (56)</td>
<td>91 (59)</td>
<td>40 (64)</td>
<td>131 (60)</td>
<td>63 (59)</td>
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<tr>
<td>Ever-smoker</td>
<td>122 (69)</td>
<td>26 (67)</td>
<td>71 (59)</td>
<td>39 (69)</td>
<td>148 (68)</td>
<td>81 (64)</td>
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<tr>
<td>DAS1</td>
<td>3.4 (1.1)</td>
<td>4.0 (1.3)</td>
<td>3.5 (1.2)</td>
<td>3.5 (1.2)</td>
<td>3.5 (1.2)</td>
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<tr>
<td>vDHS score</td>
<td>4.0 (1.5–8.0)</td>
<td>4.5 (2.0–10.0)</td>
<td>4.5 (2.0–8.0)</td>
<td>3.5 (1.5–10.0)</td>
<td>4.0 (1.5–8.0)</td>
<td>NA</td>
</tr>
<tr>
<td>Vim2–17 cit4</td>
<td>87 (49)</td>
<td>1 (3)</td>
<td>80 (52)</td>
<td>8 (13)</td>
<td>88 (41)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Fib591 cit4</td>
<td>66 (37)</td>
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<td>6 (10)</td>
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<td>2 (2)</td>
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<tr>
<td>Fib74 cit4</td>
<td>60 (34)</td>
<td>6 (15)</td>
<td>54 (35)</td>
<td>12 (19)</td>
<td>66 (30)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

### Conclusions

The prevalence of ACPA reactivities differed in subgroups of DMARD-naïve early RA patients according to anti-CCP status and RF status. All RA subgroups, including RF- and anti-CCP- patients, had higher prevalence of ACPA reactivities compared to healthy controls.

References:

Disclosure of Interest: M. Jonsson: None declared, H. Hensvold: None declared, M. Hansson: None declared, M. Mathsson-Alm Employee of: Thermo Fisher Scientific, A.-B. Aga: None declared, J. Sexton: None declared, B.-T. Fevang Grant/research support from: Novartis, S. Lillegraven: None declared, A. Catrina: None declared, L. Mathsson-Alm Grant/research support from: AbbVie, MSD, Pfizer, Roche, UCB

DOI: 10.1136/annrheumdis-2017-eular.2915

## FRIO112 SERUM LEVELS OF IL-33 AND SST2 ARE ASSOCIATED WITH FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS

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Background: Interleukin 33 (IL-33) is a cytokine related to amplification of the articular inflammation in rheumatoid arthritis (RA) animal models. Elevated IL-33 serum levels have been described in RA patients, suggesting a possible participation of this cytokine in the physiopathology of the disease. IL-33 soluble receptor (sST2) is a decoy receptor that functions as an inhibitor of the interaction of the transmembrane receptor with IL-33.

Objectives: To identify the association between serum levels of IL-33 and its soluble receptor (sST2) with clinical and laboratory characteristics of RA.

Methods: Cross-sectional observational study in which RA patients were submitted to clinical and laboratory evaluation. IL-33 and sST2 serum levels were measured by ELISA (R&D System Inc, Minneapolis, MN, USA).

Results: 102 RA patients were included, 92.5% women, mean age of 55.5±10 years and mean disease duration of 10 years. Eighty-four (82.4%) patients had seropositive RA. The median (interquartile range) IL-33 serum level was 69.1 pg/ml (31.6 - 114.5). Higher scores on the visual analogue scale (VAS) of disease activity assessed by the examiner were associated with higher IL-33 values (C195%; 0.01–0.65). In the group of patients with high titres of rheumatoid factor (RF), IL-33 levels were higher, compared to the group with negative RF (95% CI: 0.05 - 2.34). In 34 (33.3%) patients, IL-33 was undetectable and the presence of metabolic syndrome represented a 63% lower chance (OR =0.37, 95% CI: 0.15–0.90) of having IL-33 detected. In addition, 1-unit increase in HAQ-DI increased by 2.43 times the chance of detecting IL-33 (95% CI: 1.23 - 4.80). The median sST2 serum level was 469.8 pg/ml (336.3–651). sST2 was associated with worse functional capacity by the classification of Steinkroger (IC95%: 0.01–0.05). In the group of patients with negative RF (95% CI: 0.02 - 0.53) use (current or in the past) of tobacco was associated with IL-33 and sST2 serum levels.

Conclusions: These findings may suggest that both IL-33 and its soluble receptor play a role as a marker of RA severity and functional disability. The negative association of IL-33 with metabolic syndrome is in agreement with the possible protective role of this cytokine in relation to lipid metabolism.

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1Mean (SD); 2n (%); 3Median [IQR]; 4ACPAs reactivity; n positive (%).

References:
References:

Disclosure of Interest: None declared


FR0113 VALIDATION AND RESULTS OF THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

M.V. Beers-Tas 1, M. Ter Wee 1, B. Maat 1, W. Hoogland 1, A. Hensvold 3, A. Catrina 4, E. Mosor 4, A. Finch 1, D. Courvoisier 1, K. Raza 1.

Background: A range of symptoms can be present in persons at risk of rheumatoid arthritis (RA). However, information on the nature, location, timing, severity and predictive value of these symptoms is largely lacking. The Symptoms of At Risk of Rheumatoid Arthritis (SPARRA) questionnaire has been developed with support from EULAR, informed by data from a qualitative study.

Methods: The SPARRA questionnaire contains questions about presence, severity, impact and location of 13 symptoms. 240 individuals (69% rheumatoid factor and/or ACPA positive, 23% seronegative with clinically suspect arthralgia and 8% first degree family members of patients with RA) completed the questionnaire in the Netherlands (N=125), United Kingdom (N=70), Sweden (N=15), Austria (N=11) and Switzerland (N=19). Individuals had no history or presence of clinically diagnosed arthritis at the time of first physical examination. Reliability (test-retest) and validity (face, content and construct validity) were tested.

Results: Face validity was tested by a group of experts on the at-risk phase of RA and feedback on the questionnaire was asked and received from 30 arthralgia patients, leading to only minor comments. The test-retest within 7–14 days (N=51) showed moderate to good agreement (kappa mean 0.565, range 0.309–1. agreement mean 71%, range 59–100%). The content validity was high, in line with the fact that the items were derived from a qualitative study in seropositive arthralgia patients. In contrast, the construct validity (relation to visual analog scale scores (VAS) for pain and well-being) was low (R-square 0.040–0.199), suggesting that the questions measure different elements in different time frames and grasp symptom content not captured with regular VAS pain/well-being. Most symptoms were present in a high percentage of individuals, with pain, stiffness and fatigue as the most common ones. When a symptom was present, it was usually experienced as moderate to severe, and with moderate impact. ACPA positive individuals reported lower presence of symptoms than ACPA negative individuals (mean 47% for ACPA-positive (N=118), 41% for only RF positives (N=53) and 59% in seronegative individuals (N=69)), but functional impact was higher in ACPA positive individuals (51%, versus 42% in seronegatives, NS). Note that the inclusion criteria for the seronegative individuals was presence of symptoms.

Conclusions: This study provides evidence of good psychometric properties of the SPARRA questionnaire, except for low construct validity. This means the questionnaire adds information to currently available clinical measures in persons at risk of RA. Future studies are needed to evaluate whether SPARRA data can help to improve the prediction of RA.

References:

Disclosure of Interest: None declared


FR0114 ALLOGRAFT INFLAMMATORY FACTOR 1 (AIF1) POLYMORPHISMS RS4711274 (G/A) AND RS2269475 (C/T) MAY PREDICT ETANERCEPT PLUS METHOTREXATE RESPONSE IN FRENCH CAUSATIVE PATIENTS WITH RHEUMATOID ARTHRITIS

D.F. Azzouz 1, M. El Haddad 1, S. Kanaan 1, N. Blandraud 2, M. Martin 2, C. Picard 2, J. Rouder 2, 3, T. Auger 2, N.C. Lambert 2.

INSERM UMR1097; 2Rheumatology, AP-HM; 3HILA Laboratory, Etablissement Français du Sang, Marseille, France

Background: Several risk loci for Rheumatoid Arthritis (RA) have been identified by Genome Wide Association Studies (GWAS), but they do not include Allograft Inflammatory Factor 1 (AIF1). Nevertheless, a few studies have shown that AIF1 rs2269475 (C/T) is associated with RA.

Objective: We propose to analyze Allogeneic associations in French Caucasian patients with RA, of the seven most described AIF1 SNPs; 2 To study their linkage disequilibrium with HLA-DRB1 alleles; 3 To evaluate whether AIF1 single nucleotide polymorphisms (SNPs) could predict first line treatment responses in RA.

Methods: We amplified the AIF1 gene region containing the 7 SNPs and sequenced PCR products on a total of 469 individuals, including 95 Anti-Citrullinated Protein Antibody (ACPA) positive RA patients, 146, patients with scleroderma, 132 healthy controls and 69 additional healthy controls selected from a large database of volunteers bone marrow donors (VMD) for carrying at least one RA associated SNP. Patients and controls were HLA-DRB1 genotyped. Patients with RA were divided into 2 groups, a first group called “non responders” was defined as patients who did not respond to first-line methotrexate (MTX) combined with Etanercept and a second group called “good responders” was defined as patients who did respond to methotrexate combined with Etanercept.

Results: Two SNPs were associated with RA: rs4711274 (G/A) and rs2269475 (C/T). The frequency of minor allele carriers was respectively 37% (A) and 36% (T) in patients with RA versus 18% among controls (p=0.0014 and p=0.001). Furthermore, patients with RA-associated HLA-DRB1 alleles carried more often minor alleles for both SNPs (p=0.0005). Preliminary clinical data show that 56% of non-responders (N=16) carried the minor alleles of both rs4711274 and rs2269475 compared to only 21% of good responders (N=24, p=0.02).

Conclusions: AIF is an inflammation-responsive protein encoded within the HLA class III region on chromosome 6 (6p21.3). As already described in British and Polish Caucasians, we found a significant AIF1 Rs2269475 association with RA. We also found an association with Rs4711274 in linkage disequilibrium with the former. The increased frequency of minor AIF1 alleles in RA was not associated with a particular HLA-DRB1 allele, but to any HLA-DRB1 allele carrying the C minor allele.

Finally, patients who failed to respond to Etanercept and MTX carried more often minor alleles of the 2 described AIF1 SNPs.

Further analysis on a larger groups of patients is required to confirm whether AIF1 SNPs can predict response to therapy with Etanercept and Methotrexate.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4872

FR0115 EVER-SMOKING IS ASSOCIATED WITH DISEASE SEVERITY AND OPIOID USE IN RHEUMATOID ARTHRITIS

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Background: Cigarette smoking, both current and past, is a risk for incident rheumatoid arthritis (RA), even for those with low exposure rates of 1–10 pack years. Current smoking is also associated with severity of disease and poorer response to treatments. It is however not known whether any exposure to cigarettes impacts disease expression, especially for those who have discontinued smoking.

Objectives: To assess the disease severity in RA according to smoking status (ever-, past-, current-, non-smoker).

Methods: As part of a study to examine cigarette and marijuana smoking in rheumatic disease patients, consecutively attending rheumatology patients completed an anonymous self-administered questionnaire including: pain severity on visual analog scale (VAS), patient global assessment (PGA) and cigarette or marijuana smoking status. Concomitant physician recorded information included: sociodemographics, co-morbidities, treatments for RA, physician global assessment (PGA). Patients were categorized according to smoking status. Categorical variables were compared between groups with the Chi-Square test and continuous variables with the Student’s t-test. Variables showing a statistical trend (p<0.15) in univariate analysis were considered in multivariable logistic regression.
Results: Over a 2-month period (April-May 2014), there were 248 (25%) RA attendees of 1000 participants. Significant differences were observed between current, past and non-smokers in regard to age [mean (SD): 59.5 (10.0) vs. 65.2 (10.6) vs. 61.0 (18.2) years; p<0.034], gender (male: 23.9% vs. 30.3% vs. 14.6%; p=0.027), unemployment due to disability (13.3% vs. 3.1% vs. 4.9%; p=0.044), number of RA medications (mean (SD): 2.3 (1.1) vs. 2.1 (1.1) vs. 1.8 (1.1); p=0.019), DMARD use (78.3% vs. 82.8% vs. 64.1%; p=0.008), opioid use (19.6% vs. 10.1% vs. 3.9%; p=0.009), pain [mean (SD): 5.0 (3.3) vs. 4.0 (2.9) vs. 3.7 (2.6) cm; p=0.040] and PGA [mean (SD): 3.8 (2.8) vs. 3.1 (2.8) vs. 3.0 (2.4); p=0.039]. Recreational marijuana was used by 3 non cigarette smokers only, with 1 also reporting medicinal marijuana use. Ever smokers vs. non-smokers used a greater number of RA medications [mean (SD): 4.3 (3.0) vs. 3.7 (2.6); p=0.081], were more likely to use DMARDs (81.4% vs. 64.1%; p=0.003) and opioids (13.1% vs. 3.9%; p=0.014), and showed a trend towards more pain [mean (SD): 4.3 (3.0) vs. 3.7 (2.6); p=0.081]. In multivariate analysis, male gender (OR=2.193; p=0.025) and DMARD use (OR=2.376; p=0.010) were significantly associated with ever smoking while opioid use (OR=2.784, p=0.103 for ever smoking; OR=3.561, p=0.040 for current smoking) showed a statistical trend.

Conclusions: Current, but also ever cigarette use, was associated with worse RA disease as indicated by the use of more drug categories, and more likely use of DMARDs to treat RA, and a trend to more pain and opioids. The combination of opioids and cigarettes may be a manifestation of a patient "chemical coping" strategy in RA patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3777
Clinical Utility of Area-Under-Curve (AUC) of a Proposal for a SDAI, CDAI, and RAPID3-Based Definition of Minimal Disease Activity for Use in Routine Care of Rheumatoid Arthritis: Results from a Japanese National Database

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Background: The standard of care in RA is treat-to-target of remission or low disease activity state (LDA). Integral to this is the regular assessment of disease activity. Patient-derived Disease Activity Score 2 (PDAS2) was developed to allow RA patients to self-assess. Validation, corresponding disease activity statuses cut-points and response criteria had been published. PDAS2 scores >3.8, 3.8–4.5, 4.6–5.0, >5.0 correspond to remission, LDA, moderate and high disease activities respectively. PDAS2 can be recorded by patients in-between clinic visits.

Objectives: To explore the clinical utility of PDAS2 on remission, flare and need of drug adjustment

Methods: A cohort of 100 consecutive RA patients was recruited to complete PDAS2 score at home fortnightly in between two consecutive rheumatology clinic visits. Patients would return the forms when they attended the second clinic. Rheumatologists adjusted treatment according to disease activity while blinded to the scores of PDAS2 recorded at home. AUC of PDAS2 was calculated from the mean of (PDAS2 score multiplied by the time interval between scores). They were compared with disease activity at the first and second visits. The change of PDAS2 score for those patients having SDAI flare-up (from remission/LDA to moderate/high disease activity) was compared to those didn’t flare-up using unpaired T-test. Receiver Operator Characteristic curve was used to determine the cut-point for AUC-PDAS2 increment to predict flare-up and the cut-point of PDAS2 score for rheumatologists to escalate anti-rheumatic drugs.

Results: Mean age of the cohort was 60 years, mean RA duration 14 years. 90% female, 71% sero-positive and 48% in remission/low disease activity. 89 patients (89%) returned written questionnaires which were done 7.8±3.5 times on average (mean±standard deviation) (range 1–16) for a follow-up interval of 17.5±9.4 weeks (range 3–35.2) weeks. Disease activities in first and second visits are shown in Table 1. Remission: For the 14 patients in SDAI remission in both visits, 13/14 were in AUC-PDAS2 remission, and 1/14 in LDA. There were 47, 45 and 37 out of 89 patients in SDAI, CDAI and DAS28 remission/LDAS respectively – they were all in AUC-PDAS2 remission/LDA. Flare-up: There were 10/89 patients in SDAI remission/LDAS in first visit and moderate/high disease activity in second visit. Their AUC-PDAS2 score rose by 0.33±0.35 points compared to 0.01±0.32 who had no flare-up (p=0.002). ROC curve AUC was 0.80 (95% CI: 0.64, 0.95) (p=0.002), with optimal cut-point at increment of AUC-PDAS2 score by 0.11 to predict flare, sensitivity and specificity being 80%. Moreover, rheumatologists decided to escalate anti-rheumatic drugs in 15/89 patients. ROC curve AUC was 0.71 (95% CI: 0.56, 0.86) (p<0.01), with optimal cut-point at PDAS2 score 4.33 to predict the need of escalating anti-rheumatic drugs, sensitivity being 60% and specificity 77%.

Conclusions: PDAS2 scoring by patients in-between follow-up is feasible and useful in reassessing RA patients kept in remission/LDAS, informing a potential flare from previous remission/LDAS state, and predicting rheumatologists’ decision to escalate anti-rheumatic drugs. AUC-PDAS2 concept is useful in development of smartphone application for patient use.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1902
Conclusion: Serum calprotectin is not predictive for successful TNFi dose reduction or discontinuation in the context of RA patients with low disease activity, and calprotectin was only weakly correlated to CRP levels. These results might be caused by the lack of variability in calprotectin levels at baseline as all patients were in low disease activity state.

References:

Disclosures: None declared.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1729
FRI0122 PREDICTING FACTORS FOR DISAPPEARANCE OF ANTI-MUTATED CITRULLINATED VIMENTIN ANTIBODIES IN SERA FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Mutated citrullinated vimentin (MCV) is one of the important targets of anti-citrullinated protein/peptide antibodies (ACPA) and is found in synovial fluid in rheumatoid arthritis (RA). The disappearance of anti-MCV antibody (anti-MCV titer) may be better correlated with RA disease activity and radiographic progression than anti-cyclic citrullinated peptide antibody (anti-CCP) titer.

Objectives: In the present study, we tried to determine the predicting factor of anti-MCV disappearance in sera from RA patients.

Methods: Both anti-MCV (ORGENTEC Diagnostika, Germany) and anti-CCP (MESACUP(TM)-2 test CCP, MBL, Japan) in sera from 280 RA patients who met 2010 ACR/EULAR classification criteria in Kyoto University RA Management Alliance (KURAMA) cohort 2013 and 2014 were measured by ELISA. Then, we determined retrospectively the predicting factors of anti-MCV disappearance using a multivariate logistic regression analysis.

Results: In 2013 cohort, anti-MCV and anti-CCP positiveitivities were 64.6 and 84.6%, respectively. The majority (97.8%) of anti-MCV-positive patients was also anti-CCP-positive and there was significant correlation between anti-MCV and anti-CCP positivities (p<0.001). In 2013 baseline, there was no difference in patients’ age, gender and disease duration between anti-MCV-positive (n=181, 64.6%) and -negative (n=99, 35.4%) groups. DAS28, however, was higher in anti-MCV-positive group than in -negative group (3.08±1.22 vs. 2.68±1.07, p=0.011), while anti-CCP-positive (n=237, 94.9%) and -negative (n=43, 15.4%) groups had no significant difference of DAS28. Of note, while decrease of DAS28 positivity rate did not change during 2013 and 2014, anti-MCV changed to positive and to negative were recognized in 20 (7.2%) and 41 (14.6%, disappeared group) patients. So we next compared anti-MCV disappeared and sustained-positive groups (n=140, 50.0%). There was no difference in patients’ age, gender, disease duration and DAS28 in 2013. While decrease of DAS28 from 2013 to 2014 (△DAS28) in disappeared group was more apparent than that in sustained-positive group (-0.58±1.1 vs. -0.02±0.34, p=0.028). Methotrexate monotherapy was rarer in disappeared group than in sustained-positive group (26.8% vs. 53.8%, p=0.015), while continuous use of biological disease modifying antirheumatic drug (bDMARD) was more frequent in disappeared than sustained-positive group (64.7% vs. 25.2%, p<0.0001). Also serum levels of KL-6, a serum marker of intestinal lung disease, were lower in disappeared than in sustained-positive group (255±146 vs. 315±183, p=0.006). To clear the most effective factor in anti-MCV disappearance, we choose variables including anti-MCV titers in baseline, KL-6 levels, △DAS28 and bDMARD use, and performed multivariable analysis. Analysis showed that anti-MCV titers and bDMARD use, especially TNF inhibitor (Odds Ratio =7.2, p<0.001) were significantly associated with anti-MCV titer disappearance. These analyses aimed to characterize temporary interruptions of study drug during the BARCITINIB PHASE 3 RHEUMATOID ARTHRITIS PROGRAM

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Background: Temporary interruption of RA therapy is common in clinical practice; therefore, rapid clearance and low immunogenicity may be useful DMARD attributes. Baricitinib (bari) is a non-biologic Janus kinase (JAK) 1/2 JAK2 selective inhibitor with a pharmacokinetic half-life in RA patients of approximately 19 hours. It has demonstrated improved clinical efficacy compared to MTX, adalimumab and placebo (pbo) with a satisfactory safety profile when administered once daily to RA patients in 4 completed Phase 3 studies.

Objectives: These analyses aimed to characterize temporary interruptions of study drug during these studies and explore the kinetics of RA symptoms during and following interruption.

Methods: During bari Phase 3 studies, investigators were required to document temporary interruptions of study drug, including timing, reason and duration, using electronic case report forms. In 2 studies, patients recorded RA symptoms (duration and severity of morning joint stiffness, worst tenderness and worst joint pain) daily for 12 weeks. Post hoc analyses investigated changes in these scores among patients randomized at least 7 days prior to interruption, having an interruption that lasted at least 3 days, and retreated.

Results: Across the 3 pbo-controlled studies, interruptions occurred in a larger proportion of patients with bari than pbo only in the biologic DMARD-inadequate responder (IR) study RA-HEACON. In the 2 active comparator-controlled studies, the lowest rates of interruption were in the bari monotherapy arm of the DMARD-inadequate responder bari responder (IR) study RA-HEACON, and proportions similar for bari and adalimumab in the MTX-IR study. RA-HEAB (Table 1). Adverse events (predominantly non-serious, mild or moderate infections, most commonly of the respiratory tract) were the most frequent reason for interruption. Few patients interrupted for the reason of abnormal laboratory results. Most interruptions lasted for 2 weeks or less; in RA-BEAM, interruptions appeared shorter in duration for bari than for adalimumab. Diary measures indicated modest symptom increases during interruption compared to the last pre-interruption value, with a return to pre-interruption values or better after resumption of study drug (Table 2).

Conclusions: Consistent with its pharmacologic properties, brief temporary interruptions of bari during Phase 3 studies were associated with minor increases in RA symptoms, which resolved following resumption of therapy. A small molecule with a short half-life may offer advantages over injectable biologic therapies with respect to drug interruption for clinical cause in RA patients.

Disclosures of Interest: P: speakers bureau: Abbvie, BMS, JCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, using specific HLA DRB1 typing kits (Dyonal RELI SSO). The presence of shared epitope (SE) was determined based on this genotyping. The statistical analysis was performed using Stata 12.1. Chi-Square and Kruskal-Wallis tests were used for the bivariate analysis. A multivariate logistic regression was performed to determine which factors may be related to ACPA positivity, including BMI, anti-CCP titers and smoking habit, number of SE alleles and study level as independent variables.

Results: Patients were 54.9 years old [44.2-67.5] (median [p25-p75]); disease duration was 5.3 months [3-8.4]. Table 1 shows the main variables significantly associated to BMI. In addition, we observed less ACPA positivity with increasing BMI (57% low weight vs. 43% in obese [p=0.06]), as well as a lower frequency of SE in patients with a higher BMI. The multivariate analysis confirmed that being smoker (ever or current) and carrying SE alleles is associated with the presence of ACPA. Adjusted by these variables, overweight and obesity were associated with ACPA positivity during an ACPA positive disease (OR 0.49, p=0.027 and OR 0.39, p=0.019 respectively).

Table 1. Variables significantly different according to BMI

<table>
<thead>
<tr>
<th>Variable</th>
<th>BMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Low weight</td>
<td>52.3 ± 22.64</td>
</tr>
<tr>
<td></td>
<td>Normal weight</td>
<td>50.36 ± 26.64</td>
</tr>
<tr>
<td>Sex (W/M)</td>
<td>Low weight</td>
<td>7/0</td>
</tr>
<tr>
<td></td>
<td>Normal weight</td>
<td>142/245</td>
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<tr>
<td>Level of studies (N/P/S/L/%)</td>
<td>Low weight</td>
<td>64.6%</td>
</tr>
<tr>
<td></td>
<td>Normal weight</td>
<td>35.4%</td>
</tr>
</tbody>
</table>

Conclusions: In our early arthritis register, patients with a higher BMI have predominantly ACPA negative disease, a more intense perception of pain and higher disability. These findings should be validated in other populations.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4456
Anti-acetylated-peptide antibodies (AAPA) have recently been described in rheumatoid arthritis (RA) patients. [1] Patients that show multiple autoantibody positivity have a higher likelihood to flare when stopping biological treatment. The role of AAPA antibodies for response to Tumor-Necrose-Factor-Inhibitor treatment (TNFi) has not been explored.

**Objectives:** To determine the prevalence and serological overlap of AAPA to rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) in a cohort of RA patients starting their TNFi-treatment. Therefore, AAPA might add additional information to estimating the chances of RA patients for responding to TNFi-inhibitors.

**Methods:** Longitudinal data from the METEOR database were used. Fifteen definitions of remission were tested: ACR-EULAR boolean-based; Simplified Disease Activity Index (SDAI); Disease Activity Score (DAS) and 28-joint count DAS (DAS28), both with ESR/CRP, with ≥ 4 variables (3/4/4), and various cut-offs tested. Disability was measured by the Health Assessment Questionnaire (HAQ) and HAQ≤ 0.5 as dependent variable and the various remission criteria as independent variables. Potential confounding factors (age, body mass index, gender, rheumatoid factor positivity, erosions and biologic treatment) were also tested. Sensitivity analyses were performed using first visits only and using patients with no missing data for all definitions of remission.

**Results:** Data from 32,915 patients and 157,899 visits were available. The most stringent definition of remission (table 1) was the ACR-EULAR boolean definition (4.5%). The proportion of patients with HAQ≤ 0.5 among patients in remission was 54.6%. The proportion of patients for responding to TNFi treatment was 57% for ACPA and 61% for RF (for overlap of antibodies see figure). There were no significant differences in baseline characteristics of autoantibody positive and negative patients, and their association with a 50% response by the Simplified disease activity index (SDAI50), and with achieving of SDAI low disease activity or remission at 6 months after starting the first TNFi. Likelihood ratios were calculated from logistic regression analyses. To better determine differences in SDAI change over time General Estimated Equation analyses (GEE) was used.

**Conclusions:** AAPA positivity, in contrast to RF and ACPA positivity, appears to have a tighter association with greater levels of response in patients who are initiating TNFi-treatment. Therefore, AAPA might add additional information to estimate the chances of RA patients responding to TNFi-inhibitors.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5374
was higher for the most stringent definitions. However, this also meant that, for the most stringent criteria, many patients in non-remission had HAQ>0.5. The strongest degree of association between remission and HAQ=0.5 was observed for the SDAI. However, only minor differences were noted between definitions (table 1). Sensitivity analyses yield similar results (not shown).

Conclusions: The remission definitions confirmed their validity in terms of physical function in a large international clinical practice setting. However, many patients in non-remission will still have good functional status and being in clinical remission does not equate to having HAQ<0.5. A multidimensional approach should be taken to help patients achieve this functional goal. Achievement of remission according to any of the indices is more important than the use of a specific index.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3929

FR0127 OUTCOMES OF DISEASE ACTIVITY IN A 5-YEAR LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS AND A MULTIDISCIPLINARY CARE MODEL – A REAL-LIFE EXPERIENCE

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Background: Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA). PRISM was easy to use and most patients understood the simple disease activity (ptGbl), assessed at wks 12 and 24, using the sign test.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed; those patients were followed-up under T2T standards and a multidisciplinary approach. Each patient had a minimum of 6 follow-up visits. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 >3.1 and ≤5.1), and every 11–13 weeks (DAS28 ≤3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 >3.2 unless patient’s condition didn’t permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson’s statistics.

Results: 3618 patients meet the inclusion criteria. 72% were receiving conventional DMARDs therapy and 28% were receiving biological therapy. 83% were woman and 17% were men. Mean age was 61 years ±11. Mean DAS28 at beginning was 3.3±1.3 and at the end of five year period was 2.8±0.7. The difference was statistically significant (p

Conclusions: This study show evidence of an improvement in DAS28 and level disease activity in a cohort of RA patients from a Colombian center specialized in RA center.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4450

FR0128 PRISM – PICTORIAL REPRESENTATION OF ILLNESS AND SELF ACTIVITY: THE USE OF A SIMPLE NON-VERBAL TOOL AS A PATIENT-CENTRED OUTCOME MEASURE IN EARLY RHEUMATOID ARTHRITIS COHORTS

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Background: Treatment recommendations in early RA advocate a treat to target approach, the ideal goal being remission. But not all patients attain this goal. There is a need for outcome measures that are meaningful to patients and inform management of which alleviation of suffering is a key aim. PRISM® is a novel, validated, brief method of measuring suffering consistent with Cassell’s seminal conceptualisation.

Objectives: To understand the relationships between a patient’s perception of the totality of the impact of RA and commonly used clinical assessments of disease activity, depression and illness intrusiveness.

Methods: Basic sociodemographic and clinical data were collected from 182 RA patients from 3 international centres, assigned to one of four cohorts (two early RA and two established RA), at baseline, weeks 12 and 24. The two early RA cohorts (diagnosis <2 yr) comprised Group 1 on stable treatment (n=37) and Group 2 requiring csDMARD adjustment (n=34). Using the iPRISM App on a tablet, all patients were asked to complete the basic PRISM task to measure self-illness separation (SIS). The smaller the SIS, the greater the person’s perceived suffering. In the PRISM+ task, patients were asked to identify two valued aspects of their life at the moment (X and Y) which bring pleasure, satisfaction, a sense of achievement, or a sense of purpose. The iPRISM App automatically records the distance between the centres of each of these disks and the Self disk to measure patients’ perceptions of the intrusiveness of their illness on two personally valued aspects of their lives.

For both groups, direction of change in SIS and the PRISM+ measures were compared with direction of change in disease activity measures and patient global disease activity (ptGbl), assessed at wks 12 and 24, using the sign test.

Results: PRISM was easy to use and most patients understood the simple instructions. Of 182 patients at baseline, SIS showed significant correlations with ptGbl (r

Conclusions: PRISM is a novel PRO that quantifies factors salient to each individual with respect to the impact of RA and its treatment while allowing for incorporation of a wide range of such influences. It may have utility as an adjunct to references for disease activity measures in setting agreed personalised therapeutic targets.


Acknowledgements: This work was financially supported by UCB in the context of an Investigator Initiated Study.


DOI: 10.1136/annrheumdis-2017-eular.5589

FR0129 COMPARATIVE SAFETY OF BIOLOGIC DMARD INITIATION IN RA: A POPULATION-BASED OBSERVATIONAL STUDY OF MALIGNANCY RISK

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Background: Patients (pts) with RA are at increased risk for some malignancies and the use of biologic (b)DMARDs has been reported to further increase this risk. A retrospective cohort study comparing the safety of bDMARDs with other treatment options in RA patients, is not often prescribed as a first-line bDMARD, but long-term effects are unknown.

FRIDAY, 16 JUNE 2017

Rheumatoid arthritis - comorbidity and clinical aspects

FR0129
Objectives: To assess in a real-world, observational study whether treatment with ABA had a similar malignancy risk as other biologics, with or without MTX, when used as the initial bDMARD for RA.

Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify adult pts diagnosed with RA who initiated bDMARD treatment with ABA or another bDMARD between Jan 2007 and Dec 2014. Other bDMARDs included adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab. Pts were required to have ≥ 6 months (M) of continuous health plan enrolment before bDMARD initiation (index date) and deemed to have initiated a treatment if there was no claim for any bDMARD, other bDMARD, or csDMARD within the 6M period before bDMARD initiation. Pts who had a malignancy in the baseline 6M period were excluded. Pts were followed up from the date of the first bDMARD prescription initiation, either ABA or another bDMARD, until occurrence of a malignancy (identified by ICD-9 diagnosis code), end of enrolment, database or end of data collection, whichever occurred first. A 6M latency period was included. Propensity scores of ABA initiation were estimated from the baseline covariates using a logistic regression model, and trimmed to include only pts with ranges common to both ABA-exposed and comparator bDMARD cohorts. The Cox proportional hazard regression model was used to provide an estimate of the hazard ratio (HR) of malignancy associated with ABA initiation compared with initiation of another bDMARD, adjusted for age and deciles of the propensity score after trimming.

Results: A total of 3591 pts were identified as above as having initiated bDMARD therapy with ABA and 17,415 initiated with another bDMARD, with follow-up of > 6 years (median 7.5 yrs). Pts who initiated ABA vs other bDMARDs were older (mean 55 vs 52 yrs), had more comorbidity, used less MTX (49 vs 57%) and more other non-bDMARD (41 vs 36%) at baseline. After trimming on propensity scores, 565 pts developed a malignancy after ABA (incidence rate 5.0 per 100 yr) compared with other bDMARD (incidence rate 3.8 per 100 yr). When adjusted HR (95% CI) of any malignancy with ABA initiation relative to other bDMARDs was 1.18 (1.06, 1.30), while for any malignancy excluding non-melanoma skin cancer it was 1.17 (1.02, 1.34). The risk (HR; 95% CI) was not significantly elevated for lung cancer (1.11; 0.70, 1.76), female breast cancer (1.21; 0.91, 1.62) and lymphoma (1.21; 0.77, 1.90).

Conclusions: In this large, real-world study of pts treated for RA, the incidence of the most common malignancies of breast, lung and lymphoma were not significantly increased in pts using abatacept as first-line bDMARD treatment compared with other bDMARDs, though the confidence intervals were wide. The significantly increased in pts using abatacept as first-line bDMARD treatment was for any malignancy excluding non-melanoma skin cancer. This large, real-world study of pts treated for RA, the incidence of the most common malignancies of breast, lung and lymphoma were not significantly increased in pts using abatacept as first-line bDMARD treatment compared with other bDMARDs, though the confidence intervals were wide. The significantly increased in pts using abatacept as first-line bDMARD treatment was for any malignancy excluding non-melanoma skin cancer.

References:

Disclosure of Interest: A. Strangfeld: Speakers bureau: BMS, MSD, Pfizer, Roche, Sanofi-Aventis, L. Baganz: None declared, A. Richter Consultant for: Pfizer, B. Manger Consultant for: Abbvie, BMS, MSD, Pfizer, Roche, UCBB, G.-R. Burmester Consultant for: Abbvie, BMS, MSD, Pfizer, Roche, UCBB, C. Eisterhues: None declared, S. Wassenberg Consultant for: Abbvie, Pfizer, Novartis, Janssen, Roche-Chugai, Celltrion, BMS, Fuji, Speakers bureau: Abbvie, Cellgen, Novartis, Pfizer, MSD, Lilly, Janssen, UCB, A. Zink Speakers bureau: Abbvie, BMS, MSD, Pfizer, Roche, UCB, J. Listing Consultant for: Sandoz, Pfizer
DOI: 10.1136/annrheumdis-2017-eular.2887

FRID1301
RATES AND RISK FACTORS OF NEW-ONSET PSORIASIS UNDER DIFFERENT BIOLOGIC AGENTS AND CONVENTIONAL SYNTHETIC DMARD TREATMENT

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Background: Psoriatic skin disease is a burdensome, sometimes painful, dermatologic condition which was reported to occur as an adverse event (AE) during the initial treatment with bcsDMARDs and to investigate risk factors.

Objectives: To compare incidence rates of psoriasis in RA under treatment with different biologic and conventional synthetic (b/cs)DMARDs and to investigate risk factors.

Methods: We used data of 12,722 patients (53,585 patient years (py)) enrolled with the start of a b/csDMARD in the German biologics register RABBIT. Patients were required to have psoriasis at baseline and at least one follow-up. All psoriatic events (PsE) reported until 30 April 2016 were selected and assigned to treatments administered within 3 months prior to the event. Crude incidence rates (IR) of PsE were calculated per 1,000py. Cox regression was applied to investigate risk factors for the occurrence of PsE with and without inverse probability weights (IPW) to adjust for confounding by indication.

Results: 98 PsE were reported, with only 6 of them categorized as being serious. The median time between enrollment in the cohort and onset of psoriasis was 19 months (IQR:11–45 months). 21 of all PsE (22%) were palmoplantar manifestations of which 9 were reported as pustular type.

Conclusions: PsE under biologic treatment with the crude IR of 0.44/1,000py (95% CI 0.20;2.9) were not significantly different from csDMARD patients. Across TNFi, the IR varied insignificantly. Adjusted regression analysis showed higher risk for PsE with TNFi, abatacept and rituximab (graph). Female sex (adjusted hazard ratio (HR) 1.8 (1.03;3.3)) and being rheumatoid factor negative (HR 1.6 (1.02;6.2)) were additional significant risk factors. Smoking (HR 1.6 (1.1;2.5)), age (HR 1.0 (0.97;2.01)), glucocorticoids per 5 mg/d increase (HR 1.1 (0.8;3.4)) or tocilizumab (HR 0.7 (0.1;2.0)) IRs for PsE were not significantly associated. Replacing glucocorticoids with DAS28 did not show differing results. Adjustment with IPW attenuated the effect of rheumatoid factor (p=0.4) but smoking was significantly associated with a higher risk (p<0.01).

Acknowledgements: RABBIT is supported by a joint, unconditional grant from AbbVie, BMS, Celltrion, MSD, Pfizer, Roche, Samsung and UCB.

References:

Disclosure of Interest: A. Strangfeld Speakers bureau: BMS, MSD, Pfizer, Roche, Sanofi-Aventis, L. Baganz: None declared, A. Richter Consultant for: Pfizer, B. Manger Consultant for: Abbvie, BMS, MSD, Pfizer, Roche, UCBB, G.-R. Burmester Consultant for: Abbvie, BMS, MSD, Pfizer, Roche, UCBB, C. Eisterhues: None declared, S. Wassenberg Consultant for: Abbvie, Pfizer, Novartis, Janssen, Roche-Chugai, Celltrion, BMS, Fuji, Speakers bureau: Abbvie, Cellgen, Novartis, Pfizer, MSD, Lilly, Janssen, UCB, A. Zink Speakers bureau: Abbvie, BMS, MSD, Pfizer, Roche, UCB, J. Listing Consultant for: Sandoz, Pfizer
DOI: 10.1136/annrheumdis-2017-eular.5052
**FR0132** HIGH DISEASE ACTIVITY IS A PREDICTOR OF DEPRESSION AND PERSISTENT DEPRESSION IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRi)

R. Joshi 1, M. Movahedi 2,3, E. Rampakakis 2, A. Cesta 4, X. Li 5, S. Couto 5, J. Sampalis 6, C. Bombardier 6,7, B. Kuriya 2 on behalf of OBRi investigators.

1Departments of Rheumatology, Brampton Civic Hospital, William Osler Health System, Brampton; 2JSS Medical Research, Montreal; 3Ontario Best Practices Research Initiative, Toronto General Hospital, University Health Network; 4Division of Rheumatology, Mount Sinai Hospital; 5Department of Medicine (DOM) and Institute of Health Policy, Management, and Evaluation (IHPEM); 6Sinal Health System, University of Toronto, Toronto, Canada

**Background:** The prevalence of depression among individuals with rheumatoid arthritis (RA) may be as high as 40% but persistence of depression over time is relatively unknown. Uncontrolled inflammation may drive severe disease and, in turn, inflammation and high disease activity are hypothesized to mediate depression and associated symptoms.

**Objectives:** The aims of this analysis were to: (1) describe the prevalence of depression at baseline and determine how often depression persists over time; (2) determine whether there is an association between changes in disease activity and depression over time among individuals with early RA (ERA).

**Methods:** ERA patients enrolled in the Ontario Best Practices Research Initiative (OBRi) with ERA (<1 year disease duration) and >2 years of follow-up were included. Persistent depression was defined as self-reported depression at baseline and at >50% of visits over the first 2 years. The association between baseline disease activity, measured by the Clinical Disease Activity Index (CDAI), and depression at baseline or persistent depression was evaluated with multivariate logistic regression. The General Estimation Equation was also used to explore the association between changes in CDAI disease activity over time and risk of depression.

**Results:** 469 patients with ERA (72.9% female) were included with a mean (SD) age of 56.8 (13.6) years. Mean (SD) disease parameters were: CDAI: 22.9 (14.1); DAS28: 4.6 (1.5); and HAQ disability Index: 1.1 (0.75). At baseline, the prevalence of depression was 26%, and 23% reported persistent depression. Persistent depression was significantly higher in patients with moderate CDAI (19%) and high CDAI (29%) compared to those in CDAI low disease activity (LDA) or remission (16%; p<0.001). After adjusting for potential confounders (sex, rheumatoid factor status, prior use of csDMARDs, current use of bDMARDs, HAQ disability index, number of comorbidities), increased CDAI at baseline was significantly associated with both baseline depression and persistent depression (OR: 1.04; 95% CI: 1.01–1.06, p<0.002). Female gender (OR: 3.17; 95% CI: 1.50–6.80, p=0.002) and greater number of comorbidities at baseline (OR: 1.68; 95% CI: 1.47–1.93, p<0.001) were also associated with persistent depression. Over the course of follow-up, the risk of depression was significantly higher among patients with moderate disease activity compared to those in CDAI LDA or remission (OR: 1.16; 95% CI: 1.04–1.29, p=0.006). The risk of depression was substantially greater for those with high disease activity (OR: 1.32; 95% CI: 1.15–1.52) over time compared to those achieving LDA or remission states.

**Conclusions:** Depression in ERA is common and initial high disease activity increases the risk of depression as well as its persistence. High CDAI during the early years of follow-up was also an independent predictor of depression. This highlights the importance of intervening during the “window of opportunity” to control disease activity and the potential to mitigate adverse health outcomes, including depression.

**Disclosure of Interest:** R. Joshi Grant/research support from: OBRi was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbiev, Amgen, Celgene, Hospira, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, Sanofi, & UCB. M. Movahedi Employee of: OBRi/JSS Medical Research, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRi, X. Li Employee of: OBRi, S. Couto Employee of: OBRi, J. Sampalis Employee of: Head of JSS Medical Research, C. Bombardier Grant/research support from: OBRi was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbiev, Amgen, Celgene, Hospira, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, Sanofi, & UCB. B. Kuriya Grant/research support from: OBRi was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbiev, Amgen, Celgene, Hospira, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, Sanofi, & UCB.

**DOI:** 10.1136/annrheumdis-2017-eular.3994

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**FR0133** IS THERE INCREMENTAL MENTAL HEALTH BURDEN ASSOCIATED WITH RHEUMATOID ARTHRITIS?

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**Background:** Rheumatoid arthritis (RA) patients are more likely to experience depression.1 This comorbidity is associated with increased disability, use of healthcare services, and mortality risk.2 3 The association between RA and other mental health disorders has received limited attention and there remains a need to further demonstrate and understand the impact of RA on mental health.

**Objectives:** Evaluate the mental health burden of RA patients based on the analysis of Short Form-36v2 Health Survey (SF-36v2) mental health (MH) and role emotional (RE) domain scores from two independent general population databases in the US and Europe.

**Methods:** The mental health burden associated with RA was analyzed by comparing mean SF-36v2 MH and RE scores of individuals self-reporting RA (with or without depression) and the scores from 2 benchmark samples (individuals without RA, individuals with depression and no RA) in two large cross-sectional survey studies (QualiMetrix’s 2009 General US Population Norming Study of the SF-36v2 and the 2014 European National Health and Wellness Survey). Multivariate regression methods were used to adjust each benchmark sample to the distribution of the RA sample in terms of age and gender. Differences between groups were interpreted with respect to minimally important differences: 3 points for MH; 4 points for RE.

**Results:** The US (2009) and European (2014) samples included 4,042 and 81,366 individuals, respectively. Compared with individuals without RA or depression, mean RE scores were significantly (P<0.001) lower for RA patients without depression in the US (-7.75 points) and Europe (-5.31 points). Likewise, mean MH scores were significantly (P<0.001) lower among RA patients without depression in the US (-4.85 points) and Europe (-5.03 points) compared with individuals without RA or depression. Compared with individuals with depression and no RA, mean RE and MH scores were 5 to 10 points higher (P<0.001) for RA patients without depression in both the US and Europe. Comparisons of RA and RE/MH scores between RA patients with and without comorbid depression showed that comorbid depression was associated with 2 to 6 points lower scores (P<0.01) in RE and MH domains, in both the US and Europe.

**Conclusions:** RA is associated with significant and clinically meaningful mental health burden as measured by SF-36v2 MH and RE domains. Results comparing scores between RA patients with and without comorbid depression suggest that there is an incremental mental health burden associated with RA, often exceeding minimally important differences among US patients.

**References:**

**Disclosure of Interest:** V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, BiogenIdec, Boehringer Ingelheim, Celtrion, Crescendo, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, M. Kosinski Employee of: Optum, R. Rendas-Baum Employee of: Optum, D. Brooks Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline.

**DOI:** 10.1136/annrheumdis-2017-eular.3575

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**FR0134** CLUSTER ANALYSIS OF PULMONARY LESIONS IN RHEUMATOID ARTHRITIS (RA): AIRWAY DISEASE IS SHARED AND CRITICAL PULMONARY ABNORMALITY IN RA

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**Background:** Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects joints and various organs including the lung. The pulmonary involvement is critical for prognosis of the patients and decision of the treatment. Moreover, the pulmonary involvement showed various abnormalities such as interstitial pneumonia (ILD) and airway disease (AD). Importantly, a pulmonary abnormality coexists with other ones in RA patients. There have been large numbers of studies on the prevalence of pulmonary abnormalities and clinical features of patients with these lesions. However, it remains to be elucidated what existence pattern of pulmonary abnormalities RA patients have.

**Objectives:** To reveal the existence pattern of the pulmonary abnormalities in RA patients using cluster analysis, and to clarify the clinical features of patients with multiple pulmonary lesions.

**Methods:** Subjects were consecutive 208 RA patients who were treated by bDMARDs as the first one from Feb. 2004 to Sep. 2015 in our department and received HRCT scan before and after the therapy. Pulmonary abnormalities were classified into 4 categories (ILD, nodular lesions, AD and other) and 20 lesions such as ground-glass opacities, consolidation, reticular pattern, bronchiectasis and were examined their existence and distribution. Cluster analysis was conducted according to the existence of the lesions by Ward method. Clinical features were analyzed through reviewing medical records.

**Results:** Subjects were 208 RA cases (M/F: 64/144, mean age 59.2 year-old,
Conclusions: Pulmonary abnormalities were found in 70% in RA. AD was found in 55% of RA patients and coexisted with other pulmonary lesions such as ILD and nodular lesions. Patients with AD frequently showed newly emerging or exacerbation of pulmonary abnormalities developed in AD patients compared to those without pulmonary abnormalities or AD. No significant differences were found in clinical features, among AD alone, AD with ILD and AD with nodules.

Disclosures: None declared

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5828
A. Emamifar1, R. Hvid Larsen2, R. Asmussen Andersen1, I. M. Jensen Hansen1,2,3,4, A. Hansen1,3,4, R. Dolhain Hansen1,3.

**Background:** Rheumatoid Arthritis (RA) should be treated instantly to prevent further joint destruction. The first few months after treatment initiation are critical for long-term treatment outcome. [1] Patients with RA are at increased risk of thyroid disease with direct effect on initial treatment response. [2]

**Objectives:** To characterize the prevalence of thyroid disease among RA patients as well as to evaluate the correlation between presence of thyroid disease in RA patients and initial treatment response.

**Methods:** All RA patients who were registered in the local part of Danish Danbio registry were included in this study. Patients' demographic data, serology results (IgM Rheumatoid Factor, Anti-CCP, Fibrinogen, C-reactive protein (CRP) at the time of diagnosis and after 4 months (±1–2 months) of treatment (anti-ccp) as well as disease activity score in 28 joints-C-reactive protein (DAS28- CRP) at the time of diagnosis and after 4 months (±1–2 months) of treatment initiation were extracted. DAS28 was calculated as follows: DAS28 at the time of diagnosis – DAS28 after 4 months (±1–2 months) of treatment initiation. Patients' electronic hospital records including laboratory results were reviewed to reveal if they had been diagnosed with thyroid disease.

**Results:** 1035 patients were included in the study (Table 1). Prevalence of thyroid disease was 11.8% (122/1035). Multiple linear regression analysis showed a negative correlation between DAS28 and presence of thyroid disease adjusted for age, gender, disease duration, RF, anti-ccp and DAS28 at the time of diagnosis (Regression coefficient (95% Confidence Interval): -0.157 (-0.312 to -0.002), P = 0.047) (Table 2). RA patients with thyroid disease had significantly poorer initial response to RA treatment compared to patients with isolated RA after 4 months of treatment (P<0.002).

**Conclusions:** Presence of thyroid disease in RA patients worsens initial treatment response and is suggestive of poor long-term prognosis. The authors propose routine measurement of serum thyroid stimulating hormone (TSH) in all RA patients at the time of diagnosis and with yearly interval.

**References:**

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.4270

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**FR0137**

**PRESENCE OF THYROID DISEASE IN RHEUMATOID ARTHRITIS PATIENTS IS PREDICTOR OF WORSE INITIAL TREATMENT RESPONSE: AN OBSERVATIONAL, COHORT STUDY**

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**Background:** Rheumatoid Arthritis (RA) should be treated instantly to prevent further joint destruction. The first few months after treatment initiation are critical for long-term treatment outcome. [1] Patients with RA are at increased risk of thyroid disease with direct effect on initial treatment response. [2]

**Objectives:** To characterize the prevalence of thyroid disease among RA patients as well as to evaluate the correlation between presence of thyroid disease in RA patients and initial treatment response.

**Methods:** All RA patients who were registered in the local part of Danish Danbio registry were included in this study. Patients' demographic data, serology results (IgM Rheumatoid Factor, Anti-CCP, Fibrinogen, C-reactive protein (CRP) at the time of diagnosis and after 4 months (±1–2 months) of treatment initiation were extracted. DAS28 was calculated as follows: DAS28 at the time of diagnosis – DAS28 after 4 months (±1–2 months) of treatment initiation. Patients' electronic hospital records including laboratory results were reviewed to reveal if they had been diagnosed with thyroid disease.

**Results:** 1035 patients were included in the study (Table 1). Prevalence of thyroid disease was 11.8% (122/1035). Multiple linear regression analysis showed a negative correlation between DAS28 and presence of thyroid disease adjusted for age, gender, disease duration, RF, anti-ccp and DAS28 at the time of diagnosis (Regression coefficient (95% Confidence Interval): -0.157 (-0.312 to -0.002), P = 0.047) (Table 2). RA patients with thyroid disease had significantly poorer initial response to RA treatment compared to patients with isolated RA after 4 months of treatment (P<0.002).

**Conclusions:** Presence of thyroid disease in RA patients worsens initial treatment response and is suggestive of poor long-term prognosis. The authors propose routine measurement of serum thyroid stimulating hormone (TSH) in all RA patients at the time of diagnosis and with yearly interval.

**References:**

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.4270
Objectives: To define the prevalence of PHP in patients with RA.

Methods: All RA patients who were registered in the local part of Danish Danbio registry were included in this study. Patients’ demographic data and serology results (rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-ccp)) were extracted from Danbio. Patients’ electronic hospital records including laboratory results (Parathyroid hormone (PTH) and calcium levels) were reviewed to reveal if they had been diagnosed with PHP as well.

Results: 1035 RA patients were included in this study [table 1]. Prevalence of PHP was 2.8% (29/1035). RA Patients with PHP had significant longer disease duration compared to patients with isolated RA (p<0.003). There was no significant difference between RA patients with and without PHP with respect to age, gender, RF and anti-ccp positivity (Table 1).

Conclusions: Clinicians should pay special attention to higher prevalence of PHP among RA patients compared to the general population. Presence of PHP in RA patients may aggravate the effect of RA on bones and joints by means of interaction with cytokines and inflammatory markers involved in RA. Concurrent PHP can be diagnosed at early stage by testing PTH and calcium levels which minimize the future morbidities e.g. fracture due to osteoporosis.

References:

Acknowledgements: We thank Mrs. Maryam Mousavi for her contribution to data collection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4282

FR10141 | LEFT VENTRICAL CONCENTRIC REMODELING IS MORE PREVALENT IN RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

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Background: Patients with rheumatoid arthritis (RA) have a higher risk to develop cardiovascular complications than general population (1), leading to a decrease in life expectancy of 3 to 10 years (2). RA is associated to increased left ventricle mass, pericardial effusion and diastolic dysfunction (3).

Objectives: The aim of this study was to assess the structure and function of the left ventricle in patients with RA and compare the results with matched controls.

Methods: We designed an observational cross-section case-control study. Patients diagnosed with RA according to the 1987 ACR and/or 2010 ACR/EULAR classification criteria, 40–75 years old, with no overlap syndromes, atherosclerotic cardiovascular disease or hypertension were included. Subjects for the control group were matched by sex, age and comorbidities. A board-certified cardiologist performed a transthoracic echocardiogram.

Results: We included a total of 44 RA patients and 26 control subjects. Table 1 summarizes the demographic characteristics for each group. Left ventricular concentric remodeling (LVCR), defined as a relative wall thickness (RWT) ≤ 0.42 cm and a left ventricular mass index (LVMI) > 95 g/m² in women and > 115 g/m² in men, was found in 14 patients (32.6%) of the RA group and 2 subjects (8%) of the control group; this difference was statistically significant (p=0.021). When we analyzed general abnormalities of left ventricle (either LVCR or left ventricular concentric hypertrophy [RWT > 0.42 cm and LVMI > 95 g/m² in women, > 115 g/m² in men]) we found 15 RA patients (34.1%) with abnormalities and 3 subjects in the control group (11.5%) (p=0.037). There were no statistically significant differences among the groups in LVMI, diastolic dysfunction, global longitudinal strain or ejection fraction.

Table 1. Demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA group (n=44)</th>
<th>Control group (n=26)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>62.35±7.34</td>
<td>53.94±6.81</td>
<td>0.371</td>
</tr>
<tr>
<td>Disease duration (years), mean ± SD</td>
<td>10.68±2.3321</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>DAS-28 CRP, mean ± SD</td>
<td>3.36±1.42</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Women, % (%)</td>
<td>43 (97.7)</td>
<td>24 (92.3)</td>
<td>0.079</td>
</tr>
<tr>
<td>Body Mass Index, mean ± SD</td>
<td>26.98±6.13</td>
<td>28.31±12.12</td>
<td>0.096</td>
</tr>
<tr>
<td>Active smoking, n (%)</td>
<td>4 (9.1)</td>
<td>0 (0)</td>
<td>0.113</td>
</tr>
<tr>
<td>Type 2 Diabetes mellitus, n (%)</td>
<td>2 (4.5)</td>
<td>2 (7.7)</td>
<td>0.568</td>
</tr>
</tbody>
</table>

Conclusions: Left ventricle concentric remodeling is more prevalent in RA-patients when compared to controls. Further research is needed to determine the impact of these findings in the clinical prognosis of RA-patients.

References:
[1] Solomon DH, Currin GC, Rimm EB, Cunnancio CC, Karlson EW. Cardiovas-
**Background:** Neutropenia is an uncommon finding in the context of rheumatoid arthritis (RA). The incidence and association with RA features is not yet well-defined.

**Objectives:** To determine the incidence and severity of neutropenia in an early RA inception cohort, explore possible association with RA features and describe its impact on patient's management.

**Methods:** The Scottish Early Rheumatoid Arthritis (SERA) inception cohort prospectively recruited newly diagnosed RA patients (ACR-EULAR 2010 criteria), who were followed-up every 6 months. Patients who developed at least one episode of neutropenia (grade 1: <1000/μL, grade 2: <1500/μL, grade 3: <5000/μL, grade 3: <10000/μL) were compared with patients who never developed neutropenia. Binominal logistic regression was performed, exploring the enter model and using the occurrence of neutropenia as dependent variable.

**Results:** 77 episodes of neutropenia were observed in 60 (8.6%) out of 698 RA patients, who were followed-up for a median (range) time of 18 (6–48) months. Neutropenia occurred in 12 (0–120) [median (range)] months after RA diagnosis. The majority had mild neutropenia (grade 1: n=49, grade 2: n=9, grade 3: n=0; grade 4: n=2) and the mean ± SD number of neutrophils/μL was 1.68±0.35. Of the 77 neutropenic episodes recorded, coexistent lymphopenia was found in 11.5%, leukopenia in 70.1%, thrombocytopenia in 1.3% and anaemia in 32.5%. At the time of the neutropenia, most of the patients were in remission (DAS28<2.6: 53%, DAS28>3.2: 15.5%, DAS28<5.1: 22.4%, DAS28>5.1: 8.6%). Neutropenia was a single episode in the majority (76.7%) of the patients and led to treatment discontinuation in 11.7% of them.

Patients who subsequently developed neutropenia, were more likely females (p=0.03) and non-smokers (p=0.009) [Table 1]. Treatment received for RA was comparable between the two groups. Binominal regression analysis confirmed female gender [p=0.017, Exp(B): 2.587] and not smoking [p=0.032, Exp(B): 2.880] as predictors of neutropenia development. During total follow-up time, patients who had at least one episode of neutropenia they also manifested more commonly anaemia (p=0.04) and lymphopenia (p=0.03). The rate of infections/1000 person-months did not differ between patients who developed neutropenia and those who did not [5.75 (2.47–11.33) vs 4.1 (3.13–5.47), p=0.399].

**Conclusions:** Neutropenia was observed in about 9% of patients in this early RA cohort. It was usually mild, transient and not associated with increased infection rates. Interestingly, not-smoking and female gender were associated with neutropenia.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5623
Methods: A total of 141 patients (103 female, 38 male) who were diagnosed RA according to ACR (American College of Rheumatology) diagnostic criteria were included in the study. Fatigue Symptom Inventory (FSI) was used for evaluation of fatigue. While the disease activity was determined using the Disease Activity Score-28 (DAS28), the Health Assessment Questionnaire (HAQ) was used to determine functional status. The pain intensity was determined using 10 cm Visual Analogue Scale-Pain (VAS-pain).

Results: The mean age of the patients is 54.67±10.70 years and the mean duration of illness is 14.31±10.89 years. When the relationship between fatigue and other factors was examined, a statistically significant relationship was found between FSI fatigue severity scores (maximum, minimum, mean, current), FSI duration scores (number of days felt tired, amount of time felt tired), FSI interference score and HAQ, number of swollen joints, number of tender joints, VAS rest and VAS motion values (p<0.05). There was a statistically significant lower correlation between FSI fatigue scores (at least, mean) and DAS28 (r: 0.216, r: 0.181, respectively). There was no significant relationship between FSI scores and age, duration of illness, steroid use.

Conclusions: Fatigue affects patients independently of disease duration in patients with RA. Fatigue is associated with disease activity, functional status, and pain. For this reason, fatigue in RA patients should be considered as an important symptom that should not be overlooked and should be struggled.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3979

FR0145 | DOES PAIN HAVE INFLUENCE ON HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX (HAQ-DI) IN RHEUMATOID ARTHRITIS PATIENT? AN ATTEMPT TO EVALUATE EFFECTIVENESS OF PAIN VAS (PS-VAS) ON HAQ-DI IN REAL CLINICAL PRACTICE –

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Background: Health Assessment Questionnaire Disability Index (HAQ-DI) is the most important index in treatment for rheumatoid arthritis (RA) patient. HAQ-DI expresses patient’s disability in daily life (ADL), and this is influenced by disease activity (ACT-HAQ) and joint structural damage (DAM-HAQ), and aging when patient gets older in senectitude (AGE-HAQ) (1–3). One more factor that possibly makes influence on HAQ-DI is patient’s pain. However, this problem is not discussed in all.

Objectives: We have investigate patient’s pain and its effect on HAQ-DI in our clinical data in order to evaluate whether pain influences on HAQ-DI, and to make assessment existence of pain related HAQ-DI (PAIN-HAQ).

Methods: RA patients who have been treated continuously for more than five years, who had visited later than October 31th, 2016, were picked up in this study. Patients average 28-joints disease activity score with C-reactive protein (DAS28-CRP), modified HAQ (mHAQ), Sharp/van der Heijde Score (SvdHS), age, and pain score calculated by visual analogue scale (VAS-PS) were calculated in five treatment years. Means and operation values of these parameters have been calculated. Relationships among these factors have been investigated statistically using multiple linear regression analysis (MLR). After evaluation of relationship of each pair of these factors, the relationship between HAQ-DI and the other factors had been evaluated from modified data of these patients in minimize the effect of parameters other than PS-VAS and data that minimized effectiveness of PS-VAS with MLR.

Results: 382 patients had been picked up. Their sex distribution was 87 for male and 295 for female, and their average values and standard deviations of age, DAS28-CRP, HAQ-DI, SvdHS, and PS-VAS were 68.99 and 13.47, 1.91 and 0.54, 0.43 and 0.55, 54.97 and 67.30, and 22.96 and 17.85, respectively. HAQ-DI demonstrated significant regression with all of DAS28-CRP, SvdH, age, and PS-VAS (<0.01). DAS28-CRP demonstrated positive correlation with PS-VAS, HAQ-DI, and SvdHS, but negatively correlated significantly with age (<0.01). PS-VAS demonstrated positive correlation with HAQ-DI and DAS28-CRP, but negatively correlated with SvdHS significantly (<0.01), while no significant correlation demonstrated with age. SvdHS demonstrated positive correlation with DAS28-CRP and HAQ-DI, but negative correlation with PS-VAS significantly (<0.01), while no significant significant correlation demonstrated with SvdHS. Age demonstrated positive correlation with HAQ-DI, but negatively correlated with DAS28-CRP and SvdHS (Figure 1).

After minimizing the data effectiveness of DAS28-CRP, Age, and SvdHS on HAQ-DI, HAQ-DI demonstrated significant regression only with PS-VAS. When the effectiveness of PS-VAS was minimized, HAQ-DI demonstrated significant regression with parameters other than PS-VAS. Threshold of PS-VAS was 15mm.

Conclusions: These results suggested that HAQ-DI is influenced PS-VAS when it is no less than 15mm. Therefore, we conclude that HAQ-DI consists with PAIN-HAQ in adding with ACT-HAQ, DAM-HAQ, and AGE-HAQ.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3979

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2593

FR0147

ANTI-MÜLLERIAN HORMONE LEVELS IN FEMALE RHEUMATOID ARTHRITIS PATIENTS TRYING TO CONCEIVE – THE ROLE OF OVArian FUNCTION IN TIME TO PREGNANCY IN A NATIONALWIDE COHORT STUDY

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Background: Subfertility, a time to pregnancy (TTP) >12 months, is present in 40% of women with rheumatoid arthritis (RA) actively trying to conceive. Since RA patients appear to reach menopause at a younger age, the reduced fertility may be caused by a lower ovarian reserve (OR). Serum anti-Müllerian hormone (AMH) levels are currently the most reliable way to measure the OR.

Objectives: Our objective was to study preconception AMH levels and their association with TTP in women with RA.

Methods: A post-hoc analysis was performed in patients of the Pregnancy-Induced Amelioration of RA (PARA) cohort who were assessed preconceptionally. Serum AMH levels were measured using the pico AMH ELISA assay (Ansh Labs, Texas, USA), and compared to converted AMH values from a cohort of 554 healthy adult controls.

Results: Preconception serum was available in 209 women aged 32.1±3.9 years, of whom 45% were subfertile. The median AMH level was 2.5 ug/L (IQR 1.5–4.6). Reduced AMH levels were more pronounced in ACPA positive patients, suggesting the OR may be compromised more strongly in patients with a more severe disease. However, since preconception AMH levels were not associated with TTP, the reduced levels do not explain the reduced fertility in women with RA.

Conclusions: Women with RA have lower AMH levels than healthy controls. Reduced AMH levels were more pronounced in ACPSA positive patients, suggesting that the OR may be compromised more strongly in patients with a more severe disease. However, since preconception AMH levels were not associated with TTP, the reduced levels do not explain the reduced fertility in women with RA.

References:

Disclosure of Interest: None declared.

FR0148

THE EFFECT OF TNF INHIBITORS, METHOTREXATE (MTX), AND THE OTHER DMARDs THERAPIES ON DIABETIC CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA): TREATMENT WITH MTX ALONE IMPROVED DIABETES CONTROL MORE THAN TNF INHIBITORS PLUS MTX

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Background: It has been shown that inflammation directly influences insulin and glucose metabolism through cytokines such as TNFα and IL-6. It has also been reported that certain RA drugs such as TNF inhibitors, hydroxychloroquine, and MTX were associated with lower diabetes risk among people with RA, but it is still clinically unknown. On the other hand, it has been shown that MTX is involved in activation of intracellular AMP-kinase and promotes glucose uptake in skeletal muscle (Diabetes, 2015).

Objectives: We examined medical records of patients with new RA patients complicated with glucose intolerance to measure HbA1c, body weight, and HbA1c-ESR for 6 and 12 months treated with TNF inhibitors, MTX, and the other DMARDs.

Methods: Newly registered 20 RA patients complicated with glucose intolerance (HbA1c ≥5.6%) at our hospital from May 2013 to December 2015, have treated with as follows: Treatment with infliximab (1 case), golimumab (3 cases), and etanercept (2 cases) in combination with 4–12mg/week of MTX (group A: 6 cases, TNF inhibitors + MTX), MTX (4–10 mg/week) alone (group B: 8 cases MTX alone). The other DMARDs (group C: 6 cases, the other DMARDs including bucillamine (BCL) + sulphasalazine (SASP) + metformin (MTX); 1 case, BCL+SASP; 1 case, BCL alone; 2 cases and SASP alone; 2 cases) had been registered. We have compared the changes of HbA1c levels, body weight, DAS-ESR from the beginning of the treatments and 6 and 12 months later. RA patients treated with glucocorticoid were excluded. Diabetic treatment were diet and exercise in all the groups. Metformin (500 mg) and DPP4 inhibitor were used in 4 cases (Group A and C). However, each patient in Group B did not use anti-diabetic agents. We analyzed these results with paired and unpaired t test using JMP12.2.0.

Results: These registered RA patients with female were 60.0%. The mean age were 62.1, 53.5 and 63.6 for group A, B, and C, respectively. There were significant changes in DAS-ESR after treatment for 6 months in group A and B, respectively (p<0.01 in group A and p<0.05 in group B). Groups A and B showed significant improvement of DAS-ESR after treatment with 12 months (P<0.0001 in group A, p<0.01 in group B), but no significant differences between DAS-ESR-SR mg and DPP4 inhibitor were used in 4 cases in Group A and C. Each patient in Group B did not use anti-diabetic agents. We analyzed these results with paired and unpaired t test using JMP12.2.0.

Conclusions: In this study, MTX was thought to contribute not only to suppress chronic inflammation but also to improve the glucose tolerance as compared with TNF inhibitors plus MTX and the other DMARDs. Further studies concerns about the interrelationship between glucose tolerance and RA treatments may require.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2105

FR0149

DOES THYROID SUBSTITUTION PREDICT NON-RESPONSE TO METHOTREXATE IN EARLY RA?

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Background: Response to treatment varies widely between RA-patients. Our means to predict disease course and treatment response is limited, leading to substantial over- as well as under-treatment. Whereas female gender and smoking have been identified as predictors of non-response, the impact of autoimmune co-morbidities remains largely unknown. Autoimmune thyroid disease (AID) is one of the most frequent autoimmune diseases in the population. AID is more prevalent in RA-patients and has also been identified as a risk factor for RA. AID can be readily identified via thyroxin substitution. We aimed at assessing the impact of prevalent AID in relation to 3- and 6-month EULAR response to methotrexate in early RA.

Objectives: To investigate whether thyroid substitution impacts response to methotrexate as the first-line therapy in RA.

Methods: We identified patients with incident RA (symptom duration <1 year), included in the Swedish Rheumatology Quality Register, who were treated with MTX between January 2011 and October 2015 (n=7099). All patients starting treatment with methotrexate and who had a follow-up visit at 3 months (n=4364) and/or at 6 months (n=3148) were included. Prevalent AID was defined as prescription of thyroid substitution before RA-diagnosis (n=347), based on linkage to the Swedish Prescribed Drug register,
and excluding participants with prescriptions for iodine-containing drugs or history of thyroid cancer (e.g. non-autoimmune cause of thyroxin use). We used a case-control design with thyroxin substitution as exposure, cases defined as EULAR DAS28 3- and 6-month non-responders, and controls defined as moderate/good responders at these time-points. Odds Ratios (OR) were calculated adjusted for study center and age. Results: At 3 months, the proportion of thyroxin users did not differ between responders and non-responders 12% vs. 11%, (OR non-response =1.1, 95% CI 0.9–1.4). At 6 months, the corresponding figures were 13% vs. 11%, respectively, (OR non-response =1.3, 95% CI 1.0–1.7). However, a significant difference was observed between RF and/or ACPA positive patients at 6 months, where 15% of non-responders and 10% of responders used thyroxin (OR non-response=1.6, 95% CI 1.1–2.1), while no such difference was observed for seronegative RA. When stratified for gender, thyroxin substitution was significantly associated with non-response in men but not in women.

Table 1. Relative risk of prevalent AITD before RA diagnosis in non-responders compared to moderate and good responders according to EULAR response criteria, at the 6 month follow-up visit among 3148 RA-patients starting methotrexate as first ever DMARD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-responders (718)</th>
<th>Responders (254)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of AITD in non-responders</td>
<td>Overall</td>
<td>93 (13%)/254 (11%)</td>
<td>1.28 (0.98–1.66)</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>81 (16%)/231 (14%)</td>
<td>1.19 (0.89–1.57)</td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>12 (5%)/23 (2.8%)</td>
<td>2.20 (1.05–4.60)</td>
</tr>
<tr>
<td></td>
<td>Serostatus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RF and/or ACPA positive</td>
<td>73 (15%)/163 (10%)</td>
<td>1.57 (1.14–2.14)</td>
</tr>
<tr>
<td></td>
<td>RF and ACPA Negative</td>
<td>20 (8%)/80 (11%)</td>
<td>0.82 (0.48–1.42)</td>
</tr>
<tr>
<td></td>
<td>Serostatus unspecified</td>
<td>0/11</td>
<td>NA</td>
</tr>
</tbody>
</table>

Values are the number. RA = rheumatoid arthritis; AITD = autoimmune thyroid disease; OR = odds ratio; 95% CI = 95% confidence interval.

Conclusions: This large real-life study of response to methotrexate in early RA suggests that AITD, measured as thyroxin replacement therapy, may be linked to treatment response in seropositive patients (and among males). Exploratory by nature, these findings call for replication.

Disclosure of Interest: K. Waldenlid: None declared, S. Saevarsdottir: None declared, C. BengtsGott: None declared, J. Asking Grant/research support from: Abbvie, Pfizer, Lilly, Samsung, MSD, UCB, Roche, Janssen.

RHEUMATOLOGISTS’ EXPERIENCES AND VIEWPOINTS TOWARDS MANAGING RHEUMATOID ARTHRITIS IN ELDERLY PATIENTS: A QUALITATIVE STUDY

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Background: The number of elderly individuals with rheumatoid arthritis (RA) is expanding in Europe mainly due to an increased life expectancy. As a result, management of these patients, e.g. the application of the treat-to-target and tight control principles, shall have to account for frailty and comorbidity. However, knowledge about how rheumatologists perceive and manage RA in the elderly patient population is limited.

Objectives: To explore the viewpoints of rheumatologists on management goals in elderly RA patients and the influence of factors such as age, frailty and comorbidity on these goals. Furthermore, experiences of rheumatologists with regard to outcome instruments to guide management in elderly patients were assessed.

Methods: A qualitative study involving semi-structured interviews with rheumatologists was conducted. Two readers independently annotated the transcripts of the interviews. Important concepts were taxonomically categorized and later combined in overarching themes by using NVivo 11.

Results: Seventeen rheumatologists were purposively sampled from nine medical centres (mean age 44.6 years (SD 7.7 years; 85.3% female)). High levels of frailty and comorbidity frequently influenced management goals of rheumatologists. In these cases, preserving an acceptable functional status prevailed over the treat-to-target and tight control principles. For instance, most rheumatologists accepted the presence of tender and swollen joints when overall functioning and social participation were not or only minimally impaired. In patients >80 years, age instead of frailty and comorbidity was the most prominent factor that steered management. On that line, almost all rheumatologists admitted that their management strategy is less driven by the result of the Disease Activity Score-28 (DAS28), since comorbidity (e.g. osteoarthritis) and an age-related physiological Erythrocyte Sedimentation Rate (ESR)-elevation might distort the DAS28 value. Instead, before adapting anti-rheumatic therapy, rheumatologists weighted the frailty and comorbidity levels of a patient and the functional consequences of these factors such as cognitive and physical decline, dependency and polypharmacy (quote 1, Table 1). This frequently resulted in a less future-oriented management approach that was not aimed at the maximal prevention of joint erosions and deformities (quote 2, Table 1). Rheumatologists reported that a lack of time to evaluate all comorbid conditions, as well as contradictory advices of other medical specialists often complicated the management of elderly RA patients.

Conclusions: Commonly accepted RA treatment paradigms such as treat-to-target and tight control are not automatically adopted in the elderly patient population. Maintaining a patient acceptable functional status prevails. Future RA management recommendations for elderly RA patients are needed and should account for factors such as frailty and comorbidity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2291

COMPARISON OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS vs METHOTREXATE: RESULTS AT 24-MONTHS OF FOLLOW-UP

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Background: Rheumatoid arthritis (RA) is associated with increased risk of atherosclerosis. Cardiovascular (CV) disease. Treatment with conventional systemic disease modifying drugs (csDMARDs) such as methotrexate (MTX), as well as biological DMARDs (bDMARDs), has been shown to decrease CV risk. Although bDMARDs specifically target inflammation common to RA and atherosclerosis, whether or not cardioprotective effects associated with bDMARD use is superior to csDMARD use remains to be determined.

Objectives: To investigate 10-year CV risk, and incidence of new myocardial infarctions (MI), in RA patients treated with either MTX or bDMARD mono/combination therapy, in a Canadian routine clinical care setting

Methods: RA patients were prospectively followed between January 2011-March 2014. Parameters collected were patient demographics, RA disease activity parameters, traditional CV risk factors, lipid parameters, and 10-year CV risk, assessed using the Framingham Risk Score (FRS). Between-group differences in change from baseline to month 24 in FRS, disease activity, and lipid parameters were assessed with the two sample t-test or the Chi-Square statistic; within-group differences were assessed with the paired-sample t-test or the McNemar-Bowker test. Adjusted change in FRS was ascertained using general linear models, and logistic regression identified predictors of MI.

Results: A total of 517 RA patients receiving bDMARDs (n=313) or MTX (n=199), were included. Mean (SD) age was comparable between cohorts [57.57 (11.71) vs. 59.58 (11.0)], N=0.11; bDMARD vs. MTX, respectively], as was female gender [76.7% vs. 73.9%, p=0.268]. Patients receiving bDMARDs had significantly (p<0.05) longer mean (SD) RA duration [12.63 (9.95) vs. 7.86 (6.94) years] and higher total comorbidities [3.96 (2.53) vs. 3.38 (2.32)]. Mean (SD) baseline FRS was 11.84 (9.38) vs. 12.36 (9.19) percent (p=0.564; bDMARDs vs. MTX, respectively), and patient distribution across low (62.3% vs. 54.8%), intermediate (9.9% vs. 12.2%) and high (27.8% vs. 33.2%) FRS risk categories was comparable (p=0.239).

At month 24, FRS category remained stable in bDMARD patients (low: 58.6%; intermediate: 14.2%; high: 27.0%; p=0.380), whereas a shift in FRS category was observed in MTX patients (low: 69.6%; intermediate: 10.1%; high: 27.0%, p=0.006). Within-group changes in FRS were significant for both MTX (p<0.001) and bDMARD patients (p=0.016). Adjusted mean change (SE) in FRS was higher in MTX patients [-1.37 (0.30) vs. -0.72 (0.25)], although not statistically different (p=0.08). Similar between bDMARDs and MTX [OR (95% CI): intermediate: 1.3% vs. 2.7%; p=0.153; MTX vs. bDMARD: 0.3%; p=0.421], and predictors [OR (95% CI)] identified were: higher total comorbidities [1.45 (1.24, 2.20), p<0.001], age [1.07 (1.00, 1.13), p=0.037], and male gender [4.00 (1.38, 11.57), p<0.01].

Conclusion: FRS decreased in significant manner in CV risk at 24 months was observed during treatment with both MTX and bDMARDs. As predictors of MI did not include several established CV risk factors, longer studies, as well as the development of an RA-specific tool, may permit better assessment of CV risk in RA patients.

Disclosure of Interest: M. Khraish Grant/research support from: Roche Canada. M. Stutz: None declared. A. Lewis: None declared. C. Mota: None declared. E. Rampakakis: None declared

DOI: 10.1136/annrheumdis-2017-eular.2789
from: Roche, Pfizer, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, S. Valleva Grant/research support from: Roche, Bristol-Myers Squibb, Speakers bureau: Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Medac, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, K. Isawa: None declared, E. Kashchenko Grant/research support from: Novartis, A. Karaseva: None declared

DOI: 10.1136/annrheumdis-2017-eular.5944

FR0155 PREVALENCE OF HBV INFECTION AND RISK OF REACTIVATION ON BIOLOGIC TREATMENT: A POPULATION-BASED OBSERVATIONAL STUDY OF RHEUMATOID ARTHRITIS SUBJECTS IN A NORTHERN ITALY AREA
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Background: The introduction of biologic agent’s treatment in rheumatic diseases dramatically changed their outcome, but raised many concerns about infections reoccurrence. Due to the prevalence of hepatitis B virus (HBV) among Italian general population (1.2%) and the possibility of HBV reactivation in case of an immunosuppressive treatment has to be considered.

Objectives: Aim of this prospective, population-based observational study was to assess the prevalence of HBV (both in chronic carriers and reactivated) rheumatoid arthritis (RA) patients in our setting; to verify if these findings were in line to the Italian and European-reported data; finally, to evaluate the final outcome of HBV RA subjects.

Methods: We enrolled the totality of RA patients treated by biologics and, therefore, considering our Unit at least every 12th of November 2015 to January 2017. Acme of action. We collected called FESITEST (FRA) and ASSL) guidelines, every subject was screened for HBV before starting biologic treatment. Descriptive statistics was performed. Acute infection; previous (resolved) infection; inactive and active carrier; and vaccine-immunized subjects were defined according to

Results: A totality of 265 RA patients (female 56.3%; male 43.7%; mean age 36±20 years) underwent biologic treatment after the screening (HBSAg subjects were excluded). The huge majority of them (82%) was treated by TNF-alpha inhibitors (TNFi), since the remaining received biologic agents with different mechanisms of action. We overall detected 33 (12.5%) inactive carriers, for whom HbsAg and HBV DNA periodical monitoring was suggested; in 3 of them (1.1% of the study population), HBV DNA became detectable, with a low viral load (<2000 UI/ml); they prosecute the biologic therapy after the introduction of the standard prophylaxis (lamivudine 100 mg daily) and a more strictly (periodic liver enzymes elevation and liver ETG evaluation) monitoring.

In occasion of the screening, we observed 6 (2.3%) HBV-immunized (due to vaccine) and 6 (2.3%) previously infected (HbcAb+) patients: for the first ones no action is required, since the latter were put on standard prophylaxis before undergoing biologic agent and monitored. One of them (0.38%) developed, after 6 months of treatment, HBV reactivation with high-level (>2000 UI/ml) detectable DNA and liver enzymes elevation (<normality x3). She was therefore stopped from receiving biologic agent and put on entecavir 1 mg daily.

Interpretation of HBV serologic test results

Conclusions: Our prospective, population-based observational study, performed in a first-level referring Hospital in a highly populated area, suggests some considerations. In a way, our data reported a significantly higher prevalence of HBV infection “contact” among our RA population, in comparison to the general one (p<0.05). This issue has previously been reported and could be justified but the generally higher HBV diffusion in certain area (i.e., Italy); by the age/ethnicity of the sample; and, finally, by the bias consisting in an extensive screening of these patients. On the other hand, our experience suggests that a light monitoring of parameters predicting infectious flare should lead to a prompt diagnosis and a lower number of complications for these peculiar patients, as observed in our population.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2833

FR0156 DO CHANGES IN ADIPOCYTOKINES CORRELATE WITH CHANGES TO DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS? FINDINGS FROM THE TOMORROW STUDY
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Introduction: Cytokines released from mast cells evoke inflammation and correlate with arteriosclerotic lesions and autoimmune disease. The relationship between autoimmune disease activity and lipid metabolism is a notable in research surrounding rheumatoid arthritis (RA). RA patients without disease control reportedly show high titers of leptin or adiponectin as adipocytokines.

Objectives: We analyzed the interaction between changes in disease activity and adipocytokines using data from the TOMORROW (Tomorrow: Risk factors in Rheumatoid arthritis patients to lower morbidity and mortality clinical trial) study, a 10-year prospective study (registration number, UMIN000003876).

Methods: We analyzed data collected from the cohort of the TOMORROW study including 193 patients with RA and age- and sex-matched 194 healthy individuals (controls). We compared changes in leptin and adiponectin (Δleptin and Δadiponectin) in both groups between baseline and after 3 years. Correlations with the change in disease activity (ΔDAS28ESR) during 3 years and changes in Δleptin and Δadiponectin in RA were investigated by univariate analysis.

Results: Leptin levels increased in both groups. No significant differences in Δleptin were seen between RA (0.29 μg/ml) and controls (0.18 μg/ml; p=0.37). On the other hand, adiponectin was significantly decreased in controls (-3.3 μg/ml) compared to RA (-1.8 μg/ml; p=0.01). Negative correlations between Δleptin and Δadiponectin were detected in the RA group (r=-0.29, p<0.01). The correlation between adiponectin and DAS28ESR was positive both at baseline (r=0.22, p=0.01) and after 3 years (r=-0.18, p=0.01). However, no such tendencies were seen for leptin. Table 1 shows details of the correlations with changes in adipocytokine. In terms of the relationship with ΔDAS28ESR, no correlation was seen with Δleptin (r=0.07, p=0.31) or Δadiponectin (r=-0.01, p=0.91). Changes in lipid metabolic markers and fat percentages were detected as predictive factors for Δadiponectines.

Table 1. Correlations with changes in adipocytokine by univariate analysis

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔAdiponectin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline age</td>
<td>-0.199</td>
<td>0.006</td>
</tr>
<tr>
<td>ΔHigh-density lipoprotein</td>
<td>0.265</td>
<td>0.001</td>
</tr>
<tr>
<td>ΔFat percentage</td>
<td>-0.144</td>
<td>0.046</td>
</tr>
<tr>
<td>ΔDAS28ESR</td>
<td>-0.099</td>
<td>0.906</td>
</tr>
<tr>
<td>ΔLeptin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline age</td>
<td>0.258</td>
<td>0.001</td>
</tr>
<tr>
<td>ΔLow-density lipoprotein</td>
<td>0.347</td>
<td>0.001</td>
</tr>
<tr>
<td>ΔFat percentage</td>
<td>0.554</td>
<td>0.001</td>
</tr>
<tr>
<td>Fall</td>
<td>-0.145</td>
<td>0.045</td>
</tr>
<tr>
<td>ΔDAS28ESR</td>
<td>0.074</td>
<td>0.311</td>
</tr>
</tbody>
</table>

Conclusions: Leptin increased and adiponectin decreased over the course of 3 years. Correlations between Δadiponectin and ΔDAS28ESR were not detected. RA patients with high disease activity show higher adiponectin levels.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2833

FR0157 FERTILITY IN WOMEN WITH RHEUMATOID ARTHRITIS COMPARED TO HEALTHY CONTROLS
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Background: Data suggest infertility is increased in women with rheumatoid arthritis (RA) compared to healthy women. Therefore, it is possible that diminished ovarian reserve and ovulatory dysfunction may be more common among women with RA.

Objectives: To compare differences in ovarian reserve and ovulatory frequency, as well as self-reported infertility, between women with and without RA.

Methods: Women with RA aged 20–40 yrs in a university clinic without a history of ovarian surgery or prior exposure to possible ovary-toxic medications were invited to participate in a cross-sectional survey. Healthy controls were women aged 20–40 without an autoimmune disease, matched for age and current use of hormonal contraceptives. Infertility was defined as a patient reporting physician-diagnosed infertility or being unable to get pregnant after a certain number of attempts of trying. Ovarian reserve was assessed by measuring anti-Müllerian hormone (AMH). In women who were not taking hormonal contraceptives, progesterone level was measured from a serum sample drawn between days 21 and 23 of the menstrual cycle. Anovulation was defined as a progesterone level <3 ng/mL. In
In patients with RA, increased serum levels of vWF and impaired group with thicker IMT (p=0.046), as well as the percentage of men (p=0.030). Patients with RA is divided into two groups according to the value of the IMT, than in controls (0.89±0.13 mm) (P=0.001). FMD% was significantly lower in patients with RA (3). Prothrombotic markers have been shown to be able to have been found to be useful in the assessment of the cardiovascular risk of disease, as a consequence of accelerated atherosclerosis found in this diseases (1). Finding methods for assessing vascular dysfunction during the early stages of the disease is important, particularly in patient groups at high CV risk (2).

Background: In rheumatoid arthritis (RA), higher mortality is mainly due to cardiovascular comorbidities over time. Previous studies have shown that this is attributable to cardiovascular and respiratory disease. Over recent years earlier and more aggressive treatment with higher dosage of methotrexate and the earlier use of biologic drugs has improved disease outcomes. The effect on cause of death is unknown. In this retrospective cohort study we found the major cause of death in RA was infection followed by malignancy and found no correlation with seropositivity or gender.

Objectives: To analyse the causes of death in RA patients treated with aggressive disease modifying anti rheumatic drugs (DMARD) and Biological therapies over a 6 year period.

Methods: Patients with RA who died between 2010 and 2016 were identified using the DAWN software DMARD monitoring database. A cohort of 3106 patients with RA are monitored using DAWN software in Berkshire, UK. The causes of death were identified from medical records, general practice records or the local coroner’s office.

Results: 198 patients on DAWN monitoring died during the 6 year study period. Treatment details and cause of death was identified for 131 RA patients. 71% were seropositive for rheumatoid factor and 61% were female. 91 patients (69%) were treated with methotrexate, 28 hydroxychloroquine (21%), 14 sulphasalazine (21%) and 7 with leflunomide (5%). The majority of patients (81) were on monotherapy (61%), 32 were on 2 DMARDS (24%) and only one was on triple therapy. 4 patients with RA who died were on biologic monotherapy, 10 were treated with biologic and combination DMARD. The most commonly prescribed biologics were etanercept (35%) and rituximab (35%). The leading causes of death in this cohort were pneumonia (39 patients 29%), cerebrovascular disease (16 patients 12%), septicaemia (11 patients 8%) and lung cancer (6 patients 4%). Infection accounted for 57% patients’ deaths (43%) followed by malignancy in 24 patients (18%). Cerebrovascular disease (20 patients, 15%) and cardiovascular disease (13 patients, 9%) were less frequent causes of death in our cohort. Comorbidity data for the cohort was recorded pre-mortem. 49 patients (37%) had cardiovascular disease and 23% had an endocrine comorbidity (predominantly diabetes).

Conclusions: In our large cohort of aggressively treated RA patients, infection followed by malignancy and not cardiovascular disease, was the leading cause of death. Larger prospective studies will be required to see if cumulative drug toxicity of more aggressive early treatment improves outcome from RA but changes mortality from comorbidities over time.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5442

FR10159 Infection and malignancy are now the major causes of death in aggressively treated rheumatoid arthritis patients


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Background: Patients with rheumatoid arthritis (RA) have an increased mortality compared to the general population. Previous studies have shown that this is attributable to cardiovascular and respiratory disease. Over recent years earlier and more aggressive treatment with higher dosage of methotrexate and the earlier use of biologic drugs has improved disease outcomes. The effect on cause of death is unknown. In this retrospective cohort study we found the major cause of death in RA was infection followed by malignancy and found no correlation with seropositivity or gender.

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Conclusions: In our large cohort of aggressively treated RA patients, infection followed by malignancy and not cardiovascular disease, was the leading cause of death. Larger prospective studies will be required to see if cumulative drug toxicity of more aggressive early treatment improves outcome from RA but changes mortality from comorbidities over time.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5442

FR10158 Evaluation of inflammatory cardiovascular (CV) risk factors in pre- and post-menopausal females with rheumatoid arthritis (RA)

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Objectives: To assess inflammatory markers and peripheral vessels involvement as markers of cardiovascular risk in female patients with RA.

Methods: 105 female patients who fulfill ACR/EULAR 2010 criteria were examined. Laboratory assessments consisted of biochemistry and hematological analysis, measuring of CRP level, rheumatoid factor, anti-CCP level, total cholesterol, HDL, LDL, triglycerides, apolipoprotein A1, apolipoprotein B, uric acid, HbA1c, microalbuminuria. DAS28 was used in characterizing RA activity. CV risk was defined per mSCORE. Tibial artery and carotid artery ultrasonography examination included the measurement of IMT in 3 points, detection of focal plaques in the extracranial carotid tree, blood flow velocity and morphology of the extracranial carotid tree.

Results: 83.3% reproductive age patients were without CV risk, 11.1% experienced middle level and 5.6% low level of CV risk on mSCORE. In 96.1% postmenopausal patients moderate, high and very high CV risk was detected. According to multiple logistic regression analysis we identified CV risk factors:
NON-INVASIVE ASSESSMENT OF MYOCARDIAL PERFUSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Cardiac involvement among patients with rheumatoid arthritis (RA) is common, potentially life-threatening, but often underdiagnosed at presymptomatic stages. Subendocardial viability ratio (SEVR) reflects microvascular coronary perfusion and it correlates with the ratio of subepicardial to subendocardial blood flow, that can be non-invasively estimated by applanation tonometry. Although it has been studied as a surrogate measure of myocardial perfusion in high-cardiovascular risk populations, it remains unclear whether it is affected in RA patients.

Objectives: The purpose of the study was to compare SEVR between RA patients and healthy controls. We additionally sought predictors of SEVR in RA among a wide range of disease-related parameters, hemodynamic factors, and markers of atherosclerosis, arteriosclerosis, and endothelial dysfunction.

Methods: Consecutive patients with RA and healthy, nontreated volunteers were recruited. SEVR was estimated from applanation tonometry with the Sphygmocor device (AtCor Medical, Sydney, Australia), which was also used to evaluate arterial stiffness (aortic index, Aix; pulse wave velocity, PWV). In the RA group, carotid atherosclerosis was additionally evaluated by ultrasound (carotid intima-media thickness, cIMT); cardiac and hemodynamic parameters by impedance cardiography, and endothelial dysfunction by measurement of asymmetric dimethylarginine (ADMA) in serum samples.

Results: A total of 122 participants, 91 RA patients and 31 controls, were studied. SEVR was significantly lower among RA patients compared to controls (141.4±21.9 vs 153.1±18.7%, p<0.005), and the same was observed when the subgroup of RA patients without cardiovascular comorbidities (n=29) was studied separately (139.7±21.7 vs 153.1±18.7%, p=0.013). In the univariate analysis, SEVR significantly correlated with cardiac and hemodynamic parameters, but not with PWV, Aix, cIMT, ADMA, or disease-related parameters. In the linear regression analysis accounting for sex, statin use, markers of atherosclerosis, carotid, and hemodynamic parameters, female gender (p=0.007), blood pressure (p=0.028), heart rate (p=0.025), cholesterol levels (p=0.008), cardiac index (p<0.001), and left ventricular ejection time (p=0.004) were identified as independent predictors of SEVR among patients with RA.

Conclusions: Patients with RA exhibit lower values of SEVR compared to healthy individuals, suggesting a disturbed balance between oxygen supply and demand that might lead to an additional pathophysiological link for the increased cardiovascular burden in RA. Cardiac and hemodynamic parameters, rather than markers of atherosclerosis, arteriosclerosis, and endothelial dysfunction, may be useful as predictors of impaired myocardial perfusion in RA.

INVESTIGATION OF THE PERIODONTAL CONDITION AMONG RHEUMATOID ARTHRITIS (RA) PATIENTS AND ANALYSIS OF INFAMMATORY MEDIATOR IN THEIR SERUM AND GINGIVAL CREEVICAL FLUID (GCF)

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Background: Rheumatoid arthritis (RA) and periodontitis (PD) are common chronic inflammatory diseases with remarkable pathological and clinical similarities. A lot of similarities exist between RA and PD at cellular and molecular levels.

Objectives: To analyse the PD incidence among RA patients, measure the level of tumor necrosis factor-alpha (TNF-α), Interleukin-1 (IL-1) and Interleukin-6 (IL-6) in their serum and gingival crevicular fluid (GCF), and to investigate their correlations.

Methods: The experimental group was composed of 350 patients with RA and the control group consisted of 426 age and gender matched healthy individuals. checks and record periodontal condition by dentist, analyse the PD incidence of the two groups, then select 64 PD patients without systemic diseases and 47 PD patients with a stable condition of RA. Detect and compare their periodontal status and the level of TNF-α, IL-1β and IL-6 in their serum and GCF.

Results: The percentage of PD was 67.7%, which was statistically significant higher than control group (43.6%) (P < 0.001). The periodontal disease index (PDI), Probing depth (PD) and Clinical attachment loss (CAL) in patients with RA and PD are significantly higher than those with simple PD (P < 0.05). But the bleeding on probing (BOP) in the two groups was not statistically significant (P > 0.05). Meanwhile, the level of TNF-α, IL-1β and IL-6 in serum and GCF are significantly higher in all PD patients than oral healthy individuals (P < 0.05). Although those inflammatory mediators in serum are much higher in patients with PD and RA than in those with simple PD (P < 0.01), there is no difference in the two groups about those inflammatory mediators in GCF. The serum level of TNF-α, IL-1β and IL-6 in patients with PD and RA are positively correlated with the corresponding inflammatory mediators in their GCF (r = 0.510.422 and 0.777 respectively, P < 0.01).

Conclusions: Individuals with RA are more likely to experience periodontitis compared to healthy subjects, and the periodontitis is much more serious in patients with RA and PD than those with simple PD. The serum and GCF inflammatory factors' level increased significantly in patients with RA and PD even during their RA stable period. The serum level of inflammatory factors in patients with PD and RA are positively correlated with the corresponding inflammatory mediators in their GCF. There is correlation between periodontitis and RA, and they may be the risk factors for each other. The improvement of the periodontal status of RA patients with RA and PD may help to control systemic inflammatory symptoms.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5919

Differences Between RA Patients With and Without ILD From a United States Tertiary Referral Center

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Objectives: To describe the characteristics of RA patients with and without ILD and to determine if medication use constitutes a risk factor for the development of ILD.

Methods: The medical records of RA patients with and without ILD treated at one academic center between 2008 and 2016 were analyzed. Data extracted include: patient demographics, serology, medication use, prednisone (mMARDs, biologics or small molecule drugs), and self-reported disease activity as MDHAQ and Rapid3 scores. The subtype of ILD was based upon HRCT imaging, and some patients through histology. Differences between RA-ILD patients and RA patients without ILD were determined by Fisher's exact test, and t-tests with a P < 0.05 were considered statistically significant.

Results: The demographics and clinical data of 1,024 RA non-ILD patients and 96 RA-ILD patients indicate ILD patients were older males, had a higher mortality and were less likely to have been never smokers (Table 1). At the onset of ILD (diagnosis, 31% were on no medication, 35% on monotherapy (MTX 16%, prednisone 13%, Etanercept 7%, Adalimumab or LEF 5%, Rituximab 4%, HCO 3%, and ≤1% on infliximab, SSZ or tocilizumab) and 11% received combination therapy. Twenty percent of the RA-ILD patients developed ILD preceding or coinciding with the diagnosis of RA. After the onset of ILD those patients were more likely to receive prednisonex and less likely to receive MTX than those without ILD (P < 0.05). The predominant types of ILD were as follows: UIP 27%, NSIP 15%, NSIP vs UIP 14%, and unclassifiable 9%.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>RA-ILD</th>
<th>RA without ILD</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>96</td>
<td>1,024</td>
<td></td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>48 (50%)</td>
<td>238 (23%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age (&gt;65)</td>
<td>57 (59%)</td>
<td>337 (33%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Never smoker</td>
<td>33 (34%)</td>
<td>504 (50%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FOS (≥14 units)</td>
<td>64 (67%)</td>
<td>671 (66%)</td>
<td>NS</td>
</tr>
<tr>
<td>CCP3 (≥20 units)</td>
<td>62 (65%)</td>
<td>617 (61%)</td>
<td>NS</td>
</tr>
<tr>
<td>MDHAQ</td>
<td>0.7</td>
<td>0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Rapid3</td>
<td>10.6</td>
<td>12.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusions: RA-ILD patients differed from RA patients without ILD in demographic characteristics, but not in self-reported measures of disease activity or serology. Thirty one percent of RA-ILD patients were not on any immunomodulatory medications at the time of ILD diagnosis, and 25% of RA-ILD patients developed ILD preceding, or coinciding with, the onset of active RA. Our results did not identify a specific drug class or biologic agent as a risk factor for developing ILD in RA patients.

Disclosure of Interest: R. Meehan

DOI: 10.1136/annrheumdis-2017-eular.4134

SERUM FREE LIGHT CHAINS OF IMMUNOGLOBULINS IN RHEUMATOID ARTHRITIS: CORRELATION WITH INTERSTITIAL LUNG DISEASE

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Background: Lungs in Rheumatoid arthritis (RA) seem to play an important role, not only as an extra-articular manifestation but also as a site of initiation of the disease and activation for the immune response. B lymphocytes are thought to be involved in the pathophysiology of RA and interstitial lung disease (ILD). The encouraging results of the use of Anti-CD20 treatments to stabilize articular symptoms and lung involvement reinforce this theory. Serum Free immunoglobulin Light Chains (FLC) might represent, in this context, an interesting marker of B lymphocytes activation during this disease.

Objectives: To determine the serum FLC levels in RA patients with and without ILD and to study their possible association with disease characteristics and activity.

Methods: Fifteen RA patients with clinically symptomatic interstitial lung disease, confirmed by computed tomography (RA-ILD) (53.3% females; mean age 61.27±6.48 years) and age matched RA patients (66.7% females) with no evidence of interstitial disease (non-ILD) were studied. Clinical and immunological inflammatory characteristics were assessed for all patients. FLC levels were quantified by turbidimetry (Freelite TM Kappa and Lambda Kits, The Binding Site, UK).

Results: The mean serum FLC-κ levels (RA-ILD: 40.74±16.94 ng/ml vs non-ILD 24.88±8.87 ng/ml, p=0.003) and FLC-λ levels (RA-ILD: 37.34±16.56 ng/ml vs non-ILD 26.28±7.22 ng/ml, p=0.028) were significantly higher in patients with ILD compared to non-ILD, while the serum FLC-κ/λ (RA-ILD: 1.15±0.38 vs non-ILD 1.00±0.43, p=0.304) were comparable.

There was no significant difference for the DAS28 disease activity score between both groups (RA-ILD: 4.6±1.5 vs non-ILD 4.38±1.46, p=0.69). No significant correlations were found between the DAS28-score and FLC-κ, FLC-λ and FLC-κ/λ (p=0.05). FLC-κ levels correlated significantly with ESR and CRP levels (p=0.01), while FLC-λ levels (p=0.005) but not with ESR (p=0.247) and FLC-κ/λ did not correlate with both ESR and CRP levels.

Conclusions: High levels of serum FLC are associated with RA-ILD and with a higher degree of inflammation, supporting the role of B cell activation in the pathophysiology of RA with ILD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5919

DIFFERENCES BETWEEN RA PATIENTS WITH AND WITHOUT ILD FROM A UNITED STATES TERTIARY REFERRAL CENTER

FR0165

RADIOPHORIC STRUCTURAL DAMAGE IS WORSE IN THE DOMINANT THAN THE NON-DOMINANT UPPER EXTREMIT Y IN PATIENTS WITH RHEUMATOID ARTHRITIS

FR0166

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Background: The relationship between mechanical stress and radiographic damage in rheumatoid arthritis (RA) has been detected in patients with hemipelgingia or poliomyligitis. In patients without neurological disorder, Kohn reported that radiographic damage was worse and progressed faster in the dominant hand in patients with RA.
individuals with early RA\(^2\). However, few studies have detected the radiographic damage in the whole upper extremity on the mechanical stress. **Objectives:** To examine the relationship between mechanical stress and radiographic damage in RA, we evaluated the joint destruction of the dominant and non-dominant upper extremity.

**Methods:** The joint destruction of the upper extremity (shoulder, elbow, wrist, metacarpophalangeal, interphalangeal, proximal interphalangeal) in 295 patients with RA, who were from 25 years to 91 years (mean age 64 years, mean disease duration 183 months, 86% females and 97% right-handed), was assessed according to the eroded joint, which was defined as ≥ 2 by Larsen scores for radiographic damage. These were divided into the dominant and non-dominant upper extremity. The Wilcoxon signed-rank test was used to examine the difference between the eroded joint count (EJC) in the dominant and the non-dominant upper extremity.

**Results:** The mean EJC in the dominant and the non-dominant upper extremity was 2.4 and 2.05 respectively. The EJC was significantly more in the dominant than the non-dominant upper extremity. And, in regards to every joint of upper extremity, the eroded joint rate was higher in the dominant than the non-dominant extremity.

**Conclusions:** The joint destruction was significantly more in the dominant than the non-dominant one, therefore it was suggested that the mechanical stress influenced the radiographic damage in patients with RA.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3621

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**FR0167**

**COMPARATIVE CARDIOVASCULAR SAFETY OF ABATACEPT AND TUMOR NECROSIS FACTOR INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT CARDIOVASCULAR DISEASE: A POPULATION-BASED COHORT STUDY**

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**Background:** Rheumatoid arthritis (RA) patients have an increased risk of cardiovascular disease (CVD). Recent studies suggested that treatment of RA with tumor necrosis inhibitors (TNFi) can reduce the risk of cardiovascular events. However, it is unknown whether a selective costimulation modulator, affects cardiovascular risk among RA patients compared with TNFi.

**Objectives:** To evaluate the comparative cardiovascular safety of abatacept versus TNFi in RA patients with and without underlying CVD.

**Methods:** We identified RA patients aged ≥18 with ≥2 RA ICD-9 codes (714.xx) separated by >7 days but <365 days, from two large insurance claims data across the U.S.: Medicare (2008–2013) and Truven MarketScan (2006–2015). Only new users of abatacept or TNFi (adalimumab, etanercept, certolizumab, golimumab, and infliximab) were included. The primary outcome of interest was a composite endpoint of CVD including myocardial infarction (MI), stroke/transient ischemic stroke, or coronary revascularization. Secondary outcomes were each component of the primary outcome, incident heart failure (HF), and venous thromboembolism (VTE). 1:1 propensity score (PS) matching was performed separately in each database and each subgroup (with or without baseline CVD). Then the PS-matched subgroups were aggregated to form the overall matched cohort. Cox regression model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) of risk of each outcome. Estimates from two different databases were combined through an inverse variance-weighted fixed-effects model.

**Results:** After 1:1 PS matching, there were 6,102 patient pairs from Medicare and 6,934 pairs from MarketScan. Among them, patients with baseline CVD were 35.3% in Medicare and 14.0% in MarketScan. Baseline characteristics were well balanced between two treatment groups after matching (standardized mean difference <0.1). In Medicare cohort, abatacept consistently showed a decreased risk of composite CVD compared with TNFi in overall and each subgroup (Figure). However, in MarketScan cohort, proportion of patients younger than Medicare cohort, there was no association between abatacept and CVD compared to TNFi. After combining the two databases, abatacept was significantly associated with reduced risk of composite CVD outcome vs. TNFi in overall cohort (HR =0.79, 95% CI=0.67–0.92) and baseline CVD subgroup (HR =0.79, 95% CI=0.64–0.98). We also observed similar trend for secondary outcomes, where abatacept had decreased risk than TNFi.

**Conclusions:** In this large multi-database population-based study of RA patients, abatacept treatment was associated with reduced risk of CVD compared to TNFi, especially among older population and patients with prior CVD conditions.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2727

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**FR0168**

**RESTORATION OF DECREASED LYMPHOCYTES, CD8+ T CELL SUBSETS WITH TH1 SKewed PHENOTYPE ASSOCIATE WITH SPONTANEOUS REGRESSION OF LYMPHO-Proliferative DISORDERS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE**

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\(^1\)Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo; \(^2\)Division of Rheumatology, Saitama Medical Center, Saitama Medical University; \(^3\)Division of Hematology, Saitama Medical Center, Saitama Medical University, Saitama, Japan

**Background:** Lympho-proliferative disorder (LPD) is known as a relatively rare but life-threatening complication in RA patients under MTX administration. Spontaneous regression of LPD after MTX withdrawal is regarded as a distinct character of LPD under MTX administration. Previous study from our institution [1] and others [2] reported the link between decreased lymphocyte counts at LPD diagnosis and restoration after MTX cessation and the regression of LPD.

**Objectives:** To investigate the immunological factors including lymphocyte subset which involved in spontaneous regression of LPD following MTX withdrawal.

**Methods:** We studied 35 RA patients complicated with LPD under MTX administration in our institution. Age, sex, RA disease duration matched control MTX-treated patients (N=25) were selected. LPD patients were divided into two groups regarding to the status of LPD after MTX cessation: regressive group (N=22) and persistent group (N=13). Clinical features were compared among 3 groups. Flowcytometric analysis of the whole blood sample and measurement of cytokine core concentration in RA patients under MTX administration. Following MTX cessation, significant increase in proportion and absolute number of these subsets were observed only in the regressive group, but not in persistent group. Regression of Th1 cells and EMCD8+ T cells significantly correlated with increase of serum IFN-γ, and expansion of EMCD8+ T cells inversely correlated with change of serum IL-15.

**Conclusions:** Restoration in proportion and absolute number of Th1 cells, EMCD8+ T cells and EBV specific CD8+ T cells coincided with increase of IFN-γ, and associated with regression of LPD developed under MTX administration. Since changes of those immunological factors were not observed in persistent LPD, this study would be the first report to demonstrate the difference of...
GLOMERULAR FILTRATION RATE IS LOW IN RHEUMATOID ARTHRITIS COMPARED TO HEALTHY POPULATION: ESSENTIAL ROLE OF INFLAMMATION

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Background: Rheumatoid Arthritis is associated with subclinical renal impairment which contributes to increase mortality and morbidity. The role of inflammation on kidney function in inflammatory arthritis is not well studied.

Objectives: To investigate the association between estimated glomerular filtration rates (eGFR), traditional cardiovascular risk factors, and markers of inflammation in rheumatoid arthritis compared to healthy controls.

Methods: RA patient were recruited through a specialized rheumatology clinic at the Ministry of Health and Prevention of UAE, from January 2013 to January 2016. Healthy subjects were recruited from the community through brochure advertisement. The Modification of Diet in Renal Disease Study (MDRD) formula was used to calculate the eGFR, ttest was used to compare the laboratory values and renal function parameters between two groups. Linear regression analysis used to look for the correlation between the eGFR and each of the traditional cardiovascular risk factors and inflammatory markers

Results: 98 RA patients and 82 controls were recruited. None of the patients has history of diabetes, atherosclerosis or renal impairment. The mean age for the total participants was 49±13 years (M±6 – Max 82). The mean eGFR of the inflammatory arthritis patients was 118±30 ml/min (range 60–227) and 128±37 ml/min (range 62–286) for the controls. Patients and control had no significant difference in Systolic and diastolic blood pressure. Inflammatory arthritis patients had lower GFR, albumin (P<0.001), and total protein (P=0.03) levels, and had higher Erythrocyte Sedimentation Rate (ESR) (P<0.001), C-reactive protein (CRP) (P<0.001), and uric acid level (P=0.01). Negative linear relationships were found as follows:

Among RA patients and controls: There was a negative linear relationship between GFR and each of the age of the participants; (p<0.001, CI: -1.24 – 0.40 for the patients and p=0.01, CI: -1.82, -0.26 for the controls), and the systolic blood pressure; (p=0.04, CI: -0.61 for the patients and, -0.0 and p=0.022, CI: -0.61, -0.05 for the controls).

Among RA patients: The GFR had a negative linear relationship with the age of the patients (p<0.001, CI: -1.24, -0.05, diastolic blood pressure; (p=0.02, CI: -0.05, systolic blood pressure; (p=0.04, CI: -0.61, -0.05 for the patients and, -0.0 and p=0.022, CI: -0.61, -0.05 for the controls).

Conclusions: In RA non-traditional cardiovascular risk factors such as inflammatory markers are associated with sub-clinical presence of renal injury. Our data indicate that in RA, inflammation is involved in the early stages of impaired kidney function. Whether anti-inflammatory therapies are effective in slowing down the deterioration of kidney function in the arthritis diseases remain to be established.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4662

FR0169

FR0171 OSTEOPOROSIS CONTRIBUTES TO SUBOPTIMAL PHYSICAL FUNCTION IN RHEUMATOID ARTHRITIS

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1McGill University, Montreal, Canada; 2Johns Hopkins, Baltimore, United States

Background: Aggressive, early treatment of RA with new therapeutic agents has dramatically improved the management of RA. However, many studies have failed to show greater improvements in function or disability reduction between targeted control vs. less-aggressive care. The prevalence of obesity is increasing dramatically globally, and may be even higher in RA patients.

Objectives: Because obesity is also a risk factor for disability, we evaluated the extent to which excess weight may independently contribute to poorer physical function (PF) in RA.

Methods: RA patients enrolled in an observational study at an academic inflammatory Arthritis Clinic in Baltimore USA completed the patient global, pain VAS, SF 36, SICMS measured oxygen during PF, fatigue, sleep, and depression. RA clinical indicators were also collected at the visit. Outcomes were compared in obese and non-obese patients using t-tests and chi-square. Multiple regression was used to evaluate the effects of pain, fatigue, and BMI on PF, after controlling for age and eGFR. The c-statistics were calculated using the Harrell's C statistic.

Results: Participants were mostly female (82%) and white (83%) with mean (SD) age of 55 (13) years; 24% had < high school; RA duration 12 (9). Mean CDAI was 8.1 (8.1). Most were in CDAI remission (n=57; 32%) or LDA (n=64; 36%); 40 (23%) were in MDA and 16 (9%) in HDA. 49 (28%) was classified as normal weight (BMI 18.5–24.9), 46 (26%) were overweight (BMI 25–29.9) and 82 (46%) were obese (BMI>30). Men had a significantly higher mean BMI than women (33.6 [8.4] vs. 29.5 [7.2], p=0.006). As compared to non-obese participants, obese participants had a significantly higher BMI and HbA1c (6.1 vs. 4.9; p<0.005, respectively) and worse PF, pain, fatigue, sleep, and depression (mean differences -5.0, -4.6, 4.6, 3.8, 2.9, 3.6, and -4.7, respectively). In regression analyses, pain, fatigue, and BMI (but not sleep or depression) were inversely related to PF, after controlling for age and disease activity. In the final model, pain, fatigue and BMI were significantly and inversely related to PF (≤–3.9, -2.4, and -1.53, respectively) after controlling for age and disease activity (F (5, 170) =55.5, p=0.000, adjusted r2=0.61).

Conclusions: Our results suggest that excess weight also contributes to poor PF in addition to pain and fatigue. As the prevalence of obesity continues to

Table: Indicators of Contribution of Factors in RA

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Stderr</th>
<th>Sig</th>
<th>T</th>
<th>VIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>-3.36</td>
<td>.405</td>
<td>-4.0</td>
<td>1.01</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-2.40</td>
<td>.266</td>
<td>-1.5</td>
<td>.49</td>
</tr>
<tr>
<td>BMI</td>
<td>-1.53</td>
<td>.128</td>
<td>1.01</td>
<td>1.07</td>
</tr>
</tbody>
</table>

Adjusted for age and CDAI.
PREVALENCE AND FEATURES OF THE “MASKED” ARTERIAL HYPERTENSION IN WOMEN WITH RHEUMATOID ARTHRITIS IN THE ABSENCE OF CARDIOVASCULAR DISEASES BASED ON AMBULATORY BLOOD PRESSURE MONITORING

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Background: Cardiovascular (CV) events are the main reason of increased mortality at patients with rheumatoid arthritis (RA). Arterial hypertension (AH) takes a leading position among CV risk factors in RA. Ambulatory blood pressure monitoring (ABPM) has to be executed for persons with high cardiovascular risk and can be used for evaluation of “masked” arterial hypertension (MAH), according to the current recommendations.

Objectives: To estimate the frequency of identification and peculiarities of the MAH according to ambulatory blood pressure monitoring in women with RA without CV diseases.

Methods: The study included 36 women with RA (ACR 1987 and/or EULAR/ACR 2010 criteria) without CV diseases and AH (according to the anamnesis and 3-fold “office” blood pressure (BP) measurement). Mean age of RA patients was 55.7±15 years; mean duration of RA was 10 [3; 17] years, mean DAS 28 – 5.25 [4.6; 5.7]. As controls were involved 39 women with RA and AH (mean age 58.3±6.8 years; mean duration of RA - 8 [4; 14] years, mean DAS 28- 5.08 [4.04; 5.85]) and 30 women with AH without inflammatory joint diseases (mean age 55.9±6.2). Exclusion criteria were smoking, diabetes mellitus, symptomatic AH (except controls), cardiovascular diseases.

ABPM was measured using the BPlab with the program VASOTENCE® (Russian). Criteria for MAH were out-of-office BP ≥135/85 mmHg and/or average daily out-of-office BP ≥130/80 mmHg according to ABPM and considering optimal office BP.

The anamnesis, laboratory and instrumental methods of inspection were considered. Statistical analysis was performed with STATISTICA 7.0 (State Soft, USA).

Results: According to ABPM 24 of the 36 (66.6%) RA patients had optimal BP, 12 (33.3%) patients had the MAH phenomenon.

The patients with RA+AH and RA patients had the comparable levels of a daily BP [132.1/80.7 and 126.9/78.0 mmHg respectively, P>0.05]. The RA patients with MAH had statistically significant differences of BP in day and night hours [137.5/87 mmHg and 137/84 mmHg, respectively] compared to the RA+AH patients [131.8/80.7 mmHg and 126.3/73.8 mmHg, respectively, P=0.004] and AH patients [126.9/78 and 118/98.5 mmHg, respectively, P=0.001] with what MAH had.

Nocturnal systolic BP correlated with ESR (Spearmen's r=0.64, P<0.05). Daily diastolic BP correlated with SCORE/EULAR (r=0.40, P<0.05) and arterial stiffness index (r=0.86, P<0.05) in RA patients with MAH; nocturnal systolic BP correlated with C-reactive protein (r=-0.36, P<0.05) in RA+AH patients.

More than 60% of the RA+AH patients and RA+MAH patients had high variability of BP. High variability of nocturnal systolic BP occurred at 34.3% and 44.4% of RA+AH and RA+MAH patients, respectively.

In RA patients were found correlations between indices of a BP variability, duration of RA (r=0.33, P<0.05); C-reactive protein (r=-0.36, P<0.05); daily diastolic BP (r=-0.35, P<0.05); pulse BP (r=0.31, P<0.05); and frequency of non-steroidal anti-inflammatory drugs intake (r=-0.42, P<0.05).

Conclusions: In RA patients AH can proceed subclinically. Activity of RA and increased arterial stiffness can predict the masked arterial hypertension's development in RA patients. ABPM measurement can be use full in early evaluation of AH and optimization of RA treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.s500

CORRELATION BETWEEN ASYMMETRIC DIMETHYLPARTINE AND HOMOCYSTEINE LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis is a chronic inflammatory condition associated with increased cardiovascular disease (CVD) morbidity and mortality due to high coronary and cerebral atherosclerotic burden. Asymmetric dimethylarginine (ADMA) is the most potent endogenous inhibitor of nitric oxide synthase - is an emerging marker of endothelial dysfunction and CVD in several conditions such as coronary artery disease and diabetes mellitus. ADMA levels are higher in RA patients compared to controls suggesting a role in the development of atherosclerosis. In addition ADMA is involved in the metabolism of homocysteine (Hcy) which is considered a novel, non-traditional CVD risk factor contributing to excess CVD risk in this population.

Objectives: The aim of our study was to determine whether asymmetric dimethylarginine (ADMA) levels are associated with Hcy and methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism in patients with RA.

Methods: Serum ADMA and Hcy levels were measured in 201 RA individuals [155 (77.1%) females, median age 67 years (interquartile range 59–73)]. The MTHFR C677T polymorphism was assessed by using the LightCyclerTM System. Initially, ADMA was compared across the categories of MTHFR using a one-way analysis of variance (ANOVA), followed by a multivariate model, which accounted for Hcy, age, erythrocyte sedimentation rate (ESR), and homeostatic model assessment (HOMA).

Results: In univariable analysis, ADMA differed significantly across the categories of MTHFR C677T (p=0.037). Patients with the MTHFR C677T genotype had the highest ADMA levels, with a median of 0.62 (SE =0.03), significantly higher than either those patients carrying the MTHFR 677CT (0.55, SE =0.01) or the MTHFR 677CC (0.55, SE =0.01) genotype (p=0.042) in both cases. In the multivariable model, Hcy (p=0.023) and ESR (p<0.001) were found to have significant positive associations with ADMA before the relationship between MTHFR gene variants and ADMA was found to be non-significant (p=0.102).

Conclusions: The results of our study indicate an association between ADMA and Hcy in patients with RA without any genetic background as no relationship was established between ADMA and MTHFR gene variants. Abnormal metabolism of Hcy and dimethylarginines may interfere with each other resulting in endothelial dysfunction and accelerated atherosclerosis in RA individuals.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.s512
Conclusions: ILD is a serious complication in RA with a significantly increased mortality compared with a large matched cohort of RA comparisons without ILD.

Disclosure of Interest: None declared


FR0175 USING SMARTPHONES TO IMPROVE REMOTE MONITORING OF RHEUMATOID ARTHRITIS: COMPLETENESS OF PATIENTS’ SYMPTOM REPORTS

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Background: Clinical decisions about management of rheumatoid arthritis (RA) happen at intermittent clinic visits. In the absence of objective measures of disease severity between visits, understanding fluctuating disease severity largely relies on patients’ symptom reports, and thus on patients’ recall, eloquence, stoicism and willingness to discuss symptoms.

The Remote Monitoring of Rheumatoid Arthritis (REMORA) study aims to improve monitoring of disease severity in RA. Patients, clinicians and researchers co-designed a smartphone app to enable RA patients to report daily symptoms between clinic visits, and integrate these data into a patient electronic health record. The data presented here were collected as part of the REMORA feasibility evaluation.

Objectives: To evaluate the completeness of patient-reported symptom data submitted through the REMORA smartphone app over three months.

Methods: We invited 23 RA patients treated at the outpatient clinic of Salford Royal Foundation Trust (UK) to record their symptoms for three months using the REMORA smartphone app. Participants received notifications to record: daily scores for the seven items of the RA Impact of Disease score, as well as morning stiffness on a scale from 0 to 10; weekly scores for thirteen items of the Health Assessment Questionnaire (HAQ) 20-item disability scale. We calculated the time that participants were in the study as the number of days between the first and last day of submitting daily scores. We then explored patterns of data entry, as well as entry completeness.

Results: Twenty patients accepted the invitation to participate. Eight (40%) were male, all but one were white British, and their mean age was 56.9±11.1 years. The median number of days in the study was 82 (interquartile range [IQR], 80 to 82). Of all 213 weekly entries, fifteen (7%) had missing values, but never more than two. No more than nine (<1%) of the 1325 daily entries were incomplete, with only nine (~1%) having missing values for up to two individual items. Participants submitted weekly scores for a medium of 11 out of 13 weeks (IQR, 10 to 12). Of all 213 weekly entries, fifteen (7%) had missing values, but never more than two. Lastly, 8/20 participants provided monthly HAQ scores only once, while a further 9/20 and 3/20 participants did this for two and all three months, respectively. No monthly entries had any missing values.

Conclusions: Our feasibility study showed that smartphones have the potential to support collection of daily patient reports of symptoms with high levels of completeness over three months. Lengthier monthly question sets were less likely to be completed compared to briefer daily and weekly ones. Future steps include exploring methods of data entry frequency to (fluctuations in) disease severity in order to support sustained symptom reports over longer time periods and in a wider group of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4032

FR0176 | CORRELATION BETWEEN DISEASE ACTIVITY AND MENTAL HEALTH IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS: THE ASSESSMENT WITH SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILES TOOLS

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1. Arthritis UK Centre for Epidemiology, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester; 2. Centre for Primary Care, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester; 3. Centre for Primary Care, Faculty of Biology, Medicine and Health, University of Manchester; 4. Department of Rheumatology and Immunology, Jiangsu Province Hospital, Nanjing, China

Background: Rheumatoid arthritis (RA) patients can cause joint swelling and tenderness, and affect the patient’s mental health. Previous studies showed that 13–47% of RA patients suffered from anxiety and/or depression. Hospital anxiety and depression scale (HADS) is usually used to evaluate patients’ mental health, which consists of 14 items divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Disease activity score in 28 joints (DAS28) is one of the most used tools to measure disease activity in RA patients. The activity, both HADS and DAS28 assessments were commonly led by health professionals with paper questionnaire. This study applies the mobile platform of Smart System of Disease Management (SSDM) for evaluating DAS28 and HADS by RA patients.

Objectives: The purpose of this study is to describe the morbidity of mental conditions in Chinese patients with RA and analyze the potential association among DAS28 and HADS.

Methods: SSDM is a mobile application includes physicians’ and patients’ interfaces. The patient’s terminal system includes self-assessment (DAS28, HADS), lab test results and medication management. After data entry, patients can synchronize data to the mobile terminal of their authorized rheumatologist. A cohort study was conducted with patients who were diagnosed with RA in tertiary hospital across China. All participants self-assessed both DAS28 and HADS with SSDM at least one time. Descriptive statistics were performed for patient and disease characteristics, assuming normality for DAS28 distribution and the level of disease activity was analyzed using Pearson’s statistics. One-way analysis of variance was employed to explore for difference between sub-groups. Bivariate correlation and linear logistic analysis were employed to explore for potential factors among DAS28 and HADS.

Results: From June 2016 to January 2017, 230 patients (male 66, female 164) from 12 hospitals performed 311 times HADS and 517 times DAS28 self-assessment. The mean (±SD) age was 34.17±13.11 (11–71) years, with the median disease duration of 24.70 (0–572) months. As the standard of HADS score, less than 10, 10 to 11, 12 to 13 and above 13 points, patients could be divided into four levels of anxiety and depression respectively. According to the DAS28 assessment results, the proportion of patients with remission, low disease activity, moderate activity and high activity were 18%, 19%, 46% and 18% respectively. Bivariate correlation showed that DAS28 was positively correlated with HADS, p<0.001. Both HADS-A and HADS-D showed linear regression association with DAS28 score. The regression equation as “HADS-A = 5.962 + 0.435*DAS28” and “HADS-D = 6.379 + 0.694*DAS28” respectively, p<0.001.

Conclusions: DAS28 was positively correlated with HADS. SSDM is an effective mobile interface to serve for RA patients performing self-management of both disease activity and mental health as well as to supply physicians with valuable data.

Disclosure of Interest: None declared


FR0177 | THE UNDERRATED PREVALENCE OF DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Significant evidence in the scholarly literature suggests that depression is a common comorbidity among patients with rheumatoid arthrit (RA) (1) Comorbid depression in RA patients is especially troublesome because it often goes unrecognized and untreated (2) often because rheumatologists and their patients seldom communicate about depression (3). In addition, evidence of depression in RA patients is limited in Asia studies.

Objectives: To determine the prevalence of depression among patients with RA and explore the relationships between depression and an array of variables.

Methods: Cross-sectional online survey (n=500) of RA patients including the Patient Health Questionnaire [PHQ-9] (4) to measure the presence and severity of depressive symptoms were performed. The survey included demographic, clinical characteristics such as functional impairment as assessed using the Japanese version of the Stanford Health Assessment Questionnaire (J-HAQ score), and the participant’s current medical treatment. Ordered logistic regression was used to identify the determinants of depression conditions among survey respondents.

Results: The mean age of the 500 patients with RA was 54.3 years old and 67% were female. While only 25 (5%) of the population studied had been officially diagnosed with depression, 176 (35%) had PHQ-9 scores indicating depression was present. Comorbidity conditions, except for migraine and heart conditions, were not different between patients with depression and those without. Logistic regression analysis revealed a negative correlation between the prevalence of depression and younger age with odds ratio (OR) of 0.96 (95% confidence interval (CI), 0.92–0.99); higher education level (OR, 1.06; 95% CI, 0.96–1.18); and a bachelor’s degree (or higher) and an income level of 0.6–1.6 million yen (OR, 0.45; 95% CI, 0.22–0.91). Positive correlations with depression was found in RA patients with high J-HAQ score (OR, 1.99; 95% CI, 1.47–2.71). Patients treated with biologic monotherapy were significantly less likely have depression compared to those treated with non-biologic anti-rheumatic drugs (OR, 0.36; 95% CI, 0.17–0.75).

Conclusions: It is a potential risk of under-diagnosis and under-reporting of Depression in patients in Asia patients are more likely to experience depression if they are younger, have greater functional impairment, or whose treatment regimen includes pain medications without biologic drugs.
RITUXIMAB IS EFFECTIVE IN THE TREATMENT OF RHEUMATOID ARTHRITIS REGARDLESS OF BODY MASS INDEX

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¹Hanyang University Hospital for Rheumatic Diseases, Seoul; ²In-HA University, School of Medicine, Inchon; ³Apu University School of Medicine, Suwon; ⁴Chungnam National University Hospital, Daejeon; ⁵Celltrion Inc., Incheon, Korea, Republic Of

Background: High body mass index (BMI) is known to be associated with inadequate clinical response to anti-TNF agents in rheumatoid arthritis (RA) patients. However, there are limited data on the effect of high BMI on the response to rituximab in RA patients, who showed an inadequate response or intolerance to anti-TNF agents.

Objectives: To investigate the impact of BMI on clinical response in the post-hoc analysis of randomized controlled trial that demonstrated clinical equivalence between a biosimilar of rituximab, CT-P10 and innovator rituximab, RTX 2

Methods: A total of 332 patients who received two courses of either CT-P10 or RTX were included in this analysis. Patients were classified into 3 groups; normal weight (<30 kg/m²), overweight (≥25 kg/m² – <30 kg/m²) and obesity (≥30 kg/m²) as per WHO BMI category. Improvement in disease activity by the Disease Activity Score using C-reactive protein (DAS28-CRP), remission (≤2.6), low disease activity rate (LDA, <2.2) and ACR response at Week 24 (Week 24 of 1st course) and Week 48 (Week 24 of 2nd course) and duration of sustained LDA (from the 1st LDA observed to the last LDA observed up to Week 48) were analysed by BMI categories in the each and combined group of CT-P10 and RTX.

Results: In the pooled group of CT-P10 and RTX, the mean weights were 59 kg in normal weight, 73kg in overweight and 91kg in obesity. All other baseline characteristics were comparable among BMI groups including baseline disease activity based on DAS28; Moderate disease activity, 22.3% vs. 22.8% vs. 25.7%, respectively; High disease activity, 77.7% vs. 77.2% vs. 74.3%, respectively. There was no statistical difference among BMI groups in terms of DAS28 change from baseline and ACR 20/50/70 response (Table). No particular trend was observed in remission and LDA rate by DAS28 at Week 24 and Week 48 among BMI groups (Figure). Mean duration of sustained LDA (months) were also comparable among the groups (4.5 vs. 4.7 vs. 5.0, respectively). Additionally, similar trends in all analyses were observed in each treatment group; CT-P10 and RTX.

Conclusions: The BMI does not affect the clinical response in RA patients with rituximab treatment. Therefore, this result supports that rituximab could be a reasonable therapeutic option for obese RA patients with inadequate response to anti-TNF agents.


Table 1. DAS28, ACR responses by BMI subgroups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal (N=148)</th>
<th>Overweight (N=114)</th>
<th>Obesity (N=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.88 (0.95)</td>
<td>5.81 (0.89)</td>
<td>5.69 (0.78)</td>
</tr>
<tr>
<td>Week 24*</td>
<td>-2.43 (1.12)</td>
<td>-2.13 (1.19)</td>
<td>-2.39 (0.99)</td>
</tr>
<tr>
<td>Week 48*</td>
<td>-2.76 (1.37)</td>
<td>-2.47 (1.32)</td>
<td>-2.74 (1.01)</td>
</tr>
<tr>
<td>ACR20, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td>122 (62.4%)</td>
<td>96 (75.4%)</td>
<td>56 (80.0%)</td>
</tr>
<tr>
<td>Week 48</td>
<td>119 (80.4%)</td>
<td>86 (77.2%)</td>
<td>60 (85.7%)</td>
</tr>
<tr>
<td>ACR50, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td>80 (54.1%)</td>
<td>56 (49.1%)</td>
<td>39 (55.7%)</td>
</tr>
<tr>
<td>Week 48</td>
<td>76 (51.4%)</td>
<td>62 (54.4%)</td>
<td>43 (61.4%)</td>
</tr>
<tr>
<td>ACR70, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td>51 (34.5%)</td>
<td>33 (28.6%)</td>
<td>21 (30.0%)</td>
</tr>
<tr>
<td>Week 48</td>
<td>47 (31.8%)</td>
<td>36 (31.6%)</td>
<td>26 (37.1%)</td>
</tr>
</tbody>
</table>

Table A: Baseline characteristics of mothers and infants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All mothers (N=148) (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>36.1 (0.007)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>66.9 (0.000)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>29.6 (0.000)</td>
</tr>
<tr>
<td>Indication for CZP treatment, p [b]</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>0.000</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>0.012</td>
</tr>
<tr>
<td>Axial spondylarthritis</td>
<td>0.016</td>
</tr>
<tr>
<td>Cauh's disease</td>
<td>0.007</td>
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</tbody>
</table>

Table B: Concentrations of CZP (μg/mL) in breast milk

<table>
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<tr>
<th>Mother no</th>
<th>Relative time (days)</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>14</th>
<th>18</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>5.3</td>
<td>0.092</td>
<td>0.092</td>
<td>0.074</td>
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<tr>
<td>2</td>
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<td>0.092</td>
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<tr>
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<td>0.092</td>
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<td>4</td>
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<td>4.0</td>
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<td>6</td>
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</tr>
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<td>7</td>
<td>3.8</td>
<td>0.092</td>
<td>0.092</td>
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</table>

Figure 1. Remission and LDA by DAS28 by BMI group.
safe profile consisting of events occurring in unexposed infants of similar age.

Conclusions: C2P was below the lower limit of quantification in 56% of the milk samples. When detectable, C2P concentrations were less than 3x LLOQ (<1% of expected plasma concentration of a therapeutic dose), indicating no to minimal transfer of C2P from plasma to breast milk. RID was below 0.5% of maternal dose and is thus unlikely to be of clinical concern. C2P absorption in breast milk is unlikely, due to low bioavailability and its Fc-free molecular structure. These findings support continuation of C2P treatment during breastfeeding.

References:

Acknowledgements: This study was funded by UCB Pharma. We are indebted to the mothers and their infants for their altruistic participation. We thank the nurses, investigator teams and Nicole Hurst, PPD, and acknowledge Amanda Golembsky and Gerry Parker, UCB Pharma. Editorial services were provided by Costello Medical Consulting.


References:
endpoint was disease worsening according to disease-specific composite measures and/or consensus between investigator/patient leading to major treatment change. Exploratory subgroup analyses examined disease worsening and safety in RA. The primary endpoint was analysed using logistic regression, adjusted for diagnosis and disease duration.

**Results:** Demographics, occurrence of disease worsening, change in disease measures and treatment-emergent adverse events (TEAE) were similar (Table). Serum drug levels for INX and CT-P13 were similar throughout the study (Figure).

**Conclusions:** Explorative analyses in the NOR-SWITCH study showed similar efficacy, serum drug levels and safety in RA patients switched to CT-P13 as those on continuous INX. The study was not powered to show non-inferiority within each diagnosis.

**References:**


**Disclosure of Interest:** G. Goll Consultant for: Orion Pharma, Pfizer, Novartis, Boeringer Ingelheim, AbbVie, I. Olsen: None declared, N. Bolstad: None declared, K. Jørgensen Consultant for: Intercept, Celtrion, Tillot, M. Lorentzen: None declared, C. Merk Consultant for: Cellgene, AbbVie, Novartis, LefoPharma, ACHUd, Galdena Nordic, J. Jahnssen Consultant for: OnornPharma, Celtrion, Pfizer, MSD, AbbVie, Takeda, NappPharma, AstroPharma, E. Haavardsholm Consultant for: AbbVie, UCB, Roche, MSD, Pfizer, T. Kvien Consultant for: Biogen, BMS, Boehringer Ingelheim, Celtrion, Eli Lilly, Epirus, Hospira, Merckserono, Novartis, OnornPharma, Pfizer, Sandoz, UCB DOI: 10.1136/annrheumdis-2017-eular.2319

Data are n (%), mean (SD) or median (25–75 percentiles). 95% CI, 95% confidence interval of the adjusted treatment difference. DAS28, Disease Activity Score in 28 joints. FAS, Full Analysis Set. PPS, Per Protocol Set. TEAE, treatment emergent adverse events.

**FR0183 ASSESSING ADHERENCE OF RA PATIENTS TREATED WITH ETANERCEPT USING ETANERCEPT SERUM TROUGH CONCENTRATIONS AND PATIENT SELF-REPORT**

E. Vogelzang1, R. Hebing2, M. Nurmohamed3, L. A’Ami1,3, C. Kriekdaert4, G. Wolbink1,2.

1. Rheumatology; 2. Rheumatology, Pharmacy, Amsterdam Rheumatology and immunology Center | Reade; 3. Immunopathology, Sanquin Research and Landsteiner Laboratory, Amsterdam, Netherlands

**Background:** The EULAR recommendations for the management of rheumatoid arthritis (RA) update 2013 contained the following research question: "How good is patient adherence to biological agents and can lack of adherence be related to loss of efficacy?"[1] Limited studies are published in which adherence of RA patients treated with biological disease-modifying antirheumatic drugs (bDMARDs) has been assessed. Previous studies regarding adherence of RA patients treated with etanercept did not take into account that patients are instructed to temporarily discontinue bDMARDs therapy during e.g. a serious infection. In addition, etanercept concentrations have never been utilized in determining adherence to etanercept in RA patients.

**Objectives:** The aim of our study was to determine the percentage of non-adherent RA patients treated with etanercept, using etanercept concentrations and patient self-report, and to assess the relationship between adherence and clinical outcome during 52 weeks.

**Methods:** Non-adherence was defined as an etanercept trough concentration <0.1ug/mL at least once and non valid/medical reason to miss an etanercept dose. In this retrospective cohort study patients visited our clinic at baseline and in 4, 16, 28, 40 and 52 weeks after initiation of etanercept treatment. At baseline and following visits disease activity score of 28 joints (DAS28) was calculated and blood was drawn to measure etanercept concentrations. During each visit patients were asked if they missed an etanercept dose, at which date and for which reason. Remission was defined as DAS28 <2.6 at least for two consecutive visits. Low disease activity (LDA) was defined as DAS28 <3.2 during a minimal of two consecutive visits.

**Results:** In total 292 patients were included. Mean age was 53 years (SD 12.7), 82% were women and median disease duration was 8 years (IQR 3–16). In total 24 patients had an etanercept concentration <0.1ug/mL. Most patients had a medical reason to miss an etanercept dose, see table 1.

Table 1. Reasons for patients to miss an etanercept dose

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number of patients</th>
</tr>
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<tbody>
<tr>
<td>Medical</td>
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<tr>
<td>Did not start</td>
<td>3</td>
</tr>
<tr>
<td>Logistical problem</td>
<td>1</td>
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<tr>
<td>Steped due to inefficacy</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>9</td>
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</table>

Only ten patients (3.4%) were non-adherent during the follow-up of 52 weeks. Of the adherent patients 82 out of 282 (29%) reached LDA versus 1 out of 10 non-adherent patients. A total of 127 of 282 (45%) adherent patients achieved MDA versus 3 out of 10 non-adherent patients.

**Conclusions:** Most patients had a medical reason to miss an etanercept dose. The percentage of patients who are non-adherent to etanercept therapy is very low (3.4%).

**References:**


**Disclosure of Interest:** E. Vogelzang: None declared, R. Hebing: None declared, M. Nurmohamed Speakers bureau: Abbvie, Bristol-Meyers Squibb, Merck Sharp & Dohme, Celgene, Pfizer, Roche, Janssen, UCB and Sanofi, M. A’Ami: None declared, C. Kriekdaert Speakers bureau: Pfizer and Abbvie, G. Wolbink Grant/research support from: Pfizer, Speakers bureau: Pfizer, UCB and Abbvie DOI: 10.1136/annrheumdis-2017-eular.1652

**FR0184 THE PROFILES OF PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO THEIR BELIEFS IN THEIR BIOLOGICAL DRUGS. ARCO STUDY**


**Objectives:** To describe profiles of rheumatoid arthritis (RA) patients according to their beliefs in their subcutaneous biological medication (SC).
Methods: ARCO was a study carried out on RA Spanish patients who initiated a SC biological drug 11–18 months prior to the study visit. Patients completed the Beliefs About Medication Questionnaire (BMQ). According to the scores obtained in the necessity (N) and concerns (C) sub-scales, patients were classified into 4 groups: accepting (high N \([-3\) to low C \([\leq 3\) ), ambivalent (N:3 to C:3), indifferent (N:3 to C:3) and skeptical (low N: [3] to high C: [3]). We studied demographic characteristics, expectations and satisfaction with the treatment by group.

Results: 321 patients (77% women) completed the BMQ, 92.8% scored N:3 and 58.9% C:3. A higher % of men than women scored N:3 (13.5% vs. 5.2%, p = 0.031). The % who scored C:3 was higher in those with low satisfaction with symptom control (71.1% vs. 56.7% in satisfied/very satisfied, p = 0.098), or side effects (72.1% vs. 52.0%, p < 0.001), and in those with lower fulfilment of expectations of efficacy and tolerance (p < 0.001). The combination of N and C scores identified 116 accepting (36.1%), 182 ambivalent (57.7%), 16 indifferent (5.0%) and 7 skeptic patients (2.2%). There were no differences in age, gender, or RA duration among the groups, but differences were seen in the satisfaction with the treatment and in the fulfillment of the expectations (table). Ambivalent patients showed less satisfaction and lower fulfillment of expectations with the treatment received than accepting patients.

Conclusions: Patients with RA have strong beliefs about the need of their biological SC medication, but a high % also expresses concerns. Beliefs, and especially concerns, seem to relate to the satisfaction and fulfillment of expectations of efficacy and tolerability of the drug, rather than to demographics or RA characteristics. Discussing expectations may be important when initiating a biological treatment.

Acknowledgements: Funded by MSD, Spain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6242

FR10186 | INFLUENCE OF IMMUNOGENICITY TO THE FIRST TNF-I THERAPY ON RESPONSE TO THE SECOND BIOLOGIC AGENT IN RA PATIENTS


Background: There is currently no consensus on selecting a therapeutic target in patients (pts) non-responsive to their first TNF-inhibitor (TNF-i). The development of anti-drug antibodies (ADA) is a frequent cause of secondary inefficacy in our pts with TNF-i and there is evidence that those who develop ADA at their 1st TNF-i achieve a higher degree of response to the second, compared to ADA-pts. Thus ADA measurement can help in choosing a therapeutic target in pts who failed to respond to their 1st TNF-i.

Objectives: To assess if development of ADA to the 1st TNF-i determines better response when switching to a 2nd TNF-i versus a non-TNF-i. As secondary objective, analyze whether the presence or absence of ADA to a 1st TNF-i influences the efficacy of a 2nd TNF-i.

Methods: Of a total of 144 pts that switched from infliximab or Adalimumab to a 2nd biologic agent (Etanercept, Rituximab, Tocilizumab, Adalimumab, Abatacept, Certolizumab and Infliximab only, who had measured drug levels (DL/ADA) at discontinuation of the 1st TNF-i, were included. Clinical response was evaluated with DAS28, Delta-DAS28 (ΔDAS28) and EULAR response (E-resp) at 6 (v-6) and 12 (v-12) months after initiating 2nd biologic agent and at the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the biological therapy (v-end). DL/ADA levels were measured by ELISA. Statistical analysis was performed using SPSS version 20.0.

Results: Within the 60 pts who had measured DL/ADA at suspension of the 1st TNF-i, 26 (43%) were ADA- (i.e. DL-). In this ADA-subpopulation, 50% changed to a 2nd TNF-i; at v-end there were no differences between non-changers to a 2nd TNF-i and switchers to a non-TNF-i in DAS28 (3.7±2.1 TNF-i vs 4.2±1.1 non-TNF-i, p = 0.286), ΔDAS28 (1.4±2.1 TNF-i, 1.3±2.1 non-TNF-i, p = 0.374) and resp-E (75% good/moderate resp in TNF-i, 40% in non-TNF-i, p = 0.064). At v-12, switchers to a 2nd TNF-i showed a lower DAS28 (2.5±0.6 TNF-i, 3.9±1.0 non-TNF-i, p = 0.009) and a higher good E-resp rate with a marginally significant difference (80% in TNF-i, 22% in non-TNF-i, p = 0.071). However, at v-end, pts with a 2nd non-TNF-i had better response (ΔDAS28 = −5.1 in 50% of TNF-i pts, 0% of non-TNF-i pts, p = 0.044). Likewise ΔDAS28 at v-end was higher in the non-TNF-i group with trend to significance (0.7±2.7 TNF-i, 1.7±2.8 non-TNF-i, p = 0.06).
good/moderate E-resp rate was higher in switchers to a nonTNF-i (70% in TNF-i, 8.3% in nonTNF-i, p=0.006). In ADA+ subpopulation (n=34), no differences were found in clinical response at v-end in DAS28 (3.7±1.2 TNF-i, 3.9±1.1 nonTNF-i, p=0.564), ΔDAS28 (0.6±1.6 in TNF-i, 1.4±1.4 in nonTNF-i, p=0.35) and good/moderate E-resp rate (30% in TNF-i, 91% in nonTNF-i, p=0.073). In pts who changed to a 2nd TNF-i, those with ADA→1st TNF-i had a higher good response rate than ADA- pts (65% in ADA+ vs. 30% in ADA-, p=0.07).

Conclusions: The development of the ADA to the first TNF-i entails a better response when switching to a 2nd TNF-i, with a similar efficacy to the pts who switched to a nonTNF-i. In those pts who did not develop immunogenicity to the 1st TNF-i, there is a better response when changing therapeutic target. The ADA measurement can help to select the pts who can benefit from a 2nd TNF-i combination therapy.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6688

**Table:**

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**Figure 1:**

- **FR0187:** RADIOPHOGIC PROGRESSION BY DISEASE ACTIVITY STATES IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB2 OR REFERENCE INFLIXIMAB

- **Disclosure of Interest:** None declared.

- **Background:** Based on the totality of evidence, SB2 has shown to be similar with reference infliximab (INF) and has been approved as a biosimilar by the European Medical Agency. It is, however, ethically unknown, if SB2 also shares similar structural efficacy in the different disease activity states when compared with INF.

- **Objectives:** To evaluate the disease activity by simplified disease activity index (SDAI) and clinical disease activity index (CDAI) at weeks 14, 30 and 54 in patients with rheumatoid arthritis (RA) treated with SB2 or INF from a phase III study and to assess the radiographic progression at week 54 in patients by disease activity states (remission, low disease activity [LDA], moderate disease activity [MDA], or high disease activity [HDA]).

- **Methods:** Patients with RA were randomized to receive either SB2 or INF 3 mg/kg at weeks 0, 2, 6, and then every 8 weeks thereafter up to week 46 with background methotrexate. Dose increments were allowed after week 30 by 1.5 mg/kg up to a maximum dose of 7.5 mg/kg. Disease activities by SDAI, and CDAI were compared at weeks 14, 30, and 54. The radiographic progression was measured by modified Total Sharp Score (mTSS) at weeks 0 and 54.

- **Results:** Up to week 54, comparable proportions of patients achieved ACR-EULAR-index remission between SB2 and INF (by SDAI: 13/279 [4.7%] vs. 13/283 [4.6%] at week 14; 24/250 [9.6%] vs. 29/263 [11.0%] at week 30; 34/225 [15.0%] vs. 24/224 [10.7%] at week 54; by CDAI: 12/279 [4.3%] vs. 12/232 [5.2%] at week 14; 22/253 [8.7%] vs. 31/265 [11.7%] at week 30; 33/227 [14.5%] vs. 24/225 [10.7%] at week 54 in SB2 and INF, respectively). The proportions of radiographic non-progressors (defined as change in mTSS ≤ 2.8) at week 54 was 11.7% vs. 22.8% in TNF-i, 6.7% vs. 9.7% in non-TNF-i, p=0.006). In ADA+ subpopulation (n=34), no differences were seen even in LDA and MDA in both treatment arms. These data further confirm the comparability of SB2 and INF.

- **Conclusions:** The proportion of patients achieving remission or LDA was comparable up to week 54 upon treatment with both SB2 and INF. Inhibition of radiographic progression was also comparable in patients in active state. The proportion of radiographic non-progressors was also similarly high in patients achieving remission, and overall very low radiographic progression rates were seen even in LDA and MDA in both treatment arms. These data further confirm the comparability of SB2 and INF.


- **DOI:** 10.1136/annrheumdis-2017-eular.5524

**Table:**

<table>
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<th>Outcomes at 6 months among ADA+MTX and ADA+nonMTX csDMARD therapy</th>
<th>ADA+MTX</th>
<th>ADA+nonMTX csDMARD</th>
<th>Unadjusted</th>
<th>Adjusteda</th>
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</thead>
<tbody>
<tr>
<td><strong>Mean CDAI at 6 months</strong></td>
<td>11.9 (11.5)</td>
<td>15.7 (13.1)</td>
<td>4.07 (2.09 to 6.04)</td>
<td>3.15 (1.11 to 5.18)</td>
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<tr>
<td><strong>Change in CDAI</strong></td>
<td>-8.8 (13.4)</td>
<td>-7.4 (11.7)</td>
<td>-1.42 (-8.45 to 5.62)</td>
<td>3.15 (1.11 to 5.18)</td>
</tr>
<tr>
<td><strong>Change in mHAQ</strong></td>
<td>-0.11 (0.39)</td>
<td>-0.1 (0.4)</td>
<td>0.01 (0.07 to 0.08)</td>
<td>0.01 (0.07 to 0.08)</td>
</tr>
<tr>
<td><strong>Change in pain</strong></td>
<td>-10.1 (25.5)</td>
<td>-9.7 (20.7)</td>
<td>0.08 (4.51 to 5.88)</td>
<td>1.61 (3.56 to 6.91)</td>
</tr>
<tr>
<td><strong>Change in fatigue</strong></td>
<td>-2.7 (25.1)</td>
<td>-0.5 (25.1)</td>
<td>0.0 (5.07 to 5.57)</td>
<td>0.0 (5.07 to 5.57)</td>
</tr>
</tbody>
</table>

- **Conclusions:** In this real world study, patients on ADA+MTX had significantly greater improvements in disease activity compared to patients on ADA+nonMTX.
S. Cohen1, A. Alonso-Ruiz2, P.A. Klimiuk3, E. Lee4, N. Peter5, I. Sonderegger5, D. Assudani5, 6Metroplex Clinical Research Center, Dallas, United States; 5Boehringer Ingelheim, Ingelheim a.R., Germany

Background: PK bioequivalence of BI 695501, a biosimilar candidate, and the adalimumab originator was demonstrated previously (VOLTAIRE-PK: Wynne et al., Expert Opin Investig Drugs 2016:25:1381–70) and led to further clinical development.

Objectives: To demonstrate clinical equivalence of BI 695501 with the adalimumab originator by comparing efficacy, safety and immunogenicity using a clinical model sensitive to detect potential differences between the two biologics.

Methods: In this 58-week, multi-national, multicentre, randomised, double-blind, parallel arm Phase III study (NCT02137226), 645 pts (18–80 years) with moderate to severe active RA on stable treatment with methotrexate were randomised to receive US-licensed SC adalimumab originator or BI 695501 40mg Q2W for 24 weeks. At Wk 24, pts on adalimumab originator were re-randomised to continue the adalimumab originator or switch to BI 695501 until Wk 48. Pts on BI 695501 were dummy re-randomised. Co-primary end points were proportions of pts achieving ACR20 at Wks 12 and 24. Equivalence between BI 695501 and the adalimumab originator was demonstrated if the relevant confidence intervals (CI) for differences in ACR20 response rate at Wks 12 and 24 were within the predefined margins (Wk 12: 90% CI −12%, 15%; Wk 24: 95% CI −15%, 15%). This pre-specified secondary end point was powered to detect equivalence, demonstrating clinical equivalence between BI 695501 and the adalimumab originator (Table 1).

The proportion of pts with treatment-emergent adverse events (TEAE) was similar between BI 695501 and the adalimumab originator treatment groups (Table 2).

Table 1. Response at Weeks 12 and 24

<table>
<thead>
<tr>
<th></th>
<th>BI 695501 (n=321)</th>
<th>Adalimumab originator (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20*</td>
<td>67.0</td>
<td>61.1</td>
</tr>
<tr>
<td>ACR50</td>
<td>29.3</td>
<td>31.0</td>
</tr>
<tr>
<td>ACR70</td>
<td>10.1</td>
<td>11.1</td>
</tr>
<tr>
<td>DAS28-ESRt, mean change from baseline (95% CI)</td>
<td>-2.1 (-2.28, -2.01)</td>
<td>-2.0 (-2.18, -1.91)</td>
</tr>
</tbody>
</table>

*Week 12 risk difference (RD) and 90% CI for BI 695501-adalimumab originator are 5.9% and 90% CI (−0.9%, 12.7%); Week 24: RD and 95% CI are 4.5% and (−3.4%, 12.5%).

Table 2. Overview of TEAEs up to Week 24

<table>
<thead>
<tr>
<th>Pts, n (%)</th>
<th>BI 695501 (n=324)</th>
<th>Adalimumab originator (n=321)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 TEAE</td>
<td>148 (48.1)</td>
<td>148 (46.1)</td>
</tr>
<tr>
<td>≥1 TEAE related to trial drug</td>
<td>14 (43.7)</td>
<td>14 (43.9)</td>
</tr>
<tr>
<td>≥1 serious TEAE</td>
<td>12 (3.7)</td>
<td>15 (4.7)</td>
</tr>
<tr>
<td>≥1 serious TEAE related to trial drug</td>
<td>5 (1.6)</td>
<td>6 (1.9)</td>
</tr>
<tr>
<td>A TEAE leading to death</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Rates of serious AEs and discontinuation due to TEAEs were similar across the groups. No deaths were reported during the study. Similar frequencies of pts tested positive for anti-drug antibodies (BI 695501 43.2%; adalimumab originator 47.8%), and neutralising antibodies (BI 695501 16.0%; adalimumab originator 20.6%) in both groups at Week 24.

Conclusions: This study in pts with RA demonstrated that BI 695501 and the adalimumab originator are highly similar in terms of efficacy, safety and immunogenicity.

Disclosure of Interest: S. Cohen Grant/research support from: AbbVie, Boehringer Ingelheim, Celltrion, Pfizer, Consultant for: AbbVie, Boehringer Ingelheim, Celltrion, Merck, Pfizer, Sandoz, A. Alonso-Ruiz: None declared, P. Klimiuk: None declared, E. Lee: None declared, N. Peter Employee of: Boehringer Ingelheim, I. Sonderegger Employee of: Boehringer Ingelheim, D. Assudani Employee of: Boehringer Ingelheim

DOI: 10.1136/annrheumdis-2017-eular.3405

FR0190 [FR0109]

CLINICAL OUTCOMES FROM A NATIONWIDE NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR ETA NEUTERCE WITH PATIENTS IN INFAMMATORY ARTHRITIS AFTER 5 MONTHS FOLLOW-UP: RESULTS FROM THE DANBIO REGISTRY


Background: In Denmark, biological drugs are provided free by the hospitals to the patients via a tax-based system. In 2015 a non-medical switch from originator infliximab to CT-P13 was conducted (1). According to national guidelines in April 2016, a non-medical switch from originator (ETA, Enbrel® 50 mg/week) to biosimilar etanercept (SB4, Benepali®) was dictated when SB4 was marketed, including patients with inflammatory arthritis.

Objectives: To investigate 3 months’ disease activity and 5 months’ treatment withdrawal in ETA-treated patients (pts) with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (SpA), who were switched to SB4 and monitored prospectively in the DANBIO registry.

Methods: Pts with RA/PsA/SpA followed in DANBIO since start of first bDMARD were included. Disease activity at 3 months before switch (pre-switch), at the switch and after 3 months (post-switch) and changes over time (pre-switch and post-switch) were calculated. Disease flare was defined as ΔDAS28=1.2 or ΔDASAS=1.3 (SpA). Factors associated with withdrawal.

Results: In total, 1548 pts were identified (919 RA, 335 PsA, 322 SpA). 60% were women, age (median (IQR) 44 (43–46) yrs). Prior ETA treatment duration was 5.2 (3.2–8.0) yrs. ETA was the first biological treatment in 49%, and the second in 33% of pts. Concomitant MTX was given in 60% (RA)/49% (PsA)/15% (SpA). Median follow-up time was 154 (110–178) days.

Disease activity remained largely unchanged 3 months prior to vs. after the switch (Table). The proportion of patients with disease flare pre-/post-switch was 9%/13% (RA), 5%/5% (PsA), 4%/4% (SpA). Higher patient’s global score (HR 1.12/cm, 95% CI (1.05–1.21), p=0.002) and no concomitant methotrexate (HR 2.28 (1.48–3.52), p<0.001) at baseline were associated with withdrawal.

Conclusions: In 1548 patients with inflammatory rheumatic diseases treated with ETA for >5 years, disease activity was largely unaltered in the majority of patients 3 months after non-medical switch to SB4 and comparable to the fluctuations observed in the 3 months prior to the switch. Several patients (>9%)...
stopped treatment during 5 months follow-up. Higher patient's global score and no use of methotrexate were associated with withdrawal. Longer follow-up will offer additional understanding of the potential efficacy and safety consequences of the non-medical switch.

References:


DOI: 10.1136/annrheumdis-2017-eular.4545

Table 1. Incidence of disease worsening in AS and RA patients at the 2, 4, and 6-year index.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Outcome</th>
<th>Index date post IFX initiation</th>
<th>Disease worsening at subsequent visits, n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>12 months</td>
<td>24 months</td>
</tr>
<tr>
<td>AS</td>
<td>ASDAS</td>
<td>2 years 9/29 (11.4%)</td>
<td>6/59 (10.2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 years 2/42 (4.8%)</td>
<td>1/37 (2.7%)</td>
</tr>
<tr>
<td>RA</td>
<td>DAS28 ESR</td>
<td>2 years 20/184 (10.9%)</td>
<td>17/148 (11.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 years 9/121 (7.4%)</td>
<td>7/106 (6.7%)</td>
</tr>
<tr>
<td>RA</td>
<td>DAS28 CRP</td>
<td>6 years 8/73 (11.0%)</td>
<td>5/47 (10.6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 years 8/115 (7.0%)</td>
<td>6/104 (5.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 years 8/60 (7.2%)</td>
<td>5/45 (7.4%)</td>
</tr>
</tbody>
</table>

Conclusions: In this prospective longitudinal cohort, patients on long-term innovator IFX therapy show low rates of disease worsening of 2.7% to 11.5% at 1 and 2 years in AS and RA. Additional studies may elucidate the true rate of and reasons for disease worsening in rheumatologic populations.

References:


DOI: 10.1136/annrheumdis-2017-eular.5953

FR10193 | EFFECT OF VALLENCY OF ANTI-TNFs ON ELIMINATION MEDIATED BY ANTI-DRUG ANTIBODIES

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Background: There are five different anti-TNF biologics: three are bivalent full length (FL) antibodies (adalimumab, golimumab, and infliximab), one a bivalent fusion protein (etanercept), and one a univalent PEGylated Fab’ (PF) (certolizumab pegol, CZP). Administration of such protein biologics can induce anti-drug antibodies (ADAbs), of which the majority are anti-idiotypic antibodies (anti-ID). The potential cross-linking of bivalent anti-IDs with bivalent biologics can decrease in the efficacy of the biologic. Since univalent biologics, such as CZP, only have one binding Fab’ arm, such large cross-linked anti-ID-mediated ICs are unlikely to form. Therefore, anti-IDs may have a different effect on the elimination and bioavailability of univalent and bivalent biologics in vivo.

Objectives: To determine if the valency of a biologic will affect the in vitro size and in vivo elimination from the plasma of ICs formed with an anti-ID following intravenous (IV) administration to BALB/c mice.

Methods: An anti-ID antibody to CZP was generated and used for subsequent studies to mimic an ADA response. Univalent PF CZP was reengineered as a bivalent FL humanized IgG1 antibody (similar to adalimumab) to directly

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Background: Anti TNF therapy, has been used for the treatment of RA patients for several years. Yet, cancer and infections are among the most serious adverse effects described. Unfortunately, little is known about the effect of anti TNF therapy amongst patients with RA and previous cancer, mainly when synthetic DMARDs treatment fails.

Objectives: To review the evidence on the safety of biological therapy in RA patients with previous neoplasia.

Methods: We performed a systematic review through Medline, Cochrane Library, and EMBASE databases. Studies written in English, French and Spanish were considered. Patients 18 years or older, with RA diagnosis (ACR 1987 or ACR/EULAR 2010 criteria), and cancer diagnosis before starting biological therapy were included. While Systematic reviews, clinical trials and observational studies with a minimal follow-up of 6 months were considered; case reports or narratives reviews were excluded.

Results: 1077 studies were potentially identified, and 6 cohort studies were finally included, (Aaltoinen 2015, Dixon 2010, Phillips 2015, Raaschou 2015, Silva-Fernández 2016, Strandfeld 2010). Studies were based on registries of patients with RA treated with DMARDs and biological therapy. Registries evaluated etanercept with adalimumab and 14.16% of patients. The number of patients with documented previous cancer was around 122 to 425 as a whole. Biological therapies evaluated were: IFX, ETN, ADA, RTX, certolizumab pegol, Golimumab, ANAKinRA and synthetic DMARDs. Studies results were organized as anti TNF vs. DMARDs. All studies assessed were cohort trials, SIGN 2+ (Quality Scale). They included solid tumours as breast cancer, lymphoproliferative tumours, skin cancer, neck and brain tumours, as well as in situ uterus cancer. There was no increment in the risk of incidence of previous cancer in patients treated both with synthetic DMARDs and with anti TNF therapy in all studies assessed.

We point out, that 1 SR (LaForest Divonne 2016) evaluated biological therapy safety in patients with RA. It included 124 trials, while in 27 metanalysis was performed. From these 27, only 3 (Dixon 2010, Mercer 2013 and Stranfeld 2010) where the only studies which assessed risk of recurrence of previous cancer in vivo. In RA patients, The RR 0.77 (IC 95% 0.29–2.03), did not exhibit an increment in the risk of cancer in these patients.

Conclusions: Studies showed no differences in the incidence of previous cancer in patients treated either with synthetic DMARDs or with anti TNF. However, we suggest precaution in the use of these therapies, as the real risk in this population is still unknown.

• The final decision of treating or not treating these patients (risk factors, limitations etc.) needs to be performed in accordance with oncologists.
• There is no strong evidence that could identify the real risk of anti TNF therapies in RA patients, with previous cancer.
• The Individual impact of different anti-TNF therapies in this population could not be performed due to incomplete data. Yet, there is not real time schedule considering time since previous cancer and the start of anti TNF therapy.

Well designed studies with long follow-up periods are needed to answer these questions.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5953
compare the effect of valency on IC-mediated clearance. This FL antibody showed very similar TNF neutralization compared to the conventional PF molecule in a bioassay. To generate ICs, the anti-ID was incubated overnight with either IFX or FL CZP, and the size of the resultant ICs determined by an ultrafiltration assay (AU). The anti-ID complexes and FL or PF molecules were then administered IV to the mice, and the elimination of the anti-TNFs from the circulation was monitored by quantitative liquid chromatography-mass spectrometry (LC-MS) in serial plasma samples.

Results: AU analysis of the immune complexes formed between FL CZP and the anti-ID showed the presence of one peak corresponding in size to one anti-ID molecule bound to two PF molecules (~3.5x10^6 Da). In contrast, the FL CZP/anti-ID mixture showed ICs of various sizes up to very large molecular weights (~1x10^6 Da), with the predominant species corresponding to a complex of two anti-IDs bound to two FL CZP molecules (~1x10^6 Da). The in vivo studies showed that the FL CZP/anti-ID ICs were much faster eluted than the FL CZP alone (t1/2=44.5 hours), whereas the PF CZP/anti-ID ICs were eliminated much more slowly (t1/2=60.5 hours) than the PF CZP alone (t1/2=19.7 hours).

Conclusions: The FL CZP molecule formed large ICs with the anti-ID, which led to much faster elimination than the FL molecule alone. This result suggests that an ADAs response to a FL antibody could lead to rapid elimination and loss of efficacy of the drug in patients. In contrast, the FL CZP/anti-ID complex had a longer half-life than the PF CZP alone, presumably because this molecule was not seen as an IC due to the presence of only one Fc. These results showed that an ADA to a univalent biological reagent may not lead to elimination and instead, may actually increase the in vivo half-life of the molecule.

References:

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by the Medical Communications Unit.


FR01094 USE OF GLORESPONSE™ NF-κB-RE-LUC2P HEK293 CELLS TO MONITOR DRUG AND ANTI-DRUG ANTIBODY LEVELS IN SERUM


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Background: Rheumatoid Arthritis (RA) is often treated with anti-TNFα such as infliximab (IFX) which in a long-term treatment can lead to the development of anti-IFX antibodies (ATI), resulting in an interference with the drug activity. The investigation of the bioactivity of the circulating drug and antibodies present in patients sera with inflammatory diseases will allow to harmonize the different published data using both bioassays as well as immunoassays.

Objectives: To compare the bioassay using GloResponse™ NF-κB-RE-LUC2P HEK293 cell line, which responses to TNFα in the quantification of both IFX and ATI in serum from RA patients.

To compare the bioassay performance between capture- and bridging-ELISA.

Results: Serum IFx-trough levels were determined in 50 samples from patients with RA. To measure IFx, the bioassay uses GloResponse™ NF-κB-RE-LUC2P HEK293 cell line, which responses to TNFα in the quantification of both IFX and ATI in serum from RA patients.

Results show an almost perfect agreement between specimens and with the reference ELISA technique. Measurement of anti-drug antibody in serum samples treated with anti-TNFα antibodies. Comparison with ELISA method shows in most of the case the same data.


Disclosure of Interest: No competing interests declared.

DOI: 10.1136/annrheumdis-2017-eular.6352

FR01095 POINT-OF-CARE MONITORING OF ANTI-INFliximAB ANTIBODIES IN PATIENTS TREATED WITH THE REFERENCE INFliximAB OR CT-P13 IN ROUTINE CLINICAL PRACTICE

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Background: Loss of clinical response and infusion reactions to infliximab (IFX) are associated to the development of antibodies to IFX (ATI). ATI detection is a key step of patient management. However, current techniques may require additional patient appointments for sample collection, processing and batching in certain facilities. Testing report usually takes several days or weeks impairing effective decision making.

Objectives: To clinically validate the use of a new rapid test to detect ATI in capillary blood in a real-life point-of-care (POC) setting where patients attend the infusion center for the reference IFX (Remicade®, RMC) or CT-P13 (Inflectra®)/IFT, or Remsima®) infusions.

Methods: POQ-EF1 and POQ-EF2 are prospective, observational studies designed to evaluate and compare the performance of a rapid POC test (CE-marked Promonitor®), Quick Anti-IFX, Progenika, Spain) to detect ATI in routine clinical practice. A total of 60 rheumatic and gastroenterology patients treated with IFX or the biosimilar CT-p13 attending the infusion center with the ELISA technique as a reference. The POC test is a qualitative immunochromatographic assay based on lateral flow technology to detect ATI (including biosimilar CT-P13) in either fingerprick or serum or venous whole blood. Consecutive patients (initiating or under maintenance therapy) were recruited and tested in La Paz and Basurto University hospitals with the rapid test in capillary and venous whole blood specimens immediately before the infusion. ATI test results were read visually with the POC test in 30 min, just before the patient started the infusion. Trough sera were also collected for subsequent analysis with the rapid test and benchmarked with Promonitor®-Anti-IFX ELISA (Progenika, Spain). Follow-up time was 6 months. ELISA quantitative results were categorized as positive and negative to allow comparisons with the qualitative rapid test.

Results: Ninety consecutive patients were recruited (a total of 137 visits in the 6 months follow-up) accounting for a total of 137 sera, 137 fingerpricks and 71 venous whole blood samples. Overall, 8 (8.9%) patients developed ATI (5 ankylosing spondylitis, 1 Crohn’s disease, 1 ulcerative colitis and 1 juvenile idiopathic arthritis). ATI were detected in 5 patients treated with Remicade® and 3 treated with Inflectra®. Overall agreements between fingerprick vs venous whole blood and fingerprick vs serum measured with the rapid POC test were 100% and 99%, respectively. Positive (PPA) and negative (NPA) agreements between POC test vs venous and capillary whole blood specimens immediately before the infusion. ATI test results were read visually with the POC test in 30 min, just before the patient started the infusion. Trough sera were also collected for subsequent analysis with the rapid test and benchmarked with Promonitor®-Anti-IFX ELISA (Progenika, Spain). Follow-up time was 6 months. ELISA quantitative results were categorized as positive and negative to allow comparisons with the qualitative rapid test.

Conclusions: ATI can be reliably detected in either venous or capillary circulation. Results show an almost perfect agreement between specimens and with the reference ELISA technique. Measurement with the POC test allows the clinician to detect ATI in a quick and fully decentralised mode facilitating immediate POC decision making.


DOI: 10.1136/annrheumdis-2017-eular.5056

FR01096 BIOSIMILARS IN THE UK: EARLY REAL WORLD DATA FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTERS FOR RHEUMATOID ARTHRITIS

D. De Cock, K. Watson, K.L. Hrylicz, on behalf of BSRBR-RA Control Centre Consortium. 1Arthritis Research UK Centre for Epidemiology, University of Manchester; 2National Institute of Health Research Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NRS Foundation Trust, Manchester Academic Health Science, Manchester, United Kingdom.

Background: Biosimilars, biopharmaceuticals assessed by regulatory agencies monitor therapeutic drug of TNFα blocker are and useful to detect the presence of anti-drug antibody in serum samples treated with anti-TNFα antibodies. Comparison with ELISA method shows in most of the case the same data.


Disclosure of Interest: No competing interests declared.

DOI: 10.1136/annrheumdis-2017-eular.6352
Adherence, satisfaction and fulfillment of expectations on the subcutaneous (SC) biological treatment is better with monthly administration.

Objectives: We further assessed if there are differences in patients expectations and satisfaction with efficacy and tolerance that could contribute to explain such finding.

Methods: ARCO was a retrospective study on RA patients who had been prescribed a SC biological 11–18 months prior to the study. Adherence was calculated with the medication possession ratio (MPR). Satisfaction and expectations were assessed with the Spanish validated Carbonell questionnaire [1].

Results: We included 364 patients (age 54.9 years [SD 12.5], 77.5% women, median duration of RA 7.8 years, period studied for the SC biological 14.8 months). Non-adherence (MPR <80%) was lower in patients with monthly (6.4%) than with weekly (17.4%, p=0.034) or every 2 weeks administration (14.4%, p=0.032). The % of satisfied patients (quite/very satisfied) was 86.2% for efficacy and 64.4% for side effects or tolerance. Non-adherence was similar in satisfied and in neutral/unsatisfied patients (14.7% vs. 8.3%, p=0.399), or in patients satisfied/not satisfied with side effects (13.1% vs. 15.4%, p=0.504). The fulfillment of expectations is shown in the table. With regard to expectations on the effect, non-adherence was 15.5% (higher than expected), 12.6% (as expected) and 10.7% (lower than expected) (p=0.677), and with regard to discomfort/side effects, it was 15.6% (greater than expected), 18.5% (as expected) and 11.1% (lower than expected, or no side effect) (p=0.189). Fulfillment of expectations on efficacy was similar for the 3 dosing schemes, but the % reporting lower than expected discomfort or no discomfort was greater with fewer SC injections (table).

Conclusion: In particular, the % reporting no discomfort/side effects with the administration of 2 or 4 injections was greater than expected. Therefore, the % reporting lower than expected discomfort or no discomfort was greater with fewer SC injections (table). In particular, the % reporting no discomfort/side effects with the administration were 17.8% (weekly), 28.3% (every 2 weeks), and 35.0% (monthly) (p=0.013).

References:

Background: In patients with rheumatoid arthritis (RA), we previously described that adherence to the subcutaneous (SC) biological treatment is better with monthly administration.

Objectives: We further assessed if there are differences in patients expectations and satisfaction with efficacy and tolerance that could contribute to explain such finding.

Methods: ARCO was a retrospective study on RA patients who had been prescribed a SC biological 11–18 months prior to the study. Adherence was calculated with the medication possession ratio (MPR). Satisfaction and expectations were assessed with the Spanish validated Carbonell questionnaire [1].

Results: We included 364 patients (age 54.9 years [SD 12.5], 77.5% women, median duration of RA 7.8 years, period studied for the SC biological 14.8 months). Non-adherence (MPR <80%) was lower in patients with monthly (6.4%) than with weekly (17.4%, p=0.034) or every 2 weeks administration (14.4%, p=0.032). The % of satisfied patients (quite/very satisfied) was 86.2% for efficacy and 64.4% for side effects or tolerance. Non-adherence was similar in satisfied and in neutral/unsatisfied patients (14.7% vs. 8.3%, p=0.399), or in patients satisfied/not satisfied with side effects (13.1% vs. 15.4%, p=0.504). The fulfillment of expectations is shown in the table. With regard to expectations on the effect, non-adherence was 15.5% (higher than expected), 12.6% (as expected) and 10.7% (lower than expected) (p=0.677), and with regard to discomfort/side effects, it was 15.6% (greater than expected), 18.5% (as expected) and 11.1% (lower than expected, or no side effect) (p=0.189). Fulfillment of expectations on efficacy was similar for the 3 dosing schemes, but the % reporting lower than expected discomfort or no discomfort was greater with fewer SC injections (table). In particular, the % reporting no discomfort/side effects with the administration were 17.8% (weekly), 28.3% (every 2 weeks), and 35.0% (monthly) (p=0.013).
Results: A total of 49 patients were enrolled and 48 patients completed the study. The mean injection site pain score was 2.3 in PFS vs 2.0 in PFP immediately post-injection and 0.8 in PFS vs 0.7 in PFP at 15–30 minutes post-injection. At both time points the score was equivalent between PFS and PFP: the 97.5% CI was (0.09, 0.30) and (0.07, 0.25) immediately and 15–30 minutes post-injection, respectively.

The overall impression was also comparable between PFS and PFP. There were no patients who had an overall impression of extremely unfavorable and the proportion of patients who had a favorable impression was higher than that of unfavorable impression in both PFS and PFP. The overall preference for PFP (56.5%) was higher than PFS (30.4%) as presented in the Table. Both PFS and PFP were well tolerated and there were no serious treatment-emergent adverse events. Only one patient after administration of PFS experienced injection site reaction.

Conclusions: The injection site pain score of PFS and PFP was comparable with overall preference rate higher for PFP. Both PFS and PFP were well tolerated with similar safety profiles.

References:


FRIO1099 SYSTEMATIC REVIEW AND META-ANALYSIS ON CERTOLIZUMAB PEGOL FOR RHEUMATOID ARTHRITIS IN ADULTS
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Background: The appearance of tumor necrosis factor-alpha (TNFalpha) inhibitors dramatically changed the prognosis of rheumatoid arthritis. Certolizumab pegol (CZP) is a human Fab fragment of anti-TNFalpha monoclonal antibody which is approved for the treatment of rheumatoid arthritis. We performed a systematic review and meta-analysis, with Cochrane methodology, of the effects of CZP in rheumatoid arthritis.

Objectives: To assess the clinical benefits and harms of CZP in patients with rheumatoid arthritis.

Methods: We performed a search of electronic database (Cochrane Database, MEDLINE, EMBASE, Web of Knowledge and clinicaltrials.gov) until 26th September 2016. We searched for randomized controlled trials of CZP in rheumatoid arthritis compared to any other agent including placebo.

Results: 14 trials were included for the meta-analysis, 12 (5422 patients) in the pooled analysis for benefits and 14 (5499 patients) in the pooled analysis for safety. The overall possibility of bias seemed to be low but the quality of the evidence was low due to the risk of attrition bias.

With the approved dose - CZP 200 mg subcutaneous every other week with the first three doses of 400 mg - CZP showed statistically significant improvements at 24 weeks compared to placebo in: ACR20 improvement 27% (95% CI 20% to 33%); RR 3.8 (95% CI 2.42 to 5.95) and NNT=4 (95% CI 3 to 8); DAS28 <2.6 - original definition of remission - with RR 3.79 (95% CI 1.90 to 7.56); HAQ with 12% absolute improvement (95% CI -9% to -14%); and erosion score with -0.29% (95% CI -0.42% to -0.17%). There are also data available at 12 weeks with -12% absolute improvement (95% CI -9% to -14%); and erosion score with -12% improvement (95% CI -9% to -14%).

Use of an enhanced communication strategy, together with more experience and absence of group think effects, resulted in much higher acceptance and persistence rates after open label shared decision making biosimilar transitioning in patients with a rheumatic disease.

Acknowledgements: This study was funded by Biogen

Disclosure of Interest: L. Tweehuysen: None declared, V. Huiskes: None declared, B. van den Berk Speakers bureau: Pfizer, AbbVie, Mundipharma, F. van den Hoogen Consultant for: Biogen, Celtrion, Janssen, Mundipharma and Sandoz, A. A. den Broeder Consultant for: AMGEN

DOI: 10.1136/annrheumdis-2017-eular.2889
ETANERCEPT RETENTION PATTERNS AND FACTORS ASSOCIATED WITH TREATMENT DISCONTINUATION: A RETROSPECTIVE COHORT STUDY USING CANADIAN CLAIMS-LEVEL DATA

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Background: Etanercept is a soluble TNF receptor (humanized protein) indicated for the treatment of immune-mediated inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and psoriasis (PsO). Limited data exists on the factors associated with long-term retention and use of etanercept in Canada in a real-world setting.

Objectives: To evaluate the 6-year retention rates of etanercept patients in Canada, and to identify factors associated with discontinuation.

Methods: A retrospective cohort study was conducted using longitudinal pre-prescription drug claims data from QuintilesIMS Private Drug Plan database (PDP), Ontario Public Drug Plan database (OPDP), and Quebec Public Drug Plan database (RAMQ). Between 07/2008 and 06/2010, bio-naïve patients who initiated etanercept were identified and followed for 72 months. 12-month retention rates were evaluated in 1-year increments for all patients retained on therapy at year 1, 2, 3, and beyond. The retention rates in the first year were compared to retention rates in the first year. Covariates associated with time to discontinuation over the entire 72 month period were identified using a Cox proportional hazards regression model.

Results: The study identified 4,528 etanercept patients (61% female, 85% rheumatoid arthritis, and 15% PsO) across Canada who started their therapy in the period 07/2008 - 06/2010. The study identified 4,528 etanercept patients (61% female, 85% rheumatoid arthritis, and 15% PsO) across Canada who started their therapy in the period 07/2008 - 06/2010. Between 07/2008 and 06/2010, bio-naïve patients who initiated etanercept were identified and followed for 72 months. 12-month retention rates were evaluated in 1-year increments for all patients retained on therapy at year 1, 2, 3, and beyond. The retention rates in the first year were compared to retention rates in the first year. Covariates associated with time to discontinuation over the entire 72 month period were identified using a Cox proportional hazards regression model.

Conclusions: Etanercept patient retention likelihood increased the more years a patient was retained on therapy. This pattern was consistent across therapeutic areas, sex, age, and payers. Age, indication, and payer were found to have a significant impact on etanercept retention. With better understanding of factors associated with retention, patient support programs can be designed to address the specific needs of at-risk groups while supporting patients stable on therapy.

FRI0201

GOLIMUMAB IN BIOLOGIC-NAÏVE PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS (RA), PSORIATIC ARTHRITIS (PSA) OR ANKYLOSING SPONDYLITIS (AS) - SUBANALYSIS FROM THE NON-INTERVENTIONAL EVALUATION GO-NICE

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Background: Golimumab (GLM) has demonstrated efficacy and safety in several randomized clinical trials with biologic-naïve patients. However, data from effectiveness and patient-reported outcomes (PROs) parameters in daily clinical practice in Germany are scarce.

Objectives: The aim of this subanalysis is to assess Golimumab on the effectiveness, and PROs in biologic-naïve patients with established RA, PsA or AS.

Methods: This is a subanalysis of the non-interventional, prospective, 24-month study GO-NICE. Biologic-naïve patients with established RA, PsA or AS starting with GLM 50mg Sc once monthly in a real life setting in Germany. Endpoint measures: disease activity DA28S, PsARC and BASD1. PROs included QoL (EQ-5D-3L), functionality (FFbH), fatigue (FACIT-F). Safety data were also collected.

Results: RA patients (n=265): Mean age 54.5 yr, 82.1% of the patients were female, 77.3% (n=204) were rheumatoid factor (RF) positive, and 76.4% (n=201) anti-cyclic citrullinated peptides (anti-CCP) antibodies at BL. The BASDAI at BL was 5.0 and dropped significantly to 2.9 within 24 months (p<0.0001 vs BL). After 3 months of treatment, 45.2% of patients had LDA (DAS28 ≤ 2.6), which increased to 50.8% after 6 months and 64.9% after 24 months. PsA patients (n=247): Mean age 49.7 yr, 53.8% of the patients were female, 42.1% (n=104) had a nail involvement, 25.5% (n=63) dactylitis and 13.8% (n=34) enthesitis at BL. The proportion of patients achieving a response (mod PsARC) was 64%, 72.5% and 77% at 3, 6 and 24 months, respectively. AS patients (n=246): Mean age 41.9 yr, 70.7% of the patients were male, 80.5% (n=198) were HLA-B27 positive. Most common extraarticular manifestations were: enthesitis (12.6%), iritis (12.2%), IBD (3.7%), and dactylitis (2.8%) at BL. The BASDAI at BL was 6.6 and significantly improved to 4.0 (p<0.0001 vs BL) within 24 months. The proportion of patients achieving a response (BASDAI 50) was 62.2%, 66.9% and 76.9% at 3, 6 and 24 months, respectively.

An improvement of quality of life (QoL) by EQ-5D-3L was seen after 6 months and was maintained over 24 months. The patients’ health state today (EQ VAS) improved from 52.3 at BL to 64.9 (RA), from 49.0 to 66.3 (PsA) and from 49.2 to 70.6 (AS). The functional ability (FFbH) improved significantly (p<0.0001 vs BL) from 73.1 to 80.4 points (RA), from 73.0 to 82.2 (PsA) and from 72.8 to 81.2 (AS). The Mean Fatigue score (FACIT-F) increased from BL: 33.3 to 39.5 points (RA), 25.6 to 33.8 (PsA) and 28.4 to 32.9 points (AS) (each p<0.001 vs BL) within 24 months.

No new safety signals were detected.

Conclusions: GLM SC once-monthly showed after 3 months remarkable improvements in clinical effectiveness, patient-reported quality of life, functionality, and fatigue. Functional parameters were maintained over 24 months in biologic-naïve patients with established RA, PsA or AS. At month 24, 64.9% of RA patients achieved LDA status, 77.7% of PsA achieved positive PsARC response and 76.9% of AS patients achieved BASDAI 50. No new safety signals were detected.
FR010204 | COMPARISON THE LONG-TERM CLINICAL OUTCOMES BETWEEN NONTNF-INHIBITORS VERSUS TNF-I IN RA PATIENTS WHO FAILED TO A FIRST TNF-I

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Background: There are many biological therapies for Rheumatoid Arthritis (RA) with different mechanisms of action and good efficacy rate; however, up to 40% of patients (pts) fail to respond to the 1st biologic agent, and it is still not clear what strategy to follow after showing inadequate response to tumor necrosis factor inhibitors (TNF-i).

Objectives: To assess the clinical response and survival (SV), in our cohort of RA pts that discontinued the 1st TNF-i, of a 2nd TNF-i vs a non-TNF-i, both in the global cohort and in the subpopulation that dropped out the 1st TNF-i due to ineffectivity.

Methods: This observational study included 110 pts in the RA-Paz cohort who previously suspended Ifx (68%) or Ada (32%) between 1999–2016. Two groups were established: they switched to a TNF-i or non-TNF-i. Clinical response was evaluated by DAS28, Delta-DAS28 (∆DAS28) and EULAR response (E-resp). The assessments were performed at 6 (v-6) and 12 months (v-12) since initiating 2nd biological agent and during the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the drug (v-end). Statistical analysis was performed using the R program version 3.4.0.

Results: Of the 110 pts who had stopped Ifx or Ada as 1st TNF-i, 65% changed to a 2nd TNF-i. The 84% of the overall pts were women. The mean age was 64±14 years and the mean time of 2nd biologic drug was 3.0±1.3 years. 61% associated methotrexate at the beginning of 2nd biologic agent and 56% at the v-end, without differences between those who switched to TNF-i and those who did to non-TNF-i. At v-6 and v-12, there was no difference in ∆DAS28 [at v-6: 6.3±1.4 in TNF-i and 1.2±1.2 in non-TNF-i (p=0.199), at v-12: 1.3±1.5 in TNF-i and 1.2±1.1 in non-TNF-i (p=0.852)]. In contrast, at v-end, pts with non-TNF-i showed a higher clinical improvement (∆DAS28: 0.68±1.7 in TNF-i, 1.8±1.1 in non-TNF-i, p=0.002). At v-6, the TNF-i group achieved higher good E-resp rate (41% vs 18%, p=0.035), but there was no difference at v-12 (36% in TNF-i vs 23% in non-TNF-i, p=0.435). However, at v-end, the non-TNF-i group achieved better E-resp (good resp: 38% in non-TNF-i vs 25% in TNF-i, no resp 18% in TNF-i vs 56% in non-TNF-i, p=0.01). Likewise, 100% (n=7) of the pts that finished 2nd biologic agent by remission, had changed to a non-TNF-i (p<0.0001).

There were no differences regarding 2nd biologic drug SV (mean SV time of 5.7±0.66 in TNF-i, 4.3±0.59 in non-TNF-i, p=0.197). When analyzing the cohort that discontinued 1st TNF-i because of ineffectivity, at v-6 and v-12 there were no differences between switchers to TNF-I and non-TNF-I in ∆DAS28 [v-6: 1.4±1.4 vs 0.9±1.0 (p=0.164); v-12: 1.5±1.4 vs 1±1, (p=0.192)], but at v-end, the non-TNF-i group reached a higher ∆DAS28 (0.9±1.5 in TNF-i, 1.6±1 in non-TNF-i, p=0.031) between a TNF-i and a non-TNF-i within the 1st year of treatment. However, in the long-term, switching to a non-TNF-I shows enhanced clinical benefits with no impact on survival vis-à-vis a 2nd TNF-I. Despite the efficacy of TNF-I, new therapeautic targets are needed for those who fail to respond to these biological agents.

Disclosure of Interest: None declared

FR010205 | CORRELATION OF PATIENT PREFERENCES TO TREATMENT OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH ANTI-TNF AGENTS IN GREECE. THE PANORAMA STUDY

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Background: Route and frequency of administration of treatment options may be an important differentiator between drugs that are used to treat RA and patient preferences may influence adherence to and outcomes of therapy.

Objectives: The objective of this study was to assess the correlation between the fulfillment of patient preferences and clinical and patient reported outcomes.

Methods: PANORAMA was a non-interventional, prospective, multicenter, cohort study. Patients who discontinued a 1st biologic failure or experienced who initiated/switched to anti-TNF at enrollment. Post physician’s anti-TNF choice, patients completed a preferences questionnaire over attributes related to anti-TNF treatment. Satisfaction with treatment was assessed with the TQSM questionnaire and compliance (proportion of full doses/pillaged) was recorded via the use of a patient diary. Persistence was defined as the time period from the last anti-TNF administration. The observational period was 12 months, with study visits every 3 months.

Results: A total of 254 patients were enrolled in the study. The mean patient age was 58.3±13.4 years, 82.7% were female, 65.4% were biologic naive and 66.1% had severe disease (DAS-28 >5.1). The mean DAS-28 and HAQ-DI scores at enrollment were 5.5±1.1 and 1.4±0.6 respectively, while mean disease duration was 67.6±6.2 years with 53.2% of patients being seropositive (RF+) (49.2%, Anti-CCP+) (40.5%). A monthly administration was most preferred by patients (65.7% vs. 20.1% for twice per month, 11.8% for once per week and 3.9% for twice per week), and the large majority of patients (75.2%) preferred the subcutaneous mode of administration. The mean compliance and 12-month persistence rates were 97.0% and 72.3% respectively. At 12 months, good EULAR response rate was achieved by 56.5% of patients and 40.8% were in DAS-28 remission. Univariate analysis demonstrated that fulfillment of patient preferences was correlated to good EULAR response (p<0.001), increased probability of being persistent (p=0.019) and satisfaction with treatment (p=0.063). Multivariate logistic regression analysis revealed that a good EULAR response was associated with satisfaction of patient preferences (OR 5.560, p<0.001), good patient knowledge of the disease (OR 1.327, p=0.006), absence of history of comorbidities (OR 2.42, p=0.014) and lower SJC (OR 1.10, p=0.021), whereas anti-TNF persistence at 12 months was associated (Cox regression analysis) with seropositivity (HR 0.566, p=0.047) and a high baseline ESR (>35 mm/h (HR 0.587, p=0.071)).

Conclusions: In anti-TNF treated RA patients, fulfillment of expressed treatment preferences was independently associated with a good EULAR response and correlated with drug persistence at 12 months, emphasizing the importance of patient preferences in treatment outcomes.

Acknowledgements: The study was funded by Merck Sharp & Dohme S.A., Greece

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4383

FR010206 | CORRELATION BETWEEN THE SERUM ETANERCEPT LEVEL AND RESPONSE TO ETANERCEPT TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: It is well documented that the blockade of TNF-a significantly reduces disease activity in patients with rheumatoid arthritis (RA). However, at least one third of patients receiving etanercept either do not respond to treatment, or lose initial responsiveness [1]. Recent findings indicate that lack of clinical response may be related with lowering the serum drug levels.

Objectives: To investigate the relationship between serum etanercept levels and response to etanercept treatment in patients with RA.

Methods: The study population consisted of fifty eight patients with rheumatoid arthritis (RA), all treated with etanercept. Disease activity was assessed according to the 28-joint count Disease Activity Score (DAS28) at baseline and 6 months of
therapy. Clinical response was assessed using the European League Against Rheumatism (EULAR) response criteria [2]. Serum etanercept levels were measured by sandwich ELISA based on the ability of etanercept to bind TNF. Antibodies against etanercept were measured by bridging ELISA (Promonitor).

**Results:** The 47 female and 11 male were of a mean age 52±11.2 years (23 yrs–75 yrs), responding with RA for a mean of 13.2±8.2 years (2–24). At baseline the DAS28scores mean score was 6.1±1.0. After six months of etanercept treatment, 20 (34.5%) patients were in remission, 20 (34.5%) were in low disease activity and 18 (31%) were in moderate disease activity. The serum etanercept levels were significantly higher in patients in remission compared with patients in moderate disease activity (p<0.05). According to the EULAR response criteria, RA patients were divided into responders (52pts, 89.7%) and non-responders (6 pts, 10.3%). Median etanercept levels in all patients were 3.937mcg/ml. There were no statistical differences in etanercept levels between responders and non-responders (p=0.41). In addition, we stratified all patients into quartiles according to height of the etanercept level. The percentage of EULAR good responders was significantly different between the highest and the lowest quartiles (p<0.05).

Anti-etanercept antibodies were not found in any of the studied patients (0/58).

**Conclusions:** Patients with RA who did not respond to etanercept treatment achieved lower etanercept levels compared with responding patients. Higher concentrations of the drug were associated with a better response to treatment. Further studies are needed to provide evidence for this approach.

**Reference:**

Table 1. Number of patients in clinical remission at 6 months, one year and two years

<table>
<thead>
<tr>
<th>Group</th>
<th>6 Mo</th>
<th>1 Year*</th>
<th>2 Years*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFX+MTX (N=38)</td>
<td>10 (26%)</td>
<td>6 (17%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>MTX (N=38)</td>
<td>12 (32%)</td>
<td>5 (14%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>PL (N=16)</td>
<td>9 (24%)</td>
<td>1 (3%)</td>
<td>1 (19%)</td>
</tr>
</tbody>
</table>

*p<0.05 across the three groups.

**Disclosure of Interest:** None declared.

DOI: 10.1136/annrheumdis-2017-eular.5957
Objectives: This abstract presents results from three clinical trials of infliximab biosimilar, BCD-055, including comparative data on pharmacokinetics (PK), efficacy and safety in a variety of patient populations.

Methods: All three studies were conducted as international multicenter randomized double-blind studies in direct comparison with innovator IFX. ASART-1 study (biosimilar adalimumab vs. innovator adalimumab) was conducted in Russia and Brazil. A total of 200 patients - 119 patients with AS and 81 patients with RA were enrolled in ASART-1 study. 90% (181 out of 200 patients) received concomitant therapy with methotrexate. AUC was calculated for AUC-inf, AUC-0-<inf>∞, AUC-0-tau, Cmax, and Cmax-inf. AUC comparisons were made with 0.80 to 1.25 ratio as non-inferiority margin, for Cmax with 0.75 to 1.33 ratio as non-inferiority margin, and for 2-way ANOVA test for significance.

Results: ASART-1 study demonstrated that the BCD-055 is non-inferior to innovator IFX both in RA and AS patients: AUC <inf>0-τ 0 10.1136/annrheumdis-2017-eular.2357 10.1136/annrheumdis-2017-eular.2357

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4723

Scientific Abstracts

FR02020 REAL-LIFE SAFETY PROFILE OF BIOSIMILAR ADALIMUMAB IN PATIENTS WITH INFLAMMATORY ARTHRITIC CONDITIONS

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Background: Biologic therapies have dawned a new era in the management of patients with chronic inflammatory arthritis by nudging the goal post from control to induction of remission. Adalimumab, a TNF-α inhibitor, has been proven to be safe and effective in improving the disease activity and quality of life in patients with conditions like rheumatoid arthritis (RA) and ankylosing spondylitis (AS). 1,2 A biosimilar adalimumab (developed by Cadila Healthcare Ltd. India) has been approved for clinical use in 2014 in India. While the initial biosimilarity has been established for physicochemical, functional as well as clinical efficacy and safety aspects, 3,4 ongoing evaluation of safety in real-life patients is crucial for such biosimilar therapies.

Objectives: We share our experience on the real-life safety profile of biosimilar adalimumab following its clinical use in patients with RA and AS.

Methods: Patients with RA or AS treated with biosimilar adalimumab in our outpatient clinic at Arthritis and Rheumatism Centre during the period of 17 months (1 March 2016 to 10 October 2017) were considered for this analysis. Primary outcome was ADR analysis. The patients were prescribed biosimilar adalimumab 40 mg subcutaneously every fortnight for a minimum of 6 months. The patients were followed up till the end of the treatment, and any safety signals or adverse events reported were collected and analysed.

Results: A total of 200 patients - 119 patients with AS and 81 patients with RA - who received biosimilar adalimumab therapy for a period of 6 months were included. The median age for the group was 36 (17–68); and 138 patients were males. The mean BMI was 25.7±4.83; and the median duration of disease for the entire group was 4.5±(0–15.3) years - 4.5±(0–9.5) years for the patients with RA and 4.5±(2.4–15.5) years for the patients with RA. About 90% (181 out of 200 patients) received concomitant therapy with methotrexate. Biosimilar adalimumab therapy was well tolerated by all patients, with no serious adverse events. Adverse events were noted in only 2 patients - one patient had developed pulmonary tuberculosis in the 4th month of treatment, biosimilar adalimumab was discontinued and AKT treatment was started; while another patient experienced rise in transaminases for which, the dose of methotrexate was reduced. Overall assessment of tolerability as “Excellent” was 65.5% by the treating physician and 82% by patients.

Conclusions: To the best of our knowledge, this is the first report on “real-life” use of biosimilar adalimumab in such a large number of patients. The analysis reveals a safety and tolerability profile of biosimilar adalimumab comparable to that of the innovator product.

References:
[3] FRI0209

Disclosure of Interest: None declared

FR02010 REAL-WORLD HAWK STUDY: LONG-TERM SAFETY AND EFFECTIVENESS OF ADALIMUMAB WITH HIGHER-DOSE METHOTREXATE IN JAPANESE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: TNF inhibitors are first-line biologic therapy used in combination with MTX for treatment of RA. However, in Japan, limited real-world data exist on this combination with relatively higher doses of MTX (>8 to <16 mg/week).

Objectives: The HAWK study was designed to assess real-world, long-term safety and effectiveness of the TNF inhibitor ADA with MTX (>12 mg/week) in Japan. Week 52 results are presented.

Methods: This multicenter, prospective, observational study, enrolled biologic-naive, early (<2 years) RA patients with DAS28-CRP >3.2 despite MTX therapy or who required Eligible healthcare providers received ADA (12 mg/week at beginning of ADA) for 104 weeks. Primary endpoint was DAS28-CRP <2.6 at week 52. Secondary endpoints included CDAI, SDAI, HAQ-DI and inhibition of structural joint damage using the mTSS. ADRs and dosage of ADA and MTX were recorded.

Results: As of April 15, 2016, 346 patients were enrolled (safety set 301; effectiveness set 293). Effectiveness set comprised 79% women; mean (±SD) age, 54.3 (13.9) years; duration of RA, 12.1 (6.2) months; MTX dosage, 13.4 (1.8) mg/week; DAS28-CRP, 4.5 (0.9); and mTSS, 7.7 (10.0) at baseline. At week 52, DAS28-CRP <2.6 and low disease activity (<3.2) were achieved in 77% and 92% patients, respectively. Remission rates of CDAI (<28), SDAI (<3.3), and HAQ-DI (<0.5) were 49%, 51%, and 82%, respectively. Although average MTX dosage was decreased (<2 mg/week), unchanged, and increased (<2 mg/week) from baseline in 19.6%, 78.9%, and 1.4% patients over 52 weeks, respectively, there was no significant difference in disease activity improvement across these MTX dosage groups at week 52 (p=0.350). Structural remission rate at week 52 was 86% (ΔmTSS <0.5) (Figure). A total 110 ADRs occurred in 80 (26.6%) patients, 23 were serious in 21 (7.0%) patients (Table).

Conclusions: Results show that ADA with MTX (>12 mg/week at the beginning) displayed a consistent safety profile and was effective with a DAS28-CRP remission rate of 77% in routine clinical practice. The ADR rate of 26% was similar to a previous, short-term (28 weeks) postmarketing surveillance report (1).

References:

Disclosure of Interest: Y. Tanaka Grant/research support from: Mitsubishi-
A DESCRIPTIVE ANALYSIS OF REAL-WORLD TREATMENT PATTERNS OF INNOVATOR INFlixIMAB (REMICADE) AND BIOSIMILAR INFLIXIMAB IN A TREATMENT NAÏVE TURKISH RHEUMATOLOGIC DISEASE POPULATION

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Objectives: This retrospective healthcare claims analysis examined treatment patterns of innovator infliximab (IFX) and biosimilar infliximab (CT-P13) in a Turkish rheumatologic disease population after CT-P13 availability in July, 2014. Methods: Adult patients (pts) with ≥1 diagnosis code (ICD-10-CM) for rheumatoid arthritis (RA) were identified in a national Turkish healthcare database during the study period (01DEC2010–01DEC2015). Eligible pts had continuous medical/pharmacy enrollment ≥1 year before and ≥6 months after IFX or CT-P13 initiation (index date). Patients were naïve to IFX or CT-P13 (i.e. had no IFX or CT-P13 within 12 months before the index date). Demographics, comorbid conditions and medications, and treatment patterns, were tested. Confirmed discontinuation was defined as a switch to another biologic medication or the absence of an index biologic claim for ≥120 days without censoring.

Results: Key results are shown in the Table. A total of 1044 patients initiated either medication. The majority (80%; n=831) initiated IFX. The IFX cohort had a larger age, female (58%), and mean age and mean follow up was 12 months. The CT-P13 cohort consisted of 213 pts with mean age of 45 years; 58% women; and mean follow up of 9 months. Approximately one-third of pts in each cohort had a concomitant diagnosis of ankylosing spondylitis (AS; TABLE). Other concomitant disease and medications appeared balanced between cohorts. Pts in the IFX cohort had an average of 5.2 infusions and mean dose of 4.7 vials per infusion approximately every 8 weeks. Pts in the CT-P13 cohort had an average of 3.6 doses and mean dose of 5.8 vials per dispensing approximately 9 weeks apart. A confirmed discontinuation occurred in 55% of the IFX cohort; driven in part by switching, 24% of IFX pts had ≥1 biological switch with 8% initially switching to CT-P13. Time to any discontinuation or censoring of IFX is shown in the Table. In the CT-P13 cohort, a confirmed discontinuation was observed in 63%; 31% switched to another biologic therapy; and 20% initially switched to IFX. Time to any discontinuation or censoring of CT-P13 is shown in the Table.

Conclusions: These findings in a single country indicate that real world utilization patterns may differ between innovator IFX and CT-P13, with predominantly greater overall CT-P13 discontinuation and a higher proportion of patients switching from CT-P13 to IFX. Further studies are needed to understand the reasons for these observed differences.

Compared to monotherapy, combination therapy was associated with a lower drug failure (crude HR 0.75 [95% CI 0.68–0.82]; adjusted HR 0.78 [95% CI 0.70–0.86]; p < 0.0001). In patients in monotherapy, considering ETA as reference and adjusting for the above mentioned clinical characteristics, the HR for bDMARD failure was 1.32 for ADA (95% CI 1.07–1.63) and 2.38 for INF (95% CI 1.85–3.07).

Conclusions: Monotherapy with bDMARDs is consistently associated with lower retention rate in first-line therapy for anti-TNF drugs. Comparing bDMARDs administered in monotherapy, INF and ADA show a higher risk of withdrawal than ETA. Real life data support the currently recommended use of bDMARDs in association to csDMARDs.


FR0214 LONG-TERM EFFICACY AND SAFETY OF SIRUKUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE ANTI-TUMOR NECROSIS FACTOR THERAPY: RESULTS OF THE RANDOMIZED, PHASE 3 SIRROUND-STUDY

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Background: Sirukumab, a selective, high-affinity human monoclonal antibody to the interleukin-6 (IL-6) cytokine, is under development for rheumatoid arthritis (RA) and other diseases.

Objectives: To evaluate long-term efficacy and safety of sirukumab in patients (pts) with RA refractory or intolerant to anti-tumor necrosis factor (TNF) agents.

Methods: This phase 3 study included pts ≥18 years with moderate to severe active RA, and a lack of benefit to ≥1 anti-TNF or intolerance to ≥2 anti-TNFs. Eligible pts were initially randomized 1:1:1 to sirukumab subcutaneous (SC) 50mg q4w, sirukumab SC 100mg q2w, or placebo SC q2w for 24 wks. Placebo-treated pts with <20% improvement in tender and swollen joints at Wk 18 (early escape [EE]) and those remaining on placebo at Wk 24 (crossover) were re-randomized to sirukumab through Wk 52. Efficacy endpoints included ACR response, HAQ-DI scores, DAS28 (CRP) remission rates, and SF-36 scores. Results are presented for these key endpoints at Week 52.

Results: 678 pts were initially randomized to placebo (n=294), sirukumab 50 mg q4w (n=292), or sirukumab 100 mg q2w (n=292). Of placebo-treated pts, 94 met EE criteria at Wk 18 and 158 crossed over at Wk 24 and were re-randomized to sirukumab. 60% of pts had received ≥2 prior biologics, including non-TNF–targeted biologics. RA signs and symptoms and patient-reported outcomes (PROs [SF-36 scores]) improved significantly with sirukumab versus placebo through Wk 54. Improvements were maintained through Wk 52 with no dose response (Table 1). Through Wk 52 in the combined sirukumab 50mg q4w and 100mg q2w groups, respectively, an adverse event (AE) was reported for 79.6% and 81.3% of pts and a serious AE was reported for 14.2% and 13.2% of pts; injection-site reactions and alanine aminotransferase increases were the most commonly reported AEs.

Conclusions: In this population intolerant or refractory to anti-TNFs/other biologics, sirukumab SC 50mg q4w and 100mg q2w were well tolerated and reduced signs and symptoms of RA and improved PROs through 52 wks of treatment, also among pts who switched from placebo to sirukumab.

Disclosure of Interest: Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, and Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Astellas, Eli Lilly, and GlaxoSmithKline. D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche. P. Agarwal Shareholder of:...
RESULTS:

p = 0.001. Similar trends were observed after correction by LUNDEX formula at 6 months (TCZ 58.8% vs TNFis 53.7%; p = 0.021). No significant differences were achieved (p = 0.17) in 6-20% from baseline, mean (SD) 5.19 (10.84) 5.60 (10.62) 4.65 (10.10) 5.60 (10.62) 4.46 (10.51) 4.85 (10.51) DAS28 (CRP) decrease from baseline, mean (SD) 3.64 (8.44) 5.19 (10.84) 4.65 (10.10) 5.60 (10.62) 4.46 (10.51) 4.85 (10.51) ACR20 response, n (%) 41 (33.1) 74 (31.5) 115 (32.0) 38 (30.9) 77 (32.0) 115 (31.6) ACR50 response, n (%) 68 (54.8) 127 (54.0) 195 (54.3) 71 (57.7) 145 (60.2) 216 (69.3) ACR70 response, n (%) 26 (21.2) 52 (22.2) 97 (26.9) 46 (37.7) 95 (40.0) 130 (38.2) SF36 summary scores Physical Component Summary (PCS) change from baseline, mean (SD) 4.47 (7.70) 6.33 (7.23) 5.69 (7.44) 5.45 (7.22) 5.98 (7.25) 5.80 (7.24) Mental Component Summary (MCS) change from baseline, mean (SD) 3.64 (8.44) 5.19 (10.84) 4.65 (10.10) 5.60 (10.62) 4.46 (10.51) 4.85 (10.51)

Background: Despite a demonstrated superiority of interleukin-6 over tumour necrosis factor (TNF) blockade when used as monotherapy, the choice of the first biologic agent (bDMARD) for treating rheumatoid arthritis (RA) in combination with methotrexate (MTX) is still a challenge for rheumatologist.

Objectives: To retrospectively evaluate in a multicentre observational cohort of Northern Italy (the LORHEN registry) the 6- and 12-month comparative drug survival and remission rate of tocilizumab (TCZ) and TNF inhibitors (TNFi) used as first bDMARD in combination with MTX.

Methods: All RA patients treated with TCZ or a TNFi as first-line bDMARD with at least 12-month follow-up were selected from the LORHEN registry. The analysis was limited to the period from January 2009 to May 2016 and to patients receiving either TCZ or TNFi in combination with MTX, excluding bDMARD monotherapy.

Six- and 12-month clinical remission rate was defined as achievement of disease activity score 28 calculated by using erythrocyte sedimentation rate (DAS28-ESR) <2.6. Drug persistence was calculated by Kaplan-Meier method. The comparison between treatment subgroups was performed by a chi-square test for remission data and by a log-rank test for drug survival. Moreover, DAS28-ESR remission rate has been corrected for drug discontinuation by using the LUNDEX formula [1].

Results: The overall study population included 591 patients (female 77.3%, mean age ± standard deviation, SD) 54.2±13.2 years, mean disease duration ±SD) 7.4±7.7 years, positive rheumatoid factor 67.5%, positive anti-citrullinated peptide antibodies 77.6%, mean baseline DAS28-ESR 5.1±1.2 treated with TCZ (n=61) or TNFi (n=530) infliximab 43, adalimumab 163, etanercept 195, golimumab 60, certolizumab pegol 69). Baseline characteristics were similar in the two groups, with the exception of mean age (TCZ 58.2 vs TNFi 53.7 years; p=0.021). No significant differences were observed in the 6- to 24-month period (TCZ 88% vs TNFi 84.3%; p=0.752) and 12-month period (TCZ 76.4% vs TNFi 71.5%; p=0.17) between TCZ and TNFi. Clinical remission was achieved in overall 35.7% patients at 6 months (TCZ 59% vs TNFi 35%: p=0.001) and in 36.8% patients at 12 months (TCZ 76% vs TNFi 63.9%: p=0.001). Similar trends were observed after correction by LUNDEX formula at 6 months (TCZ 58.8% vs TNFi 53.7%; p=0.021). No significant differences were observed in the 6- to 24-month period (TCZ 88% vs TNFi 84.3%; p=0.752) and 12-month period (TCZ 76.4% vs TNFi 71.5%; p=0.17) between TCZ and TNFi. Clinical remission was achieved in overall 35.7% patients at 6 months (TCZ 59% vs TNFi 35%: p=0.001) and in 36.8% patients at 12 months (TCZ 76% vs TNFi 63.9%: p=0.001). Similar trends were observed after correction by LUNDEX formula at 6 months (TCZ 58.8% vs TNFi 53.7%; p=0.021). No significant differences were observed in the 6- to 24-month period (TCZ 88% vs TNFi 84.3%; p=0.752) and 12-month period (TCZ 76.4% vs TNFi 71.5%; p=0.17) between TCZ and TNFi.

Conclusions: Despite a similar 1-year remission rate, the proportion of patients achieving DAS28-ESR remission was significantly higher in TCZ+MTX treated group compared with TNFi+MTX, suggesting a deeper clinical response in patients receiving IL6 blockade.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4771


Acknowledgements: Funded by MedImmune. Medical writing support: R Plant, OX2 Comms, an Ashfield company, funded by MedImmune.

Senior author.


Acknowledgements: Funded by MedImmune. Medical writing support: R Plant, OX2 Comms, an Ashfield company, funded by MedImmune.
IMPACT OF RITUXIMAB IN COMBINATION WITH LEFLUNOMIDE AND RITUXIMAB RETREATMENT WITH TWO DIFFERENT DOSAGES ON PATIENT-REPORTED OUTCOMES: RESULTS FROM A MULTICENTER RANDOMIZED PLACEBO-CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL IN ACTIVE RHEUMATOID ARTHRITIS (AMARA-STUDY)


Methods: A total of 189 patients with active RA (DAS28≥3.2 and at least 3 SJC and 3 TJC) despite stable LEF treatment were screened for a 52-weeks placebo-controlled RCT. Patients were randomized to receive either two-times 1000mg RTX i.v. followed by a retreatment at week 24 with two-times 1000 (RTX-RTXhigh) or 500mg (RTX-RTXlow) or two times PLA at baseline, followed by a retreatment of RTX of either two-times 1000 (PLA-RTXhigh) or 500mg (PLA-RTXlow) at week 24. Adult patients who had inadequate response to more than one antiTNF or failed more than three cDMARDs were excluded. PROs (HAQ, FACIT-F, SF36) were measured at each visit until week 52. Treatment effects on PROs were determined by differences from baseline to week 16, 24 and week52.

Results: Of 189 screened patients 148 were randomized (mean age 56 years; mean proportion of RF- and anti-CCP-positivity 58.4% and 55.7% in the RTX-group; 74% female). DAS28 at baseline was 5.55 for RTX and 5.53 in the PLA-group. All baseline-characteristics were well balanced between treatment groups. An improvement in HAQ from baseline to week 16 was seen with a mean delta of -0.23 in the RTX-group (MCID) vs. -0.11 for PLA. In the RTX-group, retreatment at week 24 resulted in stable HAQ-values compared to week24 independent from its dosage. FACIT-F values increased in the RTX-group from baseline to weeks 16, 24 and 52 by 11.87, 12.3 and 14.25, respectively. All physical and mental domains of the SF36 showed a pronounced increase of levels at week 16 compared to baseline in the RTX-group (Figure 1). A total of 372 adverse events (AE) were observed during the one-year studyperiod, only 14 classified as severe (10 in RTX and 4 in PLA). 43 serious adverse events were reported, 28 of them in the RTX-group during the placebo-controlled period.

Conclusions: Efficacy of LEF plus RTX was demonstrated not only by measurements of disease activity (as presented previously) but also by measurements of PROs (HAQ, FACIT-F, SF36). This treatment regime showed equal effect sizes compared to the combinational therapy of MTX plus RTX. The treatment with LEF plus RTX illustrated an acceptable safety profile.

Disclosure of Interest: M. Köhn Grant/research support from: Pfizer, Janssen, Consultant for: Janssen, T. Rossmanith Grant/research support from: Janssen, Pfizer, Roche, S. Dauth: None declared, R. Alten Grant/research support from: Roche, M. Aringer Grant/research support from: Roche, M. Backhaus Grant/research support from: Roche, G. Burmester Grant/research support from: Roche, E. Feist Grant/research support from: Roche, H. Kellner Grant/research support from: Roche, K. Krüger Grant/research support from: Roche, U. Müller-Ladner Grant/research support from: Roche, A. Rubbert-Roth Grant/research support from: Roche, R. G. Burmester Grant/research support from: Roche, S. Wassenberg Grant/research support from: Roche, Pfizer, Speakers bureau: Pfizer, Roche, Pfizer, AbbieVie

DOI: 10.1136/annrheumdis-2017-eular.6238
ASSOCIATION BETWEEN CONVERSION TO ACPA/RF SERONEGATIVE STATUS AND CLINICAL OUTCOMES FOLLOWING TREATMENT WITH ABATACEPT IN COMBINATION WITH METHOTREXATE COMPARED WITH METHOTREXATE ALONE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND POOR PROGNOSTIC INDICATORS

D. Jansen, P. Emery, J. Smolen, R. Westhovens, M. Le Bars

Background: RA is characterized by the production of autoantibodies, including anti-citrullinated protein antibodies (ACPA) and RF, which are associated with poor prognosis in RA. More data on the clinical significance of ACPA/RF anti-citrullinated protein antibodies (ACPA) and RF, which are associated with remission achievement in SE positive patients was needed.

Methods: Logistic regression analysis was done in this retrospective cohort. The EULAR good response rate at week 24 were 74.5%/20.0% (SE positive/SE negative, p=0.001, Fisher's exact test), respectively. Simplified Disease Activity Index (SDAI) remission rate at week 24 were 55.3%/20.0% (SE positive/SE negative, p=0.004, Fisher's exact test), respectively. Multivariate logistic regression revealed the odds ratio of EULAR good response and SDAI remission achievement in SE positive patients was 23.2 and 6.73 (95% CI: 5.10–152.0, p<0.0001 and 1.70–32.5, p=0.006), respectively.

Conclusions: Abatacept is strictly effective to SE positive RA patients.

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ASSOCIATION BETWEEN CONVERSION TO ACPA/RF SERONEGATIVE STATUS AND CLINICAL OUTCOMES FOLLOWING TREATMENT WITH ABATACEPT IN COMBINATION WITH METHOTREXATE COMPARED WITH METHOTREXATE ALONE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND POOR PROGNOSTIC INDICATORS

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Conclusions: Abatacept is strictly effective to SE positive RA patients.

References:
DOES SEROPOSITIVITY INFLUENCE DIFFERENTIALLY DRUG DISCONTINUATION OF BIOLOGIC ANTIHEMATIC AGENTS WITH NON-ANTI-TNF MODE OF ACTION?

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Background: Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) are used as diagnostic tools, but may also be used as prognostic factors or as predictors of response to therapy, as these biomarkers have been associated with better clinical responses to some bDMARDs.

Objectives: To examine whether seropositivity has a similar impact on drug discontinuation of different bDMARDs with a non-anti-TNF mode of action (non-aTNF bDMARDs).

Methods: This is a pooled analysis of 10 observational European RA registries (FR, CZ, DK, NO, PT, RO, ES, SE, CH, NL). Inclusion criteria were a diagnosis of RA, initiation of treatment with abatacept (ABA), rituximab (RTX) or tocilizumab (TCZ) and available information on RF and/or ACPA status. The exposure of interest was seropositivity, which was defined as positive if RF or ACPA was positive and negative if both were negative. The primary endpoint was overall drug discontinuation, defined as the period between treatment initiation and treatment discontinuation. Because national differences may constitute a potential confounder, we only included national registries with information for all 3 bDMARD and pooled data across registries only after excluding significant effect modification by country. Drug discontinuation was analyzed using a Cox proportional hazard model, including drug, seropositivity, and their interaction, adjusting for age, gender, disease duration, baseline DAS28, concomitant DMARD (sDMARDs), number of previous sDMARDs and bDMARDs, and stratifying by country and calendar year.

Conclusions: Data from this pooled European registry analysis suggests that seropositivity is associated with lower drug discontinuation of non-aTNF bDMARDs. This effect differed between drugs and was significant for ABA, but not for TCZ or RTX. The impact of seropositivity on other measures of effectiveness still needs to be investigated.

DOI: 10.1136/annrheumdis-2017-eular.1106

DOES SEROPOSITIVITY INFLUENCE DIFFERENTIALLY DRUG DISCONTINUATION OF BIOLOGIC ANTIHEMATIC AGENTS WITH NON-ANTI-TNF MODE OF ACTION?

SUSTAINED RESPONSE FOLLOWING DISCONTINUATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL (COMP-ACT)


1Albany Medical College and The Center for Rheumatology, Albany, NY; 2Geisel School of Medicine, Dartmouth College, Lebanon, NH; 3School of Medicine, MetroHealth System, Case Western Reserve University, Cleveland, OH; 4Genentech, Inc., South San Francisco, CA, United States

Background: Methotrexate (MTX) is frequently administered in combination with biologics for the treatment of rheumatoid arthritis (RA). MTX may be subsequently discontinued due to intolerance or nonadherence, and/or to reduce medication burden once disease control is achieved. Previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO), but the impact of discontinuing TCZ in patients with RA who have been treated with MTX for an extended period cannot be ascertained.

Methods: This randomized, controlled, double-blind, placebo-controlled trial included all patients with RA (moderate-severe disease activity) who had been on MTX treatment for at least 3 months and who had not received prior biologic therapies. The primary endpoint was the proportion of patients achieving ACR50 response at week 48. Secondary endpoints included ACR20, ACR70 responses, and other measures of clinical and functional improvement. The trial had a 6-week run-in period, followed by a 48-week randomized treatment phase. Patients were randomly assigned to receive either subcutaneous placebo or TCZ 40 mg weekly.

Conclusions: The results of this study suggest that discontinuing MTX and initiating TCZ monotherapy can lead to sustained clinical improvement in patients with RA who have been on MTX treatment for an extended period. This finding may have important implications for the management of RA patients who have been treated with MTX but are not achieving adequate disease control with current pharmacotherapies.

DOI: 10.1136/annrheumdis-2017-eular.6006
of MTX withdrawal in patients achieving good clinical response to TCZ+MTX (COMBO) has not been evaluated.

Objectives: To evaluate whether TCZ-MONO is non-inferior to TCZ-COMBO in maintaining clinical response in patients who achieve low disease activity with TCZ-COMBO.

Methods: 118 patients with RA who were inadequate responders to MTX were enrolled: initial combination therapy included MTX (15 mg/week orally) plus TCZ 162 mg subcutaneous (SC) either weekly (qw; for patients >100 kg) or every 2 weeks (q2w; for patients <100 kg). Dose escalation from q2w to qw was allowed at week 12 in patients who had not achieved low disease activity (DAS28 ≤3.2) at week 24. Patients achieving DAS28-ESR ≤3.2 were randomized (double-blind) 1:1 to receive either TCZ-MONO or continue TCZ-COMBO until week 52. Patients who did not achieve DAS28 ≤3.2 were assigned to an open-label arm and continued TCZ-COMBO until week 52. The primary outcome was the proportion of patients achieving DAS28-ESR ≤3.2 in the randomized cohort between weeks 24 and 40, between the TCZ-MONO or TCZ-COMBO arms (non-inferiority margin of 0.6). Secondary outcomes included the proportion of patients achieving DAS28 ≤2.6, DAS28 ≤3.2 and American College of Rheumatology 20%/50%/70% (ACR20/50/70) responses at weeks 40 and 52, and safety. Trial registration number: NCT01385789.

Results: Of 718 patients enrolled, 296 were randomized at week 24 (TCZ-COMBO, n=148; TCZ-COMBO, n=148). Early discontinuation in the randomized cohort occurred in 12.2% of patients in the TCZ-MONO group and 10.2% in the TCZ-COMBO group. Baseline characteristics were balanced between treatment groups (mean age 55.5 years: 74.8% female; mean RA duration 6.8 years; mean DAS28-ESR 6.3). At week 24, DAS28 scores were similar in both groups, but ACR responses were ~8–11 lower in the TCZ-MONO group prior to MTX withdrawal (randomization). The mean change in DAS28 was similar between the randomized treatment groups (Table 1). For the primary efficacy analysis, the mean changes in DAS28 from week 24 to week 40 were 0.46 and 0.14 in the TCZ-MONO and TCZ-COMBO groups, respectively (95% CI: 0.04–0.592). This study met the primary endpoint by demonstrating that discontinuing MTX in TCZ responders was non-inferior to continuing MTX. The safety of TCZ-SC in this study was consistent with the known safety profile with no new safety signals observed (Table 2). The most common SAE was infection, occurring in 4.1% of patients. TCZ-COMBO had greater frequency of AEs, SAEs and serious infections than TCZ-MONO.

Conclusions: These results demonstrate that patients receiving TCZ-COMBO who achieve low disease activity can discontinue MTX and maintain disease control.


DOI: 10.1136/annrheumdis-2017-eular.2797

FR10223 ANTI-CCP IS AN INDEPENDENT PREDICTOR OF 12-MONTH EULAR RESPONSE IN PATIENTS WITH RA TREATED WITH ABATECTAE

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Background: Although anti-cyclic citrullinated peptide (anti-CCP) positivity is regarded as a strong predictive factor for untreated RA outcome, the benefit of anti-CCP tests for personalized medicine is controversial.1 Illustratively, anti-CCP was not predictive for response to anti-TNF in RA, as shown in meta-analyses, although some predictive value was shown for rituximab.2–4 There are, however, indications that better response to abatacept (ABA) is predicted by anti-CCP positivity.5–7

Objectives: To test whether anti-CCP level at baseline (BL) is an independent predictor for treatment response (DAS28 [CRP]-based EULAR response criteria) at 12 months (M) in patients (pts) with RA treated with ABA.

Methods: Conscient pts with RA from Radboud UMC and Sint Maartenstinkelijk were consecutively included if they started treatment with ABA (BL). The anti-CCP values closest before BL were used. DAS28 (CRP) was assessed at BL and at 12M by trained rheumatology nurses or rheumatologists. Demographic and disease-related variables, treatment history and co-morbidity were also assessed. Primary outcome was response to treatment based on DAS28 (CRP) EULAR response criteria at M12. Therapy cessation was regarded as non-response. Multiple imputation with 20 repetitions was used to replace missing predictors. Multivariate logistic regression was used to examine whether anti-CCP positivity was an independent predictor for treatment response, taking confounding BL covariates (Table variables) into account.

Results: Data were available for 200 pts with RA starting ABA. Mean (SD) age was 58 (13) years, 165 (83%) were female and median (p25–p75) disease duration was 12 (7–19) years (Table). Overall, 121 (61%) pts were anti-CCP positive at BL. At 12M, 86 (43%) pts remained on ABA. In the univariate model, anti-CCP was a predictor for treatment response (odds ratio 2.51; 95% CI 1.1, 6.0; p=0.038). No relevant confounding was present.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Abatacept (n=200)</th>
</tr>
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<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>58 (13)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>165 (83)</td>
</tr>
<tr>
<td>RF+, n (%)</td>
<td>128 (64)</td>
</tr>
<tr>
<td>Anti-CCP+, n (%)</td>
<td>121 (61)</td>
</tr>
<tr>
<td>No. of previous dDMARDs*</td>
<td>3 (3–4)</td>
</tr>
<tr>
<td>Oral glucocorticoids, n (%)</td>
<td>79 (40)</td>
</tr>
<tr>
<td>Disease duration, years*</td>
<td>12 (7–19)</td>
</tr>
<tr>
<td>Treatment duration, months*</td>
<td>8 (4–24)</td>
</tr>
<tr>
<td>NSAIDs, n (%)</td>
<td>117 (59)</td>
</tr>
<tr>
<td>Comorbid DM, n (%)</td>
<td>117 (59)</td>
</tr>
<tr>
<td>Overweight (BMI ≤25.0 kg/m2), n (%)</td>
<td>98 (48)</td>
</tr>
</tbody>
</table>

*Median (p25–p75). RA,+: IgM-Rheumatoid factor positivity. b/cDMARD-biologic/conventional synthetic DMARD.

Conclusions: Anti-CCP positivity was confirmed as an independent predictor for treatment response at 12M in pts with RA treated with abatacept. As indicated by meta-analysis and systematic reviews, anti-CCP is not predictive for the response to anti-TNFs.2–4 Additional studies are needed to evaluate whether abatacept could be a preferable treatment in anti-CCP-positive pts.

References:

**FR10224** RITUXIMAB SELECTIVELY REDUCES IgG4 LEVELS IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Rituximab has been applied as a therapeutic strategy in a variety of diseases, including Rheumatoid Arthritis (RA) and IgG4-Related Disease (IgG4-RD). On IgG4-RD, it has been shown that apart from B-cell depletion, rituximab induces remission by reducing IgG4 levels.2

**Objectives:** On this regard, we investigated weather B-cell depletion in RA is also associated with a selective reduction of any IgG subclass, especially IgG4.

**Methods:** 31 RA patients, 25/6 female/male, median age 59 years (34–73), duration of disease 9.5 years (1–30) on standard care DMARD treatment and rituximab administration every 6 months for 2 years were investigated for alterations on disease activity along with IgG subclasses levels. All parameters were assessed at enrollment (T0), after 6, 12 and 24 months. On this 2-year period all patients had been periodically receiving rituximab every 6 months.

**Results:** After 2 years of rituximab administration, patients achieved a good response to treatment (EULAR criteria). IgG levels were not statistically altered, though all of them declined (data for IgM and IgA not shown). Furthermore, from IgG subclasses, only IgG4 levels statistically declined.

**Conclusions:** This is the first time that IgG4 variations are investigated in a non-ILD RA population after rituximab administration. Our results imply that IgG4 may be actively implicated in RA pathophysiology, since disease remission is accompanied by only IgG4 level reduction among all classes and subclasses of IgGs. Furthermore, in RA patients, rituximab may exert its therapeutic results not only via B-cell depletion, but also via IgG4 levels reduction.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6690

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**FR10226** ANEMIA IS A BETTER PREDICTOR FOR RADIOGRAPHIC DAMAGE IN RHEUMATOID ARTHRITIS THAN DAS28 WHEN DETERMINED BEFORE START OF TOCILIZUMAB-TREATMENT – A SECONDARY ANALYSIS FROM THE ACT-RAY TRIAL

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**Background:** Clinical remission, or at least low disease activity, as measured by DAS28 may not be sufficient to prevent radiographic damage in RA patients. Anemia and low Hb levels are associated with progression of joint damage due to an increase in erythropoiesis, add importantly to the growing body of evidence for the studied association.

**Objectives:** To study the predictive value of anemia in relation to DAS28 when determined before the start of tocilizumab treatment (T12), compared to DAS28 when determined during RA treatment (T12). To analyze the association of anemia to DAS28 and radiographic data over time when obtained in patients already on tocilizumab (TCZ).

**Methods:** We studied 18 patients (13 women /5 men) with ILD associated to RA. The mean age was 65.2 years (58.7 – 71). Of 556 randomised patients, complete datasets for fully adjusted models were available from 285 patients. Overall radiographic progression was regarded to be minimal, with insignificant differences in favor of the add-on strategy. Median DAS28 before inclusion was 2.9 (IQR 1.5–6.4) in patients without and 5.5 (IQR 2.7–11.1) in patients with baseline anemia, but evolved subsequently similar when being on TCZ. Anemia at baseline was a strong predictor of mTSS (per WHO definition: coefficient 14.6, 95% CI 7.6–21.9, p < 0.001; per NHANES definition: coefficient 14.6 95% CI 7.6–21.5 p < 0.001), as well as baseline DAS28 (coefficient 3.9, 95% CI 0.7–7.0, p = 0.016). Mean DAS28 over time (p < 0.001), in contrast to anemia data over time when obtained in patients already on TCZ, was significantly associated with subsequent ΔmTSS. Baseline anemia in contrast to baseline DAS28 remained a significant predictor of mTSS for up to two years on TCZ in fully adjusted multivariate analyses (p < 0.05), including time-variant DAS28.

**Conclusions:** Anemia may be a strong and DAS28-independent long-term predictor of radiographic joint damage progression. Present data from patients on IL-6R blockade, a potent target-specific RA treatment with major impact also on erythropoiesis, add importantly to the growing body of evidence for the studied association.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6685

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**Abstract FR10224** – Table 1. DAS28 and IgG class and subclasses variations. Because of non-normal distribution of our sample, the results were expressed as median and range and statistical analysis was performed by using the Kruskal Wallis tests.

<table>
<thead>
<tr>
<th></th>
<th>DAS28</th>
<th>IgG3</th>
<th>IgG1</th>
<th>IgG2</th>
<th>IgG4</th>
</tr>
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<tr>
<td>T0</td>
<td>4.46</td>
<td>12.2</td>
<td>7.7</td>
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</tr>
<tr>
<td>T6</td>
<td>3.06</td>
<td>11.6</td>
<td>7.28</td>
<td>2.7</td>
<td>0.445</td>
</tr>
<tr>
<td>T12</td>
<td>4.01</td>
<td>11.1</td>
<td>6.81</td>
<td>2.53</td>
<td>0.423</td>
</tr>
<tr>
<td>T24</td>
<td>3.27</td>
<td>11.2</td>
<td>6.59</td>
<td>2.42</td>
<td>0.405</td>
</tr>
</tbody>
</table>

p<0.05
MTX (3), HCQ (1), AZA (1) MMF (1). A significant improvement of the dyspnea was observed. FVC and HRCT showed an improvement in the period between 6 and 12 months. DLCO remained stable in the majority of the patients (%). DAS28 also improved. After a follow-up of 12 months, the only serious adverse effect was a severe infection respiratory. table 1

<p>| Table 1. Median Percent Change From Baseline in Serum Concentrations of Circulating Biomarkers |</p>
<table>
<thead>
<tr>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMP9, n (%)</td>
<td>18</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Improvement</td>
<td>5 (33)</td>
<td>6 (37)</td>
<td>6 (37)</td>
</tr>
<tr>
<td>Worsening</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No change</td>
<td>10 (67)</td>
<td>10 (63)</td>
<td>10 (63)</td>
</tr>
<tr>
<td>CRP (0.009) mg/dL</td>
<td>2.01±0.9</td>
<td>1.12±0.9</td>
<td>1.98±1.95</td>
</tr>
<tr>
<td>JOINT, n (%)</td>
<td>18</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Improvement</td>
<td>1 (14)</td>
<td>1 (11)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>Worsening</td>
<td>0</td>
<td>1 (11)</td>
<td>0</td>
</tr>
<tr>
<td>No change</td>
<td>6 (86)</td>
<td>7 (78)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>DAS28 – Mean</td>
<td>4.32±1.35</td>
<td>3.21±0.73</td>
<td>3.44±0.87</td>
</tr>
<tr>
<td>CVF , n (%)</td>
<td>16</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Improvement</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Worsening</td>
<td>0</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>7 (44)</td>
<td>7 (44)</td>
<td></td>
</tr>
<tr>
<td>Lp(a), Wk 12 -35.0 † -0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td>0</td>
<td>2.2 (67) 7.2 (17)</td>
<td></td>
</tr>
<tr>
<td>Worsening</td>
<td>1 (17)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>5 (83)</td>
<td>1 (33)</td>
<td>8 (66)</td>
</tr>
<tr>
<td>CRP (mg/dl)-, Mean</td>
<td>2.01±2.35</td>
<td>1.12±0.9</td>
<td>1.98±1.95</td>
</tr>
<tr>
<td>HRCT, n (%)</td>
<td>7</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Improvement</td>
<td>0</td>
<td>2.2 (67) 7.2 (17)</td>
<td></td>
</tr>
<tr>
<td>Worsening</td>
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</tr>
<tr>
<td>Lp(a), Wk 24 -83.2 † -17.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td>0</td>
<td>2.2 (67) 7.2 (17)</td>
<td></td>
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<tr>
<td>Worsening</td>
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<td>0</td>
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<td>CRP (mg/dl)-, Mean</td>
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<td>1.12±0.9</td>
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<tr>
<td>CVF , n (%)</td>
<td>16</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Improvement</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Worsening</td>
<td>0</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>7 (44)</td>
<td>7 (44)</td>
<td></td>
</tr>
<tr>
<td>Lp(a), Wk 24 -18.3 † 10.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td>0</td>
<td>2.2 (67) 7.2 (17)</td>
<td></td>
</tr>
<tr>
<td>Worsening</td>
<td>1 (17)</td>
<td>0</td>
<td></td>
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<td>No change</td>
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<tr>
<td>Improvement</td>
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<td>9</td>
<td></td>
</tr>
<tr>
<td>Worsening</td>
<td>0</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>7 (44)</td>
<td>7 (44)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: RTX seems to be an effective and relatively safe treatment in RA patients with ILE. However, these data should be verified in prospective and randomized studies.

Disclosure of Interest: None declared

DoI: 10.1136/annrheumdis-2017-eular.3275

SARILUMB SIGNIFICANTLY SUPPRESSES CIRCULATING BIOMARKERS OF BONE RESORPTION AND CARDIOVASCULAR RISK COMPARED WITH ADALIMUMAB: BIOMARKER ANALYSIS FROM THE PHASE 3 MONARCH STUDY

C. Gabay1, J. Mishii2, C. Paccard3, M. Zilberstein3, N.M. Graham4, A. Boypati4, 1University Hospitals of Geneva, Geneva, Switzerland; 2Sanofi R&D, Chilly-Mazarin, France; 3Sanofi R&D, BridgeWater; 4Regeneron Pharmaceuticals, Inc, Tarrytown, United States

Background: MONARCH (NCT02332590) was a randomized, active-controlled, double-blind, double-dummy, phase 3 superiority trial comparing sarilumab monotherapy with adalimumab monotherapy. Exploratory biomarkers associated with inflammation, bone erosion, and cardiovascular (CV) risk were evaluated in this study.

Objective: To compare the effects of sarilumab monotherapy vs adalimumab monotherapy on circulating biomarkers associated with acute-phase response (CRP serum amyloid A [SAA]), bone resorption [RANKL and osteoprotegerin [OPG]], and CV risk (lipoprotein (a) [Lp(a)]) in patients from MONARCH.

Methods: Sera were analyzed at baseline and posttreatment through wk 24 from patients who consented to biomarker analyses and received SC sarilumab 200 mg q2w (N=153) or adalimumab 40 mg q2w (N=154). Biomarkers were assessed using validated ELISAs. Nonparametric methods were used to evaluate differences in the percent change from baseline in biomarker levels between treatments at each time point. Percent change from baseline in biomarkers at wk 24 was also compared, separately by treatment group, between ACR50 responders and nonresponders at wk 24. The Benjamini-Hochberg procedure was used to correct P values for multiplicity and control false discovery rate. Significance level was P=0.05.

Results: A significant difference in RANKL was observed at wks 2 and 24 between sarilumab and adalimumab groups (P<0.0001; Table). Numerically, RANKL decreased after sarilumab and increased after adalimumab treatment. Significantly greater reductions in Lp(a), SAA, and CRP were observed at wks 12 and 24 after treatment with sarilumab vs adalimumab. The difference in OPG between groups was significant at wk 2 only.

Table 1. Maximum Total Bilirubin in Sarilumab-Treated Patients by rs6742078 Genotype

<p>| Table 1. Maximum Total Bilirubin in Sarilumab-Treated Patients by rs6742078 Genotype |</p>
<table>
<thead>
<tr>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum total bilirubin, n (%)</td>
<td>0 ≤ ULN</td>
<td>&gt;1.5 × ULN</td>
<td></td>
</tr>
<tr>
<td>GG/GT</td>
<td>352 (92)</td>
<td>4 (27)</td>
<td>356 (90)</td>
</tr>
<tr>
<td>TT</td>
<td>381 (81)</td>
<td>11 (73)</td>
<td>40 (10)</td>
</tr>
<tr>
<td>Total</td>
<td>381 (81)</td>
<td>15 (7)</td>
<td>396 (100)</td>
</tr>
</tbody>
</table>

OR=34.7; p=1.2×10−4. Elevations remained ≥2 × ULN. Logistic regression with recessive genetic model, adjusting for ancestry covariates.

Conclusions: The association observed between the rs6742078 TT genotype in UGT1A1 and unconjugated bilirubin elevations in sarilumab-treated patients is consistent with previous observations in tocilizumab-treated patients. These findings suggest that sarilumab-related increases in bilirubin levels are likely benign and caused by common genetic variation in UGT1A1 and are not due to underlying liver injury.

References:


DOI: 10.1136/annrheumdis-2017-eular.5016

FR1022 | SURVEY ON TRANSPORTATION AND STORAGE OF BIOLOGICAL THERAPIES BY PATIENTS


Background: In order to ensure the psychological protection of medicinal drugs, it is mandatory to keep the cold chain unbroken from manufacturing to administration since this tolerance of rules may compromise their efficiency (1,2).

Objectives: To ascertain key aspects of transportation and storage of Biological Therapy (BT) on the part of the patients.

Methods: survey among outpatients who either were treated in the centre or attended the centre for the administration of a BT. Inclusion criteria: patients of over 18 years of age, who were receiving a BT (at least one dose over the last 12 months) whose patient information leaflet indicated, “… must be refrigerated at 2° C to 8° C (36° F to 46° F). Do not freeze.” The survey comprised 31 questions about transportation and storage of the BT. This study was approved by the Bioethics Committee. Every patient signed an informed consent form.

Results: Eighty-three patients were interviewed (76% female and 24% males), 31 years of age at diagnosis was 47.1 (SD=13.4) years with a mean disease duration of 7.2 (7.8) years, and a mean QOL of 43.1 (32.5) at baseline. No significant differences in retention rates were observed in the ABA and anti-TNF groups (Table, Figure). On average, pts treated with anti-TNFs and ABA maintained their treatment for 1.59 (1.91) and 1.90 (2.08) years, respectively. Lack of efficacy (47.6%) and adverse effects (22.0%) were the most commonly cited reasons for treatment discontinuation.

Table 1. Retention of the first bDMARD

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>TNFi</th>
<th>Abatacept</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 Months</td>
<td>71.66% (1.92%)</td>
<td>70.71% (5.15%)</td>
</tr>
<tr>
<td>24 Months</td>
<td>59.85% (21.1%)</td>
<td>62.16% (5.60%)</td>
</tr>
<tr>
<td>60 Months</td>
<td>44.28% (2.26%)</td>
<td>48.37% (2.46%)</td>
</tr>
<tr>
<td>96 Months</td>
<td>35.29% (2.46%)</td>
<td>41.17% (7.43%)</td>
</tr>
<tr>
<td>bDMARD retention time (years)</td>
<td>Mean (SE)</td>
<td>4.83 (0.18)</td>
</tr>
<tr>
<td></td>
<td>Lower quartile, (95% CI)</td>
<td>0.86 (0.72–1.00)</td>
</tr>
<tr>
<td></td>
<td>Median, (95% CI)</td>
<td>3.83 (2.87–4.67)</td>
</tr>
</tbody>
</table>

*% (standard error) survival.

Conclusions: Abatacept and TNF inhibitors demonstrate similar sustainability at 8-year, supporting studies that demonstrate that abatacept used after csDMARDs inadequate response is as safe and effective as a TNF targeting agents in the long term.
BMI dynamic was independent of TOFA dose, achieving RA activity, dynamic of DAS 28, SDAI. Use of cardioprotective therapy. Dynamic of lipid levels dependent on statins treatment. An increase in HDL-C level from 1.35 [0.88; 1.91] to 1.90 [1.64; 2.17], p < 0.05, a decrease in LDL-C level from 3.75 [3.11; 4.40] to 2.60 [2.55; 2.93], p < 0.03 was observed in pts treated with statins (n=11). An increase in total cholesterol level from 4.80 [4.14; 5.45] to 5.54 [4.56; 6.64], p < 0.001 was observed in pts who didn’t receive statins (n=17). The change in HDL-C level correlated negatively with dynamic of DAS 28, SDAI (r = 0.4, p < 0.05).

Conclusions: TOFA therapy of RA pts contributes to dramatical increase of BMI. Greater BMI dynamic associated with higher disease activity at baseline. BMI dynamic was independent of achieving RA activity and dynamic of DAS 28, SDAI. Co-administration TOFA and statins resulted in significant favorable changes of LDL and HDL-cholesterol levels.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2968

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**References:**


**Disclosure of Interest:** D. Choquette Consultant for: BMS, Speakers bureau: Abbvie, Roche, BMS, L. Coupal: None declared


DOI: 10.1136/annrheumdis-2017-eular.2968

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**FRIO232**

**E. Alemao**, 1 K. Knapp, 2 V. Anupindi, 2 S. Annamalai, 3 G. Craig, 3 Bristol-Myers Squibb, Princeton; 2 Discus Analytics, Spokane; 3 Mu Sigma, Princeton, United States; 4 Mu Sigma, Bangalore, India; 5 Arthritis Northwest, Spokane, United States

**Background:** Poor prognostic factors (PPFs; e.g. elevated anti-citrullinated protein antibody/RF levels and erosions) are associated with higher disability and mortality in RA. 1 2 In addition, high seropositivity or CRP/ESR levels are correlated with erosive disease. 3

**Objectives:** To evaluate if the presence of specific PPFs of seropositivity with erosions (PPF+) in patients (pts) with RA have an effect on treatment with abatacept (ABA) and anti-TNFs.

**Methods:** This retrospective study was based on electronic medical record data. This database includes >6500 pts with RA from 50+ rheumatologists. At each visit, data on diagnosis, medications and test results were collected. A homunculus was used to record joint tenderness, swelling, deformity or decreased range of motion. Disease activity was measured by DAS28 (ESR/CRP), SDAI, CDAI, RAPI D3 and Vectra DA blood tests. For this analysis, pts aged ≥18 yrs with an RA diagnosis from 1 Jan 2009 to 3 Mar 2016 were followed until lost to follow-up, death or end of study period. Date of first ABA/anti-TNF prescription was designated as index date, preceded by the baseline (BL) period. The ABA cohort comprised pts with a record of ABA in the study period, while the anti-TNF cohort comprised pts with a record of anti-TNF and no record of ABA in the study period. Primary outcome was change (Δ) in CDAI at 6 months (M); other outcomes were SDAI, DAS28 (CRP), pain, RAPI D3 and Patient Global Assessment. Descriptive statistics were used for BL characteristics. Univariate and multivariate regression analyses were
used to evaluate \( \Delta \text{CDAI} \). Subgroup analyses were conducted by line of therapy, after excluding switch pts.

**Results:** Overall, 3959 pts met inclusion criteria and 2045 had data on PPF; 344 and 814 pts received ABA and anti-TNF. Mean (SD) age of ABA pts was 60.3 (12.5) yrs and median (interquartile range; IQR) CDAI was 25.5 (18.1). Mean (SD) age of anti-TNF pts was 56.4 (13.3) yrs and median (IQR) CDAI (IQR) was 19.8 (18.1). PPF+ pts treated with ABA (vs all other ABA pts) had a better CDAI outcome at 6M (9.7 [16.1] vs –7.5 [14.4]). In sensitivity analyses, the difference persisted (–10.4 vs –8.4; Fig). PPF+ pts treated with ABA as first-line therapy (vs all other ABA pts) had a better CDAI outcome (–13.4 vs –10.3). Similar trends were not observed in the anti-TNF cohort (Fig). Adjusted mean (SE) \( \Delta \text{CDAI} \) in PPF+ vs PPF– pts treated with ABA was –12.1 (2.01) vs –9.5 (0.79); covariates included in the model were age, sex and BL CDAI (p=0.24). During follow-up, more PPF+ pts treated with ABA changed from high/medium to LDA or remission vs all other pts (34% vs 25%), while this was not seen in anti-TNF pts (45 vs 42%).

**Conclusions:** Pts with RA treated with abatacept had higher disease activity at BL and a greater reduction in disease activity was observed in seropositive pts with RA and erosions compared with all other abatacept pts. Similar trends were not observed in anti-TNF pts. No direct comparisons between treatments were conducted in these cohorts.

**References:**

number of previous anti-TNF use of concomitant DMARDs and prednisone, drug retention rate at 1 year was significantly better for ABA compared to anti-TNF (p=0.02) and for TCZ compared to anti-TNF (p<0.04), but no difference was found between TCZ and ABA (p=0.62) (Figure).

Conclusions: Patients who received ABA following failure of RTX, seem to be better treated with than concomitantly, compared with ABT mono-therapy group. It may reflect rapid rates of ABT at 24 weeks were higher among patients receiving ABT and mPSL. This is the first real world study to investigate whether ABT can be used in a real-world setting. Conclusions: The rates of non-retention were comparable between non-TNFi and TNFi patient groups both at 6 (mean [SD]: -1.16 (2.93) and -1.07 (1.55) respectively, p=0.296) and at 12 months [1.41 (2.93) and -1.39 (1.26) respectively, p=0.670]. In patients who did not receive co-therapy with methotrexate, significantly greater IDAS28 was observed with a non-TNFi (-1.25 (2.93) vs. -0.68 (1.61), p=0.006). When the first TNFi fails, the primary or secondary failure to the 1st TNFi (-0.81 vs -1.48, p=0.18), but this did not reach statistical significance, probably due to the low number of available patients. The 2-year drug survival was higher for non-TNF (64% vs. 39%, log rank p<0.001) due to lower frequency of discontinuations for primary failure (p<0.001) and adverse events (p=0.019). IDAS28 was comparable between non-TNF and TNFi patient groups both at 6 [mean (SD): -1.16 (2.92) and -1.08 mg/dl (± 2.17) in non-mPSL group (p=0.22), and those in ESR were = -8.23 mm/h (± 18.40) in mPSL group and -6.61 mm/h (± 17.93) in non-mPSL group (p=0.75), respectively.

Conclusions: This is the first real world study to investigate whether ABT administrated with intravenous mPSL maintain higher retention rates in rheumatoid arthritis. Although there were no statistically significant differences, the retention rates of ABT at 24 weeks were higher among patients receiving ABT and mPSL concomitantly, compared with ABT mono-therapy group. It may reflect rapid improvement of the disease activity.

Disclose of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6817

**Safety of Biosimilar Infliximab Use in a Medical Day Hospital: A Case-Series**


1 Family Doctor,
2 Internist Medicine; 3 Rheumatology, HU Virgen del Rocio, Sevilla, Spain

**Background:** The first biosimilar anti-TNF (infliximab) approved by the EMA (European Medicines Agency) began to be used throughout Europe in 2015. Since then, it has been widely used throughout the world, even replacing the original treatment approved 1999 Remicade® with Remsima®, a biosimilar drug.

**Objectives:** To report intrainfusion and postinfusion adverse events related to intravenous Remsima® use in a medical day hospital. Besides, we will describe the rehospitalizations and continuation of treatment in the follow up.

**Methods:** We designed a prospective uncontrolled case-series study. Patients referred from March 2015 to October 2016 to our MDH to receive intravenous Remsima® were consecutively enrolled. Demographic data were collected, and a harmonised active monitoring strategy was applied. We recorded the indication for treatment, the doses administered and the number and symptoms of acute transfusion reactions (ATR) occurring both in the infusion period and during the 3 hour postinfusion observation interval.

**Results:** 2828 doses were administered, 0.67% presented ATR, all of them during the infusion and reported to the Regional Pharmacovigilance Center. 53% of those ATR were women and they were on average 35.78 years (SD 14.71). The mean dose used was 4.49 mg/kg (SD 0.47). The indications for treatment in patients suffering ATR were: EC (47%), CU (26%), Spondylitis (21%) and Psoriasis (5%). As a predominant symptom during ATR we found: shortness of breath (36.89%), pruritus (15.75%), flushing sensation (15.75%), urticaria (10.4%), alopecia (5.2%), chest pain (5.2%), paraesthesia (5.2%) and nausea (5.2%). 95% of ATR showed complete recovery of the symptoms, 47% disappeared with the pause of infusion. However, they had prolonged in MDH stay, the infusion was stopped for 30 minutes and restarted at a lower rate according to the protocol. 21% of patients presenting ATR dropped out because of the symptoms, which represents 0.14% of the total infusions.

**Conclusions:** Biosimilar Infliximab seems to be safe in a MDH setting, given the

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**Concomitant Use of Intravenous Methylprednisolone to Obtain Higher Retention Rate of Abatacept in Rheumatoid Arthritis**

H Sawada, M. Suda, M. Kishimoto, M. Okada.

**Immuno-Rheumatology Center, St Luke’s International Hospital, Tokyo, Japan**

**Background:** Abatacept (ABA) is a widely used biologic for treating rheumatoid arthritis (RA).

**Objectives:** Concomitant use of intravenous corticosteroids with ABA infusion may contribute to achieve earlier remission and higher retention rates.

**Methods:** We conducted a retrospective cohort study in 2012, St Luke's International Hospital, Tokyo, Japan, from January 2010 to June 2016. Patients who met the 2010 ACR/EULAR classification criteria for RA and treated with ABA were included in the study. We excluded patients who used two or more biologics prior to initiation of ABA. Our primary outcome was treatment retention rates of ABA at week 24. Secondary outcomes were changes in C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) during follow-up (week 0 vs. week 8). We compared these outcomes between the patients receiving concomitant intravenous methylprednisolone (mPSL) with first 3 consecutive doses of ABA and those not receiving it. Log-rank analysis and Fisher’s exact test were applied for statistical analysis.

**Results:** 64 RA patients were included in the study. Mean age was 67.3 ± 14.2 and 55 (85.9%) were female. Among them, 13 (20.3%) received concomitant ABA and mPSL. The dosage of mPSL ranged from 30mg to 250mg (median dosage was 40mg). At week 24, the cumulative retention rates of the patients receiving mPSL (mPSL group) and those not receiving it (non-mPSL group) were 92.3% and 76.5%, respectively. There was no significant difference in the retention rates between the two groups (log-rank test, p=0.21) (Figure). Changes in CRP between week 0 vs. week 8 were -1.56 mg/dl ± 2.92 in mPSL group and -1.08 mg/dl ± 2.22 in non-mPSL group (p=0.75). Changes in ESR between the two groups (log-rank test, p=0.21) (figure). Changes in CRP between week 0 vs. week 8 were -1.56 mg/dl ± 2.92 in mPSL group and -1.08 mg/dl ± 17.93 in non-mPSL group (p=0.75), respectively.

**Conclusions:** This is the first real world study to investigate whether ABT administrated with intravenous mPSL maintain higher retention rates in rheumatoid arthritis. Though there were no statistically significant differences, the retention rates of ABT at 24 weeks were higher among patients receiving ABT and mPSL concomitantly, compared with ABA mono-therapy group. It may reflect rapid improvement of the disease activity.

**Disclose of Interest:** None declared.

DOI: 10.1136/annrheumdis-2017-eular.4716

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**Safety of Biosimilar Infliximab Use in a Medical Day Hospital: A Case-Series**


1 Family Doctor,
2 Internist Medicine; 3 Rheumatology, HU Virgen del Rocio, Sevilla, Spain

**Background:** The first biosimilar anti-TNF (infliximab) approved by the EMA (European Medicines Agency) began to be used throughout Europe in 2015. Since then, it has been widely used throughout the world, even replacing the original treatment approved 1999 Remicade® with Remsima®, a biosimilar drug.

This medicine is currently approved to treat people who have been diagnosed with rheumatoid arthritis, ankylosing spondylitis or psoriatic arthritis in the field of rheumatology, in addition to ulcerative colitis (UC) or Crohn's disease (EC) in gastroenterology. However, safety data of the use of Remsima® infliximab in a medical day hospital (MDH) are lacking.

**Objectives:** To report intrainfusion and postinfusion adverse events related to intravenous Remsima® use in a medical day hospital. Besides, we will describe the rehospitalizations and continuation of treatment in the follow up.

**Methods:** We designed a prospective uncontrolled case-series study. Patients referred from March 2015 to October 2016 to our MDH to receive intravenous Remsima® were consecutively enrolled. Demographic data were collected, and a harmonised active monitoring strategy was applied. We recorded the indication for treatment, the doses administered and the number and symptoms of acute transfusion reactions (ATR) occurring both in the infusion period and during the 3 hour postinfusion observation interval.

**Results:** 2828 doses were administered, 0.67% presented ATR, all of them during the infusion and reported to the Regional Pharmacovigilance Center. 53% of those ATR were women and they were on average 35.78 years (SD 14.71). The mean dose used was 4.49 mg/kg (SD 0.47). The indications for treatment in patients suffering ATR were: EC (47%), CU (26%), Spondylitis (21%) and Psoriasis (5%). As a predominant symptom during ATR we found: shortness of breath (36.89%), pruritus (15.75%), flushing sensation (15.75%), urticaria (10.4%), alopecia (5.2%), chest pain (5.2%), paraesthesia (5.2%) and nausea (5.2%). 95% of ATR showed complete recovery of the symptoms, 47% disappeared with the pause of infusion. However, they had prolonged in MDH stay, the infusion was stopped for 30 minutes and restarted at a lower rate according to the protocol. 21% of patients presenting ATR dropped out because of the symptoms, which represents 0.14% of the total infusions.

**Conclusions:** Biosimilar Infliximab seems to be safe in a MDH setting, given the
low rate of adverse transduction reactions during the 18 months analyzed. The most frequent adverse reaction was shortness of breath.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6470

FR0238  EFFECT OF BASELINE ANTI-CYClical CITRULLINATED PEPTIDE 3 ANTIBODY TITRE ON LONG-TERM DRUG SURVIVAL OF SUBCUTANEOUS ABATACEPT IN RHEUMATOID ARTHRITIS: A PROSPECTIVE CohORT STUDY

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Background: Clinical response to biologics varies widely between individuals with rheumatoid arthritis (RA). To date, there are few, and in some cases, conflicting results in the personalized approach of patients with RA treated with abatacept. Only the seropositive subphenotype (anti-cyclic citrullinated peptide, CCP) was validated in several populations, including a real-life registry (ORA) [1], and non-inferiority trial (AMPLE) [2].

Objectives: To assess whether baseline anti-CCP3 antibody status and concentration correlated with drug survival of subcutaneous (SC) abatacept among patients with RA in a real-world setting.

Methods: This was a prospective study in which well-characterized patients with RA (by 1987 ACR criteria) were included from April 2014 to December 2016. Patients were evaluated at a single rheumatology outpatient center in Bogotá, Colombia. Baseline anti-CCP3 antibody status (positive/negative) and concentration were determined using an anti-CCP3 IgG ELISA (INOVA Diagnostics). Patients with a baseline anti-CCP3 IgG concentration of ≥20 U were considered to be positive and were further divided into equal quartiles according to concentration [Q1–Q4 (highest concentration)]. The Cox proportional hazards regression model was used to test if there were any differences in drug survival curves according to baseline anti-CCP3 antibody status and concentration. The test was performed by the coxph function of the “survival” R package [3].

Results: A total of 129 patients were included. Baseline characteristics: female gender 86%, mean age 52±13 years, median disease duration 10 (IQR 11) years, and erosions 35%. Treatment background was as follows: biological naïve (n=54), switched from IV to SC abatacept administration (n=24), and inadequate response to at least 1 biologic disease-modifying antirheumatic drug (n=51). Forty-three patients (33%) discontinued treatment. The most frequent reasons for drug suspension were loss of efficacy. Rheumatoid Factor and anti-CCP3 was positive in 94%, and 89%, respectively. Median titre of anti-CCP3 was 248 U (IQR 352), and number of patients in each quartile group were Q1 (22–122); Q2 (123–248); Q3 (249–475); Q4 (476–1544). A total of 129 patients were included to obtain parallel descriptive information.

Conclusions: Baseline anti-CCP3 positivity was associated with a better response to SC abatacept in a real-world setting. Patients with lowest baseline anti-CCP3 antibody concentrations had better drug survival than patients with higher concentrations. Our results highlight the importance of identification of factors associated with response to biologics in order to optimize treatment and reduce costs.

References:

Disclosure of Interest: None declared


FR0229  RESULTS OF A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN-6 RECEPTOR NANOBODY, AS MONOTHERAPY IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS


Background: Vobarilizumab is a Nanobody® consisting of an anti-IL6 receptor domain and an anti-human serum albumin domain in development for treatment of RA.

Objectives: To assess the efficacy and safety of several dose regimens of vobarilizumab monotherapy administered subcutaneously to patients with active RA.

Methods: Patients with active RA who were intolerant to methotrexate (MTX) or for whom continued MTX treatment was inappropriate were randomized in a 1:1:1:1 ratio to 1 of the 3 blinded dose groups of vobarilizumab or to open-label tocilizumab (TCZ), all of which were given subcutaneously. Efficacy was evaluated descriptively at Week 12 using a number of widely accepted clinical endpoints. Adverse events and routine safety parameters including laboratory assessments were recorded. TCZ administered weekly or biweekly according to local labeling directed us to obtain patient descriptive information.

Results: The study enrolled 251 patients in Europe, Latin America and the United States. Baseline demographics and disease characteristics were well balanced across groups with mean DAS28CRP between 5.9 and 6.2.

At Week 12, 73% to 81% of the patients assigned to one of the vobarilizumab groups achieved an ACR20 response, while ACR50 and ACR70 response rates between 37% - 49% and 16% - 24%, respectively, were observed (see table). At the end of the 12-week treatment period, clinically meaningful improvement in HAQ-DI scores and remission based on DAS28CRP and DAS28ESR was observed in a substantial number of patients treated with vobarilizumab, either q4w or biweekly. Between 5% and 10% of the patients achieved remission defined by the more stringent CDAI or SDI criteria. In total, 94% of patients randomized to open-label TCZ received drug weekly. In spite of this disparity in dosing frequency similar efficacy results were obtained in the vobarilizumab and TCZ groups. One vobarilizumab treated patient (225mg q2w treatment group, 1.6%) experienc ed a SAE due to the treatment period as did 2 patients in the TCZ group (3.1%). Frequencies of treatment-emergent adverse events were similar across the groups. Of the vobarilizumab treated patients, 2.1% discontinued study drug due to TEAEs compared with 6% in the TCZ group. One case of severe hypersensitivity, not considered serious, was reported in the 225mg q2w treatment group. Liver function abnormalities were infrequent across all study groups. Grade 3 neutrophil toxicities were less commonly observed with vobarilizumab (1.1%) than with TCZ (4.3%).

Conclusions: In patients with active RA, treatment with vobarilizumab monotherapy had a positive impact on disease activity with no unexpected safety findings.


DOI: 10.1136/annrheumdis-2017-eular.5746

FR0240  RHEUMATOID ARTHRITIS (RA) IMPACT FOLLOWING TREATMENT WITH SARILUMAB: PATIENT REPORTED OUTCOMES USING THE RAID SCALE FROM TWO RANDOMIZED PHASE III TRIALS

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Background: Patients with RA experience a variety of signs and symptoms and report significant physical and psychological impairment. The RA Impact of Disease (RAID) scale is a disease-specific measure of the impact of RA on patients’ lives. RAID was assessed in two Phase 3 randomized trials of sarilumab,
A human monoclonal antibody directed against the IL-6 receptor-α (TARGET [NCT01709578]; MONARCH [NCT02332590]).

Objectives: To evaluate patient-perceived impact of sarilumab on RA using the RAID scale vs either placebo + conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or adalimumab.

Methods: TARGET (NCT01709578): Regired sarilumab 150mg and 200mg added to csDMARDs vs placebo in patients with RA intolerant of or not responding to anti-TNF therapy. MONARCH assessed sarilumab 200mg monotherapy vs adalimumab 40mg monotherapy in patients with RA either intolerant of, inadequate responders to, or considered inappropriate candidates for continued treatment with methotrexate. Treatments were administered subcutaneously every 2 weeks. RAID has 7 single-item domains, each rated by patients on an 11-point numeric rating scale from 0 (absence) to 10 (extreme). A total score from 0 to 10 (with lower scores indicative of less impact of disease) is calculated by weighting responses for each item based on patient assessment of the relative importance of the item. RAID was assessed at baseline (BL), Weeks 12 and 24. Least square mean (LSM) changes from BL in total score (Weeks 12 and 24) and domains (Week 24 only) were analysed with a mixed model for repeated measures, including treatment, region, visit, and treatment-by-visit interaction (and prior csDMARD therapy in TARGET) as fixed effects and BL as a covariate. RAID was tested outside of trial hierarchy and statistical significance is not claimed; nominal p-values are provided. Post-hoc categorical change analyses were conducted to identify “responders” in the total score (improvements ≥ 25% in total score) in patients continuing therapy requiring rescue medication prior to endpoint were classified as non-responders.

Results: Sarilumab was superior (nominal p<0.05) to placebo (TARGET) and adalimumab (MONARCH) at Weeks 12 and 24 for RAID total score (Table). There was a greater proportion of responders in sarilumab groups vs placebo at Week 24 at both time points (TARGET) and in sarilumab 200mg vs adalimumab at Week 24 (MONARCH). The effect of sarilumab was consistent across all 7 individual RAID domains (nominal p<0.05) at Week 24, except for sleep difficulties vs placebo in TARGET. Effects of placebo were least on pain and effects of sarilumab were lowest on emotional well-being (TARGET) and coping (MONARCH).

Conclusions: Assessed using RAID, sarilumab either with csDMARDs or as monotherapy reduced the impact of RA on patients’ lives to a greater extent than placebo+csDMARDs or adalimumab monotherapy, with benefits shown on total RAID and all 7 individual domain scores.

Acknowledgements: This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: L. Gossec Consultant for: Abbvie, Celgene, Janssen, Lilly, Novartis, MSD, Roche, and UCB; V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Biogen, BMS, Celtrion, CORRONA, Crescendo, Genentech/Roche, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Sandoz, Sanofi, and UCB; C. Pouldfoot Shareholder of: Sanofi; Employee of: Sanofi; C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc; Employee of: Regeneron Pharmaceuticals, Inc; C. Guillonneau Shareholder of: Sanofi; Employee of: Sanofi; T. Kimm Shareholder of: Regeneron Pharmaceuticals; Inc; Employee of: Regeneron Pharmaceuticals, Inc; H. van Hoogstraten Shareholder of: Sanofi; Employee of: Sanofi; S. Guillonneau Shareholder of: Sanofi; Employee of: Sanofi; D. Haney Shareholder of: Regeneron Pharmaceuticals, Inc; Employee of: Regeneron Pharmaceuticals; M. Haynie Shareholder of: Sanofi; Employee of: Sanofi.

DOI: 10.1136/annrheumdis-2017-eular.3448

The Effect of Abatacept on Cytokine Profile in Patients with Rheumatoid Arthritis


Background: Pathological activation of T-cells with the overproduction of pro-inflammatory cytokines is playing a major role in the pathogenesis of rheumatoid arthritis (RA). The influence of the selective co-stimulation modulator abatacept (ABA) on the dynamics of cytokine profile in patients with RA is not fully understood.

Objectives: To assess the changes in cytokine profile in patients treated with ABA.

Methods: 44 patients with RA and an inadequate response to synthetic DMARDs or biologics were enrolled in the study. Most of them were middle aged females (46,9±13.9 years) with median RA duration 2 years (1,4–3), high disease activity (DAS28=5,2±0,8), RF-positive (80%) and ACPA-positive (79,5%). 16 healthy individuals were included in the study as control. The serum levels of IL-1, IL-6, IL-17, TNF-α, VEGF, IP-10 (μg/ml) were measured by ELISA immunoassay, YKL-40 by MicroVue immunoassay at baseline and 24 weeks. Disease activity was measured by DAS28, results were assessed every 2 weeks by EULAR criteria. ABA was administered intravenously every 4 weeks.

Results: Levels of IL-6 (2,4 (1,1–6,4) vs 0.7 (0,62–1,0), p=0,0002), YKL-40 (97 (68,4–97,9) vs 64 (52,4–107,5), p=0,030), IP-10 (21 (12,9–49,6) vs 14 (9,2–15,2), p=0,005) were significantly higher in patients treated with ABA. ABA significant reduced disease activity already after 12 weeks of therapy (p<0,05). After 24 weeks of ABA therapy good and moderate response by EULAR criteria was achieved in 86%, low disease activity by DAS28 in 52%. By the 6-th month ABA significantly decreased levels of IL-6 (1,29 (0,9–2,2, p=0,006), IP-10 (7,5–8,2, p=0,007) as well as MMP3: before 30,1 (13,8–82), after 24 weeks 10 (7,4–5,5), p=0,0003 and RF: before 218 (9,6–187), after 24 weeks 159 (9,7–15,5), p=0,02. Lowering of the IL-6 (r=0,5) and IP-10 (r=0,32) levels were significantly (p<0,05) associated with a decrease of DAS28.

Conclusions: ABA therapy leads to a significant reduction in serum levels of IL-6, IP-10, MMP3 and RF. The serum levels of IL-6 and IP-10 correlate with decrease activity of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6540

Association Between Clinical and Radiographic Responses, and Physical Function in a Phase 3 Study of Sarilumab Plus Methotrexate in Patients with Active, Moderate-to-Severe Rheumatoid Arthritis

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Background: In MOBILITY (NCT01061736), SC sarilumab (150 or 200 mg qw) + MTX demonstrated efficacy in adults with RA and inadequate response to MTX. The most common TEAEs were infections, neutropenia, injection site reactions, and increased transaminasins.

Objectives: To examine association between clinical response and radiographic progression and functional response (HAQ-DI) in MOBILITY.

Methods: In this post hoc analysis, associations between HAQ-DI and clinical efficacy categories (CDAI, DAS28-CRP, SDAI, and Boolean-based ACR/EULAR remission) were tested at wk 16. Trend for change from baseline (BL) in HAQ-DI across response categories was assessed using the Jonckheere-Terpstra test.

Results: Regardless of definition, percentage achieving remission (CDAI ≤ 2,8, DAS28-28,CRP ≤ 2,6, SDAI ≤ 3,3) or no x-ray progression was higher with sarilumab vs Pbo (P<0,05). Overall, there was a significant trend between magnitude of clinical response at wk 16 and improvement in physical function (Table). This trend was also observed for radiographic progression (mTSS change from BL),
regardless of cut-off (<0.5 and <0). In patients achieving remission, there was a numerically greater improvement in HAQ-DI with sarilumab vs placebo (Pbo). Even if patients did not achieve remission or LDA, the sarilumab group had generally greater numerical improvements in HAQ-DI vs Pbo.

Conclusions: Achieving LDA or remission, or absence of radiographic progression, was associated with overall greater improvement in physical function. Irrespective of whether patients achieved remission or LDA, sarilumab + MTX showed greater improvements in HAQ-DI than Pbo + MTX.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink Scripture and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.


FR0244 | LOW DOSE OF RITUXIMAB IS EFFECTIVE FOR MAINTENANCE OF CLINICAL REMISSION OR LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Although existing data support the effectiveness of the low dose regimen (LDR, 1gr every 6 months) of rituximab as initial treatment for active rheumatoid arthritis (RA) (1), the extent of improvement that this regimen may be used to maintain the therapeutic effect in patients achieved clinical remission or low disease activity (LDA) upon treatment with conventional rituximab regimen (2gr every 6 months)

Objectives: To evaluate the effectiveness of the rituximab LDR regimen in patients with RA in clinical practice.

Methods: Long-term prospective study of RA patients who received rituximab in the Rheumatology Department of the University Hospital of Heraklion during 03/2005-07/2016. All patients on clinical remission [DAS 28 (ESR) <2.6] or LDA [DAS28 (ESR) <3.2] for at least 12 months were treated with the LDR after obtaining verbal consent.

Results: We analysed 247 patients who received conventional rituximab regimen, of median age (IQR) 62 (54.7–70.4) years, females (84%), disease duration 9.6 (5.6–18.3) years, 22% seropositive (2.4% anti-CCP). Patients have failed in (median) 3 (2–3) non-biologic (ndbDMARDs) and 1 (1–2) biologic DMARD, ndbDMARDs before rituximab initiation. At baseline of rituximab treatment, 58.3% and 91.1% of them were on steroids and (ndb)DMARDs respectively, while the disease activity was high [mean DAS28 (ESR): 5.84 (5.20–6.49)] and they had impaired physical functioning [mean HAQ 1.0 (0.63–3.18)].

Overall, 27/247 patients (11%) received the LDR. Before the initiation of LDR, the duration of rituximab treatment was 24 (18–48) months and cumulative rituximab “exposure” was 8 (6–15) gr. At the time of LDR initiation, disease activity [DAS28 (ESR)] was 2.8 (2.2–3.6) and HAQ 0 (0–0.4), while the time needed for achieving remission was 9.2 (5–26) months. A median duration of follow-up of patients on LDR was 12 (6–20) months. 23 (85%) of patients remained in remission or LDA with median DAS28 (ESR) 2.85 (2.23–3.52) and HAQ 0 (0–0.5) at last follow-up. Only 3 (11%) of the patients experienced an increase of DAS28 (1.2) or LDA in 2 (2%) of patients return to conventional dose.

Conclusions: In clinical practice, RA patients who achieved remission or low disease activity with conventional dose of rituximab may sustain clinical responses if treated with LDR. These preliminary findings support the use of LDR as maintenance treatment regimen and this may allow cost savings. (1)

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4958

FR0243 | SIRUKUMAB TREATMENT REDUCES LEVELS OF IRON-SCAVENGING PROTEINS AND AMELIORATES INFLAMMATION-ASSOCIATED ANEMIA IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Anemia of chronic disease, a common comorbidity of rheumatoid arthritis (RA), is detrimental to patients’ (pts) quality of life, productivity, and long-term health.

Objectives: Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, has recently demonstrated efficacy in RA. It was hypothesized that SIR, compared to placebo (pbo) and tumor necrosis factor-inhibitors (TNFi), increases hemoglobin (Hb) concentrations in RA pts by decreasing levels of iron-scavenging proteins and increasing transferrin levels, thus ameliorating anemia. This hypothesis was tested in post hoc analyses of 4 phase 3 studies of SIR in RA: SIRROUND-M, -D, -T, and -H studies, respectively: SIR 100mg q2w, n=61, 205, 61, 128, 100; pbo, n=0, 118, 56, 0; adalimumab (ADA), n=0, 0, 0, 0.

Methods: Standard hematologic measurements, including Hb levels, were made throughout the studies by a central laboratory. Anemia was defined as Hb level <125 g/L (males) and <115 g/L (females). In a subset of pts, iron-regulatory proteins (hepcidin, haptoglobin, hemopexin, transferrin) were measured in serum at baseline (BL) and Wk 4 using the SomaLogic SOMAscanTM platform (for responders [IR]); -D (disease-modifying antirheumatic drug [DMARD] IR); -T phase 3 studies of SIR in RA: SIRROUND-M (methotrexate [MTX] inadequate therapy). This hypothesis was tested through Wk 16; however, greater changes were seen in pts anemic at BL (13±13 to 16±12 g/L increase). Significant Hb elevations were observed (mean±SD) through Wk 16; however, greater changes were seen in pts anemic at BL (13±13 to 16±12 g/L increase). Significant Hb elevations were observed at BL (13±13 to 16±12 g/L increase). Significant Hb elevations were observed at BL (13±13 to 16±12 g/L increase).

Results: SIR consistently reduced the prevalence of anemia to a greater extent than was observed for pbo (p<0.05; eg, in SIRROUND-D, anemia decreased from 25% of pts at BL to 10% at Wk 16 post-treatment with SIR 50mg q4w vs increase from 24% of pts to 28% with pbo) and ADA (SIRROUND-H). Across studies on SIR 50mg q4w, increases in Hb levels ranged from 7±10 to 10±11 g/L (mean±SD) through Wk 16; however, greater changes were seen in pts anemic at BL (13±13 to 16±12 g/L increase). Significant Hb elevations were observed at Wk 2, with comparable results for SIR 100mg q2w. Statistically significant increases in Hb levels were not observed with ADA (Fig.1) or pbo, regardless of BL anemia status. Changes in Hb levels with SIR were independent of changes in RA disease activity. Mean haptoglobin levels were modestly higher at BL in RA pts with anemia compared to pts without anemia. Across studies, both SIR doses similarly strongly decreased levels of hepcidin, haptoglobin, and hemopexin and increased transferrin levels at Wk 4, regardless of BL anemia status. The modulation of these proteins by ADA was considerably less (Fig.1) and by pbo non-significant. After SIR treatment, greater decreases in hepocidin levels were consistently observed in pts with vs without BL anemia across studies by Wk 4.

Conclusions: SIR consistently increased Hb levels in RA pts (DMARD-IR, TNFi-IR, monotherapy), most prominently in pts with BL anemia, resulting in significant reductions in the prevalence of anemia. These effects were independent of the extent of improvement in RA disease activity, suggesting additional benefits of SIR beyond clinical response in RA. By inhibiting IL-6, SIR may decrease key iron-regulatory proteins, such as hepcidin, and shift homeostasis towards an increase in the iron pool available for red blood cell Hb, thus ameliorating anemia of chronic inflammation associated with RA.


DOI: 10.1136/annrheumdis-2017-eular.3570

Figure 1. for the SIRROUND-H study, changes in (A) hemoglobin (week 15 change from baseline in g/L) and (B) haptoglobin (week 15 change from baseline in g/L) are plotted for each available patient stratified by treatment group and baseline (BL) anemia status (Y, blue; N, red). * p<0.05 for baseline anemia Y vs. N within treatment group; † p<0.05 vs. adalimumab, within baseline anemia group. ADA, adalimumab; SIR, sirukumab.
IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE WITH SIRKUMAB ARE STATISTICALLY SIGNIFICANT, CLINICALLY MEANINGFUL, AND MEET OR EXCEED NORMATIVE VALUES IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: POST HOC ANALYSES OF A PHASE 3 TRIAL

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Background: Rheumatoid arthritis (RA) is associated with impaired health-related quality of life (HRQoL). Sirkumab (SIR) is an anti–interleukin-6 (IL-6) monoclonal antibody.

Objectives: These post hoc analyses evaluated improvements in HRQoL compared with an age/sex-matched normative population in a phase 3 randomized, controlled trial of SIR in RA pts with inadequate response to conventional disease-modifying antirheumatic drugs (DMARD-IR; SIRROUND-D).

Methods: 1670 pts received SIR 50mg every 4 weeks (q4w), SIR 100mg every 2 weeks (q2w), or placebo (pbo) q2w. Health-related physical/emotional well-being was measured at baseline (BL) and Wk 24 by the 36-item Short Form Questionnaire (SF-36), fatigue by Functional Assessment of Chronic Illness Therapy (FACT)-Fatigue (FACT-F), and physical function by Health Assessment Questionnaire-Disability Index (HAQ-DI).

Results: SF-36 physical and mental component summary (PCS and MCS) mean scores at BL were comparable for pbo, SIR 50mg q4w and 100mg q2w (PCS: 33.8, 34.2, and 33.5; MCS: 40.5, 40.5, and 41.8) and indicative of substantial impairment. At Wk 24, treatment with SIR 50mg q4w and 100mg q2w resulted in significantly greater mean improvements from BL vs pbo in SF-36 PCS (5.4 and 5.9 vs 2.3) and MCS (4.9 and 4.2 vs 2.9) scores (all P<0.001), exceeding the minimum clinically important difference (MCID) of 2.5. Least squares mean changes in all SF-36 domain raw scores were significantly greater with both doses of SIR than pbo at Wk 24 and all ≥MCID of 5.0 (Table; Figure). Substantial proportions of pts treated with SIR 50mg q4w or 100mg q2w reported scores ≥normative values in SF-36 domains at Wk 24 (ranges: 20–33% and 21–36%) vs pbo (range: 10–28%). For pbo, SIR 50mg q4w, and SIR 100mg q2w, BL FACT-F scores were 27.2, 27.1, and 27.5. Significantly greater proportions of pts reported clinically meaningful improvements in FACT-F (MCID=4) with SIR 50mg q4w and 100mg q2w vs pbo (61.4 and 59.4% vs 43.9%; P<0.001). FACT-F scores ≥normative values were reported by 33% of pts on SIR 50mg q4w and 100mg q2w vs 22% on pbo. HAQ-DI scores at BL were 1.56, 1.50, and 1.52 with pbo, SIR 50mg q4w, and 100mg q2w, with clinically meaningful improvements (MCID=0.22) reported by 63.0 and 63.4% with SIR 50mg q4w and 100mg q2w vs 46.9% with pbo (P<0.001). HAQ-DI scores ≥normative values were reported by numerically more pts receiving SIR 50mg q4w (22%) and 100mg q2w (21%) vs pbo (10%).

Table 1. Improvements in SF-36 Domain Scores at Wk 24 (all P<0.006)

<table>
<thead>
<tr>
<th>Domain</th>
<th>LSM change SIR 50mg q4w</th>
<th>LSM change SIR 100mg q2w</th>
<th>LSM change pbo</th>
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<td>Physical function</td>
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Conclusions: Through 24 wks, SIR treatment resulted in greater improvements in HRQoL than pbo that were clinically meaningful and met or exceeded normative values in DMARD-IR RA pts, with similar effects observed with both doses of SIR.

Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, Biogenidec, Boehringer Ingelheim, Celtion, Crescendo, Genentech/Roche, GSK,

References:

Prospective, real-world data on abatacept (ABA) retention in patients (pts) with RA.

Objectives: To assess the retention rate and to identify prognostic factors of ABA retention in the overall ACTION population and by treatment line over 2 yrs.

Methods: ACTION is a 2-yr, international, observational study of pts with RA who initiated IV ABA as first- or as second/third-line biologic therapy in routine clinical practice. Biologic-naïve and biologic-failure pts were enrolled during three periods between May 2008 and December 2013. The primary endpoint was crude ABA retention rate over 2 yrs (Kaplan–Meier plot). Prognostic factors (p<0.02) from univariate analyses with no collinearity, clinically relevant variables and known risk factors were entered into a multivariate model; factors with p<0.31 were retained by backward selection. EULAR response was compared by Fisher’s exact test.

Results: In the ACTION cohort, 2350/2364 enrolled pts were evaluable for analysis; 673 (28.6%) were biologic naïve and 1677 (71.4%) had failed biologic treatment. Most biologic-failure pts (56.6%) had previously received ≥2 biologics. Some expected differences in baseline characteristics were observed between groups; mean (SD) RA duration was shorter (7.2 [8.2] vs 121 [9.1] yrs; p<0.001), more pts had RA for ≥2 yrs (35.7 vs 9.0%; p<0.001) and fewer pts had radiographic erosions (58.2 vs 71.5%; p<0.001) for biologic-naïve vs biologic-failure pts. At Yr 2, the overall retention rate was 47.9% (95% CI 45.7, 50.0). The retention rate was higher in biologic-naïve vs biologic-failure pts (54.5 vs 44.3%; p<0.001) and in pts with 1 vs ≥2 previous biologics (Fig). Reasons for discontinuation were comparable between groups; main reasons were lack of efficacy (61.4 vs 67.7%) and safety (21.3 vs 21.2%). RF and anti-citrullinated peptide antibody (ACPA) seropositivity were prognostic factors for higher retention in biologic-naïve (p=0.030) and biologic-failure pts (p=0.028); other positively impacting factors were diabetes mellitus (p=0.044); biologic naïve; geographic location (p=0.001; biologic naïve) and ABA combination therapy (p<0.001; biologic failure). Only PI Global Assessment (p=0.035) biologic failure) predicted lower retention. Among pts continuing ABA, a greater proportion of biologic-naïve vs biologic-failure pts had a good/moderate EULAR response (90.7 vs 81.6%; p=0.005) and RF/ACPA seropositivity was associated with a better response (p=0.002). There were no new safety signals.

Conclusions: In this first prospective, international, non-interventional research evaluating the long-term IV abatacept retention, RF and ACPA seropositivity were predictors of 2-yr higher retention and better outcomes. Higher retention rates may be achievable with earlier vs later initiation of abatacept treatment, consistent with prior findings from a pooled analysis of EU and Canadian registries.


FR0247 | MEDIAN TIME TO LOW DISEASE ACTIVITY IS SHORTER IN TOCILIZUMAB COMBINATION THERAPY WITH CSDMARS AS COMPARED TO MONOTHERAPY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSES TO CSDMARS AND OR TNF INHIBITORS: SUBANALYSIS OF THE SWISS AND AUSTRALIAN PATIENTS FROM THE ACT-SURE STUDY


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Background: To analyze efficacy and safety of tocilizumab in patients with rheumatoid arthritis (RA) and an inadequate response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) and/or tumour necrosis factor (TNF) inhibitors of the Swiss and Austrian patients from the ACT-SURE study.

Objectives: Methods: Sub-analysis of RA patients from Switzerland and Austria, who participated in the international phase IIIb, open-label, ACT-SURE study. Patients with an inadequate response to csDMARDs or TNF antagonists were included into the study receiving 8 mg/kg of IV tocilizumab every 4 weeks during a 24 week time period. Therapy with one or more csDMARDs could be continued as combination therapy with tocilizumab (Combo) or stopped, resulting in tocilizumab monotherapy (Mono), at the treating physician’s discretion. These two treatment groups were analyzed in separate and compared.

Results: Overall, 107 (22 on Mono vs 85 on Combo) and patients were treated with tocilizumab. The percentage of patients with at least one adverse event was significantly lower in the tocilizumab combination (58.8%) as compared to the monotherapy group (81.8%, p=0.0458). No differences in ACR20/50/70/90 response rates were observed between both treatment groups at week 24 (Mono: 63.6%, 49.0%, 22.7%, and 18.2% vs. Combo: 61.2%, 43.5%, 25.9%, and 10.6%). The median time to low disease activity (LDA) was significantly shorter in patients treated with tocilizumab combination therapy Mono: 9.1, Combo 7.9 weeks, Log Rank p<0.038.

Conclusions: This post hoc regional sub-analysis of the ACT-SURE study no differences for disease activity were found comparing the two patient groups at week 24. However, median time to LDA was statistically shorter in patients treated with tocilizumab combination therapy as compared to tocilizumab monotherapy. Consequently, adding tocilizumab to csDMARD therapy rather than changing to tocilizumab monotherapy may be, in our opinion, the safest strategy to reach remission in RA patients with active disease despite treatment with csDMARDs. csDMARDs may be withdrawn early due to adverse events or after at least low disease activity has been reached.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5903

FR0248 | INCIDENCE OF MELANOMA IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB


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Background: There have been conflicting reports whether patients with rheumatoid arthritis (RA) receiving conventional or biologic immunosuppressive therapies are at increased risk of specific malignancies. Melanoma is an aggressive malignancy with risk factors including sex, age, fair skin and elevated cumulative UV exposure. Interleukin-6 (IL-6) has a role in pro- and antiinflammatory pathways. Whether tocilizumab (TCZ), a biologic that alters IL-6 signaling, increases the risk of melanoma in patients with RA is unclear.

Objectives: This age- and sex-adjusted standardized incidence ratio (SIR) analysis compared the observed reports of melanoma in patients with RA treated with TCZ in clinical trial and postmarketing settings with the expected number of cases across geographic regions.

Methods: SIRs for melanoma were calculated from the TCZ clinical trials all exposure population. Postmarketing rates were estimated from the TCZ Global Safety Database population. Both databases were searched cumulatively from 11 April 2005 to 10 October 2015. For clinical trials, observed reports of melanoma in patients with RA treated with TCZ were compared with expected number of cases in the general population based on the 2012 US Surveillance, Epidemiology, and End Results using an age- and sex-adjusted SIR. Postmarketing regional SIRs were calculated based on the estimated commercial exposure in each region and the incidence of melanoma as reported by Globocan by age and sex (2012).

Results: In the clinical trial setting, 4 qualifying cases of melanoma were identified among 7093 patients with RA treated with TCZ (20,828 PY of exposure). The SIR (95% CI) of 1.17 (0.56–2.43) for melanoma incidence with RA treated with TCZ in clinical trials was comparable to that in the general population (Table 1). In the postmarketing setting, the number of observed reports of melanoma was comparable to the expected number of cases in Europe and Japan and fewer than expected in North America (Table 2). The exception is Australia, where SIR estimates indicated more than the expected number of cases in patients with RA receiving TCZ in Australia compared with the general population in that region (SIR 3.71 [95% CI: 2.16, 5.93]).

Conclusions: In clinical trials, no evidence was found to suggest there were more cases of melanoma in patients with RA treated with TCZ compared with the general population. Consistent with this, no evidence was found to suggest that patients with RA treated with TCZ in Europe, North America or Japan had more cases of melanoma than expected compared with the general population in each region. In contrast, the estimated SIR of melanoma in patients with RA treated with TCZ in Australia indicated more than the expected number of cases in the general population. This finding is consistent with reports of elevated risk of melanoma in patients with RA in Australia (compared with the general population), where UV exposure is high and methotrexate is a common first-line therapy.

References:
2 Buchbinder et al. BMC Musculoskeletal Disord. 2015.


DOI: 10.1136/annrheumdis-2017-eular.1314

FR0249 | CIRCULATING FOLLICULAR HELPER-LIKE T CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABACETEP

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Background: Rheumatoid arthritis (RA) is characterized by synovial inflammation and, in most cases, by autoantibodies, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide antigen (ACPA), whose presence is associated to a more severe disease. The capability of producing autoantibodies is acquired by B cells with the “help” of specialized T lymphocytes, known as Follicular helper T (TFH) cells, in the germinal centers (GC) of secondary lymphoid tissues. TFH express the inducible co-stimulator (ICOS), and are characterized by a high expression of CXC-chemokine receptor 5 (CXCR5), which mediate their migration into the GC, where its ligand CXCL13 is expressed. Here, TFH promote the GC development and B cell maturation. These cells are reported to exist in greater quantities in the peripheral blood (circulating TFH-like cells) of RA patients.

Abacetep (ABA) is a fusion protein, which through its CTLA4 portion can bind to CD80 and CD86 on antigen presenting cells, thereby inhibiting CD28 costimulation. Data from animal models and phenotypic analysis of circulating T cells in RA suggest that ABA may act in the secondary lymphoid organ, and not directly on the synovium (1,2). While experimental models show that ABA can block the generation of TFH (3), little is known on the effect of ABA on circulating TFH-like cells of RA patients (4).

Objectives: To analyze the effect of the blockade of costimulation performed by
ABA on the levels of circulating TFH-like cells of RA patients.

Methods: 55 RA patients (FM=18/7; median age: 52.5th-75th percentile): 57 (44–63 years; ACPA+: 16 (64 %); RF+: 17 (68 %)), treated for at least 6 consecutive months with ABA were evaluated. Circulating TFH-like cells were identified by flow-cytometry as CD4+ICOS+CXCR5+. The response to treatment was evaluated with the EULAR Criteria.

Results: After 6 months of therapy with ABA the percentage of circulating TFH-like cells among total CD4+ T-cells tended to decrease from a median of 1.8 (0.6–3.8) to 0.8 (0.1–2.3) (p 0.07; Wilcoxon signed rank test). The percentage of circulating TFH-like cells at baseline was higher among patients who did not respond to ABA (n:8; 2.6 (2.0–3.6)); than in those who achieved a moderate or good EULAR score (n:17; 1.0 (0.5–5.4) (p:0.01; Mann–Whitney test), but their trend of reduction was similar in the two groups of patients. No difference in the levels of circulating TFH-like cells was found between ACPA+ and ACPA− RA patients.

Conclusions: ABA tends to reduce the number of circulating TFH-like cells in RA patients, suggesting the relevance of costimulation via CD28 in their generation. A higher percentage of these cells is present in patients not responding to ABA. While this observation suggests their possible use as predictors of clinical response to ABA, further studies are destined to evaluate whether it reflects different localizations of TFH, or functional variability within this T-cell subset in patients with RA.

References:

Acknowledgements: Bristol-Myers-Squibb Italy provided an unrestricted research grant for the study conduct and did not interfere with the conception and design of the study, acquisition, analysis, interpretation of data, and manuscript drafting.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4081

FRI0250
SERIOUS ADVERSE EVENTS IN PATIENTS WITH RA TAKING ABATACEPT COMPARED WITH OTHER DMARDs BY LINE OF TREATMENT
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Background: Observational studies are critical in assessing medication safety and effectiveness in the real world. Nonrandom assignment can provide insight into how and when medications are prescribed. Since the US introduction of TNF inhibitors (TNFi) in 1998, several newer biologics with varying mechanisms of action are available to patients and physicians.

Objectives: To compare baseline characteristics and serious adverse events (serious infections (SI), malignancies) of patients who received abatacept (ABA) compared to those who received other comparison cohorts: conventional DMARDs (cD) and biologic DMARDs (bD) by line of therapy. (LT).

Methods: Participating patients from 2005–2015 with RA in the National Data Bank for Rheumatic Diseases (NDB) provided treatment and other characteristics (physical demands, time management); the 3-level EuroQol-5 Dimension (EQ-5D) questionnaire measured 5 dimensions of health status (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).

Results: A total of 2, 430, 360 patients (54.0% cD; 34.0% bD) were identified. Baseline characteristics were similar across groups. ABA patients were more likely to be female, white, and have a lower BMI, insurance, comorbidity index, RA severity, and co-medications.

Conclusions: Abatacept leads to the highest self-reported quality of life and physical demand. ABA patients had better self-reported health status compared to other DMARDs at baseline. No overall increased risk of malignancy was found for ABA compared to other DMARDs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6357

FRI0251
SIRKUMAB, AN ANTI-IL-6 CYTOKINE MONOCLONAL ANTIBODY, LEADS TO IMPROVEMENTS IN WORK PRODUCTIVITY AND GENERAL HEALTH STATUS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS REFRACTORY TO ANTI-TNF THERAPY: RESULTS FROM THE PHASE 3 SIRROUND-T STUDY
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Background: Sirkumab is an anti-interleukin-6 (IL-6) monoclonal antibody that selectively binds to the IL-6 receptor with high affinity and is in development for rheumatoid arthritis (RA) and other diseases.

Objectives: This study evaluated the effects of sirkumab on work productivity/interference and health status in patients with active RA despite treatment with anti-tumor necrosis factor (TNF) therapy.

Methods: In this randomized, double-blind, phase 3 trial, 878 eligible patients with active RA who were intolerant/refractory to anti-TNFs were randomized 1:1:1 to sirkumab subcutaneous (SC) 50mg every 4 weeks (q4w; n=292), sirkumab SC 100mg every 2 weeks (q2w; n=292), or placebo SC q2w (n=294). At Week 16, placebo patients were re-randomized to 1 of the sirkumab doses if insufficient (<20%) improvement; at Week 24, all patients remaining on placebo crossed over to sirkumab. The Work Limitations Questionnaire (WLQ) evaluated health-related job limitations and productivity loss in 4 domains (mental-interpersonal, output, physical demands, time management); the 3-level EuroQol-5 Dimension (EQ-5D) questionnaire measured 5 dimensions of health status (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).

Results: At Week 24, mean total WLQ scores improved significantly from baseline for sirkumab 50mg q4w and 100mg q2w versus placebo (mean change, −2.2 and −2.3 vs 0.2, respectively; both p<0.001), as did all 4 mean QoL domain scores (all p<0.001). Improvements from baseline in mean total WLQ and all 4 domain scores were maintained through Week 52 for both sirkumab doses. Mean EQ-5D index and health state visual analog scale (VAS) scores improved significantly from baseline at Week 24 for sirkumab 50mg q4w and 100mg q2w versus placebo (mean index change, 0.2 and 0.2 vs 0.0, respectively; mean VAS change, 13.9 and 15.4 vs 4.8, respectively; all p<0.001); improvements from baseline were maintained through Week 52 with both sirkumab doses.

Conclusions: Sirkumab treatment led to significant improvements in work-related productivity and general health status in patients with active RA despite anti-TNF therapy, consistent with demonstrated effects of sirkumab on RA disease improvement.


DOI: 10.1136/annrheumdis-2017-eular.10597
SUMMARY OF NEUTROPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SIRKUMAB IN THE SIRROND PHASE 3 CLINICAL TRIALS

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Background: Neutropenia has been reported with interleukin-6 (IL-6) pathway inhibition. However, it is not clear how much neutrophil count should be associated with increased rates of infection. The reduced neutrophil counts seen with IL-6 inhibitors may be due to effects on margination of circulating neutrophils as opposed to a decrease in bone marrow production or reduced survival. Efficacy of sirukumab (SIR), a human anti-IL-6 cytokine monoclonal antibody, has recently been shown in several phase 3 trials.

Methods: Neutrophil counts were compared for SIR 50 mg q4w and 100 mg q2w doses vs placebo (pbo) in the pbo-controlled period (Wks 0–18) of 2 phase 3 trials (SIRROND PHASE IIIA and PHASE IIIB) for the 5-trial, phase 3 program. The distribution of neutropenia by grade was similar in pts who did or did not use disease-modifying antirheumatic drugs (DMARDs) at baseline.

Grade 3 neutrophil counts were National Cancer Institute Common Terminology Criteria for Adverse Events grade 0/1, within the normal range, and the incidence of grade 3/4 decreases was low across groups (Table). Neutropenia began at Wk 2 and persisted through the study period. In long-term analysis, the proportions of pts with grade 1, 2, or 3 neutropenia were slightly higher than in the 18-wk pbo-controlled period, suggesting the majority of events occurred early. No dose effect of SIR on neutrophil counts was observed in the pbo-controlled period such that no change in dose schedule was required.

Conclusions: Across phase 3 studies, there was no dose effect of SIR on neutropenia, and the use of DMARDs did not have an apparent effect on neutropenia. The majority of grade 4 neutropenia with SIR was not associated with infections.


Conclusions: In BREVACTA, TCZ-SC + csDMARDs resulted in significantly greater improvements across all PROs and significantly more pts reporting scores ≥ minimal clinically important differences.
Efficacy of tocilizumab for suppressing radiographic progression of cervical lesions in patients with rheumatoid arthritis comparison with methotrexate treatment: Two years of follow-up - A multicenter registry study -

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Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously. In particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14 and 16. However there is still few studies of efficacy of against RA cervical lesions of Tocilizumab (TCZ), anti-interleukin 6 receptor antibody.

Objectives: To evaluate the efficacy of TCZ for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 2 years.

Methods: We used TCZ or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 38 and 71 patients received continuous TCZ and MTX treatment for at least 2 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2.

Results: In the patients receiving TCZ (n=38) and MTX (n=71), the number of female were each 28 (72%) and 51 (72%) cases (p=0.999). The mean age was 57.3±12.4 and 63.3±10.9 years (p=0.929) and the mean dose of MTX was 9.0±3.4 and 8.3±2.9 mg/w (p=0.335). Clinical findings related to RA were as follows: CRP 3.8±3.1 and 1.5±2.1 mg/dl (p<0.001); ESR 52.7±25.3 and 30.0±20.8 mm/h (p<0.001); MMP3 400±300 and 213±356 ng/ml (p=0.001); the number of RF-positive 30 (79%) and 44 (62%) cases (p=0.087) and 30 (79%) and 41 cases (58%) receiving TCZ and 49 (69%) cases (p=0.367) after 2 years. Also the number who was able to show progression in ADI, SAC and Ranawat value were each 30 (79%) and 41 (58%) cases (p=0.035); 30 (79%) and 44 (82%) cases (p=0.007) and 30 (79%) and 49 (69%) cases (p=0.367) after 2 years. Also the number who was able to suppress progression in all three parameters were each 29 cases (76%) receiving TCZ and 41 cases (58%) receiving MTX (p=0.062) after 2 years (Fig.2).

Conclusions: This study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3312

FR10254

Efficacy of tocilizumab for suppressing radiographic progression of cervical lesions in patients with rheumatoid arthritis comparison with methotrexate treatment: Two years of follow-up - A multicenter registry study -

References:

Acknowledgements: This study was funded by F. Hoffmann-La Roche/Genentech.

Disclosure of Interest: V. Strand Consultant for: Abbvie; Amgen; AstraZeneca; Biogen Idec; Boehringer Ingelheim; Celtrion; Crescendo; Genentech/Roche; GSKSmithKline; Janssen; Lilly; Merck; Novartis; Pfizer; Regeneron; Samsung; Sanofi; UCB. K. Lampi Employee of: Genentech, Inc. C. Birchwood Employee of: Genentech, Inc. J. Pei Employee of: Genentech, Inc. K. Tuckwell Shareholder of: Roche, Consultant for: Roche, Finch Shareholder of: Roche, Employee of: Roche, A. Kivitz Consultant for: Genentech; Novartis; Pfizer; Sanofi-Regeneron; UCB, G. Burmester Grant/research support from: Roche, Consultant for: Roche.

DOI: 10.1136/annrheumdis-2017-eular.4698

FR10255

Patterns of disease activity impact on organ damage in Systemic Lupus Erythematosus

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by fluctuating disease activity in which adverse long-term outcomes remain a major challenge. In the face of extreme individual unpredictability of the disease course over time, four different patterns can be defined, as elsewhere described [1], using SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index-2K) evolution in order to focus on clinical activity. The patterns are clinical quiescent disease (CQD), chronic active disease (CAD), relapsing-remitting disease (RDR) and minimal disease activity (MDA).

Objectives: The aim of our study was to assess the association between different disease activity patterns and damage accrual in SLE patients.

Methods: Patients with SLE registered at our Lupus Clinic at the Rheumatology Unit, between 1 January 2013 and 1 October 2016, were included. Demographic and clinical variables included age, gender, age at SLE onset, major organ involvement. SDI (Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index) was categorized as absent (SDI=0) or present (SDI>0). Disease activity patterns (CQD, MDA, RRD, CAD) were retrospectively assessed. Drugs used in the treatment of SLE, including hydroxychloroquine, cumulative dose of glucocorticoid (prednisone equivalent >10 g) and other immunosuppressive drugs, were also collected. Multivariate logistic regression analyses were performed to identify disease patterns associated with damage accrual. Results are presented as odds ratio (OR) and 95% confidence intervals (CI).

Results: A total of 473 Caucasian patients were observed, mainly female (89.4% F:10.6% M), mean age 52.6 years (±14.9 SD). In our cohort, the disease activity pattern distribution was as follows: 65.4% CQD (290 pts), 21.5% RDR (91 pts), 6.1% MDA (28 pts) and CAD in 19.1% of the cases (84 pts). Damage was significantly more frequent in CAD subset (81.2%, 52/64 pts) versus 54.5% in CQD (158/290 pts), 50% in MDA (14/28 pts) and 58.2% in RDR (53/91 pts). Compared to a CQD course, CAD pattern was independently associated with overall disease after controlling for factors including gender, disease duration, cumulative glucocorticoid dosage, major individual organ involvement (neuropsychiatric and renal), positive antiphospholipoid antibody profile, exposure to cyclophosphamide and hydroxychloroquine (Table 1).

Table 1. Logistic regression analysis of independent factors associated with damage in SLE patients

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<th>Factors</th>
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<th>Adjusted* Odds ratio (95% CI)</th>
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<td>Disease Activity Pattern</td>
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<td>Minimal disease activity (CQD)</td>
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<td>Relapsing-remitting disease (RDR)</td>
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<td>Chronic active disease (CAD)</td>
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*adjusted for: age, gender, disease duration, NP and renal involvement, cumulative dosage of Cs; aPL positivity, HCoC, CnC (NP), neuropsychiatric aPL, antiphospholipid; CyC, cyclophosphamide; HCoC, hydroxychloroquine; M, male; C, corticosteroid; F, prednisone.
Conclusions: Our results demonstrated that a clinically and persistently CAD triples the risk of damage compared to milder or relapsing courses, while hydroxychloroquine appeared to have a “protective” effect. Identifying the prevailing pattern of disease activity in every patient can be translated into a more effective personalized preventing strategy to reduce damage accrual and improve outcomes.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5103

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<th>ULTRASOUND CONSENSUS DEFINITIONS ON NORMAL AND ABNORMAL FINDINGS IN SALIVARY GLANDS IN SJÖGREN’S SYNDROME: RESULTS OF AN OMERACT DELPHI PROCESS</th>
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Background: Ultrasonography (US) of salivary glands (USSG) may support the diagnostic workup for primary Sjögren’s syndrome (pSS), a chronic inflammatory autoimmune disease characterized by salivary gland (SG) involvement. The OMERACT Delphi process has been utilized in the development of definitions for imaging in various areas of medicine. In limited literature, consensus definitions of salivary gland disease have been established in Sjögren’s syndrome. To our knowledge, formal consensus definitions concerning normal and abnormal USSG findings in the context of Sjögren’s syndrome have not been established.

Aims: To develop, through a Delphi process, a definition of normal and abnormal USSG findings in patients with Sjögren’s syndrome.

Methods: A 2-step Delphi process was performed. Step 1: a questionnaire with open-ended questions was administered to 25 experts from 17 countries. Step 2: An electronic Delphi questionnaire was administered with a 3-grade (1=Agree, 2=Undecided, 3=Disagree) scoring system.

Results: Of the 25 experts who completed the questionnaire, 18 agreed to participate in the Delphi process. Step 1: 120 responses were collected. The majority of experts (72%) were rheumatologists, the rest were radiologists. Step 2: 123 responses were collected. A Consensus Conference was held to discuss the draft definitions. The experts agreed on definitions for normal ultrasound findings of salivary glands. For abnormal ultrasound findings, extensive discussion took place concerning the use of ultrasound in patients with primary Sjögren’s syndrome.

Conclusions: A Delphi process successfully established definitions for normal and abnormal ultrasound findings of salivary glands in primary Sjögren’s syndrome. These definitions will be tested in a prospective cohort study to ascertain their validity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5901

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<th>FRIO257</th>
<th>URINARY ANGIOSTATIN, CXCL4 AND VCAM-1 AS BIOMARKERS FOR LUPUS NEPHRITIS</th>
</tr>
</thead>
</table>

Abstract FRIO256 – Table 1

<table>
<thead>
<tr>
<th>% of agreement</th>
<th>Definition of normal US findings</th>
<th>Procedure of scanning</th>
<th>Definition of abnormal US findings</th>
<th>SG to evaluate in pSS</th>
<th>Definition of scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid glands</td>
<td>Uniformly echoic tissue with a clear delineation from the superficial tissue. Tissue comparable to thyroid parenchyma (81%)</td>
<td>Longitudinal and transverse plane (90%)</td>
<td>Focal or diffuse an/hypoechoic areas (95%)</td>
<td>yes</td>
<td>4-grade semiquantitative scoring system (i.e. grade 0, normal parenchyma; grade 1, minimal change; grade 2, moderate; grade 3, severe; diffuse inhomogeneities occupying all the surface of the gland) (79%)</td>
</tr>
<tr>
<td>Submandibular glands</td>
<td>SMG are usually of finer granular echo texture compared to PG or to the normal thyroid parenchyma (89.1%)</td>
<td>Longitudinal and transverse plane (90%)</td>
<td>Idem PG (95%)</td>
<td>yes</td>
<td>Idem PG (79%)</td>
</tr>
<tr>
<td>Sublingual glands</td>
<td>SLG has no clear delineation from the superficial tissue because of no true fascial capsule (77%)</td>
<td>Longitudinal and transverse plane</td>
<td>Idem PG (95%)</td>
<td>no</td>
<td>Not useful</td>
</tr>
</tbody>
</table>

Background: The value of urinary angiostatin, CXCL4 and VCAM-1 in differentiating between active renal and non-renal SLE was determined by 2x2 contingency tables. In patients with active renal disease, correlation between these urinary biomarkers with clinical renal parameters was also performed.

Results: 227 SLE patients (80 inactive SLE; 67 active non-renal disease; 80 active renal disease; 94% women, age 39±13.8 years) and 53 controls were studied.

Urinary angioatin, CXCL4 and VCAM-1 levels normalized for creatinine were significantly higher in patients with active renal than non-renal disease (angiostatin 18.4±27.1 vs 1.6±2.91 pg/μg; p<0.0001; CXCL4 9.11±15.7 vs 5.12±10.4 pg/μg; p<0.003; VCAM-1 4.1±3.11X10^5 vs 0.72±1.10X10^5 pg/μg; p<0.0001). The levels of these urinary protein markers were also significantly higher in active SLE patients than inactive SLE patients or healthy controls. Urinary angiostatin, CXCL4 and VCAM-1 correlated significantly with the renal SLEDAI (Rho 0.66, 0.45 and 0.51, respectively; p<0.001 in all), total SLEDAI score (Rho 0.60, 0.46 and 0.53, respectively; p<0.001 in all) and urine protein-to-creatinine (upCr) ratio (Rho 0.73, 0.51, 0.59, respectively; p<0.001 in all) in the same patients studied. Urinary angioatin was more specific (specificity 0.82) than elevated anti-dsDNA and low C3 (specificity 0.64 and 0.66) in differentiating active renal SLE from non-renal SLE. In a subset of patients with biopsy proven active lupus nephritis (N=68), these urinary protein markers could not differentiate between proliferative (III/IV) from non-proliferative (I/II) types of lupus nephritis. However, urinary CXCL4 (Rho 0.25; p=0.049) and VCAM-1 (Rho 0.28; p=0.02), but not angiostatin (Rho 0.11; p=0.39), correlated significantly with the histologic activity index. There was no significant association between these protein markers and the histologic chronicity index or renal SLEDAI score. On the other hand, urine angioatin levels (Rho 0.36; p<0.003) were correlated with the renal SLEDAI score in SLE (Rho 0.36; p<0.003), but not CXCL4 (Rho 0.07; p=0.59) or VCAM-1 (Rho -0.11; p=0.36), correlated significantly with the upCr ratio in this subgroup of patients.

Conclusions: Urinary angiostatin, CXCL4 and VCAM-1 are potentially useful biomarkers for SLE, in particular lupus nephritis. Further longitudinal studies are necessary to delineate the sensitivity and specificity of these two urinary protein markers in predicting renal flares and prognosis in SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3951

<table>
<thead>
<tr>
<th>FRIO258</th>
<th>LONG-TERM PROGNOSISOFPATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: CSTAR-PAH COHORT STUDY</th>
</tr>
</thead>
</table>

Background: SLE-associated pulmonary arterial hypertension (PAH) is common in Asian countries, and the clinical outcome of patients with SLE-associated PAH is dramatically impaired.

Objectives: This study aimed to identify the long-term clinical outcomes and prognostic factors of patients with SLE-associated PAH confirmed by right heart catheterization (RHC).

Methods: A multicenter cohort of SLE-associated PAH was established. Baseline and follow-up records were collected. The primary endpoint was death from any cause.
cause. The secondary experimental end point was treatment goal achievement (TGA), defined as an integrated outcome.

**Results:** Among the 310 patients enrolled from 14 PAH centers, the median follow-up was 24.0 months. The 1-, 3-, and 5-year survival rates were 92.1%, 84.8% and 72.9%, respectively. The 1-, 3-, and 5-year TGA rates were 31.5%, 53.6% and 62.7%, respectively. Serositis, 6MWD >380 m and Cl × 2.5 [L/min × m²] were identified as independent prognostic factors of TGA. TGA within 5 years was identified as a factor associated with survival in patients with SLE-associated PAH (Figure 1).

Table 1. Baseline characteristics of patients with SLE-associated PAH

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SLE-associated PAH (n=310)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at recruitment, yr</td>
<td>35.0±10.1</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>99.4</td>
</tr>
<tr>
<td>WHO FC, %</td>
<td>51.7</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>408.6±98.0</td>
</tr>
<tr>
<td>NT-proBNP, pg/ml</td>
<td>1660.5±2275.1</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>6±5.5</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>46.5±12.1</td>
</tr>
<tr>
<td>CI, L/min × m²</td>
<td>2.8±0.9</td>
</tr>
<tr>
<td>RAP, mmHg</td>
<td>5.8±5.8</td>
</tr>
</tbody>
</table>

**Conclusions:** TGA was associated with the long-term survival, which supports and provides evidence to the treat-to-target strategy in SLE-associated PAH. Early diagnosis, intervention and heart function preservation are priorities for better long-term outcomes.

**Disclosure of Interest:** None declared

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**FRI0259 LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) IN PATIENTS WITH LUPUS NEPHRITIS (LN)**

D.V. Monova, S. Monov, M. Ivanov, E. Peneva. Department of Internal Medicine, Medical Institute, Sofia, Bulgaria

**Background:** Lupus Low Disease Activity State (LLDAS) is a consensus-based definition of minimally acceptable disease activity in patients with Systemic lupus erythematosus (SLE).

**Objectives:** The aim of this study was to evaluate what proportion of patients with LN fulfills the definition of LLDAS and to evaluate the effect of LLDAS attainment on damage accrual over a period of 5 years.

**Methods:** This is a retrospective analysis of data prospectively collected in a longitudinal observational cohort of LN patients. The conceptual definition of LLDAS is fulfilled when all of the following criteria are met: (1) SLE Disease Activity Index (SLEDAI-2K) ≤ 4, with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever) and no haemolytic anaemia or gastrointestinal activity; (2) no new features or changes in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever), and no increase in SLEDAI-2K of ≥3 points; (3) no new features of lupus disease activity compared to the previous assessment; (4) a Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI physician global assessment (PGA) (scale 0–3) ≤ 1; (4) a current prednisolone (or equivalent) dose ≤ 7.5 mg daily; and (5) well-tolerated standard maintenance dose of immunosuppressive drugs and approved biologic agents, excluding investigational drugs. The definition of LLDAS was applied to each patient for each visit; organ damage was calculated with the SLICC/SDI score (SDI) at study entry and at last observation.

**Results:** 294 patients were eligible for the study (89.79% females, mean age at first visit 31.4±11.9 years, mean disease duration at last visit 19.8±8.7 years). At last observation 219 patients (85.37%) were on treatment with glucocorticoids (GC) and/or immunomodulators. According with all the items of the definition, at last observation LLDAS was present in 146 patients (49.65%); among these, 37 patients (20.8%) maintained a stable LLDAS during the last 5 years of follow-up (LLDAS fulfilled for all visits). LLDAS accrued less organ damage during the follow-up; in the cohort as a whole the mean increase in SDI was 0.40±0.67 resulting in a mean final SDI of 1.2±1.8. Patients who maintained LLDAS were younger (p<0.005), had a lower disease activity score at study entry (p<0.001) and were more likely GC-free at last observation (p<0.001). Patients who maintained LLDAS accrued less organ damage but this difference did not reach statistical significance.

**Conclusions:** High percentage of patients fulfills the proposed definitions for LLDAS at last visit but only a minority maintained this state for all the follow-up period. A minimally acceptable disease activity state is associated with a successful GC tapering and, probably, better long-term outcomes. LLDAS was shown to be associated with protection from damage accrual.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6718

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**FRI0260 ULTRASOUND STUDY OF PLEURAL PROFILE AND CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT): DIAGNOSTIC ROLE IN PRIMARY SJÖGREN'S SYNDROME-INDUCED LUNG INVOLVEMENT**

F. Ferro1, A. Bulleri2, A. Delle Sedie1, E. Elefante1, N. Luciano1, M. Mosca1, C. Baldini1, 1 Clinical and Experimental Medicine, Rheumatology Unit, University of Pisa; 2 Radiology Unit, University of Pisa, Pisa, Italy

**Background:** Ultrasound pleural irregularity (PI-US) is a novel promising tool for non-invasive diagnosis of intestinal lung involvement (ILD) in connective tissue diseases (CTDs). Few data are available on its diagnostic usefulness in primary Sjögren's syndrome (pSS)-induced ILD.

**Objectives:** (a) To assess the accuracy of PI-US to diagnose ILD in pSS when compared to chest tomography (HRCT) (i.e. gold standard imaging technique); b) to explore PI-US diagnostic value in early preclinical phases of lung involvement.

**Methods:** PI-US was performed by a single operator using a MyLab-25 (Esaote), 10 MHz, 5 cm linear probe. PI was defined as the loss of the normal hyperechoic linear pleural contour (score 0–2: normal, minimal and major changes at each intercostal space). Abnormal findings at HRCT were quantified by an expert radiologist according to a semiquantitative score (0–2: absent, moderate, severe). Semi-quantitative scores assigned by PI-US and HRCT to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface) were compared. Total and partial scores (for each lung fields) were evaluated. For statistical analysis chi-square, Mann-Whitney test, R-Spearman, and ROC-curve analysis were used.

**Results:** Validation study phase (PI-US vs HRCT): We enrolled 32 pSS patients [M/F: 5/27; median age (IQR): 67 yrs (51.5–71); median disease duration (IQR): 7 (4–11) yrs; anti-Ro/SSA (+) 78.1%]. To be included patients should have performed a HRCT evaluation within 6 months. Thirteen patients (41%) presented HRCT lesions suggestive for ILD. HRCT total score and PI-US total scores were strongly correlated (r=0.744, p<0.000). Similarly, PI-US and HRCT partial scores related to the postero-inferior fields showed a strong correlation one to each other (r=0.780, p=0.000). ROC-curve analysis identified a total PI-US score of 28.5 (Youden index) as able to predict HRCT-diagnosis of ILD with a sensitivity (SE) of 84.6% and a specificity (SP) of 89.5%. Analogously, a postero-inferior PI-US score of 12.5 demonstrated a SE of 100% and a SP of 89.5% for the ILD diagnosis. Prospective study phase exploring the usefulness of PI-US for ILD early pre-clinical diagnosis: We included 24 consecutive pSS patients without overt respiratory symptoms [M/F: 12/12; median age (IQR): 65 yrs (47–67); median disease duration (IQR): 4 yrs (1–12); anti-Ro/SSA (+) 60.9%]. Out of them, at the end of the diagnostic work-up, four new cases of HRCT-proven pSS-ILD were diagnosed. Their PI-US mean total score was significantly higher than that observed in non-ILD patients (48±18 vs 16±12, p=0.001) as well as their mean postero-inferior PI-US score (19±9 vs 15±5, p=0.003). The total PI-US and postero-inferior PI-US cut-off retrieved in the first part of the study (i.e. 28.5 and 12.5) allowed us to identify those patients with an HRCT-proven pSS-ILD with a SE of 75% and 100%, a SP of 95% and 89.5%, a PPV of 75% and 57% and a NPV of 95% and 100%, respectively.

**Conclusions:** Even if preliminary, this study demonstrated a strong correlation between PI-US and HRCT in the detection of ILD-pSS also in asymptomatic patients, opening new perspectives for the early non-invasive screening of lung involvement in pSS.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1676

**FRID058**
SKIN CANCER IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS


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Background: Conflicting results about the prevalence of skin cancer in Systemic Lupus Erythematosus (SLE) have been reported in the literature [1,2].

Objectives: The aim of this study was to retrospectively evaluate the prevalence of malignancies, with a particular focus on skin cancers, in a cohort of SLE patients followed in a single Center.

Methods: All the SLE patients classified according to the ACR and SLICC criteria, attending the Rheumatology and Clinical Immunology Unit of Spedali Civili, Brescia, were retrospectively evaluated. Clinical and laboratory data were obtained from clinical charts. Diagnoses of skin cancers (melanoma and non-melanoma: basalioma, squamous cell carcinoma) and other malignancies were recorded together with the time elapsed from diagnosis of SLE. Univariate analysis was performed to compare characteristics of patients with (K+) and without (K-) cancer. We also compared the prevalence of cancer in our population to that reported in the Italian general population (from the Italian National Institute of Statistics, ISTAT, report 2014).

Results: In a cohort of 511 SLE patients (92% females, 95% caucasian) regularly followed from 1972 to 2016 (mean age at diagnosis 31 years, range 1–13 and median follow-up 12 years, range 1–40) we detected 51 cases (9.9%) with a history of malignancy: melanoma was reported in 3 (0.5%), non melanoma skin cancer (NMSC) in 11 (2%) and other malignancies in 38 cases (7.4%). Table 1 reports the comparison between patients with and without cancer. Patients with cancer, as well as cases with NMSC and non cutaneous malignancies, showed a higher age at disease onset (p < 0.0001; p = 0.002 and p < 0.0001 respectively) and higher SLE damage (p < 0.0001; p = 0.019 and p < 0.0001 respectively) compared with patients without malignancies. Patients with melanoma showed the same age at SLE onset, but a higher prevalence of discoid lupus (p < 0.0001) and oral ulcer history (p = 0.02). No difference in serological SLE features or in disease activity were detected between groups. The prevalence of melanoma in our cohort (0.5%) was only slightly higher than the one reported in the northern Italian general population (from the Italian National Institute of Statistics, ISTAT, report 2014). Its prevalence appeared to be higher than that reported in the same population (prevalence of spinocellular and basal cell cancer 0.1% and 0.5% respectively).

Conclusions: Non-melanoma was the most common skin cancer observed in our SLE cohort. Its prevalence appeared to be higher than that reported in the general population. SLE patients with melanoma showed a higher frequency of cutaneous lupus history compared with other SLE patients. Melanoma was reported in 3 (0.5%), non melanoma skin cancer (NMSC) in 11 (2%) and other malignancies in 38 cases (7.4%). The frequency of major organ involvement was as follows: biopsy-proven lupus nephritis (40.7%), nephropathic involvement (19.4%), secondary antiphospholipid antibody syndrome (6.1%) and lupus pneumonitis (1.7%). Class IV (41.1%) was the most common type of lupus nephritis followed by class V (15.5%).


References:

This abstract was published in the proceedings of the EULAR Congress 2017. For further information, please visit the EULAR Congress 2017 website.
EPIDEMIOLOGIC PROFILE OF ERECTILE DYSFUNCTION IN SLE: A MULTI-CENTER STUDY IN LATIN AMERICAN PATIENTS


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Background: Although systemic lupus erythematosus (SLE) has a higher prevalence in women, the disease usually has a more aggressive course in men. Information regarding erectile function in men with SLE is quite scant.

Objectives: The aim of this study was to describe the prevalence of erectile dysfunction (ED), as well as associated demographic and clinical features, in men with SLE from a multi-center, standardized epidemiologic study.

Methods: We performed a transversal study in eight tertiary care centers in Latin America. We included male patients ≥16 years who fulfilled ≥4 ACR criteria for SLE, and who had regular sexual activity in the previous 6 months. Patients with other rheumatic diseases (except for APS), chronic viral infections and late-onset SLE were excluded. All patients answered the IIEF-5 Questionnaire, which has been validated in Spanish. Other relevant demographic, clinical and serological characteristics were documented. We included two control groups: the first one was made up by healthy men and the second by men with autoimmune diseases different from SLE (control group).

Results: We included 279 subjects (174 SLE, 55 non-SLE and 50 healthy controls). The prevalence of ED in SLE group 68% (vs 22% in healthy group, p<0.001). The mean age of patients with ED in the SLE group was 36.1±10.3, while in patients without ED it was 32.5±12.7 (p<0.022). Whereas there was no difference regarding ED prevalence between SLE patients and the non-autoimmune group (68 vs 60%, p=0.25), patients with other autoimmune diseases were 10 years older (46.3±10.6 years, p<0.001).

Among SLE patients with and without ED, the presence of persistent lymphopenia (>1000cells/mcl at three consecutive times, p=0.006), the prednisone dose (9.3±2.1 vs 5.3±1.2mg, p=0.026), as well as the SLICC damage score (1.2±0.1 vs 0.8±0.1 points, p=0.026), were significantly different. Comorbidities and other demographic, serological and treatment variables were not different between those groups. Multivariate analysis showed the following independent risk factors for ED in SLE patients: persistent lymphopenia (OR 2.79 CI95% [2.79–7.90], p<0.001) and corticosteroid use (any dose) in the previous year (OR 2.15 CI95% [1.37–3.37], p<0.001). Only 7% of patients had been questioned about their sexual function in the previous three visits to the rheumatologist; also, 81% of subjects considered it would be appropriate to be asked about their sexual function.

Conclusions: Regardless of comorbidities, treatment (excluding steroids) and type of disease activity, SLE patients have a high prevalence of ED, especially considering most patients are young and sexually active. Rheumatologists should be aware of the relevance of this problem in male SLE patients and should ask about this issue in regular visits.

Disclosure of Interest: None declared


FR0265 CYTOKINES AND CORRELATIONS WITH PATIENT REPORTED OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS AND POPULATION CONTROLS

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Background: In open questions patients with systemic lupus erythematosus (SLE) report fatigue as the most distressing symptom. Pro-inflammatory cytokines are generally suggested to contribute to fatigue in chronic diseases, however results are contradictory (1, 2). Patient reported outcome measures (PROMs) quantify patients’ experiences of qualities like fatigue and depression, which have great impact on both physical and psychological wellbeing. If PROMs are associated with pro-inflammatory cytokine activity in SLE has not yet been well investigated.

Objectives: In this study we explored the relationship between a large set of cytokines and self-assessments of fatigue, anxiety, depression and quality of life in a large group of patients with SLE and in matched controls.

Methods: In a cross-sectional setting, persons with SLE and age- and gender-matched population controls responded to PROMs, assessing fatigue (Multidimensional Assessment of fatigue Scale), depression/anxiety (Hospital Anxiety and Depression Scale) and health related quality of life (Medical Short Form 36 (SF-36)). 30 cytokines were analyzed (MSD 30-plex cytokine assay). Spearman’s rank correlation coefficient (rs) between cytokines and PROMs were calculated.

Results: 423 patients aged 46.6±15.3 and 315 controls aged 47.5±14.6 (p=0.43) were included. Of 30 analyzed cytokines 20 gave reliable results and were correlated to PROMs. Five of the cytokines (IL-6, TNF-αf, IL-15, MCP-1 and MIP-1-beta) correlated best (rs ≥0.37) with investigated PROMs (table 1). Fatigue correlated to TNF-αf (rs=0.26**), IL-6 (rs=0.27**) and MCP-1 (rs=0.35**), as well as MIP-1-beta (rs=0.29**), p<0.01 for all. When summarizing SF-36 results we noted a pattern of stronger correlations between investigated cytokines and the physical component than the mental component. Anxiety and depression correlated, but weakly (rs<0.25).

Table 1. Correlations between cytokines and patient reported outcomes

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Fatigue</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Physical Function</th>
<th>Role Physical</th>
<th>Social Function</th>
<th>Role Emotional</th>
<th>Mental Health</th>
<th>Physical Component</th>
<th>Mental Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6</td>
<td>0.28**</td>
<td>0.32**</td>
<td>0.29**</td>
<td>0.32**</td>
<td></td>
<td>0.32**</td>
<td>0.32**</td>
<td>0.32**</td>
<td>0.32**</td>
<td>0.31**</td>
</tr>
<tr>
<td>TNF-αf</td>
<td>0.05</td>
<td>0.12**</td>
<td>0.12**</td>
<td>0.29**</td>
<td></td>
<td>0.29**</td>
<td>0.29**</td>
<td>0.29**</td>
<td>0.32**</td>
<td>0.32**</td>
</tr>
<tr>
<td>IL-15</td>
<td>0.19**</td>
<td>0.25**</td>
<td>0.21**</td>
<td>0.19**</td>
<td></td>
<td>0.21**</td>
<td>0.21**</td>
<td>0.21**</td>
<td>0.21**</td>
<td>0.21**</td>
</tr>
<tr>
<td>MCP-1</td>
<td>0.38**</td>
<td>0.15**</td>
<td>0.29**</td>
<td>0.29**</td>
<td></td>
<td>0.29**</td>
<td>0.29**</td>
<td>0.29**</td>
<td>0.29**</td>
<td>0.29**</td>
</tr>
<tr>
<td>MIP-1-beta</td>
<td>0.25**</td>
<td>0.19**</td>
<td>0.29**</td>
<td>0.29**</td>
<td></td>
<td>0.30**</td>
<td>0.30**</td>
<td>0.30**</td>
<td>0.30**</td>
<td>0.30**</td>
</tr>
</tbody>
</table>

**Spearman correlation is significant at the 0.01 level (2-tailed). From SF-36.

Conclusions: Most PROMs were positively associated with pro-inflammatory cytokines (Fatigue and PROMs reflecting physical aspect of disease correlated most convincingly, while correlations with mental aspects were weaker.

References:
BACKGROUND: Jaccoud arthropathy (JA) is a non erosive reversible joint disorder commonly associated with systemic lupus erythematosus (SLE), and occurs in roughly 5% of all cases. Some studies suggest different profiles of clinical and immunological features between SLE patients with or without JA.

OBJECTIVES: To compare the clinical and serological manifestations of patients with SLE with and without JA in a tertiary care hospital of Madrid.

METHODS: We performed a retrospective observational study of a cohort of patients diagnosed with SLE (4 or more ACR criteria) from 45 Rheumatology Units across Spain who fulfilled the Pego-Reigosa criteria and received treatment in a large Spanish cohort of SLE patients.

RESULTS: Of the 2,765 patients with SLE included in the study, 13.1% (range: 7.5–21.2) had JA. JA was more frequent in women (88.7%) and the mean age at diagnosis was 34.2±12.2 years. JA occurred in 100% of the patients with SLE with secondary Sjögren’s syndrome (SS). The main triggers of JA were infections, followed by SLE activity flares. At the time of diagnosis, in the other 2 cases the diagnosis of both entities was simultaneous.

CONCLUSIONS: JA is a rare life-threatening SLE manifestation. It must be considered in patients with persistent fever who do not respond to antibiotics, cytopenias and evidence of multiorgan involvement. Relapses and death are common in SLE associated with SLE. The diagnosis requires in order to better identify these differences, so a multicenter initiative could be of great help.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6980

HEMOPHAGOCYTIC SYNDROME IN PATIENTS FROM SLE REGISTRY FROM THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSLER)

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University Hospital A Coruña, A Coruña; Hospital Universitario Dr Negrín, Gran Canaria; University Hospital Ramón y Cajal; HGU Gregorio Marañón, Madrid; Hospital, Araba; University Hospital 12 de Octubre, Madrid; University Hospital Donostia, Donostia; Hospital Vigo; IISGS, Vigo, Spain

BACKGROUND: Systemic Lupus Erythematosus (SLE) is an autoimmune systemic rheumatic disease that, in our area, presents hematologic manifestations in approximately 70% of cases. Some of them are very rare so there are no large series whose analysis could provide relevant information.

OBJECTIVES: To study the characteristics of patients with Hemophagocytic Syndrome (HS) in a large sample of SLE patients.

METHODS: SLE patients from RELESSLER database were studied. We analysed SLE manifestations present at 12 different domains (mucocutaneous, renal, musculoskeletal, constitutional, hematologic, vascular, cardiac, respiratory, neuropsychiatric, gastrointestinal, ophthalmic and serological) before, during and after SLE diagnosis.

RESULTS: 3,656 SLE patients (≥4 ACR criteria) from 45 Rheumatology Units across Spain were studied. Seven patients (0.5%) with HS were identified. 71.4% were women, with a mean age (± S.D.) of 35.1 (± 7.1) years. In 5 of the cases the HS occurred 115.5 (± 162.9) months after SLE diagnosis. In the other 2 cases the diagnosis of both entities was simultaneous.

The main triggers of HS were infections, followed by SLE activity flares. At the time of HS diagnosis, they had high SLE activity with a high SLEDAI score of 13.1 (± 11.3) and 1.4 (± 2.3) SDI score.

CONCLUSIONS: HS is a rare life-threatening SLE manifestation. It must be suspected in SLE patients with persistent fever who do not respond to antibiotics, cytopenias and evidence of multiorgan involvement. Relapses and death are common in SLE associated with SLE. The diagnosis requires in order to better identify these differences, so a multicenter initiative could be of great help.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2542
Objectives: To assess the accuracy of US and MRI and to define possible cutoff values for the diagnosis of pSS.

Methods: Thirty-three patients with pSS according to AECG criteria and typical histology of the SG biopsy and 12 patients with sicca syndrome and normal SG histology were included in the study. Two experienced ultrasound experts (C.D. 6y, T.D.) were blinded to the identity of the SG using a B-mode score (0–48 points [1]) and real-time sonoelastography (RTS: 0–16 pts [2]). Morphology of the parotid glands was also assessed by MRI (0–12 pts). We obtained clinical data (C-reactive protein (CRP), antinuclear antibodies (ANA), Ro/La-antibodies, Gamma globulins, patient questionnaires ESSDAI and SSDI). The statistically analysis was carried out using the immunohistochemistry, student’s t-test, or Mann-Whitney-U test. Correlations were performed using Spearman-rank-correlations.

Results: Patients with pSS had significantly higher B-mode- (average =25 [2–44] vs. 9 [1–20], p<0.001) and RTS-scores (6.5 [2–13] vs. 4 [1–9], p<0.001) than sicca-patients. The same was also found for MRI-assessment (6.96 vs. 2.33, p<0.001). In a Spearman rank correlation, clinical parameters were linked to the imaging techniques. The B-mode showed significant inverse correlations with the Saxon-test (r=0.505, p<0.002) and a positive correlation with MRI (r=0.792, p<0.001). No correlation was found for the activity scores ESSDAI (p=0.221) or SSDI (p=0.219). The MRI score had an inverse correlation with the Saxon-test (r=-0.523, p<0.001). Both imaging techniques showed no relationship with ESR or CRP. We also generated ROC curves of both imaging methods to define possible cutoff values for the diagnosis. For B-Mode we would recommend a value of 12 points (sensitivity 82.6% and specificity 91.7%) and for MRI 3.5 points (78.3% and 87%).

Conclusions: Sonography and MRI detected typical morphological changes in the SG of pSS with high sensitivity and specificity. Both methods could become valuable tools for the diagnosis of pSS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6570

FR0269

"IF IT’S NOT MULTIPLE SCLEROSIS, LOOK FOR A URINARY AND SERUM NEUTROPHIL GELATINASE-ASSOCIATED DISEASE!"

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Background: Demyelinating syndrome with atypical features for MS may exhibit an underlying connective tissue disease.

Objectives: To examine whether patients with demyelinating syndrome and atypical features for MS could be distinguished from non-specific lesions of microvascular etiology. In cases of demyelinating syndromes not fulfilling criteria for MS, features of an underlying CTD, suggestive of SLE, are frequently found. A small percentage of patients may go on to develop frank MS during follow up, thus longitudinal monitoring is necessary.


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6438

FR0270

URINARY AND SERUM NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A BIOMARKER IN INDIAN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RELATION TO RENAL INVOLVEMENT AND OVERALL DISEASE ACTIVITY

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Background: Renal involvement often results in long-term morbidity in childhood Systemic Lupus Erythematosus (cSLE). Neutrophil gelatinase associated lipocalin (NGAL) has been shown to be a reliable structural biomarker for the early diagnosis of kidney injury in many clinical scenarios.

Objectives: This study aimed to detect levels of urinary and serum NGAL and changes in flare and improvement on longitudinal follow up in cSLE in a real world clinical scenario.

Methods: Children <14 years of age attending the Pediatric Rheumatology clinic, fulfilling the 1997 SLE criteria were recruited. Urine and serum samples were collected during routine clinical review and urine analysis was assessed. Children were divided into 3 categories, active renal, active non-renal and inactive lupus. Active lupus was defined as SLEDAI >4. Urinary and serum levels of NGAL (uNGAL; sNGAL) were assessed by ELISA. Urinary values were normalized for urinary spot creatinine. In addition, some patients were longitudinally followed up and resampled when their disease activity changed.

Results: The study included 122 (F:M =91:31) children, 54 had active renal,14 had active non-renal and 54 had inactive disease. Median (IQR) age was 8.8 (6.5–10.7) years and disease duration was 10 (3–24) months. 26 children with nephrotic syndrome and 49 age and gender matched healthy controls were also recruited. Children with active renal lupus had significantly higher uNGAL as compared to other categories. Although sNGAL was significantly higher in active renal as compared to inactive lupus, there was no difference between renal and non-renal active lupus (Table 1). On longitudinal follow up, uNGAL levels increased markedly prior to a flare, significantly higher in renal compared to a non-renal flare (p<0.05). On the other hand, active lupus children had a significant fall in their uNGAL on follow up. Their was good correlation between change in SLEDAI and change in absolute uNGAL levels (r=0.84, p<0.01). Overall, on ROC analysis, uNGAL classified active renal versus active non-renal and inactive combined with an AUC of 0.986 (95% CI 0.972–1.0). The sensitivity and specificity of a uNGAL cutoff off value of 25750 ng/ml was 96.3 and 91.2% respectively.

Conclusions: Urinary NGAL is a sensitive marker of renal involvement in SLE disease activity and can also be a reliable tool for monitoring renal disease activity changes.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6605

FR0270 – Table 1

<table>
<thead>
<tr>
<th></th>
<th>Inactive cSLE (n=54)</th>
<th>Active renal cSLE (n=54)</th>
<th>Active non-renal cSLE (n=14)</th>
<th>Healthy controls (n=49)</th>
<th>Nephrotic controls (n=26)</th>
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**Demographics**

<table>
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<tr>
<th>Age (years) (mean±SD)</th>
<th>10.6±3.2</th>
<th>10.9±2.5</th>
<th>10.7±1.9</th>
<th>11.0±2.0</th>
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<tr>
<td>Age at onset (years) (mean±SD)</td>
<td>8.4±3.1</td>
<td>9.4±2.3</td>
<td>8.9±2.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Female: male</td>
<td>39:15</td>
<td>41:13</td>
<td>11:3</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Disease duration (months) (mean±SD)</td>
<td>23.7±3.24</td>
<td>16.6±2.31</td>
<td>14.5±19.2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Disease activity</td>
<td>–</td>
<td>–</td>
<td>–</td>
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**SLEDAI** (mean±SD)

<table>
<thead>
<tr>
<th>SLEDAI (mean±SD)</th>
<th>2.1±1.0</th>
<th>20.9±6.6</th>
<th>7.1±2.0</th>
<th>–</th>
<th>–</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum NGAL (mg/l) (Median (IQR))</td>
<td>4400 (2332.5–5400)</td>
<td>18245 (16137.5–21062.5)</td>
<td>18375 (14375.0–26142.5)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Urine NGAL (mg/l) (Median (IQR))</td>
<td>14100 (11250–19650)</td>
<td>41875.0 (36243.75–46575)</td>
<td>18475 (15287.5–22500)</td>
<td>1170 (658.5–1714.5)</td>
<td>25040 (19637.5–31762.5)</td>
</tr>
</tbody>
</table>

**Urine NGAL/creatinine Median (IQR)**

| Urine NGAL/creatinine Median (IQR) | 14743.7 (10487.7–21051.8) | 32388.65 (24610.7–44243.9) | 14541.2 (11939.3–20432.08) | 1006 (597.7–2042.79) | 21874 (16328.5–31143.6) |
PREVALENCE AND ASSOCIATED FACTORS OF DEPRESSIVE DISORDERS IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
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Background: Psychiatric symptoms are common in patients with SLE. Most studies utilized self-rated scales of psychiatric symptoms for evaluation. Formal diagnosis of depression was not established by psychiatric interviews. 

Objectives: To determine the prevalence of depressive disorders, severity of depressive symptoms, and the associated clinical and socioeconomic factors in Chinese patients with SLE.

Methods: Patients who fulfilled ≥4 ACR criteria for SLE were randomly recruited from rheumatology out-patient clinics and hospital admission in a 9-month period. Psychiatric disorders were diagnosed by a direct interview with the psychiatrist using the Chinese-bilingual Structural Clinical Interview for DSM-IV Axis I disorders, patient research version (CB-SCID-IP). The severity of depressive symptoms was assessed by the validated Chinese Hamilton Depression Rating Scale (HAM-D). Patients were also asked to complete the Beck Depression Inventory (BDI), Medical Outcomes Study Social Support Survey (MOS-SSS-C), and the WHO Quality of Life Measure-Abbreviated Version (WHOQOL-BREF, BREF (HK)). SLE disease activity (SLEDAI), organ damage (SLICC/SDI) and socio-demographic were collected and correlated with the presence of psychiatric disorders. Logistic regression models were used to study the independent factors associated with depressive disorders and the severity of depressive symptoms.

Results: 175 SLE patients were studied (95% women, age 39.2±12.4 years, SLE duration 10.3±6.7 years). 27 (15%) and 37 (21%) patients were diagnosed with a current depressive (52%major depressive disorder, 22% dysthymia) or anxiety (29%generalized anxiety, 14%social phobia, 8%post-traumatic disorder) disorder, respectively. Patients with depressive disorders, as compared to those without psychiatric disorders, had more active SLE (p=0.03) and were more likely to have a history of psychiatric diagnosis (p<0.001) and financial assistance from Government (p=0.04). Independent factors associated with a depressive disorder were SLEDAI score (1.13 [1.02–1.24]; p=0.02), perceived poor social support (p=0.03) and a past history of psychiatric disorders (p=0.003). Age, disease duration and other socio-economic variables such as educational level and marriage status were not correlated with the presence of a depressive disorder. Being separated/divorced (β=-0.18; p=0.02), having a higher SLEDAI score (β=0.16; p=0.02), SLE duration (β=-0.18; p=0.02) and a past history of psychiatric disorders (β=0.18; p=0.01) were independently associated with higher HAM-D scores, which reflect more severe depressive symptoms. Depressive disorders and severity of depressive symptoms were significantly associated with poorer quality of life. ROC analysis showed that a cut-off of 14 points of the self-rated BDI had a sensitivity of 89% and a specificity of 83% for differentiating a current depressive disorder from those without.

Conclusion: A diagnosis of depressive disorders is prevalent in Chinese patients with SLE. Independent risk factors are more active disease, perceived poor social support and a past history of psychiatric disorders. Patients with more active SLE, shorter disease duration, a past history of psychiatric disorders and being separated were associated with more serious depressive symptoms. The self-rated BDI provides a good screening tool for identifying depressive disorders in SLE patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4327

ROLE OF PROCALCITONIN AND C-REACTIVE PROTEIN IN SCREENING OF INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Previous studies revealed conflicting results regarding the role of procalcitonin in predicting infections in patients with systemic lupus erythematosus (SLE).

Objectives: This retrospective study aimed to analyse the role of procalcitonin (PCT) and C-reactive protein (CRP) in predicting infections in SLE patients, and to determine an optimal cut-off value for PCT and CRP for defining sepsis.

Methods: This study was carried out in one single tertiary centre. Adult patients (18-year-old) with underlying SLE who were admitted to hospital between 1st Jan 2007 and 31st Dec 2015 were included. Demographic data, PCT and CRP upon admission, and other clinical parameters were obtained. Infection was defined by positive culture, or based on clinical and radiological evidence with substantial response to antibiotics. The presence of SLE activity was defined by SLEDAI, and also by SLE-related manifestations not included in SLEDAI. Mann-Whitney test was used to test the difference between numerical parameters between patients with and without infection. Spearman’s correlation was used to analyse the correlation between PCT and CRP. Receiver operating characteristic (ROC) curves were plotted to define an optimal cut-off values for PCT and CRP in infection.

Results: 33 (27 female & 6 male) SLE patients were included. Both mean and median age were 42-year-old. Among the 21 septic patients, 9 had active lupus and 12 had inactive disease. All but one of the 12 non-septic patients had active lupus. All 4 patients with underlying renal failure belonged to the infection group. There were 13 and 3 patients on immunosuppressive treatments in infection and non-infection groups respectively. In patients with infection, mean PCT was 5.74ng/ml and mean CRP was 77.22mg/L. In those without, those were 0.29ng/ml and 20.04mg/L respectively. Both PCT (p<0.014) and CRP (p=0.016) levels were significantly higher in patients with infection than those without. There was no significant difference between the PCT and CRP levels in both septic patients (PCT p=0.862, CRP p=0.247) and non-septic patients (PCT p=1.000, CRP p=0.500) regardless of their SLE disease activity.

PCT level correlated positively with CRP level (r=0.456, p=0.008), but it had no correlation with age (p=0.978), gender (p=0.424), underlying renal failure (p=0.307), and organ damage at baseline (p=0.503) or other immunosuppressants (p=0.132) use. ROC curves of PCT and CRP showed a similar area under curve (AUC) of 0.756 and 0.752 respectively. The cut-off for PCT was 0.78mg/L (sensitivity 61.9%, specificity 91.7%), giving a positive predictive value (PPV) of 92.9%. The cut-off for CRP was 9.35mg/l (sensitivity 85.7%, specificity 66.7%), giving a PPV of 81.2%. Combining both PCT and CRP above their cut-offs, the specificity of predicting infection improved to 100% but the sensitivity worsened to 52%.

Conclusions: Both PCT and CRP were useful in predicting infection SLE patients regardless of their disease activity. The cut-off of PCT at 0.78mg/L and CRP at 9.35mg/l gave satisfactory positive predictive value for infection.
References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5733

**FRI0274 MORPHOLOGICAL INDEXES IN LUPUS NEPHRITIS – DO THEY HAVE PROGNOSTIC VALUE?**

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Background: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE). With current therapies, a high remission rate is observed, thus determining the most important prognostic factor. Currently, therapy is guided by findings in the renal biopsy, following the ISN/RPS classification. Although recommended by EULAR, Austin and Hill’s morphological indexes are not routinely obtained.

Objectives: To analyze the importance and applicability of the different morphological indexes in predicting response to treatment and prognosis.

Methods: Retrospective single center study of consecutive SLE and biopsy proven LN patients, diagnosed from 2010 to 2016. We evaluated the following outcomes: clinical remission, renal function and proteinuria at end of follow-up (FUP) (g/24h). Complete remission was defined as a reduction of proteinuria to <0,5g/24h, inadmissible urinary sediment, creatinine <115% of baseline, partial remission same parameters, except proteinuria <1g/24h if initial value >3,5g/24h, or reduction to <3g/24h if initial value >3g/24h. The studied predictors were the INS/RPS LN classification and the morphological indexes described by Austin (Activity and Chronicity) and Hill, obtained after histomorphological review of renal biopsies. Statistical analysis was performed with STATA software.

Results: During 6 years, there were 46 biopsy-proven LN cases, 84,8% (n=39) woman, median 35 years old (27 – 42,5) and 57,6% (n=19) caucasian, 39 patients were already known to have SLE, 7,4% (1,5 – 12,3) years previous to the biopsy. The median FUP was 31,9 (13,2 – 45,6) months. Based on biopsy findings, 35 patients were started on immunosuppression – induction in 50% of cases with clinical activity. We observed that Class IV patients had, at presentation, lower eGFR (67,3 vs 99,8 ml/min (71,2 – 116,8) and proteinuria of 0,6 g/24h (0,2 – 3g/24h).

Conclusions: The correlations between clinical findings and morphological indexes (Hill and Austin) are summarised in table 1.

**FRI0276 PREVALENCE OF DEPRESSION BY BECK II AND IMPORTANCE OF FATIGUE BY FACIT IV QUESTIONNAIRES IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS VS CONTROLS IN A SINGLE CENTER OF ARGENTINA**

E. Avid, A. Braillard-Pocard, M. Garcia Carrasco, N. Perez, G. Nasswetter, D. Dubinsky, Rheumatology Division, Hospital de Clinicas Jose de San Martin, Capital Federal, Argentina

Background: Estimated prevalence of neuropsychiatric symptoms in SLE is among 17 to 71%2. Depressive symptoms are around 54%1,2. Fatigue is frequently referred, predicts high morbidity and may be influenced by lifestyle and individual psychological characteristics1.

Objectives: To evaluate the prevalence of depressive symptoms and its association with demographics and clinical variables in patients with SLE. To determine the predictive value of FACIT for fatigue in SLE vs controls.

Methods: Observational, retrospective case-control design. Patients ≥18 years old with SLE (ACR 97) were consecutively evaluated in our centre from January to July 2015. We analyzed age, disease duration, clinical manifestations, antibodies profile, SLEDAI (>4 scored as active) and SLICC. We recorded familiar psychiatric diseases, educational and socioeconomic level (Graffar Scale), employment and marital status. Beck II and FACIT (IV version) questionnaires were used for evaluate depression and fatigue respectively. We tested two cut points for fatigue: <22 and <40 to determine sensitivity/specificity for this tool in SLE patients vs controls.2. Continues data were compared using t Student and Mann Whitney. Categorical data: chi-square or Fisher’s exact test by SPSS version 20.0. To predict fatigue we calculated the area under the curve by Receiver Operating Characteristic (ROC). Statistical significant p<0.05.

Results: 77 SLE and 100 controls, all female. SLE vs control group: Mean of age: 34 (19–49) vs 38 (18–90). Prevalence of depression: 52% (44/77) vs 27% (27/100) (p<0.005). FACIT –40: prevalance of fatigue (FACIT–40 <22): 24% (19/77) and 36% (36/100) (p<0.05). Mean disease duration (months) 48 (24–114). Socio-demographic characteristics, SLICC/SLEDAI, clinical and serological manifestations were not correlated with major depression p>0.05. FACIT: Median values: FUP (range 22–40) SLE group: FACIT–22 total SLE: 12/77 (15%) and FACIT–40: 33/77 (42%). Cut points FACIT SLE vs controls: <22: 15% (12/77) vs 1% (1/100) (p>0.05). 30% sensitivity/100% specificity, 100% PPV and 57% NPV. AUC FACIT–22: 0.65 (0.65–0.77). FACIT–40 in SLE vs controls: 42% (33/77) vs 26% (26/100) (p<0.05). 99% sensitivity and 84% specificity, 82% PPV and 70% NPV. FACIT: AUC FACIT–40: 0.75 (0.64–0.87).

Conclusions: Prevalence of depression was high in our cohort and similar to...
ANTI-SSA ANTIBODY STATUS IN COMBINATION WITH ULTRASOUND OF MAJOR SALIVARY GLANDS: A SHORTCUT IN THE CLASSIFICATION OF PRIMARY SJÖGREN’S SYNDROME?

E. Mossel1, K. Deli2, J.F. Van Nimwegen1, A.J. Stel1, F.G.M. Kroese1, M.A. Saavedra1, D. Miranda-Hernández1, A. Sánchez 1, F. K.L. Spijkervet2, A. Vissink 2, S. Arends 1, H. Bootsma 1 on behalf of EULAR

Background: Ultrasound of major salivary glands (SUS) is an upcoming diagnostic method to assess the involvement of major salivary glands in primary Sjögren’s syndrome (pSS). In the AECG, ACR and recently published ACR-EULAR criteria, a positive salivary gland biopsy or presence of anti-SSA antibodies are necessary to classify the patient according to the AECG criteria and not included as a diagnostic item.

Objectives: To assess whether combining anti-SSA antibody status with SUS outcome can predict classification of patients as pSS in our inception cohort study.

Methods: Consecutive outpatients clinically suspected with pSS underwent SUS of the parotid and submandibular glands. Parenchymal echogenicity, homogeneity, hypoechogenic areas, hyperechogenic reflections and clearness of salivary gland border were scored according to the Hocevar scoring system (total score 0–48).1 Positive SUS was defined as total score ≥15. Patients underwent a diagnostic work-up according to the AECG, ACR and ACR-EULAR criteria. We determined the positive predictive value of the combination of anti-SSA antibody status and SUS outcome for classification as pSS or non-pSS. Separate analyses were done considering either i) parotid gland biopsy or ii) labial gland biopsy as an item, when applying these classification criteria.

Results: Anti-SSA antibody status was positive in 53 (51%) patients and SUS was positive in 40 (39%) patients. When parotid gland biopsy outcome was considered as an item of the criteria, 45 of 97 patients were classified as pSS according to the AECG, 44 of 93 according to the ACR and 52 of 99 according to the ACR-EULAR criteria. The combination of presence of anti-SSA antibodies with positive SUS showed a very high positive predictive value for classification as pSS (94–97%) and the combination of absence of anti-SSA antibodies with negative SUS highly excludes classification (negative predictive value 96–100%). When labial gland biopsy outcome was considered as an item of the criteria, 49 of 96 patients were classified as pSS according to the AECG, 43 of 93 according to the ACR and 55 of 97 according to the ACR-EULAR criteria. The combination of presence of anti-SSA antibodies with positive SUS showed a high positive predictive value for classification as pSS (94–97%). However, the combination of absence of anti-SSA antibodies with negative SUS did not per se exclude classification (negative predictive value 89–93%).

Conclusions: In our prospective inception cohort study derived from daily clinical practice, the combination of anti-SSA antibodies and positive SUS outcome highly predicts classification as pSS according to the AECG, ACR and ACR-EULAR classification criteria.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5938

PREVALENCE AND FACTORS ASSOCIATED WITH AUTOIMMUNE RHEUMATIC DISEASES IN WOMEN WITH AUTOCOLPENCHONCLE COUNSELING IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

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Background: Adequate prenatal counseling in women with autoimmune rheumatic diseases (ARDs) may help minimize maternal-fetal complications. However, the available information about the frequency and quality of prenatal counseling given to these women is limited.

Objectives: To estimate the prevalence of preconceptional counseling and associated factors in women with ARDs.

Methods: A survey was conducted on socio-demographic data, gynecological-obstetric history, and domains related to preconception counseling in women with ARDs at the reproductive stage. It was defined as adequate preconception counseling if the patient knew that the pregnancy should be medically planned, that the complications are associated with severity/activity of the disease, that they should use an effective contraceptive method and that their medications may or may not be used during pregnancy. Descriptive statistics, Student’s T test for quantitative variables with normal distribution, Mann-Whitney U test for non-normal and chi-square distribution were used for categorical or ordinal variables.

Results: Of a total of 146 surveys, 131 were analyzed. Only 49 (37.4%) patients received adequate preconception counseling. Two thirds of the patients had systemic lupus erythematosus (Table). The time of evolution of the disease was a factor associated with receiving adequate counseling (5.6 vs 3.6 years, p=0.023), illness, marital status, and level of education were not factors associated with adequate counseling.

Disclosure of Interest: None declared


PREVALENCE OF PRIMARY SJÖGREN’S SYNDROME IN A POPULATION-BASED COHORT IN THE UNITED STATES

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Background: Different studies worldwide reported highly discrepant estimates for the prevalence of primary Sjögren’s syndrome (pSS), ranging from 0.01% of the general population to more than 3%. No previous study reported the prevalence of pSS in the United States.

Objectives: To report the 2015 point prevalence of pSS in the first population-based study performed in the U.S.

Methods: Cases of all potential pSS patients living in Olmsted County, Minnesota on January 1, 2015 were retrieved using the Rochester Epidemiology Project resources, and ascertained by manual medical record review. Definite pSS cases were defined according to physician diagnosis. All patients with doubtful cases and all patients with an associated systemic autoimmune disease were excluded. The remaining cases were classified as pSS or non-pSS.

Results: A total of 106 patients with pSS were included in the study: 86% were female, with a mean (SD) age of 64.6 (15.2) years and disease duration of 10.5 (8.4) years. A majority were anti-SSA positive (75%) and/or anti-SSB positive (58%), but only 22% met American-European Consensus Group or American College of Rheumatology criteria because the other tests required for disease classification were rarely performed in clinical practice (ocular dryness objective assessment, salivary gland functional or morphologic tests, or salivary gland biopsy). According to the physician diagnosis, age and sex adjusted prevalence of pSS was 10.3/10,000 inhabitants, but according to classification criteria this prevalence would be only 2.2/10,000. The analysis based on previous incidence data projected a similar 2015 prevalence rate of 11.0/10,000. Using figures from the 2015 general U.S. population census, a total of 248,000 patients with pSS (35,000 males and 213,000 females) would currently live in the country. If only cases fulfilling classification criteria are considered, there would be only about 53,000 prevalent cases of pSS in the U.S.

Conclusions: This study reports the first prevalence rate of physician-diagnosed pSS in a well-defined population in the U.S. The estimated prevalence of 10.3/10,000 inhabitants in 2015 is higher than previous results obtained in other geographical areas, probably due to different methodological designs of the studies. Because physicians rarely used tests included in the classification criteria to diagnose the disease in this community setting, current classification criteria do not reflect accurately the diagnosis of pSS in routine clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6198
adequate counseling. The adoption of a contraceptive method and the number of pregnancies were not different between the two groups. The history of use of embolotoxic/teratogenic drugs was associated with a higher frequency of adequate counseling (79.6% vs 41.5%, p<0.001). According to the patients, adequate counseling was given by the rheumatologist in 75.3% of the cases (p<0.001).

Conclusions: Preconception counseling in the reproductive stage is deficient. A multidisciplinary strategy is required to improve the frequency and quality of preconception counseling in patients with ARDs.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5475

**FR0280**

ASSOCIATION BETWEEN INSULIN RESISTANCE, SUBCLINICAL ATHEROSCLEROSIS AND ACTIVITY/DAMAGE STATUS IN SLE PATIENTS

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Background: Insulin resistance (IR) may contribute to an increase in cardiovascular risk in general population as well as in Systemic Lupus Erythematosus (SLE) patients.

Objective: The aim of this study was to examine the association between IR and disease activity, disease characteristics, drug exposure and subclinical atherosclerosis in patients with SLE.

Methods: Cross-sectional study that encompassed 87 SLE patients and 82 sex-matched controls. IR by homeostatic model assessment (HOMA2), insulin, C-peptide serum levels and lipid profile were assessed in both groups. Activity (SLEDAI), severity (Katz) and damage (SLICC) scores, carotid intima-media thickness (cIMT) and carotid plaques (ultrasound) were assessed in SLE patients. A multivariable regression analysis, adjusted for IR related factors, was performed to evaluate the differences between groups in IR indexes and, in SLE patients, the interaction between IR and disease activity/characteristics as well as subclinical atherosclerosis.

Results: Median disease duration was 16 years (IQR 9–21). Body mass index, abdominal circumference, hypertension or dyslipidemia did not differ between groups. According to the SLEDAI score, 40% of patients were in non-active, while 32%, 21%, 18% and 1% were in mild, moderate, high and very high activity respectively. HOMA-IR-C-peptide (beta coefficient 0.53, [95% CI 0.25–0.82], p=0.00) was increased in SLE patients when compared to controls, as well as HOMA %B C peptide levels (beta coeff. 35, [95% CI 16–52], p=0.00). Similarly, insulin sensitivity estimated through HOMA-IR-C-peptide was inferior in SLE patients (-beta coeff. -37, [95% CI -63–11], p=0.01). This differences remained significant even after adjustment for IR related factors. SLICC damage index was clearly associated with IR indexes; higher index values were related to higher HOMA-IR-C-peptide (beta coeff. 37, [95% CI 16–57], p=0.00) and lower HOMA-5% levels (beta coeff. 30%, [95% CI -47–14], p=0.00). Katz severity index showed correlation with HOMA-IR-C-peptide (beta coeff. 5, [95% CI -11–0], p=0.04). These associations remained significant after adjustment for age, gender, smoking, hypertension and dyslipidemia, and, in relation with the SLICC index, also after adjustment for prednisone intake. SLEDAI activity index was not related to IR indexes. The use of prednisone was positively associated with HOMA-IR both when considered binary (beta coeff. 47, [95% CI 31–63], p=0.00) and continuous (beta coeff 2 [95% CI 0–5] per mg, p=0.03). Hydroxychloroquine (or other drugs) use was not associated with IR indexes, neither were disease duration, antiDNA titers and complement serum levels. Carotid plaques were found in 20% of the SLE patients. The presence of carotid plaques was correlated with a higher HOMA-IR-C-peptide (OR 3.15 [95% IC 1.17–8.51], p=0.02), and a higher cIMT value was associated with a lower HOMA-IR-S%-%-C-peptide (beta coeff. 0.98 [95% CI 0.96–0.99], p=0.03). Nevertheless, after adjustment for cardiovascular risk factors this relation was lost.

Conclusions: Activity and damage indexes in SLE patients are independently related to the development of IR. IR is associated with subclinical carotid atherosclerosis in SLE patients on the univariate analysis.

Disclosure of Interest: None declared


**FR0282**

CARdiovascular damage in decreasing patients with SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Cardiovascular comorbidities are a major contributor of damage in patients with SLE. They are driven by classical, as well as SLE-related risk factors, i.e. disease activity and immunosuppressive treatment.

Objectives: We aimed to analyze cardiovascular damage (CVD) in a group of 90 deceased SLE patients regularly followed-up in a routine academic setting at our Department, and to identify features associated with accrual of CVD.

Methods: We retrospectively observed 90 SLE patients (68 females) deceased within the 2002–2011 period. All patients were ≥18 years of age and Croatian residents at the time of death, fulfilling ≥4 classification criteria of the American College of Rheumatology (ACR). We identified patients with CVD, including the following components of the Systemic Lupus International Collaborating Clinics (SLICC)/ACR damage index: cardiovascular damage as defined by the index (cardiac damage), peripheral vascular damage, cerebrovascular accident, pulmonary infarction, bowel infarction and avascular necrosis. An extensive set of variables was compared between patients with and without CVD: demographics, ACR criteria at diagnosis and death, damage (according to the SLICC/ACR index) and its components one year following diagnosis and at the time of death, disease activity at diagnosis (according to the European Consensus Lupus Activity Measurement indexes, ECLAM), as well as features of the metabolic syndrome, smoking and immunosuppressive treatment. Frequencies were compared using χ2, and Fisher’s exact test, and continuous variables using the t-test and Mann-Whitney U test. Variables associated with CVD in the univariate analysis were included in a multivariate logistic regression model.

Results: We identified 63/90 patients with CVD, including 46/63 (73%) with cardiac damage, 19/63 (30%) with peripheral vascular damage, 21/63 (33%)
with cerebrovascular accident, 4/63 (6%) with bowel infarction, 14/63 (22%) with avascular necrosis and a single patient with pulmonary infarction (Figure 1). Patients with CVD had a higher disease duration at time of death compared to patients without CVD (12±8 vs. 7±6 years), as well as higher cumulative proportions of hematologic disorder (60/63 vs. 15/27), lymphopenia (48/63 vs. 10/27), peripheral vascular disease (19/63 vs. 1/27), fractures (25/63 vs. 2/27), higher overall damage (6.0±3.0 vs. 2.4±2.0) and a higher proportion of secondary antiphospholipid syndrome (14/63 vs. 1/27) (p<0.05). Conversely, patients with CVD had a lower proportion of discoid lupus at diagnosis (7/49 vs. 9/24) and a lower proportion of skin damage one year following diagnosis (2/63 vs. 5/27) (p<0.05). Parameters associated with cardiovascular damage in the multivariate model were cumulative fulfillment of lymphopenia as a classification criterion (odds ratio, OR 4.7 (95% confidence interval, CI 1.3–17.0)) and accrual of pulmonary damage (OR 13.1 (95% CI 2.2–76.3)).

Figure 1. Distribution of cardiovascular damage in the analyzed group (numbers represent frequencies of each subtype of cardiovascular damage)

Conclusions: More than two thirds of deceased patients accrued CVD over the disease course. Lymphopenia and pulmonary damage may be associated with CVD in deceased SLE patients.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5197

FR0283 | AN IMMUNOLOGICAL PROFILE COMBINING INNATE AND ADAPTATIVE IMMUNITY BIOMARKERS IDENTIFY RISK FOR EVOLUTION INTO SLE IN WOMEN WITH RECURRENT PREGNANCY LOSS

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Background: Autoantibodies, low complement levels and higher NK cell counts are present in a subset of women with recurrent pregnancy loss (RPL). The combination of these abnormalities might be a surrogate profile for the presence of a subclinical inflammatory or autoimmune condition.

Objectives: In a cohort of women with unexplained RPL we evaluated if an immunological profile combining innate and adaptive immunity mediators was associated with the presence of distinct clinical characteristics that are commonly observed in autoimmune diseases and if it was a risk factor for developing these diseases. In a small subset of women with the immunological profile we evaluated the activation status of CD4+ and CD8+ cells.

Methods: We evaluated 366 women with RPL defined as 2 or more pregnancy losses and 93 control women. We defined the immune profile as the presence of 2 or more of the following abnormalities: Peripheral blood NK cell percentages >15%, positive antiphospholipid antibodies, positive anuclear antibodies, positive anti-thyroid antibodies, low complement C3 levels and low C4 complement levels. Evolution to autoimmune diseases was detected during follow-up. Lymphocyte subsets were evaluated by flow-cytometry. Statistics: Chi-square test. Logistic regression.

Results: The prevalence of women with 2 or more immunological abnormalities was 57 out of 366 women (15.6%) and was significantly higher than in control women. Demographic clinical characteristics were similar in women with 2 or more immunological abnormalities as compared with women with only one immunological alteration or no abnormalities. The presence of the immunological profile was significantly associated with the presence of the following clinical characteristics: Leucopenia (p=0.048), lymphopenia (p=0.007), livedo reticularis (p=0.01), cutaneous rash (p=0.009), and arthritus (p=0.001). During follow-up 17 patients (4.6%) developed an inflammatory or autoimmune disease that was not present at the time of diagnosis of RPL including SLE and lupus like disease. Women with the immunological profile were at higher risk for evolution into these diseases: OR 4.19, 95% confidence interval 1.52–11.51, p=0.0055. In 10 women with the immunological profile we observed significantly higher levels of CD4+DR+ and CD8+DR+ T-cells as compared with women without the immune profile.

Conclusions: A subpopulation of women with unexplained RPL are at risk of developing clinical characteristics of an inflammatory or autoimmune disease. In this regard, the immunological evaluation of women with RPL might be necessary not only to identify a potential cause of abortion but also to identify women that could require a more careful clinical follow-up. Higher CD4+DR+ and CD8+DR+ T-cells might be a pathogenic pathway leading to development of autoimmune diseases in RPL women.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6003

FR0284 | PREDICTORS OF ARTERIAL VASCULAR EVENTS IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS


Background: Arterial vascular events (AVE) are among the major causes of morbidity and mortality in patients with Systemic Lupus Erythematosus (SLE). Several studies have been carried out to identify the main factors related to AVE in this population. The ankle brachial index (ABI) is one of the tools currently used to identify patients at greater risk of arterial events in the general population; however it has been scarcely studied in patients with SLE.

Objectives: The objectives of this prospective cohort study were to determine the predictive value of the ABI for occurrence of AVE in patients with SLE and to identify other possible factors associated with an increased risk of AVE.

Methods: 216 patients with SLE were evaluated using an ABI and followed up for 5 years. Pathological ABI is considered an ABI <0.9. Different potential vascular risk factors (traditional, non-traditional and related to SLE and/or the treatments used) were jointly evaluated. AVE: coronary events (angina pectoris, acute myocardial infarction, coronary revascularization by angioplasty or surgery), cerebrovascular events (transient ischemic attack, cerebrovascular accident), peripheral arterial disease (symptomatic intermittent claudication, distal ischemia, revascularization by angioplasty or surgery), and death related to vascular disease. Survival analysis was performed using a competitive risk regression approach, considering non-vascular death as a competitive event, to identify the predictive value of ABI and other factors studied. The Ethical Committee for Clinical Research at Cruces University Hospital approved the study protocol in accordance with the Declaration of Helsinki (CEIC 3216). All patients signed an informed consent at the time of entry into the study.

Results: During follow-up, 4/216 (1.8%) patients were lost to follow-up. 18 AVE were identified in 17 patients, with one patient having 2 episodes of angina requiring angioplasty (4 coronary events, 11 cerebrovascular events, 2 peripheral arterial disease events and 1 sudden death) and 14 deaths (6 per AVE or their sequelae, 4 due to neoplasias and 4 due to cardio-respiratory pathology).

In the competitive risk regression analysis, independent predictors of higher risk of AVE were identified: pathological ABI (subhazard ratio (SHR) 3.51, 95% confidence interval 0.96–12.79, p=0.057), family history of AVE (SHR 6.3, 95% CI 1.97–20.21, p=0.002), cumulative total prednisone (grams) (SHR 1.02, 95% CI 1.01–1.04, p=0.004) and a history of arterial thrombosis (SHR 4.60, 95% CI 1.97–20.21, p=0.002).

Conclusions: Being male, having a higher cumulative dose of prednisone, having a family history of early vascular disease and having suffered previous arterial thrombosis are independent risk predictors of an AVE in patients with SLE. Having abnormal ABI, even without statistical significance, showed a marked tendency to increase this risk despite the low number of events recorded in the studied cohort.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5303

FR0285 | LUPUS NEPHRITIS IS ASSOCIATED WITH INCREASED RATES OF HOSPITALIZATION AND IN-HOSPITAL MORTALITY COMPARED WITH NON-RENAL LUPUS AND MATCHED CONTROLS: AN ANALYSIS OF INSURANCE CLAIMS DATA

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Background: Systemic lupus erythematosus (SLE) is heterogeneous in its clinical presentation, course, and prognosis and lupus nephritis (LN) continues

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6004
to be a major cause of morbidity and mortality among children and adults with SLE. Up to 60% of adult and 80% of pediatric SLE patients (pts) will eventually develop overt renal disease [1]. To date the excess burden of comorbidities, risk of inpatient hospitalization, and in-hospital death associated with SLE and LN remains incompletely understood.

Objectives: To identify differences in comorbidities, hospitalizations, and in-hospital mortality of SLE and LN cohorts compared to: 1) each other; 2) reference populations of pts without an autoimmune condition (non-AI) matched on gender and age. Reference populations were allowed to have claims for non-autoimmune conditions.

Methods: We conducted a retrospective cohort study using the Truven Healthcare MarketScan® Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits database, which together comprise 65 million insured US lives between 1999 and 2014. Cohort identification is based on validated algorithms [2, 3] for identification of pts with SLE or LN without renal involvement using claims data. Pts were matched on age and gender at index date. All eligible participants had 365 days of enrollment prior to and after the index date. End of study for post-index follow-up was captured as whichever of the following occurred first: 1) end of enrollment; 2) end of database; 3) date of death. Results are presented separately for pediatric and adult pts.

Results: 54,813 SLE pts without renal involvement and 8,839 LN pts were identified and matched to reference non AI populations. Compared to the non-renal SLE cohort, pts in the LN cohort were older (49.9±16.6 vs. 48.6±14.3 years) with a higher proportion of males (15.4% vs. 11.2%), Pts with LN had the highest scores on the Charlson Comorbidity Index modified to exclude renal involvement (Table 1). Additionally, adults with LN had higher rates of hospitalizations and longer hospitalizations compared with adults with non-renal SLE, who already had higher rates of hospitalizations and longer hospitalizations than matched controls (Table 2). This pattern of findings was consistent for children. Rates of in-hospital mortality were highest among those with LN but also increased among those with SLE compared with matched controls (Figure 1).

Conclusions: An SLE diagnosis was associated with a higher burden of comorbidities and higher rates of hospitalizations and in-hospital mortality than non-AI matched controls. Pts with LN had the highest burden of comorbidities and rates of hospitalizations and in-hospital mortality. SLE and LN disproportionately high burden of morbidity and mortality and the medical need for safe and effective treatments of LN and SLE remains unmet. Clinicians should consider these factors in their assessment and treatment of pts with SLE and LN. The retrospective, claims-based results do not permit pt-level assessment of the relative contributions of disease, treatment, and potential confounders to these findings.

References:


DOI: 10.1136/annrheumdis-2017-eular.5526

FRIO287 SEROLOGICAL EVOLUTION IN PATIENTS WITH THROMBOTIC ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease characterized by the presence of antiphospholipid antibodies (aPL) and at least one clinical event (thrombosis and/or pregnancy morbidities). The titers of aPL can fluctuate and eventually become negative. This negativization, particularly if persistent, may be associated with a lower frequency of clinical events.

Objectives: To describe the clinical and serological course of patients with thrombotic APS as well as the factors related with the aPL negativization.

Methods: We performed a retrospective study including patients attended at the Rheumatology clinic from a tertiary hospital in Northern Spain. We included 94 patients with thrombotic APS according to Sidney criteria of 2006. They were classified according to the serological evolution as persistently negative aPL, transiently positive, and persistently positive aPL according to previously established criteria.

Results: After a mean follow-up of 145±56 months, 48.9% of patients presented a persistently negative serology, whereas in 12.8% it was transiently positive, and persistently positive in 38.3%. When analyzing potential factors related to the negativization (table 1), we found that patients with positive lupus anticoagulant tended to have a persistently negative serology during follow-up, but it did not reach statistical significance (OR 2.7; 95% CI 0.8–9.4; p=0.145). We found no association between traditional cardiovascular risk factors or previous treatments and the serological evolution.

Conclusions: After a mean follow-up of 12 years, 49% of thrombotic APS patients presented a persistently negative serology. We found no significant association between immunological, traditional cardiovascular risk factors or previous treatments and the persistently negative serology.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5106
American SLE population have shown a higher prevalence of LN, higher severity, and less favorable outcomes (1).

**Objectives:** To determine the incidence of lupus nephritis and end-stage renal failure, as well as evaluate progression of renal function and proteinuria during an 18-month follow up in colombian patients with SLE.

**Methods:** A retrospective cohort study was conducted in 1448 patients with SLE, 41 of which were diagnosed with LN between August/2014 and July/2015. Follow up was made for 18 months, analyzing glomerular filtration rate (GFR) and proteinuria, induction and maintenance therapy, renal relapses, hospitalizations and mortality. Univariate analysis was done to describe sociodemographic and clinical variables. Longitudinal data analysis was performed using linear mixed models with random intercepts. In all cases, a p value <0.05 was considered statistically significant.

**Results:** Clinical characteristics of patients with LN are shown in table 1. Eighty-five percent of LNs where biopsy-proven. Incidence of LN was 2.83 cases/100 SLE patients/year. The incidence of end-stage renal failure was 7.31 cases/100 SLE patients/year. A high proportion of patients with refractory response to multiple immunomodulatory treatments for LN were identified.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6137

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**FR01291** | **CEREBROVASCULAR DISEASE IN THE ANTIPHOSPHOLIPID SYNDROME**

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**Background:** Antiphospholipid syndrome (APS) is a thrombophilic disorder characterized by recurrent arterial and venous thrombosis, and also pregnancy losses associated to antiphospholipid antibodies (APA). Cerebrovascular disease (CVD) is the most common and severe arterial thrombotic manifestation in patients with APS.

**Objectives:** 1. To determine the prevalence and the type of CVD in patients with APS. 2. To compare the recurrent strokes, affected brain areas, hospitalization, treatment and mortality between patients with CVD, with and without APS.
Methods: Retrospective and descriptive study of patients with APS (Sidney criteria) and CVD followed for a long period of time in a specific Systemic Autoimmune Diseases and Thrombosis Unit. Subsequently, retrospective case-control study was performed. Case definition: patients with CD4 and CD8 counts in patients with APS. Control definition: patients with APS without CD4 and CD8 counts. The controls were matched by sex and age (within the same decade). Chi-square and t-student were used, according to the statistical package SPSS22.0.

Results: 25 patients (25/88 28.4%) had CVD. 19 (76%) of primary APS, 6 (21%) of secondary APS. 17 patients (71.6%) were female. The mean age was 57.48±21.52 (range 13–89), with a mean follow-up of 8.64±6.72 years. 24% of patients had atrial fibrillation, 80% had one cardiovascular risk factor and 48% had two or more factors (hypertension 68%, hypercholesterolemia 36%, diabetes 20%, tabaquism 4%). Echocardiographic study was performed in 72% of patients with APS. Mitral valve was mainly involved. Most CVD were ischemic events (92%). The brain areas most involved were the basal ganglia (36%), together with the parietal and temporal lobe (16% respectively). 40% had two or more affected regions. 44% of the patients had two or more episodes of stroke. Lupus anticoagulant was positive in 40%, and anti-cardiolipin antibodies in 70%. 20% had anti-glycoprotein antibodies in 20%. No differences were found with isotypes of APA and recurrent thrombosis or mortality. The treatment applied was oral anticoagulants (OAC) (48%), antiplatelet therapy (APT) (20%) and low molecular weight heparin (20%). In 10 patients (40%) CVD was diagnosed before APS (mean 8.64±6.7 years). The mortality was 44% and 40% of the patients were hospitalized more than once. When we compared the groups: treatment, performed echocardiogram, valvular disease, affected brain areas, recurrent strokes and follow-up time, revealed significant differences (see table 1). OAC were more used in the patients with APS and APT was the most common in control group. Valvular disease was more frequent in case group. The brainstem and the frontal lobe were the areas more affected in patients without APS. The number of strokes was higher in APS group. The patients with CVD and APS had a long-term follow-up.

Conclusions: The prevalence of CVD in our series of APS was 28.4% and most often were ischemic events. Most of the patients were women with high recurrent strokes and mortality. No differences were found with isotypes of APA and recurrent thrombosis or prognosis. CVD with APS patients had more recurrent strokes and longer follow-up. 

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4509

**FRIO290**

**INTERLEUKIN 10 GENE POLYMORPHISMS IN PRIMARY SJÖGREN SYNDROME IN A TUNISIAN POPULATION**


**Background:** Primary Sjögren syndrome (PSS) is one of the most common autoimmune rheumatic diseases although its prevalence ranging between 0.6 and 1.7%. PSS affects exocrine glands and lead to sicca syndrome. Interleukin-10 (IL-10) is a pleiotropic cytokine that is involved in the inflammation process of PSS.

**Objectives:** The aim of our study was to determine in a Tunisian population, clinical and biological characteristics of patients with primary PSS, allelic and genotypic frequencies of -1082G/A, -819C/T and -592 C/A polymorphisms in IL-10 gene and to evaluate the association of these polymorphism with PSS.

**Methods:** The population studied consisted of 242 subjects with female predominance (average age at diagnosis 49 years), divided into 84 PSS patients fulfilling the revised AECG criteria 2002 and ACR proposed criteria 2012, recruited from the internal medicine of the Rabta hospital. 158 controls recruited in the Greater Tunis. IL-10 level was assessed by ELISA. Polymorphisms genotyping of the IL-10 gene was done using PCR-RFLP technique.

**Results:** IL-10 plasma level was lower in PSS patients (23.71±9.2 ml, n=73) compared to healthy volunteers (42.2±9.2 ml, n=60) and the difference was statistically significant (p<0.01). The genotype frequencies of our population respected Hardy-Weinberg equilibrium distribution both in patients by primary SS than in controls. In PSS patients, the genotype frequencies of -592C/A are 53% for the CC genotype, 41% for the CA and 6% for the AA genotype. In controls these frequencies are respectively 60.3%, 32.9% and 6.8%. The genotype frequencies of -1082 G/A are 29.6% for the AA genotype, 63% for the AG and 7.4% for the GG genotype. In controls these frequencies are respectively 41.5%, 52.1% and 6.3%.

No significant differences in genotypic frequencies were observed between cases and controls in the three polymorphisms.

Statistical analysis preformed revealed that there was neither protective nor aggravating haplotype. However ACP haplotype seems to have a protective impact in controls (p=0.06 and OR=0.2)

**Conclusions:** IL10 level was significantly higher in PSS patients in precedent studies (1) (2). In our case IL10 level was associated with PSS in Tunisian patients but it was statistically lower than controls. Our results show that the three polymorphisms of gene of IL-10 are not a marker of SGS in the Tunisian population. This result might be explained by allelic variation or ethnic group.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6617
ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN (APS/PT) ANTIBODIES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME


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Background: Several studies have shown conflicting results regarding the presence and meaning of anti-phosphatidylserine/prothrombin (aPS/PT) antibodies. However, aPS/PT antibodies seem to be a risk factor for thrombosis. Nevertheless, most of the studies have focused on patients with SLE and secondary antiphospholipid syndrome (APS).

Objectives: To assess the prevalence of aPS/PT antibodies, as well as their association with other antiphospholipid (aPL) antibodies (specially lupus anticoagulant [LA]) and thrombosis, in a well-established cohort of primary APS from a single center.

Methods: We included 96 consecutive patients with primary APS according the Sydney classification criteria and/or patients with hematological features (thrombopenia and hemolytic anemia) attending a referral center in Mexico City. Patients from both groups fulfilled the Sydney laboratory criteria for APS. We registered demographics, disease duration and type of manifestation. aCL (IgG and IgM), antibodies to purified human anti-2GP1-IgG and aPS/PT (IgG and IgM) and aPS/PT antibodies (IgG and IgM) were assessed by ELISA (INOVA Diagnostics). LA was determined by LA/1 screening reactant and a confirmatory test LA/2 according to published guidelines. We used chi-square (χ²) test, Spearman correlation analysis and logistic regression.

Results: Most patients were females (69.7%), mean age 44.5±14.6 and median disease duration 7.3 years. The main clinical features were thrombosis (n=74.77%), hematology involvement (n=49 patients, 51%) and obstetric events (n=24, 25%) (non-exclusive groups). The prevalence of LA was 69.8%, aCL-IgG 56.8%, anti-2GP1-IgG 43.1%, aCL-IgM 31.5% and anti-2GP1-IgM 21.1%. The frequency of aPS/PT antibodies was 61.2% and 61.6% for IgG and IgM isotype, respectively. When we compared patients with LA+ (n=58) vs. LA− (n=25), the first group had a higher prevalence of aPS/PT-IgG (79.3% vs. 16%, p<0.0001) and aPS/PT-IgM antibody (81.5% vs. 8.1%, p=0.0001), as well as higher titers (aPS/PT-IgG 103.5 U vs. 2.2 U and aPS/PT-IgM 21.5 U vs. 1.1 U, p=0.0001). aPS/PT-IgG antibodies correlated with aCL-IgG (ρ=0.59, p=0.0001) and anti-2GP1-IgG (ρ=0.63, p=0.0001) and anti-2GP1-IgM (p=0.35, p=0.001). On the other hand, aPS/PT IgM antibodies correlated with aCL-IgM (ρ=0.57, p=0.0001), anti-2GP1-IgM (ρ=0.42, p=0.001) and anti-2GP1-IgG (ρ=0.48, p=0.001) and anti-2GP1-IgG (ρ=0.59, p=0.0001). We found moderate agreement between the presence of LA and both aPS/PT isotypes (κ=0.58, p<0.001 for IgG, and κ=0.47, p=0.001 for IgM). Thrombosis was associated with aPS/PT-IgG antibodies (87.7% vs. 61.1%, p<0.0001) but not with aPS/PT-IgM (73.6% vs. 81.8%, p=0.37). At the logistic regression analysis, the aPS/PT IgG antibodies remained associated with thrombosis after adjusting by all other aPL antibodies, OR 8.6 95% CI 2.1–33.8, p=0.002.

Conclusions: In this cohort of patients with primary APS, aPS/PT antibodies were highly prevalent, correlated with other aPL antibodies and were associated independently with thrombosis.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5578

CHARACTERIZATION AND RISK ESTIMATE OF CANCER IN PRIMARY SJÖGREN SYNDROME: ANALYSIS IN 1300 PATIENTS


Objectives: To characterize the risk of solid and hematological cancer in a large, well-characterized cohort of patients with primary Sjögren syndrome (SjS).

Methods: The GEAS-SEMI registry is a network of Spanish reference centers with specific clinical experience in the management of SjS patients. By January 2016, we had analyzed the development of cancer in 1300 consecutive patients fulfilling the 2002 SjS classification criteria. Multivariate Cox proportional-hazards regression analysis allowed adjustment for age at diagnosis, gender and the statistically-significant baseline variables associated with cancer for the univariate analysis. The sex- and age-specific incidence rates (SIR) of cancer were estimated from 2012 Spanish mortality data modeling, using a set of age-, sex- and site-specific incidence/mortality ratios.

Results: After a mean follow-up of 91 months (9922.3 person-years), 127 (9.8%) patients developed 133 cancers. The most frequent type of cancer was B-cell lymphoma (34% of cancers, including 27 MALT and 19 non-MALT B-cell lymphomas). Systemic activity at diagnosis of primary SjS correlated with the risk of hematological neoplasia (HR 1.06, p<0.001). Positive cryoglobulins at SjS diagnosis were independently with thrombosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5391

ULTRASOUND OF THE SALIVARY GLANDS HELPS TO DISTINGUISH BETWEEN PRIMARY AND SECONDARY SJÖGEN SYNDROME


Background: Previous studies have demonstrated typical findings in the ultrasound of salivary glands (USG) in patients with primary Sjögren syndrome (pSjS) compared with healthy controls. However, it is unknown, if these findings are only seen in patients with pSjS but also in patients with secondary Sjögren syndrome (sSjS) or other connective tissue diseases with positive Ro-SSa/La-SSb antibodies.

Methods: We used an ultrasound score developed by Zhang [1] to investigate salivary glands with a score ranging from 0–48. We compared the score from patients with pSjS according the criteria of the American-European Consensus Group (group 1) with patients who fulfilled the criteria (1–4), but were Ro-SSa/La-SSb negative (group 2), with patients who had another rheumatic disease, but had sicca symptoms and were Ro-SSa and/or La-SSb positive (sSjS) (group 3), with patients with other rheumatic disease without Ro-SSa or La-SSb antibodies (group 4), with patients with other rheumatic disease with Ro-SSa antibodies but no sicca symptoms (group 5) and with patients with no rheumatic disease (group 6), respectively. We investigated the parotid and the submandibular salivary glands bilaterally. The USG was assessed with a score from 0–48 points with a maximum of 12 points for 4 items each (hyoechoic areas, hyperrechoc reflexes, inhomogeneity and distinct organ border). If available the score was correlated with the scoritgraphically measured function of the salivary glands.

Results: We included USG of 92 patients in our study. Group 1 (n=33) had a score of 16.6±11.6; group 2 (n=7) 2.4±3.5; group 3 (n=16) 6.9±5.5; group 4 (n=16) 5.3±7.8; group 5 (n=11) 4.5±5.7 and group 6 (n=9) 1.9±2.3, respectively. The score in patients with sSjS was significantly higher than the score of patients with pSS (p<0.01), with no significant differences between all other groups. In 25 patients a scintigraphy of the salivary glands was available. The excretory function in the scintigraphy highly significantly correlated with the ultrasound score (r=0.53, p<0.001).

Conclusions: USG showed significantly higher scores in patients with pSjS, than in patients with sSjS or other rheumatic disease. USG as a non invasive investigation might be similarly helpful for the diagnosis of pSjS like salivary gland functional tests. USG findings can reliably distinguish between pSjS and sSjS associated with other rheumatic disease, also if they are positive for Ro-SSa/La-SSb.
References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8928

FR0295 HIGH RISK OF IDIOPATHIC OSTEONECROSIS IN SLE PATIENTS WITH HIGH ANTI PHOSPHOLIPID SCORE AND HYPERTRIGLYCERIDEMIA

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Background: Systemic lupus erythematosus (SLE) patients are prone to develop idiopathic osteonecrosis (ION) compared to other connective tissue disease patients or healthy subjects. ION has shown to occur as a result of ischemia, however, the involvement of antiphospholipid antibodies (aPL) in its pathophysiology remains to be elucidated. In the last years, our group introduced a quantitative marker of aPL “antiphospholipid score (aPL-S)”, which well reflected the risk of developing thrombosis [1].

Objectives: We newly identified high aPL-S as a risk factor for ION. Further-

Methods: A single center retrospective study comprising 82 consecutive patients who were diagnosed SLE at the Rheumatology department of Hokkaido University Hospital and underwent magnetic resonance imaging (MRI) of hip joints from January 2000 to December 2016. Among all the enrolled patients, aPL-S, which is calculated from 0 to 86, as well as classical risk factors for ION were evaluated.

Results: All 82 patients (13 males and 69 females) were given glucocorticoids. ION of the femoral head was diagnosed by MRI scan in 37 patients. Male ION(+): ION(-) 10/37 (27%) vs 16/45 (36%), p=0.058, malar rash ION(+): ION(-) 22/37 (59%) vs 16/45 (36%), p=0.045, aPL positivity ION(+): ION(-) 22/37 (59%) vs 15/35 (44%), p=0.026, high aPL-S ION(-30) ION(+): ION(-) 9/37 (24%) vs 3/45 (7%), p=0.001, hypertriglyceridemia (fasting triglyceride levels >100 mg/dL) ION(+): ION(-) 23/37 (62%) vs 12/45 (27%), p=0.002, and high dose infections requiring treatment or bacterial infections requiring admission due to immunosuppression, 12 (4%) had malignancy. SLE is an autoimmune disease requiring multi-faceted approach.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3253

FR0297 ROLE OF SERUM INTERLEUKIN-6 IN BLOOD BRAIN BARRIER DAMAGES IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuropsychiatric systemic lupus erythematosus (NPSE) is one of the most serious complications of the disease. We have recently demonstrated that the breakdown of blood brain barrier (BBB) plays a crucial role in the development of diffuse psychiatric/neuropsychological manifestations (diffuse NPSE), allowing influx of neuron-reactive autoantibodies from systemic circulation into the brain. However, the mechanism of BBB damages remains unclear. On the other hand, although CSF interleukin-6 (IL-6) has been shown to be elevated in NPSE, there has been no report on serum IL-6 in NPSE.

Objectives: The present study was designed in order to elucidate the roles of serum IL-6 in the pathogenesis, especially in development of BBB damages, in NPSE.

Methods: Paired serum and cerebrospinal fluid (CSF) samples were obtained from 101 SLE patients when they presented active neuropsychiatric manifestations (69 patients with diffuse psychiatric/neuropsychological syndromes [diffuse NPSE]) and 32 patients with neurologic syndromes or peripheral nervous system involvement [local NPSE] and from 22 non-SLE control patients with non-
inflammatory neurological diseases. The levels of albumin and IL-6 in CSF and serum were measured by ELISA.

**Results:** Serum IL-6 as well as CSF IL-6 was significantly elevated in acute confusional state (ACS) compared with non-ACS diffuse NPSLE (anxiety disorder, cognitive dysfunction, mood disorder and psychosis) or focal NPSLE (figure). ANA and cryo-antibodies (including anti-neutrophil cytoplasm AT, Y. Asaklu, A. Ed-Din, R. Thanawala, D. Andrew, I. Albert, C. May, M. Sokhova, T. Popkova, D. Novikova, E. Alexandrova, E. Nasonov, V.A. Nasonov Research Institute of Rheumatology, Moscow, Russian Federation

**Objectives:** This study was aimed to determine NT-proBNP serum levels in patients with untreated SLE, thus ruling out any potential effect of SLE therapy to analyze any possible correlation between NT-proBNP values and traditional risk factors (TRF), inflammatory markers and myocardial function parameters. PS matching will allow comparison of long-term organ damage in patients with untreated lupus erythematosus (SLE) have established the efficacy and safety of belimumab plus standard SLE therapy (SoC) vs SoC alone. 10.1136/annrheumdis-2017-eular.3735

**Disclosure of Interest:** None declared

**DOl:** 10.1136/annrheumdis-2017-eular.2806

**FRIO299 | APPLICATION OF PROPENSITY SCORE-MATCHING METHODS TO COMPARE DATA FROM LONG-TERM EXTENSION TRIALS WITH DATA FROM AN EXISTING LUPUS REGISTRY**

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**Methods:** Potential PS model criteria were a) Medical Decision Modeling Inc, Indianapolis, United States; b) Value Evidence & Outcomes, GSK, Stockley Park, United Kingdom; c) Value Evidence & Outcomes, GSK, Philadelphia, United States. The study included 28 pts (82% females, aged 28.5 [25.0–32.0] years (median [interquartile range 25%–75%]) with untreated SLE (ACR criteria, 1997) and 27 healthy controls (89% females, age 30.0 [23.0–49.0] years). Mean NT-proBNP levels in patients with untreated SLE were higher than in healthy controls (30.5 [12.2–94.0] vs 12.5 [5.0–26.1] pg/ml, p<0.05). NT-proBNP was significantly negatively correlated with CRP, IL-6, INF-α, immunoglobulins G, A and M, C3 and C4 complement fragments and others, autoantibodies (ANA, antiDNA, ENA-SSA, -SSB, -Sm, -RNPs-70, aPL), echocardiography was performed using standard techniques. Serum levels of NT-proBNP (pg/ml) were measured using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland). Normal NT-proBNP levels should vary within 125.0 pg/ml.

**Results:** Mean SLE duration was 21.0 [5.0–60.0] months, SLEDAI 2K score - 11 [8–9], SLICC/DI score - 0 [0–0]. SLE pts had higher levels of NT-proBNP vs control (160.7 [98.6–335.4] vs 55.2 [36.6–70.3] pg/ml, p=0.001). Elevated levels of NT-proBNP (75.0–125.0 pg/ml) was detected in 18 (64%) SLE pts. In SLE pts NT-proBNP serum levels showed positive correlation with creatinine (r=0.480, p<0.01), uric acid (r=0.427, p<0.05), ACL IgG (r=0.710, p<0.001), antiDNA (r=0.395, p<0.05), ANA levels (r=0.256, p<0.05), left ventricle (LV) end-systolic dimension (r=0.442, p<0.05), mean pulmonary artery pressure (r=0.488, p<0.05); and negative correlation with hemoglobin level (r=-0.493, p<0.01), C4 complement component (r=-0.475, p<0.05), glomerular filtration rate (r=-0.558, p<0.01) and LV ejection fraction (r=0.505, p<0.01); left ventricular diastolic dysfunction (DDLV) was only in pts with NT-proBNP levels >125.0 pg/ml. Mean NT-proBNP concentration in verified DDLV cases (n=5) (18%) considerably exceeded normal values, reaching up to 799.2 [27.6±177.0] pg/ml.

**Conclusions:** Untreated SLE patients without a history of myocardial infarction, coronary procedure or any evidence of heart failure demonstrated higher NT-proBNP concentration as compared to healthy controls (p<0.001). NT-proBNP levels showed correlation with numerous SLE markers (ACL IgG, ANA, antiDNA, C4 fragment of complement), kidney function (creatinine, uric acid, glomerular filtration rate) and myocardial function (end-systolic dimension of the LV, mean pulmonary artery pressure, LV ejection fraction). No correlation was documented between NT-proBNP concentration and TRF or inflammatory markers (CRP, IL-6, INF-α). All abovementioned data suggest presumable SLE-associated autoimmune damage of cardiomyocytes and/or mediated decrease of myocardial function caused by kidney disease.

**Disclosure of Interest:** None declared

**DOl:** 10.1136/annrheumdis-2017-eular.3735

**FRIO300 | NEUROLOGICAL INVOLVEMENT IN PRIMARY SJÖGREN SYNDROME**

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**Background:** Prevalence of neurological involvements (NI) in primary Sjögren Syndrome (pSS) varies from 10 to 60% and depends on whether they are screened systematically or only when they are symptomatic. The aim of the study was to describe the prevalence, clinical patterns and treatment of NI in pSS.

**Methods:** We performed a retrospective study of patients with pSS (American-European Consensus Group criteria) and followed in an internal medical department over a period of 15 years. Patients with NI were enrolled after excluding other potential causes. We did investigate neurologic systems only when patients were present with NI. The two groups were compared:

**Results:** Primary Sjögren Syndrome was diagnosed in 155 patients, 41 had neurological manifestations (26.4%). They were 5 male and 36 female. The mean age at disease onset was 49 ±13 years. The average delay from NI onset to pSS diagnosis was four months for peripheral nervous system (PNS) and 12
months for central nervous system (CNS). NI revealed the disease in 14 cases (34%). CNS and PNS involvements were respectively found in 27 and 19 cases (six patients had both CNS and PNS). In patients with CNS disorders, headache was the most frequent symptom (n=11). Pyramidal syndrome was found in 9 cases and cerebellar syndrome in one patient. Aseptic meningitis was noted in two cases. Brain MRI was performed in 22 cases and showed abnormalities in 82% of cases. T2 and flair weighted hyperintensities were periventricular (n=11), subcortical (n=5), frontal (n=3) and parietal (n=2). Myelitis was found in one patient.

Patients with PNS showed paresthesia (92%), motor deficit (22%) and decreased tendon reflex (12%). Sensory-motor neuropathy was described in 4 cases, pure sensory neuropathy in 6 cases (including one case of small fiber neuropathy) and motor neuropathy in one patient. Mononeuropathy multiplex was found in 4 cases and polyradiculoneuritis in one patient. Neuromuscular biopsy was performed in five patients and showed vasculitis in two cases. Trigeminal nerve and cochlear nerve were respectively involved in four and one patients. Antinuclear antibodies, anti-SSA and anti-SSB antibodies were respectively positive in 71%, 50% and 28% of cases. NI were treated with corticosteroids and immunosuppressive therapy in respectively 56% and 41% of cases. Outcome was good in 46% of the patients. Comparison of clinical and biological features in patients with and without NI showed no significant differences, only fatigue was significantly associated to NI (45.5% vs 12.9%; p<0.005).

Conclusions: In our series, NI prevalence was similar to other groups. CNS involvements were more frequent than PNS manifestations whereas in other ethnic groups they are less frequent.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2772

FR10301 | CHARACTERIZATION OF FEVER IN HOSPITALIZED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: LESSONS FROM THE JIANGSU COHORT

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Background: Fever is one of the main symptoms leading to the admission of patients with systemic lupus erythematosus (SLE) and its causes are usually complicated.

Objectives: To explore the prevalence and clinical characteristics of fever in Chinese SLE patients at the time of their first admission and to find out whether fever is related to a poor prognosis.

Methods: A follow-up study aimed to delineate SLE prognosis had been conducted by our Lupus Collaborative Group under the supervision of Jiangsu Rheumatology Association to collect the data of patients who had ever recorded first admissions during the 1999–2009 decade (1). Among which, those with admission temperature documented were extracted for the assessment of potential factors associated with fever. The independency of various clinical features linked to fever was established by binary logistic regression analysis, and the relation between fever and patient’s survival was determined by Cox regression analysis.

Results: Totally 1,348 patients were enrolled, in which 1,048 (77.8%) had normal temperature, 221 (16.4%) had low and moderate fever and 78 (5.8%) had high fever at the time of their first hospitalization. Compared with those having normal temperature, fever patients were more likely to have short disease duration (RR 0.74), concurrent infection (RR 3.29) and gastrointestinal (RR 1.57) as well as hematological involvements (RR 1.56), High C reactive protein level (RR 2.08) and positive anti-Sm antibody (RR 1.55) were the two laboratory factors related to fever at admission. However, age, gender, SLEDAI score or erythrocyte sedimentation rate was not independently associated with fever in this cohort. Cox regression analysis showed that there was no correlation between fever and overall deaths (Figure 1) as well as infection induced deaths.

Conclusions: Both infection and lupus itself (especially gastrointestinal and hematological involvements) contribute to fever in SLE patients. Although the presence of fever increases the complexity of disease treatment, it does not constitute a risk factor for patient’s long-term outcome.

References:

Acknowledgements: This study was supported by National Natural Science Foundation of China (81373198) and Jiangsu Provincial Special Program of Medical Science (BE2015602).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3140

FR10302 | ELEVATED CYSTEINE-RICH PROTEIN 61 IN SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

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Background: Pulmonary arterial hypertension (PAH) is a complex and devastating complication of connective tissue diseases that leads to severe morbidity and mortality. Unlike in Caucasians, it is systemic lupus erythematosus that recognized as the the major underlying cause of CTD associated PAH in Asian countries, especially in China [1]. Early diagnosis and intervention is vital for better long-term outcome in SLE-PAH patients. Previous study has demonstrated Cysteine-rich protein 61 (Cyr61) was highly expressed in SLE patients [2]. However, the role of Cyr61 in pulmonary arterial hypertension (PAH) remains unknown.

Objectives: To explore the value of Cyr61 for PAH in SLE patients by comparing the plasma Cyr61 levels in SLE patients with/without PAH.

Methods: Plasma samples from two tertiary medical centers were obtained from 54 patients with definite SLE-PAH, 52 age, gender and SLEDAI matched SLE patients without PAH, and 54 age and gender matched healthy controls. Plasma Cyr61 concentration was measured by enzyme-linked immunosorbent assay.

Results: Plasma Cyr61 concentration in SLE-PAH patients was significantly higher than the matched SLE patients and healthy controls (median (IQR): 172.5 (143.8, 218.2), 124.9 (104.1, 154.7), 58.17 (28.9, 80.4) respectively, P<0.001 (Figure 1). The sensitivity and specificity of Cyr61 in predicting the presence of PAH in entire SLE patients were 79.6% and 67.3%. Receiver operating characteristic curve analysis showed the area under the curve was 0.757 (95% CI: 0.682–0.852), with 140.6 pm as the cut off concentration (Figure 2). Further multivariate logistic regression analyses revealed high Cyr61 level (>140.6) is an independent risk factor for SLE patients to develop PAH (OR:7.822 (95% CI: 2.224–41.138) (Table 1)). Additionally, weak to moderate positive correlations were observed between Cyr61 concentration and serositis, hematological involvement, red blood cell distribution width, right ventricular systolic pressure and right ventricular diameter measured by echocardiography in entire SLE population.

Conclusions: Plasma Cyr61 level was significantly higher in SLE-PAH patients than SLE patients without PAH. Cyr61 may be used as a biomarker for PAH complication in SLE patients.

References:
The IgG4:IgG RNA ratio is a new and promising disease activity marker in granulomatosis with polyangiitis

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Background: Granulomatosis with Polyangiitis (GPA) is a form of vasculitis characterized by inflammation of blood vessels in lungs, kidneys, and the ear, nose and throat region. Regular monitoring and treatment adjustments are common, as the disease activity tends to fluctuate over time. Unfortunately, good markers for disease activity are lacking. This leads to both over- and undertreatment.

Immunoglobulin G4 positive (IgG4+) B-cells and plasma cells are implicated in the pathogenesis of GPA, but the level of serum IgG4 does not seem to be a good disease activity marker. Recently we developed a test that indirectly measures the presence of IgG4+ B-cells/plasma cells by measuring the IgG4/IgG RNA ratio. We hypothesized that this test could be used as disease activity marker.

Objectives: To test the IgG4:IgG RNA ratio in peripheral blood as a disease activity marker in GPA.

Methods: 27 PR3-ANCA positive GPA patients were included in this cross-sectional study. Mean age was 52 years, 56% were female, and 39% had active disease. For each patient the ESR, CRP, BVAS, and ANCA titre were measured and peripheral blood samples were obtained. Patients were defined as having active disease if the BVAS was $\geq 3$. In addition we included 10 healthy controls, and 63 patients with other immune mediated inflammatory diseases (systemic lupus erythematosus (SLE) (n=24), rheumatoid arthritis (RA) (n=19), primary sclerosing cholangitis (PSC) (n=20)). A validated qPCR test was performed in all groups to measure the IgG4:IgG RNA ratio in peripheral blood samples

Results: The median IgG4:IgG RNA ratio was significantly higher in the GPA cohort (5.7, IQR 2.6 - 19.7) compared to all control groups: 1.2 in SLE (0.7 - 4.1; p $< 0.001$), 2.5 in RA (1.0 - 2.8; p $< 0.001$), 1.3 in HC (0.6 - 1.8; p $< 0.001$). In addition, the median IgG4:IgG RNA ratio was significantly higher in patients with active disease (23.8; IQR 12.1 – 29.1) compared to patients in remission (3.5; IQR 2.0 – 5.5; p $< 0.0001$). The height of the IgG4:IgG RNA ratio significantly correlated with height of the BVAS (r² = 0.76, p $< 0.0001$), while the ESR, CRP and ANCA titre did not. Interestingly, IgG4/IgG RNA ratios among patients with active disease were consistently above 9.3, and among patients in remission they were below this threshold.

Conclusions: The IgG4/IgG RNA ratio distinguishes active GPA from GPA in remission with excellent specificity and sensitivity. Moreover the ratio shows a significant correlation with disease severity, in contrast to ESR, CRP and ANCA titre. Retesting in another, prospective study is indicated to validate the IgG4/IgG RNA ratio as a novel, highly sensitive and specific marker of disease activity in GPA.

References:

Acknowledgements: We thank D. van der Coelen for the technical assistance, the doctors of the vasculitis outpatient clinic, especially Dr. B.J.H. van der Born and Dr. A.E. Hak, for the contribution to patient inclusions, and all the patients that participated in this study.

Disclosure of Interest: None declared

limits and aorta were less in benign RPF; however, significant differences were only observed when comparing with lymphoma (p values: all <0.001) but not with metastatic carcinoma (p value: 0.396, 0.181, 0.112 and 0.64). A greater frequency of retroperitoneal lesions with high FDG-uptake (100% vs 77.5%, p value: 0.017) and a higher mean SUVmax (12.2 vs 4.8, p value: <0.001) were observed in malignant RPF. The frequencies of LNs in malignant FDG-uptake were greater with significance in malignant RPF except for hilar/mediastinal and cervical LNs, hence the rest LNs were regarded as specific LNs. At ROC analyses, the AUCs of SUVmax and specific LNs were 0.893 and 0.947. The sensitivity and specificity were 85.7% and 81.4% when the SUVmax was 6.23. The AUC of logistic regression model combining SUVmax and specific LNs was 0.974 with sensitivity of 90.5% and specificity of 90.1%.

Conclusions: PET/CT could help distinguish benign from malignant RPF, especially when taking into account the FDG-uptake of retroperitoneal process and LNs.

Disclosure of Interest: None declared


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**FR10305**  
**RELATIVE FDG ACCUMULATION OF THE AORTIC WALL LESIONS TO AORTIC BLOOD POOL IN 18F-FDG-PET AND PET/CT COULD BE A USEFUL PARAMETER FOR THE PREDICTION OF DISEASE RELAPSE AFTER SUCCESSFUL TREATMENT IN TAKAYASU ARTERITIS**

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**Background:** The assessment of disease activity of Takayasu arteritis (TA) is difficult if symptoms and serum inflammatory marker were not detected. Even in those conditions, relapses were frequently observed during the dose reduction of corticosteroid and immunosuppressant. There is accumulating evidence that 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) and PET/ computed tomography (PET/CT) is useful for monitoring patients with TA when TA was clinically active. However, it is not clear the significance of FDG accumulations when TA was inactive.

**Objectives:** To investigate a quantitative predictor in FDG-PET or PET/CT scans for the relapse of TA.

**Methods:** We retrospectively investigated 76 FDG-PET or PET/CT scans and extracted 37 scans which were performed in inactive status. These scans were divided in two groups according to relapse of TA for 5years. The relapse was defined the increase of CRP and steroid dose or addition of immunosuppressant. FDG accumulations in aortic wall lesions of TA was evaluated by semi-quantitative index; the standardized uptake value (SUV), in addition to SUVmax in the aortic wall, we also calculated SUV ratio of maximum aortic wall uptake to mean lung uptake (ratio Lu), SUV ratio of maximum aortic wall uptake to mean liver uptake (ratio Li), and SUV ratio of maximum aortic wall uptake to mean aortic blood pool uptake (ratio BP). We compared groups using these parameters. We also determined the cutoff levels, sensitivity, and specificity of 4 sets of parameters was calculated as follows: SUVmax 1.4, ratio Lu 5.31, ratio Li 1.01, and ratio BP 1.41, respectively. Using these cut-off level, relapse rates of these parameters was calculated (Table 1). Using Receiver Operating Characteristic (ROC) analysis, the AUCs of SUVmax and specific LNs were 0.893 and 0.947. The sensitivity and specificity were 85.7% and 81.4% when the SUVmax was 6.23. The AUC of logistic regression model combining SUVmax and specific LNs was 0.974 with sensitivity of 90.5% and specificity of 90.1%.

**Conclusions:** PET/CT could help distinguish benign from malignant RPF, especially when taking into account the FDG-uptake of retroperitoneal process and LNs.

Disclosure of Interest: None declared


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**FR10306**  
**LONG TERM DRUG-FREE REMISSION IS FEASIBLE IN SEVERE BEHCET’S DISEASE AFTER CESSATION OF SUCCESSFUL ANTI-TNF TREATMENT: A SINGLE CENTER, RETROSPECTIVE LONGITUDINAL OUTCOME STUDY**

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**Background:** The efficacy of anti-TNF treatment for patients with severe forms of Behcet’s disease (BD) is well established (ref), but long term data on the outcome after cessation of such treatment are lacking.

**Objectives:** To examine whether sustained long term remission of severe BD is feasible after cessation of successful anti-TNF treatment.

**Methods:** This retrospective longitudinal outcome study was conducted in December 2016 and included all patients with severe BD refractory to conventional immunosuppressive therapy who were considered complete responders to continuous anti-TNF treatment in our center, the first being treated in 2000.
Study's endpoint was the proportion of patients achieving sustained complete remission of BD for at least 3 years after cessation of the anti-TNF agent.

**Results:** A total of 28 patients in whom infliximab and/or adalimumab treatment was given, always combined with azathioprine unless not tolerated (n=2), and discontinued anytime before December 2013 were eligible for analysis. Following cessation of successful anti-TNF treatment, median duration of 2 years, 13/28 patients achieved the study's end-point. The main reason for anti-TNF administration was sight-threatening ocular disease (n=12) or intestinal disease (n=1). The remaining 15 patients relapsed within 1.5 year (main reason for anti-TNF: ocular disease, n=9; neuro-BD, n=2; severe mucocutaneous disease, n=3; intestinal disease, n=1; median treatment duration of 24 months); 12/15 were successfully re-treated with anti-TNF. So far, 3 of them (ocular disease, n=2; neuro-BD, n=1) have achieved the study's end-point (median re-treatment duration of 2 years). Overall, our 16 patients who achieved the study's end-point (57%) are in complete disease remission ranging from 3 to 12 years (5.7 years, median). Nine patients with severe ocular disease are currently any drug-free (32%), whereas the 7 remaining patients are on low doses of conventional immunosuppressive therapy (25%). Notably, those patients on drug-free remission had shorter median disease duration at initiation of anti-TNF treatment, compared to the remaining patients (1 versus 3 years, respectively).

**Conclusions:** Sustained drug-free remission for many years after cessation of successful anti-TNF treatment is feasible in some patients with severe BD. Since anti-TNF-induced "cure" can never be differentiated from a spontaneous remission by natural history, further studies should examine whether early anti-TNF treatment must be intended for every patient with severe BD.

**References:**

**Disclosure of Interest:** None declared.

**FRI0308** |

**PREDICTORS OF HYPOGAMMAGLBULINAEMIA IN RITUXIMAB TREATED PATIENTS. A RETROSPECTIVE ANALYSIS ON A MONOCENTRIC COHORT**

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**Background:** Rituximab (RTX), a chimeric monoclonal antibody against CD20, is increasingly used in the treatment of B-cell lymphomas and autoimmune conditions. It has been shown that some patients develop hypogammaglobulinaemia after treatment.

**Objectives:** To assess frequency and predictors of hypogammaglobulinaemia after RTX treatment in a monocentric cohort of patients affected with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and connective tissue diseases (CTD).

**Methods:** We retrospectively reviewed all patients receiving RTX and concomitant immunosuppressants between 2007 and 2016 in a single rheumatologic center. Serum levels of total Ig and lymphocyte subsets were recorded at the time of RTX administration and 3–6 months later. We assessed the frequency of hypogammaglobulinaemia (IgG <6 g/L) and its related events.

**Results:** 72 patients, 30 (41.6%) GPA/MPA, 25 (34.7%) systemic lupus erythematosus, 13 (18.1%) systemic sclerosis and 4 (5.6%) polyarthritis mutilans were treated with RTX. We analyzed 113 RTX infusions, with 41 (36.2%) treatments (median 2 [2–6]). We excluded 12 patients/18 infusions due to incomplete data. RTX was administered at the dosage of 1000 mg twice in 68.1% of patients and 275 mg/m² weekly in 31.9%. IgG levels after RTX infusions were available in 68 (71.6%) patients. We observed a significant decrease of IgG levels between baseline and 3–6 months after RTX infusion in all patients (0.001). The frequency of patients with IgG <6 g/L was 22.1%, and 8.8% had IgG <4 g/L, significantly higher in GPA/MPA patients (0.008), with short disease duration (0.011), lower IgG levels at baseline (0.008), higher prednisone equivalent (PDE) cumulative dosage per year (0.006) and higher daily PDE dosage after RTX (0.001) (Table 1). After RTX, all patients had complete B-cells depletion.

At univariate analysis, IgG <6 g/L was associated with GPA/MPA diagnosis (0.006, OR 6[1.5–24.2]), disease duration <1 year (0.001, OR 0.2[0.1–0.9]), RTX 375 mg²/m² protocol (p=0.017, OR 4.1[1.2–13.9]), PDE cumulative dosage per year <0.001, OR 6.6 [1.3–33.6], daily PDE intake >15 mg/day after RTX (<0.001, OR 12.7[3.5–25.2]) and IgG levels before RTX (<0.001, OR 18[1.8–178]). At multivariate analysis, daily PDE intake after RTX (>15 mg/day) and GPA/MPA diagnosis resulted independent predictive factors for hypogammaglobulinaemia (p=0.03, OR 9.5, [2.2–41.7] and p=0.43, OR 4.7, [1.1–21.5]).

Patients affected with GPA/MPA were compared to CTD, as reported in Table 2. GPA/MPA patients at infusion were older (0.002), presented shorter disease duration (0.001), lower IgG levels at baseline (<0.001) despite lower rate of nephritic syndrome (0.003). Moreover they were treated more frequently with Azathioprine (0.007), RTX 375 mg²/m² weekly protocol (<0.001) and higher PDE cumulative and daily dosage (<0.001, 0.01 respectively).

Only 5 patients (5.2%) experienced severe infections within 12 months, more frequently in IgG <6 g/L patients (0.007).

**Conclusions:** In autoimmune rheumatic diseases, diagnosis of GPA/MPA and glucocorticoid therapy resulted independent predictors of hypogammaglobulinaemia after RTX treatment. Despite low IgG levels were associated with higher infections risk, rare severe infectious events were observed.
Background: Several chronic inflammatory diseases are associated with cardiovascular disease, but the cardiovascular risk in ANCA-associated vasculitis is poorly quantified.

Objectives: The aim of the present study is to review the evidence for the increased cardiovascular risk in patients with ANCA-associated vasculitis.

Methods: A comprehensive systematic review was conducted in accordance with guidelines of preferred reporting items for systematic reviews and meta-analyses (PRISMA). The databases PubMed, Embase.com and the Cochrane Library (Wiley) were searched for original observational studies reporting an estimate of the association between ANCA-associated vasculitis and cardiovascular events, including ischemic heart disease, cerebrovascular accidents and/or peripheral arterial disease. The quality of the included studies was assessed with the Newcastle–Ottawa Scale. Summary estimates were derived with a random-effects model and reported as relative risks.

Results: 1375 studies were identified and 7 studies were included comprising 14098 ANCA-associated vasculitis patients versus general population controls in 6 studies and chronic kidney disease patients in 1 study. ANCA-associated vasculitis carried a relative risk of 1.65 (95% confidence interval, 1.23–2.22) for all cardiovascular events, 1.60 (1.39–1.84) for ischemic heart disease and 1.20 (0.98–1.48) for cerebrovascular accidents. We did not find studies that addressed all cardiovascular events, 1.60 (1.39–1.84) for ischemic heart disease and 1.20 (0.98–1.48) for cerebrovascular accidents. We did not find studies that addressed the risk for peripheral arterial disease separately. No heterogeneity was seen in the estimates.

Conclusions: This meta-analysis of observational studies supports an increase in cardiovascular risk of about 65% in patients with ANCA-associated vasculitis, similar to that found in other chronic inflammatory diseases. Hence, there is a clear need for active cardiovascular risk management in patients with ANCA-associated vasculitis.

The frequency and severity of patient-reported symptoms in giant cell arteritis

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Background: A better understanding of the patients’ perspectives is pivotal in the development of patient-reported outcomes (PROs) in vasculitis.

Objectives: To assess patients’ perspective of disease amongst cases with Giant Cell Arteritis (GCA) compared to comparator illnesses mimicking large vessel vasculitis (LVV) included in the Diagnostic and Classification Criteria in Vasculitis Study (DCVAS) database.

Methods: Patient Description (PDI) forms from 89 patients with GCA and 28 comparators (COM) were analysed. There was no difference in age and sex distribution between groups (mean age 70±8 for GCA and 69±12 for COM). The symptoms description and frequency of the first most severe aspect of disease, including the patient’s own words, is presented in Table 1. The symptom regarded as the most severe by both groups was headache. While there were no differences in the frequency of sudden visual loss, visual symptoms were reported more commonly as the most severe feature by COM vs GCA (21% vs 8%, p=0.05). Headache was the most frequently reported symptom in both groups. Patients with GCA reported jaw claudication (37%) as the second most frequently reported symptom, while COM reported arthralgia/arthritus (32%). Shoulder/neck pain was the third most important symptom in GCA (33%), while fatigue was the third most common complaint among COM (21%). Fatigue was reported as the fourth most common feature by 30% of GCA patients.

Conclusions: Headache was the most frequent and most severe symptom reported by patients with GCA and comparators. However, the reported frequencies and severities of other symptoms were significantly different between the two groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5945

References:

FR0313 THE EFFICACY AND SAFETY OF TOCILIZUMAB THERAPY IN PATIENTS WITH POLYMYALGIA RHEUMATICA WHO WERE RESISTANT OR INTOLERANT TO GLUCOCORTICOIDS AND ADDITIONAL METHOTREXATE

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Background: A recent trial of tocilizumab (TCZ) in patients with newly diagnosed polymyalgia rheumatica (PMR), conducted in Europe and the United States, has shown its efficacy and safety.

Objectives: We examined the efficacy and safety of TCZ for patients with PMR who had been primarily resistant or intolerant to glucocorticoids (GC) and additional methotrexate (MTX).

Methods: Sixty patients had been diagnosed with having PMR since 2011. The patients are all compatible with the 2012 EULAR/ACR provisional classification criteria for PMR, and had been treated first with GC, if they were resistant or intolerant to GC, were added MTX, similarly to the 2015 EULAR/ACR recommendations for the management of PMR. The disease activity were measured by PMR-AS.

Results: There were 17 patients with GC/MTX resistant or intolerant PMR (28%). Of them, 9 patients with PMR agreed to the proposal of TCZ addition, and their therapeutic responses to TCZ and its safety were determined. They were at the age of 68±10.6, including three males and six females. Before TCZ addition, the patients were treated with prednisolone (PSL) at 7.6±3.0 mg/day plus MTX at 7.1±5.1 mg/week, and serum CRP were at 1.8±1.0 mg/dL. After 8.4±5.7 months of TCZ treatment, PSL and MTX had been reduced to 1.1±1.3 mg/day and 3.3±4.5 mg/week, respectively, with CRP at 0.02±0.05 mg/dL. GC were able to be withdrawn in 5 patients, and MTX were further withdrawn in 4 patients. Two patients reached drug-free remission (PMR-AS=0.02). During TCZ therapy, each one patient showed the worsening of depression and occlusion of the central retinal vein.

Conclusions: These results indicate that TCZ may provide a therapeutic option for patients with severe PMR who were resistant or intolerant to GC and additional MTX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4051

References:


Acknowledgements: No grants or other support were received for this study.

Disclosure of Interest: None declared


FR0312 THE FREQUENCY AND SEVERITY OF REPORTED SYMPTOMS IN GIANT CELL ARTERITIS

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Background: A better understanding of the patients’ perspectives is pivotal in the development of patient-reported outcomes (PROs) in vasculitis.

Objectives: To assess patients’ perspective of disease amongst cases with Giant Cell Arteritis (GCA) compared to comparator illnesses mimicking large vessel vasculitis (LVV) included in the Diagnostic and Classification Criteria in Vasculitis Study (DCVAS) database.

Methods: Patient Description (PDI) forms from 89 patients with GCA and 28 comparators (COM) were analysed. There was no difference in age and sex distribution between groups (mean age 70±8 for GCA and 69±12 for COM). The symptoms description and frequency of the first most severe aspect of disease, including the patient’s own words, is presented in Table 1. The symptom regarded as the most severe by both groups was headache. While there were no differences in the frequency of sudden visual loss, visual symptoms were reported more commonly as the most severe feature by COM vs GCA (21% vs 8%, p=0.05). Headache was the most frequently reported symptom in both groups. Patients with GCA reported jaw claudication (37%) as the second most frequently reported symptom, while COM reported arthralgia/arthritus (32%). Shoulder/neck pain was the third most important symptom in GCA (33%), while fatigue was the third most common complaint among COM (21%). Fatigue was reported as the fourth most common feature by 30% of GCA patients.

Conclusions: Headache was the most frequent and most severe symptom reported by patients with GCA and comparators. However, the reported frequencies and severities of other symptoms were significantly different between the two groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5945

Abstract FR0312 – Table 1. Top 10 most recurrent patient-reported symptoms and correspondent severity rank in giant cell arteritis (GCA) and Comparators (COM)

<table>
<thead>
<tr>
<th>Item</th>
<th>Frequency in GCA</th>
<th>Severity in GCA</th>
<th>Frequency in COM</th>
<th>Severity in COM</th>
<th>Examples of patient’s own words</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>1</td>
<td>1, 2, 8</td>
<td>1</td>
<td>1, 2, 5</td>
<td>Headaches; Sore head; Thumping headache</td>
</tr>
<tr>
<td>Jaw claudication</td>
<td>2</td>
<td>3, 6, 6</td>
<td>0</td>
<td>3</td>
<td>Jaw ache; Pain in jaw and teeth</td>
</tr>
<tr>
<td>Shoulder/neck pain</td>
<td>2</td>
<td>3, 5, 3</td>
<td>0</td>
<td>3</td>
<td>Shoulder pain; Tiredness</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4</td>
<td>5, 6, 10</td>
<td>0</td>
<td>3, 6, 7</td>
<td>Severe tiredness; Fatigue; No energy and exhausted</td>
</tr>
<tr>
<td>Myalgia or muscle weakness</td>
<td>5</td>
<td>5, 7, 10</td>
<td>0</td>
<td>3</td>
<td>Aching muscles; Aching limbs; Loss of strength in arms and legs</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>6</td>
<td>10</td>
<td>0</td>
<td>4</td>
<td>Blurred vision</td>
</tr>
<tr>
<td>Scalp tenderness</td>
<td>7</td>
<td>8, 10</td>
<td>0</td>
<td>4</td>
<td>Irritation to the scalp; Tender scalp</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Lack of appetite</td>
</tr>
<tr>
<td>Flu-like symptoms</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>General ill feeling; Flu-like symptoms; Unwell</td>
</tr>
<tr>
<td>Arthralgia or arthritis</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>Hip, knee more on right side; Pain in back of neck, ankles, wrists, and chest</td>
</tr>
<tr>
<td>Other ENT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>Severe sinusitis; sore inside gums</td>
</tr>
<tr>
<td>Sudden visual loss</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>Loss of eyesight to both eyes; Vision loss</td>
</tr>
<tr>
<td>Night sweats</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>Night sweats; Night fever sweats</td>
</tr>
<tr>
<td>Painful eyes</td>
<td>0</td>
<td>9</td>
<td>0</td>
<td>10</td>
<td>Shooting pain left eye; Pain right eye</td>
</tr>
</tbody>
</table>
Background: Evidence supporting the classification of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) based on ANCA type is accumulating.1

Objectives: To evaluate serum cytokine profiles in patients with AAV classified by ANCA specificity (proteinase 3 (PR3)-ANCA versus myeloperoxidase (MPO)-ANCA) or by clinical diagnosis (granulomatosis with polyangitis (GPA) versus microscopic polyangiitis (MPA)) and clinical phenotypes.

Methods: An antibody array testing 30 soluble mediators, already shown to be implicated in the pathogenesis of AAV, was performed in each patient with active AAV at inclusion in the Rituximab in ANCA-Associated Vasculitis (RAVE) trial, as previously described.2,3 By means of Wilcoxon signed rank test for univariate analyses, we analyzed the association of levels of these cytokines with ANCA specificities, clinical diagnosis, and distinct clinicopathologic phenotype characteristics derived from the BVAS/WG items recorded at the time of enrollment (capillaritis, granulomatous manifestations, renal involvement, and alveolar hemorrhage; new diagnosis and relapsing disease), as described.4

Results: All cytokines tested (see Figure 1 and legend for the complete list), except for RANTES, ACE, bFGF and VCAM-1, were significantly increased in the RAVE cohort when compared to healthy controls (p < 0.05). Median Birmingham vasculitis activity score and steroid use at screening did not significantly differ between PR3-AAV and MPO-AAV, and between GPA and MPA. Within both ANCA specificities, levels of 9 mediators were significantly higher in PR3-AAV (IL-6, NGFβ, GM-CSF, IL-15, IL-18, IL-18Bβ, sIL-2Ra, IL-8, TARC) than with MPO-ANCA specificity (Table 1). Similarly, the differences associated with PR3-AAV (Figure 1).

Conclusions: Cytokine profiles separate patients more clearly by ANCA specificity than by clinical diagnosis, suggesting important differences in underlying pathophysiology and validating stratification of patients by ANCA specificity for clinical trials.

Acknowledgments: The authors report no conflict of interest.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4225

FRI0316 FACTORS ASSOCIATED WITH SURGICAL OUTCOMES OF SEVERE AORTIC REGURGITATION IN PATIENTS WITH BEHÇET’S DISEASE
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Background: In rare cases, Behcet’s disease (BD) can cause severe aortic regurgitation (AR) or aortic root destruction that might have lethal outcomes. Conventionally, simple aortic valve replacement (AVR) is performed for the management of severe AR in BD patients; however, the reoperation rate is as high as 78 to 100%, while mortality rate range from 20 to 47%. Recently, several series of case reports showed that compared to AVR, aortic root replacement (ARR) improved the surgical outcomes of AR in BD patients.

Objectives: To identify the factors associated with the long-term surgical outcomes of AR in BD patients.

Methods: We identified 23 patients who had been surgically treated for AR caused by aortic root involvement of BD from January 1996 through December 2013. We evaluated the occurrence of post-surgical adverse events, which were defined as follows: death, aortic valve/graft problem, infective endocarditis, cerebral infarction, and/or re-operation of aortic valve or root. Types of surgery were classified as simple aortic valve replacement (AVR), bioprosthesis aortic root replacement (ARR), and mechanical valve composite graft aortic root replacement (cARR). Clinical parameters including baseline characteristics, C-reactive protein (CRP), erythrocyte sedimentation rate, and medications were extracted from electronic medical records.

Results: Appropriate aortic valve or root surgery cases were 35 in total, with a mean follow up duration of 11±5 years in 23 patients. Out of the 11 cases

Table 1. Clinical features in patients with and without vascular involvement

<table>
<thead>
<tr>
<th>With vascular involvement</th>
<th>Without vascular involvement</th>
<th>OR 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>176 (25.4)</td>
<td>516 (74.6)</td>
<td>1.72</td>
</tr>
<tr>
<td>Uveitis</td>
<td>127 (17.2)</td>
<td>217 (42.2)</td>
<td>0.76</td>
</tr>
<tr>
<td>Genital ulceration n (%)</td>
<td>123 (69.9)</td>
<td>392 (76.1)</td>
<td>0.72</td>
</tr>
<tr>
<td>Patent pulmonary artery or</td>
<td>79 (45.6)</td>
<td>164 (32.2)</td>
<td>1.72</td>
</tr>
<tr>
<td>Acneiform rash n (%)</td>
<td>101 (35.5)</td>
<td>157 (27.1)</td>
<td>1.72</td>
</tr>
</tbody>
</table>

Elevated levels of 10 mediators were significantly higher in patients with vascular involvement (Table 1). AR involvement was detected in 52 (28.9%) of 176 patients with vascular involvement. Deep venous thrombosis alone was present in 125 (71%) patients, arterial involvement alone in 12 (6.8%) patients, arterial and venous involvement together detected in 40 (22.7%) patients. Arterial involvement was most commonly seen as pulmonary artery involvement in 45 (25.6%) patients (pulmonary artery thrombosis 35 (20%), aneurysm 10 (7.7%) and thrombosis + aneurysm 6 (3.4%) patients). Twenty (11.3%) patients had other arterial involvement except pulmonary, 8 of them had thrombosis and 12 had aneurysm.

Conclusions: Vascular involvement in Behcet’s disease is commonly seen in males. Deep vein thrombosis is the most common form of vascular involvement. Arterial involvement is important because of its higher risk of mortality (especially pulmonary artery aneurysm). The incidence of EN and uveitis is higher in patients with vascular involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4225

FRI0315 CLINICAL CHARACTERISTICS OF VASCULAR INVOLVEMENT IN BEHÇET’S DISEASE
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Background: Behcet’s disease (BD) is a multisystem inflammatory disorder classified as vasculitis, which can affect all types of vessels. The prevalence of vascular involvement has been reported at rates ranging from 15 to 50%.

Objectives: In this study, we aimed to determine the characteristics of vascular involvement in patients with BD.

Methods: Six hundred and ninety-two patients with BD, who applied to the multidisciplinary BD polyclinics from 2006–2016, were retrospectively analyzed. The diagnosis of vascular involvement was made on clinical signs, by Doppler ultrasonography and/or angiography using computed tomographic or magnetic resonance techniques where appropriate.

Results: One hundred and seventy-six patients (64.4%) had vascular involvement. The mean age of patients with vascular involvement (n=176) and non-vascular involvement (n=516) was similar to 42±13.2 and 42±12.2 years, respectively, while male sex frequency was significantly higher in patients with vascular involvement (72% vs 42%, p<0.001). Uveitis (45%) and erythema nodosum (EN) (47.7%) were significantly higher in patients with vascular involvement than those without vascular involvement (for Uveitis OR: 1.7, p=0.003/for EN: OR: 2.5, p<0.001) (Table 1).

Table 2. Venous involvement (%)

<table>
<thead>
<tr>
<th>With vascular involvement</th>
<th>Without vascular involvement</th>
<th>OR 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis</td>
<td>142 (80.7)</td>
<td>186 (57.4)</td>
<td>1.72</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>26 (14.7)</td>
<td>27 (14.7)</td>
<td>1.72</td>
</tr>
<tr>
<td>Femoral vein thrombosis</td>
<td>36 (20.5)</td>
<td>18 (10.2)</td>
<td>1.72</td>
</tr>
<tr>
<td>Patent pulmonary artery or</td>
<td>43 (24.4)</td>
<td>184 (57.4)</td>
<td>1.72</td>
</tr>
<tr>
<td>Acneiform rash n (%)</td>
<td>101 (51.4)</td>
<td>157 (27.1)</td>
<td>1.72</td>
</tr>
</tbody>
</table>

Conclusions: Vascular involvement in Behçet’s disease is commonly seen in males. Deep vein thrombosis is the most common form of vascular involvement. Arterial involvement is important because of its higher risk of mortality (especially pulmonary artery aneurysm). The incidence of EN and uveitis is higher in patients with vascular involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5672

FR0315 - CLINICAL CHARACTERISTICS OF VASCULAR INVOLVEMENT IN BEHÇET’S DISEASE

Cleveland, United States; 2University Medical Center, Groningen, Netherlands; 3Johns Hopkins University, Baltimore; 4Hospital for Special Surgery, New York; 5Duke University Medical Center, Durham; 6Massachusetts General Hospital; 7Boston University, Boston, United States

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5672
that underwent AVR, post-surgical events were observed in 8 (73%) cases. Out of the 12 BARR cases ( xenograft in 5 cases and homograft in 7 cases), 9 (75%) cases had post-surgical adverse events. Out of the 12 cARR cases, post-surgical adverse events occurred in 4 (33%) cases. Multivariable Cox proportional hazards model indicated that levels of CRP at 1 month after discharge and age at admission were independent prognostic factors associated with event-free probability. Notably, performing cARR was the most significant factor that affected the surgical outcome (HR [95% CI] 0.147 [0.028 – 0.766], p=0.023).

Conclusions: In BD patients with severe AR, the occurrence rate of post-surgical adverse events was associated with the levels of CRP at 1 month after discharge, age at operation, and type of surgery. cARR may be a better surgical option in BD patients with aortic root involvement

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5856

FR10317 | HUMORAL AND CELLULAR IMMUNITY TO VARICELLA-ZOSTER VIRUS IN GIANT CELL ARTERITIS PATIENTS: NO EVIDENCE OF VIRAL REACTIVATION AT ONSET OF DISEASE
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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are strongly overlapping diseases that are thought to have a shared etiology [1]. The observation of varicella-zoster virus (VZV) antigen in temporal artery biopsies of GCA patients led to the hypothesis that VZV might be a trigger for the onset of the disease [2]. Herpes zoster occurs when the latently present VZV reactivates. It has been reported that patients with GCA do not appear to be at increased risk of herpes zoster compared with age and sex matched controls, even during treatment with high dose glucocorticoids [3]. Levels of VZV specific immunoglobulin G (VZV-IgG) are known to only slowly decline again after a reactivation [4]. We therefore hypothesized, in line with the proposed etiologic role, to find higher VZV-IgG levels in GCA and PMR patients at disease onset, compared to healthy controls. Furthermore, we expected to find no differences in cell-mediated immunity to the virus between patients and controls assuming that the incidence of herpes zoster is not increased in GCA.

Objectives: To investigate humoral and cellular immunity to VZV in GCA and PMR patients and compare these to results in age-and sex matched healthy controls.

Methods: Antibody responses to VZV glycoprotein were measured in serum samples of 35 GCA patients and 26 PMR patients at baseline (before glucocorticoid treatment) and during follow up, and in 58 healthy controls by an enzyme-linked immunosorbent assay (ELISA). Cell-mediated immunity to VZV was determined by performing interferon-γ (IFNγ) enzyme-linked immunosorbent spot (ELISPOT) and intracellular cytokine flow cytometry measurements in 11 GCA patients and 15 PMR patients, and in 26 age and sex matched healthy controls.

Results: Similar levels of VZV-IgG were found in GCA and PMR patients at baseline, and healthy controls. The number of VZV specific IFNγ spot-forming cells was significantly lower in GCA patients than in healthy controls (p<0.02), but not different in PMR patients compared to healthy controls.

Conclusions: Since antibody levels at baseline were not different in GCA and PMR patients compared to healthy controls it seems unlikely that VZV has an important role in the aetiology of GCA or PMR. The finding of a decreased cell-mediated immunity in GCA patients, especially after treatment with high dose corticosteroids may indicate an increased risk of developing herpes zoster.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3756
**FR0319** PREDICTORS OF COMPLETE REMISSION IN POLYMYALGIA RHEUMATICA

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory rheumatologic condition characterized by aching and morning stiffness in the shoulders, hip girdle, and neck that typically occurs in adults over the age of 50. A rapid resolution of symptoms with low-dose glucocorticoids is a feature of PMR although some patients may experience a disease flare-up during steroid tapering.

**Objectives:** The aim of the study was to investigate possible clinical or laboratory prognostic factors of remission during a 12 month follow up in PMR patients treated with a starting low prednisone dose following the 2015 ACR-EULAR guidelines.[1]

**Methods:** From 86 consecutive outpatients, diagnosed with PMR following ACR/EULAR 2012 provisional clinical criteria for PMR,[2] 79 patients (56 women and 23 men), that achieved a complete follow up of at least 12 months, were selected. Clinical evaluation and laboratory tests were performed every 3 months. Clinical remission was defined as lack of shoulder and hip girdle pain and as levels of ESR ≤ 40 mm/h and CRP ≤ 0.5 mg/dl.

**Results:** 37 PMR patients reached a complete remission after twelve months follow-up. We didn’t find any significant difference in the mean age and in ESR and CRP values at the beginning of the disease in patients in remission after 12 month of follow up when compared with patients not in remission. Presence of obesity, dyslipidemia, hypertension, diabetes and smoking habits were not significantly different in the two groups of patients. No significant difference in steroid therapy at the beginning and after 6 month of follow up was noted between the two groups of patients. No significant difference in the mean age and in ESR and CRP levels of ESR [33.9% versus 78.2%, p=0.000] Moreover it was shown that the patients achieving clinical remission at the 12 month follow up had statistically significantly higher CRP values, instead of ESR ones, when compared with male complete clinical remission patients. A statistically significant female low clinical remission was seen at the end of 12 month follow up when compared with patients not in remission.

**Conclusions:** The sixth month of therapy is a crucial target for the management of PMR, because it can help to identify patients at greater risk of exacerbations, which may benefit from a tighter follow up and a more aggressive therapeutic strategy. Among prognostic factors female sex and high CRP values at sixth months appear to be associated with higher relapse risk and a longer duration of treatment.

**References:**

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**FR0320** PREDICTIVE VALUE OF PLATELET TO LYMPHOCYTE RATIO IN RENAL INVOLVEMENT IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS

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**Background:** Granulomatosis with polyangiitis (GPA) is a granulomatous necrotizing vasculitis with high morbidity and mortality. Anti-neutrophil cytoplasmic antibody (ANCA) is a valuable diagnostic marker, however its titer lacks predictive value for the severity of organ involvement. Platelet to lymphocyte ratio (PLR) and mean platelet volume has been regarded as a potential marker in assessing systemic inflammation.

**Objectives:** We aimed to investigate PLR and MPV as inflammatory marker in patients with GPA.

**Methods:** GPA patients and age-sex matched healthy controls were included. Demographic, clinical and laboratory information were extracted from medical records. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), platelets (PLT), lymphocyte and neutrophils counts and mean platelet volume were analyzed. Disease activity was assessed with Birmingham Vasculitis Activity Score for WG vasculitis (BVAS/WG).

**Results:** 56 patients with GPA and 53 healty controls were included. Clinical characteristics and laboratory findings of the study population are shown in Table 1. ESR, CRP, MPV and PLR were significantly higher in patients with GPA than controls. PLR positively correlated with ESR and CRP (r=0.389, p<0.005 and r=0.512 p<0.001 respectively). In contrast, MPV negatively correlated with ESR and CRP (r=-0.308, p=0.028 and r=-0.337 p=0.014 respectively). There were no significant correlation between PLR, MPV and BVAS/WG. Patients with renal involvement had statistically significantly higher PLR than patients without renal involvement (303.01±287.33 vs 177.98 + 75.43, p: 0.020 respectively). Moreover PLR negatively correlated with glomerular filtration rate (r=-0.266 and p:0.009, n=0.389). Receiver operating characteristic curve of PLR, ESR and CRP for differentiating renal involvement is presented in Figure 1. Area Under Curves (AUCs) for PLR, ESR and CRP were 0.703 (95% confidence interval [CI], 0.558–0.849, p=0.016), 0.577 (95% CI: 0.416–0.738, p=0.382), 0.508 (95% CI: 0.337–0.678, p=0.929), respectively. The cutoff level of PLR was 204 (sensitive 65.6%, specifity 62.5%, positive predictive value 70%, negative predictive value 57.7%). Patients with alveolar hemorrhage tended to have higher PLR but this difference did not reach statistically significance (266.60 + 182.90 vs 240.61 + 252.43 p=0.382, respectively).

**Conclusions:** Results suggest that PLR exhibit favorable diagnostic performance in predicting renal involvement in patients with GPA.

**References:**

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6262
Circulating IL-6 and Other Metabolic Biomarkers as Assessment of Damage and Prognosis in Patients Comparing Biopsy Proven Giant Cell Arteritis in

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Background: GCA may be an interleukin-6 (IL-6) driven disease and IL-6 blockade is emerging as an exciting therapy of IL-6. We measured serial IL-6 levels in new patients with GCA treated in an RCT of modified-release prednisone (MR) versus immediate-release prednisolone (IR) used in a tapering regimen conforming to BSR guidelines.

Methods: Patients (n=12) were randomised into two treatment arms (7 MR, 5 IR) and followed up over 26 weeks. IL-6 samples were collected at 09h at weeks 4, 10, 18 and 26 and were measured using Beckman Coulter IL-6 immunoassay, validated in a controlled study according to ACB criteria. We also measured bone markers (CTX, P1NP, vitamin D), HaB1c, cortisol, ACTH and PTH.

Results: Significantly higher overall mean IL-6 levels were seen in the IR arm (n=5) compared to MR (n=7) [unpaired two-tailed Student’s t test]. IL-6 levels in both arms were lowest between weeks 4–10 and continued to decrease in the IR arm to week 26, whereas lower but constant levels were seen in the MR arm (Figure).

Mean CTX concentration was significantly higher at week 4 (M =0.29, SE =0.04) compared to Week 26 (M =0.13, SE =0.02) p=0.002. No significant difference was seen between treatment arms.

Patients on MR had complete suppression of ACTH compared to IR (p<0.05) without a significant difference between groups in 9am cortisol levels (p=0.3412).

Conclusions: Our study suggests that elevated levels of IL-6 are better suppressed by MR prednisone therapy compared to IR prednisolone in new GCA. Bone resorption marker CTX was significantly reduced in both treatment arms. ACTH suppression with MR prednisone may reflect a greater impact on the HPA axis although cortisol levels were not affected.

Our findings suggest that MR prednisone may warrant further clinical trial investigation in GCA.

References:

Acknowledgements: Napp Pharmaceuticals Limited, Beckman Coulter, Gabriel Labinjo for technical support.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6473

Assessment of Damage and Prognosis in Patients with Adult IGA Vasculitis: Retrospective Multicentered Cohort Study

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Background: IGA Vasculitis is a leukocytoclastic vasculitis involving small vessels with depositions of immune complexes containing IgA. There is limited data for the prognosis of adult IGA Vasculitis, with also no damage assessment.

Objectives: We aimed to evaluate the clinical characteristics, treatment, outcome and damage of patients with adult IGA Vasculitis.

Methods: We assembled a retrospective cohort of patients with adult IGA Vasculitis, from tertiary Rheumatology Centers in Turkey. All data were abstracted from medical records. Birmingham Vasculitis Activity Score (BVAS),prognostic Five Factor Score (FFS) and vasculitis damage index (VDI) were calculated.

Results: The study included 52 (male/female:40/12) patients with adult IGA Vasculitis. The mean age was 42.2±17 years. Infection history within 6 weeks before presentation was present in 22 (42.3%) patients (18 upper respiratory tract, 3 gastrointestinal and 1 urinary tract). Cutaneous manifestations were the most common clinical manifestations (Table 1). All patients were treated with oral glucocorticoids (GC). As additional immunosuppressive agents, azathioprine was given to 21 (40.4%) and pulse cyclophosphamide to 11 (21.2%) patients. Twenty-eight patients (53.9%) had follow-up of 28.6 months. Five (17.8%) patients relapsed during follow-up. While 3 relapses were major, 2 of them were minor relapses. At the last visit, disease status was evaluated as active or treatment failure by the treating physician in 6 (21.4%) patients. Mortality was 3.6% (n=1) during follow-up, due to pneumonia. The mean VDI score was 0.6 in the last visit. Nine (32.1%) patients had at least one damage item at the end of follow-up period.

Table 1. Clinical characteristics of patients with adult IGA Vasculitis

<table>
<thead>
<tr>
<th>Laboratory parameters</th>
<th>Clinical Manifestations, n/52 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte Sedimentation Rate (mm/hour)*</td>
<td>Fever</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Proteinuria (&gt;300mg/24 hours)</td>
<td>Myalgia/Weakness/Leg tenderness</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>Arthritis and/or arthralgia</td>
</tr>
<tr>
<td>3.7±2.2</td>
<td>14 (26.9%)</td>
</tr>
<tr>
<td>25.2 ±1 (94.9)</td>
<td>46 (88.5%)</td>
</tr>
<tr>
<td>28 ±53.9%</td>
<td>1 (1.9%)</td>
</tr>
<tr>
<td>9.0±0.4</td>
<td>Testicular pain or tenderness</td>
</tr>
<tr>
<td>7 ±13.5%</td>
<td>Recent onset or severe hypertension</td>
</tr>
<tr>
<td>5 ±5.8%</td>
<td>2 ±3.8%</td>
</tr>
<tr>
<td>48 ±92.3%</td>
<td>Cutaneous Manifestations</td>
</tr>
<tr>
<td>39 ±75%</td>
<td>Gastrointestinal manifestations</td>
</tr>
<tr>
<td>29 ±55.8%</td>
<td>FFS=0</td>
</tr>
<tr>
<td>15 ±28.8%</td>
<td>FFS=1</td>
</tr>
<tr>
<td>8 ±15.4%</td>
<td>BVAS score at diagnosis*</td>
</tr>
</tbody>
</table>

Conclusions: Our results showed that approximately one fifth of patients with adult IGA Vasculitis had relapses during follow-up. At the end of follow-up, one third of patients had at least one damage item. Although, 45% of patients had FFS=1, the mortality rate was observed to be low in the present study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3865

Comparison of Biopsy Proven Giant Cell Arteritis in North America and Southern Europe: A Population-Based Study

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Objectives: To compare clinical characteristics, treatment, long-term follow-up and prognosis of two population-based cohorts of patients with biopsy-proven giant cell arteritis (GCA) from Olmsted County, Minnesota, USA (Olmsted cohort) and the Reggio Emilia area, Northern Italy (Reggio cohort).

Methods: All patients residing in Olmsted County and the Reggio Emilia area

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8458
with a new diagnosis of biopsy-proven GCA in 1986–2007 were retrospectively identified. Patients were followed from GCA diagnosis to death, migration or September 2011. Comparisons were performed using Chi-square and rank sum tests, Kaplan-Meier methods and Cox models.

**Results:** The study included 110 patients in the Olmsted and 144 in the Reggio cohort. Compared with the Olmsted cohort, patients from the Reggio cohort were younger (mean±SD age 74.6±7.4 years vs 77.8±7.6, p=0.002), more likely to have cranial symptoms (93% vs 86%, p=0.048), temporal artery abnormalities at physical examination (68% vs 42%, p<0.001), partial or complete unilateral or bilateral permanent vision loss (21% vs 6%, p=0.001), systemic symptoms (87% vs 46%, p=0.001) and polymyalgia rheumatica at or before GCA diagnosis (47% vs 26%, p<0.001). Scalp tenderness was less common in the Reggio cohort (36% vs 49%, p=0.033). ESR and CRP were higher (mean 88±22 mm/h vs 73±77, p=0.001 and mean 89±60.2 mg/L vs 35±24.3, p=0.001 respectively) and gait was more likely lower (mean 11.2±1.4 g vs 11.8±1.4, p=0.004) in Reggio than in the Olmsted cohort. Patients from the Olmsted cohort received a higher initial prednisone dose (mean 53.6±15.3 mg/day vs 49.5±12.8, p=0.001). There were no differences in relapse rates, cumulative glucocorticoid (GC) dosages at 1, 2 and 5 years, and time to first GC discontinuation. However, the Reggio cohort reached a prednisone dose <10 mg/day sooner (median 4.9 months vs 7.9, p=0.012) and had a first relapse later (median 13.6 months vs 7.9, p=0.003) than the Olmsted cohort. Patients from the Reggio cohort had a significantly higher mortality compared to those from the Olmsted cohort (HR 1.72, 95% CI 1.12–2.65 for age and sex).

**Conclusions:** Genetic and/or environmental factors may contribute to the differences in clinical characteristics and disease outcomes observed in this study comparing patients with GCA from North America and Southern Europe.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5156

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**FRI0324**

**SMALL VESSEL VASCULITIS SURROUNDING A PRESERVED TEMPORAL ARTERY: A DIAGNOSTIC ALGORITHM TO ASSESS CLINICAL SIGNIFICANCE**


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**Background:** Systemic vasculitides are complex and heterogeneous diseases, with overlapping features that frequently pose a diagnostic challenge to clinicians. The temporal artery biopsy (TAB) is the gold standard for the diagnosis of giant cell arteritis (GCA) but, occasionally, TAB show inflammation of small vessels surrounding a spared temporal artery (SVV) as the only pathologic finding. Ultimate diagnosis and, consequently, optimal treatment remain uncertain in these patients.

**Objectives:** To analyze the final diagnosis of patients with SVV surrounding a spared temporal artery after a pre-established diagnostic algorithm and to identify clinical and laboratory findings with potential usefulness in predicting the ultimate diagnosis.

**Methods:** Patients with TAB showing SVV were subjected to the diagnostic algorithm displayed in figure 1, completed by at least 1 year follow-up. Clinical and laboratory features at the time of diagnosis were recorded. The algorithm led to the following final diagnosis: GCA, other systemic vasculitides and undetermined condition. Chi-square and/or X2-squared and/or ANOVA tests were used for statistical comparison using IBM SPSS Statistics 20.

**Results:** From 1998 to 2007, 380 TAB were performed in our institution. Biopsy disclosing small vessel inflammation surrounding a normal temporal artery (SVV) was described in 47 (12%) patients. In all patients TAB was selected as the first invasive procedure because GCA was initially considered the most likely diagnosis. Accordingly, 24 (51%) fulfilled at least 3 ACR classification criteria for GCA. 7 patients declined to undergo subsequent work-up to complete the diagnostic algorithm, 10 died or were lost to follow-up before completing 1 year follow-up. The study cohort consisted of 30 patients (19 women and 11 men) aged 77±10.4 years followed for 55.16±55.20 months. In 13 patients the final diagnosis was consistent with GCA based on the absence of SVV in other territories, large-vessel inflammation by imaging or subsequent development of aortic aneurysm; in 12 SVV was subsequently demonstrated in other territories and were diagnosed with other systemic vasculitis (7 AAV, 0 cryo, 3 PAN, 0 vasculitis associated to autoimmune diseases, 2 unclassified small vessel vasculitis), and in 5, diagnosis remained undetermined. No significant differences in clinical or routine laboratory abnormalities were found among patient subgroups stratifying according to the final diagnosis.

**Conclusions:** Inflammation of small vessels surrounding a spared temporal artery in a TAB conveys a substantial diagnostic uncertainty. After a detailed diagnostic work-up most of patients can be diagnosed with GCA. However other systemic vasculitides requiring more aggressive treatment may disclose similar histopathologic findings and are therefore frequent diagnosis remaining undetermined in a substantial proportion of cases. Search for more accurate molecular biomarkers is necessary for a better interpretation of these findings.

**Acknowledgements:** Supported by PI15/00092, Plan Estatal de Investigación Científica y Técnica de 2013–2016 and cofinanciado by the ISCIII.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5156

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**FRI0325**

**PREVALENCE OF TAKAYASU ARTERITIS IN YOUNG WOMEN WITH ACUTE ISCHEMIC HEART DISEASE**

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**Background:** Takayasu arteritis (TA), a systemic vasculitis typically occurring in female patients aged <40, can affect the coronary arteries and cause ischemic heart disease. The prevalence of TA among young females with acute ischemic heart disease is undetermined.

**Objectives:** In this study, we investigated the prevalence of TA in young women presenting with ischemic heart disease in the Emergency Department.

**Methods:** We conducted a retrospective evaluation of the hospital records of 172,790 consecutive female patients aged <45, who accessed the Emergency Department of our institution over 8 consecutive years (2007–2015). The prevalence of TA and of other etiologies of ischemic heart disease was determined. Diagnosis of TA was established based on the 1990 American College of Rheumatology criteria.

**Results:** Overall, 2,090 women aged <45 presented to the Emergency Department with chest pain, dyspnea, palpitations, angina, heart failure, or cardiac arrest; 40 had confirmed acute ischemic heart disease. The etiology was "classic" atherosclerosis in 24 cases (60%), TA in 4 cases (10%), vasospasm and sympathomimetic drug abuse in 3 cases each (7.5%), coronary artery dissection and microvascular angina in 2 cases each (5%), Takotsubo and radiation-induced cardiomyopathy in 1 case each (2.5%).

**Conclusions:** Although a diagnosis of TA is likely to be overlooked, TA is not infrequent in younger females presenting with acute ischemic heart disease. Specifically, TA accounted for 10% of cases of acute ischemic heart disease in female patients aged <45, a finding relevant to the diagnosis and management of these young patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5504

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**FRI0326**

**RECOMMENDATIONS FOR THE MANAGEMENT OF NEURO-BEHÇET DISEASE BY JAPANESE RESEARCH COMMITTEE FOR BEHÇET DISEASE**


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**Background:** Central nervous system involvement is one of the most serious complications in Behçet’s disease (BD). This condition is referred to as neuro-
Behçet’s disease (NB) and can be classified into acute type (ANB) and chronic progressive type (CPNB) based upon differences in the clinical course and responses to corticosteroid treatment. Diagnostic criteria were generated in 2013 based on a multicenter clinical survey performed by the Behçet’s Disease Research Committee of the Ministry of Health, Labor and Welfare of the Japanese Government. Although “Guidelines for Treatment of NB” was also proposed based on the survey, it is still preliminary.

Objectives: The aim of the current study is to develop evidence-based recommendations for the management of NB supplemented by expert opinions where necessary.

Methods: First, clinical questions (CQs) on NB were extracted from a literature search for problem areas and related keywords, and draft CQs and a flow chart were prepared. The expert committee, a task force of the research subcommittee for NB, consisted of 7 board-certified rheumatologists (one was also a board-certified neurologist) and 3 board-certified neurologists. A systematic literature search was performed using Medline and the Japanese Medical Abstract Society databases from 1997 to 2016. A total of 15 initial CQs were generated. These yielded the final recommendations developed from 3 blind Delphi rounds, in which the rate of agreement scores on CQs (range 1 [disagree]–5 [strongly agree]) was determined through voting by the whole committee.

Results: Thirteen recommendations were developed for the management of NB (general 1, ANB 7, CPNB 5). The strength of each recommendation was established based on the evidence level as well as rate of agreement. There was excellent concordance between the level of agreement of rheumatologists and that of neurologists. Based on these recommendations, a flow chart was established for the management of ANB and CPNB (Figure).

Conclusions: The recommendations generated in this study are mainly based not only on expert opinions but on the results of uncontrolled evidence from open trials and retrospective cohort studies. Guidelines that can be used for international studies are needed, for which verification by further properly designed controlled clinical trials is required.

Disclosure of Interest: None declared


GASTROSCOPIC FEATURES AND CLINICAL CHARACTERISTICS IN 172 CASES OF CHILDREN WITH HENOCH-SCHONLEINPURPURA

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Objectives: To investigate gastroscopic features and explore the relationship between clinical characteristics in children with Henoch-Schönlein purpura (HSP).

Methods: To take gastroscope in 172 cases of children with HSP in our hospital and summarize the gastroscopic performance. All the case were divided into two groups by gastroduodenal mucosal bleeding or not. It was compared among the total time of abdominal pain, pain relief, hospitalization, fasting and kidney injury case in the groups.

Results: Gastroscope with varying degrees of injury of 172 cases has accounted for 169 cases (98.3%). Gastroscopic manifestations include gastroduodenal mucosal congestion, edema, rough, erosion, bleeding and ulcer, which involved 148 cases of gastric (86.0%), 158 cases of duodenal involvement (91.9%). Mucosal erosion and bleeding occurs mainly in duodenum, mostly in the descending duodenum. Duodenal bleeding accounted for 36 cases (21.8%) in the bulb and 92 cases (55.8%) in the descendant. Only five cases (2.9%) of duodenum occurred in the duodenum, where four cases of bulb ulcer, one case of descending ulcer. Esophageal and gastric cardia mucosal just occurred in one case. There were not significant difference (P>0.05) among the time of abdominal pain, pain relief, hospitalization and fasting in the group. There was no significant difference (P>0.05) in the incidence of kidney injury between two groups of children during hospitalization.

Conclusions: Gastroscopic features of HSP in children is characterized by bleeding, erosion of duodenal mucosa and occasional duodenal ulcer formation, which mostly involve the antral mucosa, rarely involving the esophagus, cardia. There was no significant difference (P>0.05) among the severity of gastroscopic performance and the time of abdominal pain, fasting, hospitalization and kidney injury of the cases during hospitalization.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2127

THE DIAGNOSTIC VALUE OF ALPHA-1-ANTITRYPSIN PHENOTYPE IN SYSTEMIC VASCULITIS

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Background: Deficiency of alpha-1 protease inhibitor, or alpha-1-antitrypsin (A1AT) is a frequent genetic disorder, which is characterized by low serum level of A1AT and usually manifests as pulmonary emphysema and liver disease. Also the deficiency of A1AT is known to be associated with granulomatosis with polyangiitis (GPA). The influence of A1AT deficiency on GPA clinical course is not clarified.

Objectives: The aim of this study was to estimate the prevalence of pathological A1AT phenotypes in GPA and other systemic vasculitides and to define the influence of A1AT phenotype on clinical course of GPA.

Methods: We enrolled 86 patients with systemic vasculitides, including GPA (N=47), microscopic polyangiitis (MPA, N=16), eosinophilic granulomatosis with polyangiitis (EGPA, N=12), polyarteritisnodosa (PN, N=11). 46 healthy donors were included in the control group. All blood samples underwent A1AT phenotyping by isoelectrofocusing (IEF) and turbidimetric A1AT measurement. The results of phenotyping were compared to clinical data, such as BVAS activity rate (Birmingham Vasculitis Activity Score), VDI index (vasculitis damage index), organs involvement, inflammatory markers, including antineutrophil cytoplasmic antibodies (ANCA), total IgG concentration and serum levels of C3, C4 complement factors.

Results: Pathological A1AT phenotypes were found in 17% (8/47) of GPA patients, 6.25% (1/16) of MPA patients, 2% (1/46) of healthy donors and were never found in EGPA, PN. The abnormal phenotypes in GPA were ZP2Z, 4P4M, 2P2M, 1P2MS, and 1P1MS phenotype was identified in MPA patient. Levels of lung and upper respiratory tract was observed in all patients with pathological phenotypes A1AT (N=4), while in normal phenotype A1AT it was present in 72% and 82% respectively. The mean concentration of A1AT was significantly lower in GPA patients with abnormal A1AT phenotypes, than in patients with normal phenotype A1AT (respectively 100±148.8 and 196±127.9 mg/L, p<0.01). The average activity index by BVAS index in GPA was significantly higher in patients with pathological phenotype A1AT than in patients with normal phenotype A1AT (24.6±2.897 and 18.5±1.44 points, p<0.05). Also we revealed excess levels of VDI in cohort of patients with abnormal phenotypes A1AT, rather than in cohort of patients with normal phenotype A1AT (6.3±3.1 versus 5.4±2.6, p<0.05). The average values concentration of antibodies to proteinase-3 in GPA patients with pathological phenotype A1AT were significantly higher compared to GPA patients with normal phenotype A1AT (11.1±3.4 and 2.3±1.1 (p<0.05)) respectively. In GPA patients with mutated A1AT phenotypes levels of serum creatinine (<0.05), levels of total IgG concentration and serum levels of C3 and C4 complement factors (<0.05) also were significantly higher than in group of GPA patients with normal A1AT phenotype.

Conclusions: Pathological A1AT phenotypes are more often observed in GPA patients who have more severe GPA clinical course and higher immunological disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4412

EFFICACY AND SAFETY OF INFlixIMAB ORIGINATOR IN PATIENTS WITH TAKAYASU ARTERITIS WITHIN THE RTU (TEMPORARY RECOMMENDATION OF USE) IN FRANCE

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Background: The benefit/risk ratio of infliximab in refractory patient with Takayasu arteritis (TA) is assumed to be favorable, based on retrospective studies with limited sample size [1, 2] in which infliximab has been prescribed off-label. Since 2013, the French Temporary Recommendation of Use (RTU) provides a temporary framework allowing the use of infliximab originator in “TA patients refractory to conventional treatment” during a 3-year period.

Objectives: The aim of the study was to evaluate the real-life efficacy and safety of infliximab originator in TA patients initiating or with ongoing infliximab treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4412
**Methods:** Prospective, multicenter, observational, open-label, study of TA patients treated with infliximab originator.

**Results:** As of 2016 (2 years of follow-up), the study included 14 patients (13/14 were female; median age 32 [range 12–56] years) with TA (diagnosis according to Ishikawa criteria). At study entry, the median TA duration was 4.7 (0.4–16) years, 11 patients had pathergy and 1 patient had pseudofolliculitis. 9 had uveitis, 9 had erythema nodosum, 12 had arthritic involvement, 5 patients had gastrointestinal involvement, 4 had pathergia, 1 had orchitis and 1 had gastrointestinal involvement. Thirtwoy seven had BVAS ≥ 1. As shown in Table 1, both the HADS-depression (HADS-D) (4.7 vs 2.5) and HADS-anxiety (HADS-A) (8.3 vs 5.7) scores were elevated in BD patients compared to healthy controls. FACIT-F was higher in healthy controls in comparison with BD group (44.1 vs 36.6), revealing lower levels of fatigue. There were no differences between gender on these scores.

**Conclusions:** In our study, fatigue and increased levels of anxiety and depression were more common in BD patients. Contrary to the study of Ilhan et al., we found that fatigue was not higher in patients with active disease. Similarly, there were no correlation between the assessed scores and gender. In spite of these results, the authors believe that controlling the symptoms may improve the quality of life in BD patients.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4459

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**FR0331 | IDENTIFICATION AND VALIDATION OF POTENTIAL METABOLOMIC BIOMARKERS FOR RELIABLE DIAGNOSIS OF BEHÇET’S DISEASE USING GAS CHROMATOGRAPHY WITH TIME-OF-FLIGHT MASS SPECTROMETRY**

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**Background:** Although many diagnostic criteria have been developed and revised by experts in the field, diagnosing Behcet’s disease (BD) is still complicated and challenging. Metabolomic studies can lead to a better understanding of pathophysiological processes and may uncover new diagnostic markers for classification of disease subgroups and assessment of disease activity in rheumatic diseases. No metabolomic studies on serum have been attempted to improve the diagnosis and to identify potential biomarkers of BD.

**Objectives:** The purpose of this study was to investigate distinctive metabolic changes in serum samples of BD patients and to identify metabolite candidate biomarkers for reliable diagnosis of BD using the metabolomics platform.

**Methods:** Metabolomic profiling of 90 serum samples from 45 BD patients and 45 healthy controls (HC) was performed via gas chromatography with time-of-flight mass spectrometry (GC/TOF-MS) with multivariate statistical analyses. Thirty-five patients with BD and age- and sex-matched 35 HCs were randomly selected to form the discovery set, and the validation set is composed of 10 patients with BD and 10 HCs.

**Results:** We identified a total of 104 metabolites in the serum samples of the discovery set. To maximise the discrimination between groups BD and HCs, we applied supervised partial least squared-discrimination analysis (PLS-DA). A PLS-DA score plot of the discovery set indicated that the cluster of BD patients is well separated from HC clusters in component 1. The variation values of the PLS-DA model were R² = 0.246, Q² = 0.852, indicating strong explanation and prediction capabilities of the PLS-DA model. The PLS-DA models did not show clear and consistent discrimination between groups according to drug administration, indicating that drugs used in patients with BD had a negligible effect on the distinct metabolic profiles discriminating BD patients from HCs. A panel of five metabolic biomarkers, namely, decanoic acid, fructose, tagatose, linoleic acid, and oleic acid were selected based on their variable importance on projection values and adequately validated as putative biomarkers of BD (sensitivity 100%, specificity 97.1%, area under the curve 0.993) in the discovery set and validation set. Principal component analysis showed clear discrimination of BD and HC groups by the five metabolite biomarkers in the validation set.

**Conclusions:** This is the first report on detection of a characteristic metabolic profile of BD and identifying and validating potential metabolite biomarkers in BD.
The topical corticosteroid therapy was prescribed in 27, 14% of cases, oral in 47, 51% and bolus in 28, 41%. 47, 51% of patients received Cyclophosphamide and 19% received Azathioprine. Cyclosporine was administered in 3 cases, interferon and Infliximab in 2 cases each. The evolution was good in 111 cases (50.22%), treatment failure was noted in 24% of cases and recidivism in 16.74% of cases. 63 patients have evolved into blindness which was bilateral in 51.1% of cases.

**Conclusions:** Only early diagnosis and appropriate management can improve the prognosis of ocular involvement in BD.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5961

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**DIFFERENCES BETWEEN TEMPORAL ARtery**

**BIOPSY-POSITIVE AND BIOPSY-NEGATIVE GIANT CELL ARTERITIS: A COMPARATIVE COHORT STUDY**

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**Background:** Giant cell arteritis (GCA) is the most common systemic vasculitis in patients aged 50 years or older. The presence of atypical features in temporal artery biopsy have historically been the primary focus for diagnosis of this condition. A notable percentage of patients with symptoms of GCA have negative temporal artery biopsies, however, few cohort studies exist comparing the presentation and outcome of patients based on temporal artery positivity.

**Objectives:** To establish a large, single institution cohort of patients with temporal artery biopsy-negative GCA. To identify differences in presentation and outcome among patients with temporal artery biopsy-negative and temporal artery biopsy-positive GCA.

**Methods:** Patients presenting with temporal artery biopsy-negative GCA diagnosed between 1/1/1998 and 12/31/2013 were identified retrospectively. Final diagnosis was confirmed by consensus among two rheumatologists and a physician abstractor. Baseline characteristics and outcomes were compared to a previously established temporal artery biopsy-positive GCA cohort (n=286) from the same institution.

**Results:** 110 patients with temporal artery biopsy-negative GCA were identified. Unilateral biopsies were performed in 73, bilateral-sequentual in 10, and bilateral same day in 27 cases. Median duration between steroid initiation and biopsy was 3 days. Median length of first biopsy was 14mm and second biopsy (if performed) was 22mm. Among biopsy-negative patients with advanced imaging with features of temporal artery vasculitis, 37% (13/35) had evidence of large vessel vasculitis.

Patients with biopsy-negative GCA were younger (72.0±9.0 vs 75.0±7.6; p<0.001), met fewer ACR criteria (≥ 3 criteria 64% vs 95%; p<0.001) and had a shorter time from symptom onset to diagnosis (median 1.1 vs 2.1 months; p<0.001). Vascular risk factors evaluated at diagnosis showed a higher rate of pre-existing hypertension and obesity among patients with biopsy-negative GCA but similar rates of smoking and diabetes mellitus. Frequency of headache and vision loss at time of presentation were similar between groups. However, biopsy-negative GCA patients had more temporal artery tenderness (35% vs 16%; p<0.001) and arm claudication (13% vs 2%; p<0.001) but less frequent jaw claudication (19% vs 52%; p<0.001). Anorexia, fatigue, and arthralgia were also more commonly noted in biopsy-negative patients. Baseline CRP was lower among patients with negative biopsies (44±53±6 vs 70±6±3 mg/L; p<0.001).

Initial prednisone dose was similar among both cohorts. Although cumulative glucocorticoid (GC) was lower in biopsy-negative patients at 1 year (6±3±2.6 vs 7±2±2.7 g; p=0.004), cumulative GC doses at 2-years and 5-years were equivalent. Biopsy-positive patients (5-years, 56±3%) were able to discontinue GC sooner than biopsy-negative patients (5-years, 30±5%; p<0.001). The number of relapses, time-to-first relapse, annual relapse rate and mortality did not differ based on biopsy positivity.

**Conclusions:** While similarities are present, notable differences are observed at diagnosis in patients with biopsy-negative GCA. Further research is needed to confirm and understand the variability in GC duration.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1936

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**WHAT IS THE ABSOLUTE RISK OF DEVELOPING DIABETES MELLITUS IN PATIENTS WITH GLUCOCORTICOID-TREATED POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS? A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are treated with glucocorticoids (GCs) but long-term GC use is associated with diabetes mellitus (DM). The absolute incidence of this serious complication in this patient group remains unclear.

**Objectives:** To quantify the absolute risk of GC-induced DM in PMR and GCA in published literature.

**Methods:** We identified literature from inception to February 2016 reporting diabetes following exposure to oral GC in patients with PMR and/or GCA without pre-existing diabetes. A random-effects meta-analysis was performed to summarise the literature. Risk of bias was assessed using the Cochrane Collaboration tool.

**Results:** 21 eligible publications were identified. In studies of patients with GCA, mean cumulative GC dose was almost two times higher than in studies of PMR (8.9g vs 5.0g), with slightly longer treatment duration but much longer duration of follow-up (8.8years vs 4.4years). The incidence proportion (cumulative incidence) of patients who developed new-onset DM was 6% (95% CI: 3–9%) for PMR and 12% (95% CI: 8–17%) for GCA. Heterogeneity between studies was high (I²=78.2%), as there were differences in study designs, patient population, geographical locations and treatment strategies. Based on UK data on incidence rate of DM in the general population, the expected background incidence rate of DM over 4.4 years in PMR patients and 8.8 years in GCA patients (the duration of follow-up) would be 4.8% and 9.7%, respectively. Very little information on predictors of DM in PMR or GCA patients was found. The overall risk of bias was high for many of the observational studies, especially relating to definition and recording of outcome and prognostic variables.

**Conclusions:** Physicians should screen patients treated for PMR/GCA for DM but it remains unclear what is the time-period of greatest risk and the influence of risk factors. Our meta-analysis produced plausible estimates of DM incidence in patients with PMR and GCA but there is insufficient published data to allow precise quantification of the DM risk or, crucially, which patients are at greatest risk.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4942
Background: Behcet’s disease (BD) is a multisystem disease in which central nervous system involvement – neuro-Behcet’s disease (NBD) – may strike young patients with devastating consequences. In this regard, early diagnosis and treatment are essential to prevent injury.

Objectives: This study aimed to analyze NBD clinical features compared to non-neurological BD in order to distinguish disease patterns.

Methods: A retrospective study was performed in 101 BD outpatients from a single tertiary center followed between 2011 and 2016. BD diagnosis was based on the 2014 International Criteria for Behcet’s Disease. Demographic, clinical and imaging features of 28 NBD patients were compared to 73 BD patients without neurological involvement.

Results: Earlier disease onset was found in NBD compared to BD (26±10.2 vs. 30±22.8 years, p=0.08). There were no differences between goiter presentations, with a female predominance in both groups (64.3 vs. 72.6%, p=0.05). Over half of patients (53.6%) presented NBD as the first symptom and the mean time between diagnosis and NBD onset was 3.8±5.9 years. Uveitis was less frequent in NBD patients (25% vs. 47.9%, p=0.04), together with cutaneous disease (95.5% vs. 73%, p=0.01), upper airways involvement (7.9% vs. 17.9%, p=0.01), and articular involvement (67.9% vs. 32.1%, p=0.001). Most patients (82.1%) had a single neurological attack whereas relapsing disease was similar in both groups. Regarding NBD presentation, brainstem involvement was the most prevalent (67.9%), followed by central venous thrombosis (32.1%), aseptic meningitis (17.9%), stroke (3.6%) and peripheral neuropathy (3.6%). Most patients (53.6%) presented NBD as the first symptom and the mean time between diagnosis and NBD onset was 3.8±5.9 years. Uveitis was less frequent in NBD patients (25% vs. 47.9%, p=0.04), together with cutaneous disease (95.5% vs. 73%, p=0.01), upper airways involvement (7.9% vs. 17.9%, p=0.01), and articular involvement (67.9% vs. 32.1%, p=0.001). Most patients (82.1%) had a single neurological attack whereas relapsing disease was found in 18.5%.

Conclusions: Our study found an earlier disease onset in NBD patients and a lower frequency of ocular, cutaneous and articular involvement. Moreover, several patients may unfold the disease as NBD, with lack of other manifestations. In addition, brainstem lesions occurred in most patients. Recognizing these disease patterns might support to expedite NBD diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5514

FR0336 Efficacy of tocolizumab in 31 patients with giant cell arteritis


Background: Giant cell arteritis (GCA) is often a disease refractory to corticosteroids and, besides, the efficacy of immunosuppressive agents is not well established. In this work, we describe the clinical characteristics and the long-term outcome of all the patients with GCA treated with Tocilizumab (TCZ).

Objectives: Our aim was to assess in a clinical practise setting the short and long-term outcomes in patients with refractory GCA.

Methods: A retrospective analysis of all GCA patients treated with TCZ between January 2014 and December 2016 at the University Hospital of Alicante - San Juan de Alicante, Spain was performed. We collected demographic data, clinical parameters, laboratory tests, and long-term outcomes in all patients. TCZ was administered intravenously at standard dose of 8 mg/kg/monthly (n=29), and subcutaneously at a dose of 162 mg/week (n=2). The dose was reduced due to side effects (n=2). The median follow-up of 18 [interquartile range, 6–30] months we observe a reduction of the median of: a) CRP from 1.9 [1.1–3.7] to 0.1 [0.1–0.7] mg/dL; b) ESR from 44 [17–74] to 12 [4–16] mm/1st hour; and c) the dose of prednisone from 20 [10–45] to 2.5 [0–7.5] mg/day. In this follow-up period, the outcome of patients was as follows: a) discontinuation of TCZ (n=8) due to sustained remission; b) dose reduction due to improvement (n=5) or side effects (n=2); c) withdrawal of TCZ because of side effects (n=7); and d) the same dose that at onset (n=8). The reasons why TCZ had to be discontinued were: severe neutropenia; colon adenocarcinoma; cytomegalovirus infection; hypertensive crisis during infusion; myelodysplastic syndrome; and overall health deterioration. The latter patient died because of stroke. Another patient also died after the second TCZ infusion due to stroke in the context of an infective endocarditis.

Conclusions: TCZ therapy leads to a rapid and maintained improvement in patients with refractory GCA and/or with unacceptable side effects related to corticosteroids. However, the risk of neutropenia and infection should be kept in mind when using this biologic agent in patients with GCA.

Disclosure of Interest: None declared


FR0337 ANCA pattern in granulomatosis with polyangiitis and micropolyangiitis. a retrospective analysis of outcomes on a multicentric inception cohort

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Background: ANCA-associated vasculitides (AAV) are characterized by their specific antibody profile (ANCA pattern). ANCA-positive granulomatosis with polyangiitis (GPA) is subdivided into ANCA-antineutrophilic cytoplasmatic antibody (c-ANCA) or anti-neutrophil cytoplasmatic antibody (p-ANCA) types. The ANCA pattern has been shown to influence disease presentation, clinical manifestations, and long-term outcomes.

Objectives: To analyze how ANCA could influence clinical manifestations and long-term outcomes in AAV-affected patients, previously classified as GPA or MPA, from three different referral centers of Northern Italy.

Methods: Clinical manifestations and long-term outcomes of GPA and MPA patients were retrospectively collected. We considered clinical (including BVASv3), laboratory (including ANCA and c-ANCA/p-ANCA ratio) and long-term outcomes1.

Recently ANCA pattern has been reported to define different clinical manifestations and long-term outcomes1.

Results: We identified 171 patients, 90 (52.6%) anti-PR3 positive, 52 (30.4%) anti-MPO positive and 25 (14.6%) ANCA negative. Patients were mainly middle aged (52.5±15.9 years), Caucasian (98.2%) and both sexes were equally represented (Female 53.2%). Anti-PR3 positive patients were older (65 [52.5–69.7] years) at disease onset (p=0.001), affected by more comorbidities (p=0.045). They presented more frequently renal involvement (p=0.001) with higher creatinine levels at diagnosis (0.98 [0.75–1.92] mg/dL, p=0.001) (Fig. 1), systemic symptoms (p=0.039) but lower frequency of upper airways involvement (p=0.005).

Anti-MPO positive patients were older (65 [52.5–69.7] years) at disease onset (p=0.001), affected by more comorbidities (p=0.045). They presented more frequently renal involvement (p=0.001) with higher creatinine levels at diagnosis (0.98 [0.75–1.92] mg/dL, p=0.001) (Fig. 1), systemic symptoms (p=0.039) but lower frequency of upper airways involvement (p=0.005).

ANCA negative showed a longer diagnostic latency (8.5 [3.5–49] months, p=0.0001) than the other two groups. They presented a higher HLA-DRB1*0401 allele frequency (p=0.001).

Conclusion: ANCA pattern is associated with clinical and long-term outcomes in AAV-affected patients.
and the highest frequencies of sinuses (p=0.031), laryngeal (p=0.026) and CNS (p=0.020) involvement.

Long-term outcomes were available only in 113 patients. A low long-term mortality rate (8.7, 1.1% deaths) was noted (mean follow-up of 66.6±30.6 months), significantly higher in anti-MPO positive patients (7.21%) when compared to anti-PR3 positive (0.8, 1% ANCA negative 0 (0%) (p=0.011). Nevertheless, the highest number of relapses/years were associated with anti-PR3 positivity (0.7±1.3 vs 0.1±0.3 in anti-MPO and 0.4±0.7 in ANCA negative, p=0.012). At multivariate analysis, anti-PR3 pattern resulted an independent predictive factor of relapses (p=0.036, OR 5.8, IC95%: 1.1–29).

Conclusions: Our study confirms the hypothesis that each ANCA pattern could define a specific disease subset with different clinical manifestations and outcomes in AAV. Furthermore, in our cohort we observed a lower rate of recurrence and a better long term survival (92.9%) than in literature.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5606

FR02338 THERAPEUTIC CONFORMITY TO GUIDELINES AND DRUG-APPROVAL IN ADAMANTIADES-BECHTSEL’S DISEASE: A RETROSPECTIVE ANALYSIS OF A MIDDLE-EUROPEAN COHORT
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Background: Adanantades-Bechtels disease is a chronic systemic vasculitic disease. Because of multiorgan involvement with diagnostic and therapeutic challenges for physicians, treatment decisions can be very difficult.

Objectives: To retrospectively assess the use of medication for ABD-therapy in view of 1) current guidelines and 2) approval by authorities in a Middle-European tertiary care center.

Methods: Data between 1997 and 2016 from a Middle-European ABD-cohort were retrospectively analysed. First, medical treatment was evaluated for conformity with the EUROLAR-recommendations for ABD-management and the anti-TNF therapy recommendations by Silfakis et al. (1,2). Second, medical treatment was evaluated for use according to indications approved by authorities. Therefore official prescribing informations of the Bundesamt für Sicherheit im Gesundheitswesen (BASG)/European Medicines Agency (EMA), exemplary for Europe, and the Food and Drug Administration (FDA), exemplary for the USA, were screened (3–5). The study was approved by the local ethics committee.

Results: A total of 174 medical interventions were identified in 76 patients. Until 2008, treatment of ABD was based only on few clinical trials. According to EUROLAR-recommendations 93.7% were considered as being treated appropriately, including 55.2% of therapeutic approaches exactly matching the recommendations. 88.9% of TNF-depletion were indicated according to the anti-TNF therapy recommendations (n=8/9). Out of 27 used drugs only prednisolone was approved by BASG/EMA- and FDA-authorities for ABD. Cyclosporin A had the specific BASG/EMA-indication for ABD-uveitis. Another 12 medications had the indications for different symptoms of ABD, and thirteen medications were not authority-approved for any ABD-treatment.

Conclusions: Approvals by BASG/EMA- and FDA-authorities are often missing the indication of ABD. Therefore physicians not only face the complexity of ABD as a rare multiorgan disease, but also have to treat their ABD-patients with unapproved drugs. We propose that medications recommended by international guidelines for the management of rare diseases should be recognized by BASG/EMA- and FDA-authorities, even in case of low evidence.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4783

FR0340 B-CELL REPOLUPATION KINETICS AFTER RITUXIMAB TREATMENT IN ANCA-ASSOCIATED VASCULITIDES COMPARED TO RHEUMATOID ARTHRITIS, AND CONNECTIVE TISSUE DISEASES: A LONGITUDINAL OBSERVATIONAL STUDY ON 120 PATIENTS
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Background: B cell depletion with rituximab (RTX) is approved for treatment of anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitides. Recently, RTX has been shown to be effective in AAV maintenance therapy, but an optimal RTX treatment schedule is unknown and the time to B cell repopulation after RTX has not been studied.

Objectives: To compare kinetics of B cell repopulation after RTX treatment in AAV, RA and connective tissue diseases (CTD) to improve the design of RTX-therapy in AAV and CTD.

Methods: Retrospective single-center analysis of patients with AAV, RA or CTD treated with RTX and a follow-up of >9 months were included. B-cell-repulation was defined as a peripheral B-cell count >0.5x and ≤5x. Prolonged B cell depletion was defined by a B cell repopulation starting later than 12 months after RTX treatment.

Results: 120 patients were included in the study. Sixty-six patients had AAV with 65 classified as granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) and 11 as eosinophilic granulomatosis with polyangiitis (EGPA). Fifty one patients had RA and 19 were treated with RTX because of CTD. There were no significant differences between the groups regarding age and sex. Most patients were treated with RTX 1000mg twice, two weeks apart. Cumulative CYC doses were higher in patients with AAV or CTD than in RA patients. In RA and CTD we observed a B-cell repopulation in all patients (100%) while only 33 AAV patients (50%) had started B-cell repopulation (<0.0001). 93% of the RA and 88% of the CTD patients showed a normal repopulation within the first 12 months after RTX compared to only 10% in GPA and 0% in EGPA (<0.0001). Mean time to repopulation was significantly longer in GPA/MPA (21 months) and in EGPA (20 months) compared to RA (8.5 months) and CTD (8.7 months). Median time of persistent depletion was 26 months in GPA/MPA, 21 months in EGPA compared to 9 months in RA and 6 months in CTD (p<0.0001). In 25 AAV patients B cell depletion persisted longer than 24 months (mean time 4.4±1.81 years). In ten of 55 GPA/MPA patients B-cells were still depleted 4 years, in six patients even after more than 5 years after only one RTX treatment cycle. One patient had a complete B cell depletion even 8 years after the second RTX treatment. Immunoglobulin production was affected by RTX-treatment with a significant decreased decrease in IgG, IgM and IgM compared to baseline values in GPA/MPA but not in RA or CTD. In EGPA only IgM declined significantly. Significantly more patients with GPA/MPA and EGPA developed a hypogammaglobulinemia (IgG<7g/L, IgM<0.4g/L). In some AAV patients hypogammaglobulinemia became clinically relevant and required IVIG treatment.

Conclusions: In contrast to RA and CTD, in AAV RTX induces long-lasting depletion of B cells that is associated with decreased antibody production. This observation points towards potential defects in the B cell compartment in AAV and has important implications for the design of maintenance treatment schedules using RTX. The TNF-inhibitors were indicated for GPA/MPA, but not in RA or CTD. In EGPA only IGM declined significantly. Significantly more patients with GPA/MPA and EGPA developed a hypogammaglobulinemia (IgG<7g/L, IgM<0.4g/L). In some AAV patients hypogammaglobulinemia became clinically relevant and required IVIG treatment.


DOI: 10.1136/annrheumdis-2017-eular.4783
RESULTS: The levels of BAFF were significantly higher in group 3 (0.88±0.19 ng/ml) compared with group 1 (0.68±0.13 ng/ml, p<0.05), but did not distinguish from the group 2 (0.90±0.35). There were not significant differences in ESR between groups. ROC analysis indicated that the AUC for ESR is 0.63±0.10 (p=0.17) and for BAFF – 0.72±0.12 (p=0.05), which indicates fair capacity for BAFF differentiation of patients with low activity or remission of SNV and pts with severe SNV (sensitivity - 61.5%, specificity - 88.9%), while it was poor for ESR (sensitivity - 85.7%, specificity - 46.4%).

CONCLUSIONS: There are significant differences in levels of BAFF between pts with BVAS≤24 and pts with BVAS<11. According to ROC analysis evaluation of serum ESR level and pts with active SNV from pts with low activity of remission better than determination of ESR.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2200

FR10341  CLINICO-PATHOLOGICAL DISCREPANCIES AND CAUSES OF DEATH IN TAKAYASU ARTERITIS: A RETROSPECTIVE ANALYSIS OF 60 FATAL CASES

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BACKGROUND: Takayasu arteritis (TA) may present with a wide spectrum of symptoms common to other diseases leading to delayed or missed diagnosis.

OBJECTIVES: To investigate the rate of undiagnosed clinically cases of TA, and provide a detailed analysis of the wrong diagnoses and the underlying causes of death.

METHODS: A retrospective clinicopathological analysis of sixty autopsy cases (52 males and 8 females aged 18 to 45 years) of TA over period of 11 years have been performed. The median age at disease onset was 25, 7 years.

RESULTS: In 33 cases (55%), TA was not diagnosed during the clinical stages but only in autopsy. The most common incorrect clinical diagnosis was atherosclerosis of the aorta and its branches (celiac trunk, renal, mesenteric and iliac arteries) that has misdiagnosed in 14 cases (42.4%) of TA. TA was misdiagnosed as myocardial infarction/ischaeic heart disease in 5 (15.1%), perforated peptic ulcer in 3 (9.1%), polyarteritis nodosa in 3 (9.1%), and infective endocarditis in 2 cases (6.1%). There were other diagnostic errors in 6 cases in 18.2%); in these cases, cerebral haemorrhage, rheumatic heart disease, pulmonary embolism, pheochromocytoma, chronic glomerulonephritis and lung cancer were the wrong clinical diagnoses. The leading position in the mortality structure due to TA belongs to septic shock that observed in 19 cases (31.7%) due to peritonitis/acute abdomen caused by mesenteric artery occlusion with subsequent intestinal necrosis in 12 (63.1%), lower limb gangrene in 6 (31.6%), and prosthetic aortic graft infection in 1 (5.3%). The second-leading cause of death was acute heart failure due to myocardial infarction, and renovascular arterial hypertension (25%).

The third most frequent cause of death was hemorrhagic shock in 14 cases (23.3%).

The acute bleeding was caused by ruptured aortic aneurysm in abdominal in part 6 cases (42.8%) and ascending aorta with cardiac tamponade in 4 (26.6%). In 2 cases (14.3%), the source of hemorrhage was ulcers of gastrointestinal tract. The surgery has complicated by lethal bleeding in 2 cases (14.3%). In other patients, causes of death were chronic renal failure in 6 (10%), facial failure in 3 (5%), respiratory failure in 1 (1.7%), and revascularization syndrome in 1 (1.7%). In one case, TA coexisted with scleroma of larynx, and asphyxia was direct cause of death.

CONCLUSIONS: Our data show a high number of cases of TA (55%) that were identified at autopsy but were not diagnosed clinically. It can be assumed that aortic atherosclerosis, myocardial infarction/ischaeic heart disease were the most common wrong diagnoses in TA. The leading causes of death in TA are septic shock, acute heart failure, and haemorrhagic shock. In addition, it should be noted that in our series of autopsy cases of TA, males (86, 7%) were most frequently affected compared with results other investigations. Interestingly, that the correct diagnosis of TA was established before death in all females’ cases. It seems to be a trend to miss the clinical diagnosis of TA in male patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5322

FR10342  DISTRIBUTION OF VASCULITIDES IN EASTERN MEDITERRANEAN: RESULTS OF A PROSPECTIVE COHORT


BACKGROUND: The ethnic and geographical differences have been commented on, mainly from European data. We lack large data sets from the eastern part of Europe.

OBJECTIVES: This study is aimed to present the distribution of vasculitides in the Pediatric and Adult Vasculitis patient groups.

Methods: Hacettepe University is one of the main referral centers in the capital of Turkey, serving approximately 470,000 adult and pediatric patients/a year. Hacettepe University Vascularitis Centre (HUVAC) was established to organize a prospective cohort in 2014. All patients starting from October 2014 have been recorded to the database. Additionally electronic patient recording database between October 2014-December 2016 was searched for the patients having any of the 10th revision of the International Statistical Classification of Diseases (ICD)-10 code for the particular vasculitis. The study group of Hacettepe University Vascularitis Centre (HUVAC) re-evaluated the ascertainment patients’ hospital records to review their diagnosis according to the 2012 revised Chapel Hill nomenclature criteria.

RESULTS: A total of 1196 patients had been newly followed in this period. 271 (22.7%) of them were pediatric patients and 31.8% of them were newly diagnosed. The leading vasculitis among adult patients was Behcet’s Disease whereas in pediatric patients it was HSP/IgA Vasculitises (Table). Granulomatous polyangiitis was the most common small vessel vasculitis in adults. Takayasu arteritis was more frequent than giant cell arteritis among the adult patients. There was a female predominance in patients with large vessel vasculitises. During prospective follow up, 22 (1.9%) patients deceased; 7 due to the primary disease, 6 due to infections, 7 due to cardio and cerebrovascular diseases.

Table. Distribution and gender of Adult and Pediatric Vasculitides Patients:

FR10343  COGNITIVE DISORDERS IN BEHÇET’S DISEASE: SOME CLINICAL AND PATHOGENESIS RELATIONS

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BACKGROUND: the cognitive disorders (CD) is a special psychopathological problem for Behcet’s Disease (BD) patients. The causes of CD aren’t enough investigated. Anxiety/depressive disorders and primary neural parenchymal lesions due to BD are the main causes of CD in these patients.

OBJECTIVES: to determine the prevalence of CD in BD patients and its associations with some clinical and magnetic resonance imaging (MRI) scan features.

METHODS: the investigation has been realized in accordance with the interdisciplinary program "Stress factors and mental disorders in immune-mediated inflammatory rheumatic diseases".

RESULTS: 106 BD patients were enrolled in the study. The majority of patients were men (72.6%), natives of the North Caucasus (51.9%), with mean age (Mt±m) 33.3±10.8 years. All the patients met the criteria of the International Study Group for BD (1990) classification. The disease activity was assessed by scoring system BDCF.

CD were diagnosed with psychology and neuropsychology methods. Mental disorders (MD) were diagnosed by psychiatrist in accordance with the ICD-10 in semi-structured interview. The severity of depression and anxiety was evaluated
**FR0344** NOVEL BIOMARKERS OF SUBCLINICAL ENDOTHELIAL DYSFUNCTION IN BEHÇET’S SYNDROME: EVALUATION OF CLINICAL, DENTAL, VASCULAR AND INTIMA-MEDIA-THICKNESS IN A HOSPITAL-BASED POPULATION

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**Background:** Growing interest exists on the role of markers of subclinical cardiovascular disease as independent predictors of cardiovascular events. Poor data are available on the role of these markers as prognostic factors for Behçet’s syndrome (BS).

**Objectives:** The primary aim was to explore Intima-Media-Thickness (IMT), mean arterial diameter and distensibility (DC) in a group of patients with BS, comparing these data with a healthy control group and a disease control group; the secondary aim was to correlate the vascular parameters with demographic clinical/critical profiles.

**Methods:** Thirty BS patients (females:12;mean age±SD:43±10.5; mean disease duration±SD:13±8.8) fulfilling the ISG criteria were prospectively enrolled. Demographic data, level of disease activity, frequency of smokers, hypertension, family history of cardiovascular risk factors, body mass index (BMI) and current therapies were analysed. For each subject, ultrasound B-mode image sequences of right common carotid arteries were acquired and analysed by an automatic system (Cardiotro Studio,Quup) for the measurement of IMT and mean arterial diameter. In addition, carotid pulse pressure was estimated between IMT and DC coefficient was obtained. The systolic and diastolic carotid diameters were automatically measured on the distal wall of the common carotid artery, 1–2 cm beneath the bifurcation. Carotid diameter was calculated as the distance between media-adventitia interfaces. Cross-sectional DC was estimated through the variations in arterial cross-sectional area and blood pressure during systole. DC was computed as DC=ΔA/(PP*A) where A is the distal lumen area, ΔA is the stroke change in lumen area, and PP is the local pulse pressure.

**Results:** At time of evaluation, 4/17 patients presented active disease (50% of them in moderate-severe and 25% joint involvement, 25% gastro-enteric involvement; mean BS activity score 5). Mean IMT±SD value resulted of 0.57±0.81, mean arterial diameter±SD value was 6.87±0.91 and mean DCs SD 27.3±14.34. All the vascular parameters considered were significant correlated with BMI, while only IMT and DC were also significantly correlated with arterial hypertension. Using a correction analysis for age and sex, we found significant correlations between mean arterial diameter and disease activity and between DC and disease duration. These data resulted significantly different compared to healthy control and a disease control groups, in terms of smaller arterial diameter and higher DC. Duration. These data resulted significantly different compared to healthy control with and without CD (28% vs 32%, p=0.44). The patients with CD were older (34.3±10.7 vs 29.9±2.14, p=0.006), more often had chronic/recurrent depressive disorders (41% vs 50%, p=0.001) of moderate severity (MADRS 16,1±5.7 vs 12.2±1.06, p=0.005), stressful life events (91.5% vs 62.5%, p=0.001) and multifocal subcortical parenchymal MRI changes (57.6% vs 9%, p=0.005).

**Conclusions:** The results have shown high rates of different CD in both BS patients. CD were not associated with BS activity and presence of neurological symptoms. CD were related to the diagnoses of stress-related mild to moderate chronic depressive disorders and minor brain multifocal subcortical parenchymal MRI lesions.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3741

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**FR0345** CLINICAL IMPACT OF ALPHA-1-ANTITRYPSIN DEFICIENCY IN GRANULOMATOSIS WITH POLYANGIITIS

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**Background:** Deficiency in α-1-antitrypsin (AAT), which is the main proteinase 3 (PR3) inhibitor, is now recognized as a pathogenic factor in some cases of anti-PR3 anti-neutrophil cytoplasmic antibodies (ANCA)-associated granulomatosis with polyangiitis (GPA). However, the clinical impact of AAT deficiency remains poorly established in this setting.

**Objectives:** The purpose of our study was to describe the clinical phenotypes and outcomes of anti-PR3 GPA patients according to their AAT status.

**Methods:** A retrospective monocentric study carried out in Caen University Hospital led to identify anti-PR3 GPA patients, from 09/21/2011 to 06/10/2016. AAT dosage and phenotype (isoelectric focusing in agarose gel) were performed for all patients. Categorical variables were reported as percentages and compared using Chi² or Fisher’s tests according to expected frequencies. Continuous variables were expressed as means and analysed using Student’s t-tests. Associations between survival, renal survival or relapse-free survival, and AAT phenotype were evaluated by the log-rank test. A p-value <0.05 was considered to be statistically significant.

**Results:** Among the 72 identified anti-PR3 GPA patients, 40 (56%) were male. Median age at diagnosis was 60.5 years old. Patients mainly had constitutional symptoms (51,71%), pulmonary (52,72%), ear, nose or throat (ENT) (49,68%), rheumatologic (45,63%), and renal (44,61%) involvements. Median initial BVAS score was 2 (IQR: 1-5). The maximum score was 17 (IQR: 12-22). Thirty (41.7%) patients were noted (median follow-up: 55 months). Forty-eight (67%) patients had MM phenotype, 10 (14%) MZ phenotype, 8 (11%) MS phenotype, 3 (4%) M variant phenotype, 2 (3%) ZZ phenotype and 1 (1%) ZS phenotype. Allele frequencies of M, Z and S allele were 81, 10 and 6%, respectively. The whole cohort had the same immunosuppressant drug regimen.

**Conclusions:** Our observations confirm the epidemiological association of anti-PR3 GPA with AAT deficiency. The frequency of neurological manifestations (headache, seizures, myelopathy, ataxia) did not differ significantly in patients with and without CD (28% vs 32%, p=0.44). The patients with CD were older (34.3±10.7 vs 29.9±2.14, p=0.006), more often had chronic/recurrent depressive disorders (41% vs 50%, p=0.001) of moderate severity (MADRS 16,1±5.7 vs 12.2±1.06, p=0.005), stressful life events (91.5% vs 62.5%, p=0.001) and multifocal subcortical parenchymal MRI changes (57.6% vs 9%, p=0.005).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4500

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**FR0346** RENAL INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS

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**Objectives:** We assessed the frequency, clinical features and prognosis of renal involvement in granulomatosis with polyangiitis (GPA) and current treatment approaches.

**Methods:** We performed a retrospective analysis of 234 patients with GPA, diagnosed according to Chapel-Hill Consensus Conference 2012 classification, 81 male and 153 female, aged 53 (41; 62) years. 54 patients (23.1%) had renal involvement developed at disease. We performed a retrospective analysis of chronological follow-up of 234 patients with GPA, 81 male and 153 female, aged 53 (41; 62) years. 54 patients (23.1%) had renal involvement developed at disease.

**Results:** 25 patients (24.3% of 103) renal involvement developed at disease.
onset, the other 78 patients (75.7%) developed glomerulonephritis after a median onset of 3 (11.12) months. Hematuria was present in 84 (91.3%), proteinuria in 85 patients (82.5%), nephrotic syndrome in 11 patients (10.7%), hypertension in 31 patients (30.1%). Rapidly progressive glomerulonephritis (RPGN) defined by the doubling of serum creatinine within ≤ 3 months developed in 29 patients (28.2% of 103). Myeloperoxidase-ANCA-positive patients (n=12) developed RPGN significantly more often than proteinase-3-ANCA-positive patients (n=78): 7 (58.3%) vs 22 (28.2%) (p=0.0049). 11 (10.7%) patients developed AKI, stage 3 being the most common (in 8 patients). 40 (38.8%) patients exhibited indolent renal disease course, i.e. without worsening of renal function. By the end of the follow-up, 33 (32.0%) patients were diagnosed with CKD grade 3-5, among them 11 patients (10.7%) developed end-stage renal disease (ESRD). 6 patients (5.8%) died. As a result, 73 patients (71.8%) developed one or more severe relapses with a relapse rate of 0.27 per patient-year. 50 (48.5%) patients had renal relapses (0.096 per patient-year).

Conclusions: Prevalence of renal involvement in the studied group was lower than expected, most likely because of a large proportion of patients with localized GPA. Our study showed that RPGN was not the most common feature of renal involvement. Almost 40% of patients developed indolent course of kidney disease. Nevertheless one third of patients developed CKD G3B or worse by the end of the follow-up. During the induction therapy with high-dose corticosteroids, cyto toxic agents and/or RTX relapses, both renal and extrarenal, are frequent.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5104

Table 1. Demographic features of 37 TA patients with inflammatory bowel disease (IBD), antikylosing spondylitis (AS) or Behcet's syndrome (BS)

<table>
<thead>
<tr>
<th>Concomitant disease</th>
<th>F/M</th>
<th>Mean age at TA diagnosis (SD)</th>
<th>Mean age at concomitant disease (SD)</th>
<th>Time of TA diagnosis in relation to concomitant disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>13/2</td>
<td>31±8</td>
<td>27±11</td>
<td>Simultaneous (n=3)</td>
</tr>
<tr>
<td>IBD</td>
<td>11/1</td>
<td>33±9</td>
<td>31±9</td>
<td>Simultaneous (n=9)</td>
</tr>
<tr>
<td>BS</td>
<td>7/3</td>
<td>35±13</td>
<td>32±13</td>
<td>Simultaneous (n=5)</td>
</tr>
</tbody>
</table>

Conclusions: TA does co-occur with IBD, AS or BS in about 1/5 of the patients, at least in a hospital setting and without a clear temporal pattern. This could be due to the close association of TA with MHC class-1 diseases. In addition, the high prevalence of inflammatory back pain in the dorsal spine in TA needs further scrutiny.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4555
them into three groups according to the allele at the SNP, AA (n=26), AC (n=43) and CC (n=16) (A is a risk allele), and investigated the association of the SNP and organ involvements.

**Results:** There were no differences in the complication rates of carotid arterial lesions among the groups (AA 78.9%, AC 63.9% and CC 80.0%). The proportion of patients with lesions in descending aorta (Numano classification22) Ilb–Vc was 75.0% in AA, 44.2% in AC 44.2% and 25.0% in CC and the proportion in AA was significantly higher than in CC (p=0.0096). Moreover, estimated glomerular filtration rate (eGFR) was significantly lower in AA than in CC (61.3±26.9 ml/min/1.73m² vs. 81.5±28.8 ml/min/1.73m², p=0.042).

**Conclusions:** The SNP rs6871626 located in 12q12 may influence on the occurrence of descending aortic lesions in TAK patients and this may lead to renal dysfunction.

**References:**
5. Disclosue of Interest: None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.2936

**FR0351**

**PAPULOPUSTULAR LESIONS ACCORDING TO AGE, SEX AND LOCALIZATION IN BEHCET'S SYNDROME PATIENTS COMPARED HEALTHY AND DISEASED CONTROLS**

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**Background:** Papulopustular lesions (PPL) are the most common skin lesions in Behcet’s syndrome (BS).

**Objectives:** To assess whether PPL are different in BS according to localization, age, sex and medications used when compared to rheumatoid arthritis patients (RA) and apparently healthy subjects (HS).

**Methods:** 209 consecutive BS patients who were routinely followed in our dedicated BS center were studied. Patients with RA (n=146) who were followed up in the rheumatology outpatient clinic of the same unit and HS (n=149) were used as controls. All subjects were clinically evaluated by the same dermatologist and all skin lesions (papules, pustules, comedones, folliculitis, cysts, nodules) on the face, trunk and legs were separately counted. Information regarding the demographic and clinical features of primary disease and medications used were obtained from patients’ charts.

**Results:** Subjects without PPL were excluded before analyses. Demographic features and mean number of PPL according to site of body were summarized in Table-1. Mean number of total PPL were similar between BS and HS and significantly higher than in RA (p<0.001). Mean number of total PPL according to sex were similar in RA and HS but higher in male BS patients compared to female BS patients (p<0.04). When we analyzed the number of PPL according to different body sites, we observed that BS patients had significantly more lesions on the legs when compared to the RA patients and HS (p<0.0001). Number of PPL lesions tend to decrease as the patient ages in BS similar to RA and HS. When leg lesions were analyzed according to age, this difference remained in the age groups 31–50 and >50 but not in the age group <30. Corticosteroid use did not impact the results.

**Conclusions:** BS patients have significantly more PPL on the legs when compared to HS and RA. Number of PPL tend to decrease as the patient ages in BS similar to RA and HS however BS patients still have more PPL on the legs after the age of 50 suggesting that these lesions somehow differ from acne vulgaris, in pathogenesis.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.6463
**EFFICACY OF BIOLOGICS IN PATIENTS WITH REFRACTORY TAKAYASU ARTERITIS AND ANALYSIS OF THEIR GENETIC BACKGROUNDS**

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**Background:** Takayasu arteritis (TAK) is a rare disease that mostly affects young females and causes inflammation, stenosis, and dilation of the aorta and its main branches. Although glucocorticoids are effective, relapses occur frequently [1]. Recently, the efficacy of biologics has been reported in refractory TAK. HLA-B*52 is a major genetic risk factor and associated with the severity [2].

**Methods:** We analyzed serum samples of 3 patients with SSc and ILD (2 limited SSc: one ANA positive and one anti-Scl70 positive, and one diffuse SSc anti-Scl70 positive), 3 patients with SSc and no ILD (ACA positive limited SSc), and 4 healthy controls. All subjects were women and age matched.

**Results:** Serum proteomic profiling was performed using the SOMAScan platform (SomaLogic, Inc., Boulder, CO, USA). Statistical analysis included Student’s t-test and were performed using the IBM SPSS software (IBM, Armonk, NY, USA).

**Conclusions:** Circulating microparticle subsets are associated with serum proteomics profile in systemic sclerosis.

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**CIRCULATING MICROPARTICLE SUBSETS ARE ASSOCIATED WITH PATIENTS WITH EXTENDED FIBROTIC PHENOTYPE IN SYSTEMIC SCLEROSIS**

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**Background:** In systemic sclerosis (SSc), systemic remodeling, microvascular injuries and production of autoantibodies are well known as disease hallmarks. However, the master regulator of these characteristics is still unclear. Microparticle (MP) is a small membranous vesicle, released from various kinds of cells, and distributes systemically through circulation [1]. Recent reports revealed that MP contains various growth factors, proteases and cytokines including TGF-β1, suggesting that MP can contribute to immune and mesenchymal responses as a conveyor [2] and involve with disease process of SSc. Although, the possible involvement of MPs in the pathogenesis of SSc is indicated, the detailed association of MPs including MP subsets with SSc is not well clarified.

**Objectives:** To elucidate the association between circulating MP subsets and patients’ characteristic of SSc.

**Methods:** Thirty-six patients with SSc and 13 healthy controls were involved in this study. Platelet-rich plasma containing microparticles was isolated from whole blood using gradient centrifugation and analyzed using flow cytometer. MP was defined as particles smaller than 1 μm diameter using Megamix® and identified each MP subsets based on expression of cell type-specific surface markers: platelet (CD31, CD41), endothelial cell (CD31, CD41) and monocyte (CD14, CD45) using fluorescence-tagged antibodies. Clinical information was retrospectively collected from medical records, and the correlation with the number of each MP subset was analyzed.

**Results:** Mean age of 36 patients with SSc was 60±1.8 years, 94% was female, and mean disease duration was 11.2±9.5 years. Patients with diffuse cutaneous SSc: one ANA positive and one anti-Scl70 positive, and one diffuse SSc anti-Scl70 positive.

**Conclusions:** The association between circulating MP subsets and patients’ characteristic of SSc.
IL-17A UP-REGULATION IN PERIPHERAL BLOOD MONONUCLEAR CELLS CO-CULTURED WITH AUTOLOGOUS SKIN FIBROBLASTS IS ASSOCIATED WITH DOWN-REGULATION OF PRO-FIBROTIC MEDIATORS AND INCREASED FIBROBLAST APOPTOSIS


Background: IL-17A has been implicated in the pathogenesis of systemic sclerosis (SSc) (1). We previously showed that skewed peripheral blood mononuclear cell (PBMC) activation by IL-17A from SSc patients can induce Fas-mediated apoptosis in co-cultured autologous skin fibroblasts (2).

Objectives: We therefore aimed to investigate IL-17A expression and effects in these co-cultures.

Methods: PBMCs and skin fibroblasts from 5 SSC and 5 healthy control patients with disease duration less than 3 years were co-cultured up to 10 days in presence of IL-17A [20 U/ml] in a 1:1 ratio, as previously described. IL17A, IL17RA, CXCL1, CCL2, CCL3, TGFB2R2, SMAD3, CTGF, COL1A1, COL3A1 mRNA expression was assessed by Sybr Green real-time PCR. Chemokine production was further investigated at the protein level by multiplex immunosassay. In subset experiments, co-cultures were treated with either IL-17A receptor A neutralizing antibody or recombinant IL-17A in order to re-activate mononuclear cells (anti-IL-17 receptor A; neutralizing monoclonal antibodies (anti-IL-17A mAb), then cells were stained with Annexin V, anti-IL17RA, and anti-FAS antibodies and were investigated by flow-citometry.

Results: IL17A mRNA in co-cultured PBMCs was increased by 11.5 fold (p < 0.01) and IL17RA by 4.3 fold (p < 0.05) in co-cultured fibroblasts. CXCL-1, CCL2, and CCL3 were also up-regulated at both mRNA (11.9 fold, 773.3 fold, and 29 fold, respectively; p < 0.05) and protein level (8.9 fold, 11.2 fold, and 252.4 fold, respectively; p < 0.05). Profibrotic mediators, such as COL1A1, COL3A1, and CTGF mRNA expression in co-cultured fibroblasts was reduced to 0.33 fold, 0.24 fold, and 0.31 fold, respectively (p < 0.05). This effects were associated with mRNA down-regulation of two key effectors of TGF-β signaling, TGFB2R2 and SMAD3 to 0.59 and 0.79 fold, respectively. Flow cytometry analysis, we observed a robust increase in co-cultured fibroblasts apoptosis by adding IL-17A neutralizing mAb to IL-17A treated cells (39% to 16.8%; p < 0.05). Compared to controls treated with IL-17A and isotype controls, moreover, IL17RA mAb addition also reduced Fas expression in co-cultured fibroblasts as compared to IL-17A treated cells (47.7% to 10.69%; p < 0.05).

Conclusions: Our results support the role of IL-17A in the pathogenesis of SSc. Furthermore, we here first show that IL-17A up-regulation in co-cultured PBMCs might play antibiotic effects in autologous skin fibroblasts and might be implicated in fibroblast apoptosis, interphering with the FAS/FASL pathway.

Disclosure of Interest: None declared

MIRCNPCASES AS A BIOMARKER AND A REDOX-DEPENDENT REGULATOR OF NEUTROPHIL ACTIVATION AND PROTEOLYTIC ACTIVITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Persistent oxidative stress and unrelenting vascular inflammation are hallmarks of Systemic Sclerosis (SSc). Platelet-derived microparticles (PD-uP) that express a bioactive redox-dependent moiety, HMGB1 accumulate in the peripheral blood of SSc patients, but their biological actions is not fully characterized.

Objectives: To verify whether PD-uP might represent a biomarker of SSc clinical involvement and whether their biological actions is regulated by environmental redox.

Methods: Fifty-four patients with SSc and 20 healthy controls were enrolled so far. Twenty healthy controls (HC) matched for sex and age were studied in parallel. PD-uP were characterized and quantified by flow cytometry. Leukocyte features, including expression and distribution of myeloperoxidase (MPO), were assessed by flow cytometry and confocal microscopy. PD-uP ability to regulate neutrophil activation and pro-inflammatory action was assessed in vitro in defined redox conditions and in vivo upon intravenous (i.v.) injection in immunocompromised NSG mice, and traced at various times based on recognition of the human platelet antigen CD61.

Results: PD-uP are present in the blood of SSc patients. Their concentration is significantly higher than in the blood of HC (p<0.001). A substantially higher fraction of SSc PD-uP express the prototypic DAMP, HMGB1 (70% SSc vs 5% HC). Among SSc patients, those with pulmonary hypertension had a significantly higher concentration of HMGB1 + PDuP (p<0.002). In contrast other disease-associated variables, including the extent of fibrosis and the presence of active SSc pattern at the NVC, were not apparently influential. Neutrophils of SSc patients were activated, as demonstrated by the MPO redistribution from the primary granules to the plasma membrane. Circulating neutrophils appeared to be viable and the fraction of cells undergoing apoptosis was similar in SSc patients and HC. The extent of neutrophil activation was associated with the concentration of HMGB1 + PD-uP (p<0.001). SSc PDuP but not HC PD-uP induced MPO redistribution in vitro. The effect was dependent on HMGB1 and increased by oxidizing moieties. Injection in immunocompromised mice resulted in time-dependent association of SSc PD-uP to mouse neutrophils, which contextually redistributed MPO at the plasma membrane.

Conclusions: HMGB1 expression on PD-uP of SSc patients could help identify functionally relevant population of microparticles, involved in neutrophil activation/function and possibly valuable as a novel biomarker of vascular remodeling.

Disclosure: None declared
DOI: 10.1136/annrheumdis-2017-eular.3980

MARKER FOR INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: Interstitial lung disease (ILD), the primary cause of death in systemic sclerosis (SSc) in early to late course, is premature and difficult to diagnose. Apoptosis is considered the first pathophysiologic event in SSc-ILD. Monitoring of apoptotic processes with nuclear imaging, a sensitive, specific and noninvasive
methodology might be a promising new approach for the diagnosis of early SSC-ILD.

**Objectives:** To evaluate the radiotracer $^{99m}$Tc-rhAnnexin V-128, which specifically targets a pathophysiological key molecule of early apoptosis, for the detection of earliest stages of lung involvement in animal models of SSC-ILD with single photon emission computed tomography (SPECT/CT).

**Methods:** C57BL/6J mice were treated with a single intratracheal injection of bleomycin or saline. Animals were euthanized at days 3, 7, 14 and 21 post-injection (n=6). Lung injury was evaluated by analysis of HE and Sirius red staining. The Ashcroft score was applied for the semi-quantitative evaluation of fibrotic changes. Immunofluorescence using the TUNEL assay and double staining with specific cell markers were performed to determine apoptotic cells. Positive nuclei were quantified by manual and automatic counting with ImageJ analysis software. Three days after injection with bleomycin or saline, mice were injected with $^{99m}$Tc-rhAnnexin V-128 (Advanced Accelerator Applications, Italy). After 1h, images were acquired using small animal SPECT/CT, followed by ex vivo autoradiography.

**Results:** In the model of bleomycin-induced lung fibrosis, inflammatory infiltrates developed from day 7 as assessed by Sirius red staining and was $^{(CD45^+)}$ occurred as early as day 3 with peak at day 7, whereas pulmonary fibrosis from day 7 as assessed by Sirius red staining was most pronounced at day 21 (mean Ashcroft score=4.6, p=0.0286). Notably, the number of apoptotic cells evaluated by TUNEL staining, was highest at day 3 (mean ± SE=6.5±1.5 positive cells/HPF, p=0.0438) compared with saline controls (mean ± SE=0.7±0.1, p=0.0095) and then decreased over time. To determine the type of cells undergoing apoptosis, we performed co- stainings with different cell markers. Data displayed that endothelial cells (vWF+) and epithelial cells (cytokeratin+), but not inflammatory cells (CD45+) were the primary cells undergoing apoptosis in earliest inflammatory stages of ILD.

In accordance with the findings on tissue level, at day 3 post-injection, we detected ex vivo with autoradiography, yet not with in vivo SPECT/CT, an increased pulmonary uptake of $^{99m}$Tc-rhAnnexin V-128 in the lungs of bleomycin-induced mice compared with saline treated controls.

**Conclusions:** Apoptosis of epithelial and endothelial cells preceded the development of pulmonary inflammation and fibrosis in the model of bleomycin-induced lung fibrosis. Thus, the use of $^{99m}$Tc-rhAnnexin V-128 might be a promising approach for the diagnosis of earliest stages of ILD. However, sensitivity of **in vivo** imaging has to be further improved.

**Disclosure of Interest:** L. Guo: None declared, J. Schniering Grant/research support from: Swiss National Science Foundation (S-85605–02–01), R. Schibli: None declared, A. Blanc: None declared, D. Chico Employee of: Advanced Accelerator Applications, S. Ye: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi:patent licensed mir-29 for the treatment of systemic sclerosis, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIDec, BMS, Boehringer Ingelheim, ChemomAb, Epipharma, eserRade foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, Medimmune, Mitsubishi Tanabe Pharma, Pharmocyclics, Pfizer, Sanofi, Sorapharm, Sinoxa, Speakers bureau: AbbVie, IQone Healthcare, Mepha, M. Béhé: None declared, B. Maurer Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Pfizer, Roche, Actelion. Patent licensed: mir-29 for the treatment of systemic sclerosis

**DOI:** 10.1136/annrheumdis-2017-eular.4945

Abstract FRIO359 – Table 1

<table>
<thead>
<tr>
<th>Percentage of Ki-67 positive cells</th>
<th>Healthy (I)</th>
<th>Bleo (II)</th>
<th>BleoHighPT (III)</th>
<th>BleoMediumPT (IV)</th>
<th>HealthyHighPT (V)</th>
<th>HealthyMediumPT (VI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average (%)</td>
<td>50.4</td>
<td>36.1</td>
<td>35.4</td>
<td>37.2</td>
<td>50.1</td>
<td>49.4</td>
</tr>
<tr>
<td>SD</td>
<td>2.6</td>
<td>3.0</td>
<td>3.2</td>
<td>2.8</td>
<td>2.0</td>
<td>1.4</td>
</tr>
</tbody>
</table>

**Conclusions:** The cumulative doses of 1200 J/cm² and 600 J/cm² of narrowband UVA1 effectively reduced the dermal thickness, and the impact was dose-dependent. Phototherapy course did not up-regulate p53 nor Ki-67 proteins in the healthy mice and mice with scleroderma skin. UVA1 radiation caused the increase of the active caspase-3 expression in the skin of mice with scleroderma reflecting the apoptotic feature of narrowband UVA1. The results of this study indicate that 365±5 nm UVA1 phototherapy is safe and effective for the treatment of dermal fibrosis.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2869
mononuclear cells (PBMCs), and a relationship among specific inflammatory mediators, ECS, and organ involvement has not been established.

**Objectives:** To analyze ECS elements and related inflammatory molecules in PBMCs of SSC patients, and evaluate their relationship with the clinical profile of the disease.

**Methods:** 24 SSCs patients [including 5 Pre-SSc, 13 limited cutaneous SSc (lc-SSc) and 6 diffuse cutaneous SSc (dc-SSc)] and 24 healthy donors (HD) were included. Purified PBMCs were used for analysis of gene expression of molecules belonging to the ECS: CB1, CB2, GPR55, P2Y1, FAAH, MAGL and TRPV1. Inflammatory mediators were evaluated in PBMCs by RT-PCR. Clinical evaluation of patients was performed and correlation/association studies were developed.

**Results:** Cannabinoid type-2 receptor, GPR55 and TRPV1 gene expression were reduced in PBMCs of SSC patients, while FAAH showed a high level of expression in the same populations. In addition, in the patient group’s of Pre-SSc, specific elevated in various cytokines was demonstrated (i.e. IL-1β, IL-17, VEGF-A), suggesting that these cytokines might act as early biomarkers of disease development. Patients’ positive for anti-centromere antibodies showed increased expression of IL-4, IL-17 and MCP-1 in relation to those positive for anti-Sc70. PBMCs expression levels of GPR55, IL-12 and MCP-1 were higher in lc-SSC compared to dc-SSc. Interestingly, we observed a direct correlation between levels of these cytokines and the occurrence of pulmonary hypertension, a pathology more frequent in lc-SSc, thus suggesting a role for these inflammatory molecules in pulmonary involvement in this form of the disease. Correlation studies demonstrated an interrelation among deregulated expression of various molecules belonging to the ECS (i.e. FAAH, GPR55 and TRPV1) and inflammatory mediators over-expressed in serum and immune cells (i.e. CRP, ESR, MCP-1, TNFα and VEGF-A).

**Conclusions:** SSCs patients show altered gene profile of ECS and inflammatory mediators in PBMCs, which might allow the discrimination between limited and diffuse forms of the disease, and are associated with the presence of specific auto-antibodies and the internal organ involvement. Our overall data suggest an appealing potential target of ECS for treatment of SSCs, as it seems to be related to the inflammatory profile.

**Acknowledgements:** TCB-794 and ISCCII (P15/01333 and RIER RD/16/0012/0015)

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4946

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**REFERENCES:**


**Acknowledgements:** We thank all the physicians and others caring for the patients enrolled in our study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3040

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**FR01361**

**INTERLEUKIN-4 INDUCES CLASS-SWITCHING TO IGG4 AND SYNERGISTICALLY CONTRIBUTES TO PLASMABLASTS DIFFERENTIATION WITH INTERLEUKIN-21 THROUGH CD40 DEPENDENT MANNER IN IGG4-RELATED DISEASE**

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**Background:** IgG4-related disease (IgG4-RD) is a lymphoproliferative disorder characterized by elevated serum levels of IgG4 and increased numbers of circulating plasmablasts. We have previously reported that class-switching to IgG4 and plasmablast differentiation are mediated by follicular helper type 2 T cells which are known to secrete interleukin (IL)-4, IL-13, IL-10 and IL-21 (1, 2). However, the cytokines which play a role in the IgG4 class-switching and plasmablast differentiation through correlation to cell contact remain unclear in IgG4-RD.

**Objectives:** The aim of this study was to elucidate the role of follicular helper type 2 T cell cytokines (IL-4, IL-13, IL-10, and IL-21) and cell to cell interaction in the IgG4 class-switching IgG4-RD.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were prepared from seven consecutive patients with active, untreated, newly diagnosed IgG4-RD and five healthy controls. To identify the cytokines which induce IgG4 class-switching, the cells were stimulated with IL-4, IL-13 or the combination with other cytokines, such as IL-10 or IL-21. The amounts of IgG4 and IgG in the culture supernatants were measured by cytometric bead arrays. The expression level of activation-induced cytokine deamidase (AID; an enzyme essential for class-switch recombination) was analyzed by quantitative PCR to confirm the induction of class-switching by stimulation with cytokines. The numbers of plasmablasts and plasma cells induced by cytokines stimulation were examined by flow cytometry. Moreover, an anti-CD40 antibody was added to the culture to elucidate the effects of cell to cell interaction on the differentiation of plasmablasts or plasma cells.

**Results:** IL-4 significantly induced CD40-stimulated PBMCs to undergo IgG4 class-switching to IgG4-RD, while IL-13 did not show any positive effects. Moreover, the IgG4/IgG ratio in culture supernatants was also significantly higher in the stimulation with IL-4 compared to other cytokines in IgG4-RD. In addition, the expression levels of AID mRNA were increased by stimulation with IL-4 compared to that by no stimulation or CD40 stimulation in IgG4-RD. On the other hand, PBMCs from healthy controls showed no significant difference in IgG4 production after stimulation with either IL-4 or IL-13. Furthermore, IgG4 production stimulated with IL-4 was significantly higher in IgG4-RD than that in healthy controls. Assessing additional effects of IL-10 or IL-21 on IL-4, IL-10 and IL-21 did not increase IgG4 production and IgG4/IgG ratio compared to IL-4 alone. However, importantly, IL-21 synergistically induced plasmablasts or plasma cells differentiation in combination with IL-4, whereas no obvious change was observed in PBMCs stimulated with IL-4 alone in IgG4-RD. Of note, the differentiation of plasmablasts and plasma cells by IL-4 and IL-21 was markedly abolished in the absence of CD40 stimulation.

**Conclusions:** Our results strongly suggest that IL-4 plays a pivotal role in IgG4 class-switching, and the effective collaboration between IL-4 and IL-21 contributes to plasmablasts and plasma cells differentiation via CD40 dependent manner in patients with IgG4-RD.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3040

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**FR01362**

**ANGIOGENIC T CELL EXPANSION CORRELATES WITH SEVERITY OF PERIPHERAL VASCULAR DAMAGE IN SYSTEMIC SCLEROSIS**

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**Background:** The mechanisms underlying endothelial cell injury and defective vascular repair in systemic sclerosis (SSc) remain unclear. Recent studies suggest that a novel T cell subset, the so-called angiogenic T (Tang) cells, may have an important impact on the repair of damaged endothelium. Tang cells are characterised by the co-expression of CD3, CD31 (platelet-endothelial cell adhesion molecule-1) and CXCR4 (or CD184, receptor for the CXC chemokine stromal cell-derived factor-1 (SDF-1)/CXCL12). Tang cells may promote the formation of new blood vessels and endothelial repair by stimulating the function and differentiation of endothelial progenitor cells possibly through the secretion of proangiogenic cytokines, thus fostering postnatal vasculogenesis.

**Objectives:** This study aimed to analyse the Tang cell population in relation to disease-related peripheral vascular features in SSC patients.

**Methods:** Tang cells (CD3+CD31+CXCR4+) were quantified by flow cytometry in peripheral blood samples from 39 patients with SSc and 18 matched healthy controls (HC). CD3+CD31+CXCR4- Tang cells were expressed as a percentage of total CD3+ T cells. Circulating levels of SDF-1α were assessed in paired serum samples by immunoassay. Skin sections from patients with early diffuse cutaneous SSc (n=7) and HC (n=6) were subjected to CD3/CD31 and CD3/CXCR4 double immunofluorescence staining.

**Results:** The percentage of circulating Tang cells was not different between the whole SSc patient cohort (median 29.9, interquartile range (IQR) 22.3–36.2) and HC (median 25.2, IQR 23.3–33.5). Subgroup analysis revealed that Tang cells were significantly increased in SSc patients with digital ulcers (DU) (median 35.5, IQR 32.2–42.5) compared either with SSc patients without DU (median 23.3, IQR 18.5–29.6) or with HC (p<0.001 for both). Furthermore, Tang cell percentage was significantly higher in SSc patients with “late” nailfold videocapillaroscopy (NVC) pattern (median 34.9, IQR 25.0–42.0) than in those with “early”/“active” NVC patterns (median 26.8, IQR 20.4–32.9) and in HC (p=0.01 and p=0.04, respectively). No difference in circulating Tang cell counts was found when comparing either SSc patients without DU or patients with “early”/“active” NVC patterns and HC. In SSc peripheral blood, the percentage of Tang cells was inversely correlated to the levels of SDF-1α (Spearman’s rho = -0.59, p<0.0001).

**Conclusions:** Our findings demonstrate for the first time that Tang cells are expanded in patients with SSc displaying most severe peripheral vascular complications. Such an expansion may be an ineffective attempt to compensate for the need increased angiogenesis and endothelial progenitor cell function. In SSc, Tang cells might represent a potentially useful biomarker reflecting peripheral vascular damage severity. Further studies are required to clarify the function of Tang cells and investigate the mechanisms responsible for their change in SSc.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3017
Scleroderma, myositis and related syndromes

**FRI0363** KL-6 AND NOT CCL-18 IS A PREDICTOR OF EARLY PROGRESSION IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE


Background: Pneumoproteins are attractive biomarker candidates in systemic sclerosis (SSc) related interstitial lung disease (ILD) because they are easily obtainable and lung-specific. KL-6 and CCL-18 (PARC) have been previously reported as promising predictive biomarkers of lung parenchymal damage in multiple disorders including SSc-ILD.

Objectives: Our goal was to determine the predictive significance of these two pneumoproteins for forced vital capacity % (FVC) decline within the first year of follow-up in patients with early SSc-ILD, in order to inform individualized care in routine clinical practice and facilitate enrichment strategies in clinical trials.

Methods: GENISOS (Genetics versus ENvironment In Scleroderma Outcome Study) cohort patients who had ILD verified by imaging and available pulmonary function tests at enrollment plus 12–18 months thereafter, were included in this study. All patients had disease duration ≤5 years at enrollment. FVC, expressed as percentage of predicted value was used as surrogate for severity of ILD. Annualized percent change in FVC at one year follow up was calculated. Baseline demographic, clinical variables and two pneumo-proteins, KL-6 and CCL-18 were investigated. KL-6 and CCL-18 were measured in the plasma by commercially available, validated ELSA. Multiple linear regression with baseline clinical and demographic variables as independent variables was performed in univariable and multivariable models. Only variables that reached p<0.1 were included in the multivariable analyses.

Results: A total of 82 patients with early SSc-ILD were included. 18 were male and 45 had diffuse cutaneous involvement. Mean disease duration was 2.3 years. Rate of FVC% predicted change over time ranged from -0.23 to 0.38, indicating a highly variable course. Baseline KL-6 levels were higher in patients than healthy controls (p=0.0001). Baseline higher KL-6 levels were predictive of faster FVC% decline at the one year follow-up (b=-0.03, p=0.04). Upon categorizing KL-6 using a previously determined optimal cut-off of 1273 u/mL (1), its predictive significance remained in the univariate (p=0.01) and multivariable analyses adjusted for Sci-70, disease type and gender (b=-0.03, p=0.04). Twenty-nine (34.5%) patients had KL-6 levels equal or above 1273 u/mL. Although CCL-18 was higher in patients than controls (<0.0001), its levels did not predict rate of FVC decline (provide p-value).

Conclusions: KL-6 but not CCI-18 is predictive of early SSc-ILD progression. In this study, we also validated the previously proposed cut-off of 1273 for KL-6 in an independent cohort. KL-6 is a promising pneumoprotein that can inform individualized clinical care and contribute to enrichment strategies in clinical trials of SSc-ILD.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5145

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**FRI0364** USEFULNESS OF SERUM HAPTOGLOBIN LEVELS AS A NOVEL MARKER FOR PULMONARY ARTERIAL HYPERTENSION COMPLICATED WITH CONNECTIVE TISSUE DISEASE


Background: Pulmonary arterial hypertension (PAH) is of great clinical significance as a life-threatening complication of connective tissue diseases (CTD). Pulmonary artery thrombotic microangiopathy (PATM) is an important pathophysiology of PAH. The concept of PATM refers to localized thrombotic microangiopathy to be defined histologically and should be discriminated from systemic thrombotic microangiopathy characterized by microangiopathic haemolysis and thrombocytopenia. The degree of PATM has been suggested to be associated with vascular remodeling, severity and prognosis of PAH, and anticoagulation therapy might be effective in PAH patients with features of PATM [1]. Haptoglobin (Hp) is a plasma protein mainly produced by hepatocytes, which binds free haemoglobin released from erythrocytes and protects the kidneys from damage induced by haemoglobin. The Hp is measured in clinical setting as a sensitive marker to detect intravascular haemolysis including thrombotic microangiopathy [2].

Objectives: We hypothesized that serum Hp levels decreased in patients with PAH due to pulmonary microangiopathic haemolysis. The aim of this study was to investigate the association between serum Hp levels and pulmonary artery systolic pressure estimated by echocardiography (ePASP) in patients with CTD.

Methods: This study included CTD patients with suspicion of PAH who were attending Rheumatology Department in Hokkaido University Hospital between August 2015 and August 2016 and underwent echocardiography. PAH was diagnosed based on right heart catheter findings. Serum Hp levels were measured by standardised turbidimetric immunoassay in all patients. Demographic data, laboratory results, and echocardiographic findings were extracted from the medical records. Decreased serum Hp levels were defined as below 15 mg/dL based on the 95th percentile of healthy controls.

Results: Twenty-four CTD patients with confirmed PAH (CTD-PAH) and 32 CTD patients without PAH (non-PAH) were enrolled. Decreased serum Hp levels were significantly frequent in patients with CTD-PAH compared with non-PAH patients (29% vs 6%, p=0.03). In patients with CTD-PAH, serum Hp levels had a significant negative correlation (r = -0.692, p<0.0001, Figure 1) with ePASP, and serum lactate dehydrogenase (LDH) levels were significantly elevated in patients with decreased Hp levels (233±47 U/L vs 187±42 U/L, p=0.01). Follow up study showed lowering ePASP led to normalizing serum Hp levels.

Conclusions: Serum Hp levels correlated negatively with ePASP in patients with CTD-PAH, and serum LDH levels were higher in CTD-PAH patients with decreased Hp levels. These findings suggest that decreased Hp levels in CTD-PAH patients may reflect PATM and subsequent subclinical haemolysis. Serum Hp levels are a candidate of additional non-invasive marker of CTD-PAH to assess the degree of PATM.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5145
References:

Disclosure of Interest: None declared


FR10365 NEW COLLAGEN BIOMARKERS PREDICT PROGRESSION OF FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a complex autoimmune disease with extensive fibrosis of the skin and internal organs in which extracellular matrix (ECM) remodelling is a key pathogenic process. Imbalance in the formation and degradation of collagens results in fibrosis. Quantifying the tissue turnover in a highly fibrotic disease such as SSc is very important for the prediction of disease progression and therapeutic efficacy. Given the clinical heterogeneity of SSc patients, biomarkers facilitating personalized medicine approaches are highly needed.

Objectives: To evaluate the potential of selected ECM neo-epitopes as serological biomarkers for diagnosis, prediction of clinical outcomes and disease progression in SSc.

Methods: Healthy controls (HC; n=29), stable SSc (n=149), and progressive SSc patients (n=23), progression defined either as 10% decrease in FVC% predicted or increase in mRSS >25% and 5 points on one year clinical follow up), meeting the 2013 ACR/EULAR classification criteria were analyzed. Longitudinal clinical assessment, data recording and sera collection were done according to EUSTAR standards. ECM-degradation (C3M, VICM, C4M2, BGM) and ECM-formation biomarkers (P1NP, P4NP7S, Pro-C3, Pro-C5, Pro-C6) were measured in serum using newly developed ELISA-based assays (Nordic Bioscience). Differences in biomarker levels were analyzed with respect to several fibrosis-related clinical outcomes. Statistical analysis was performed by Man-Whitney U, Kruskal-Wallis and Spearman tests. Biomarkers’ sensitivity and specificity was examined by ROC analysis.

Results: Both ECM-degradation and ECM-formation biomarkers differed between SSc patients and HC: The expression of C4M2, Pro-C3, BGM and C3M was significantly increased in SSc patients compared to HC (p<0.0001, AUC=0.93; p<0.0001, AUC=0.74; p=0.003, AUC=0.67; p<0.0001, AUC=0.94, respectively), whereas P1NP was significantly lower (p<0.0001, AUC=0.78), Figure 1. Furthermore, Pro-C3, VICM and Pro-C6 levels were significantly higher in SSc progressors vs. HC (p<0.0001, AUC=0.86; p=0.003, AUC=0.75; p<0.0005, AUC=0.81, respectively).

Conclusions: There is no fully validated biomarker predicting worsening of fibrosis. In this regard, most interestingly, the ECM-degradation markers C4M2, BGM, C3M were significantly lower in SSc patients showing progression of fibrosis on follow up versus SSc patients being stable on follow up (p<0.0001; p<0.008; p<0.0001, respectively). Consistently, the formation marker Pro-C6 was significantly increased (p<0.001, AUC=0.71) indicating a profound imbalance of ECM turnover in progressors. The strongest difference between progressive and stable SSc patients was seen for the ratio between the formation and degradation biomarkers Pro-C3/C3M which showed an AUC of 0.86 in progressive vs. stable SSc patients (p<0.0001).

FR10366 A PILOT STUDY ON ISCHEMIA AND REPERFUSION INJURY DURING A RAYNAUD’S ATTACK: SEQUENTIAL ASSESSMENT OF REDOX STRESS PARAMETERS IN A UNIQUE COOLING AND REWARMING EXPERIMENT

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Background: Oxidative stress plays a role in systemic sclerosis (SSc), but the molecular mechanisms involved are incompletely understood. During an attack of Raynaud’s phenomenon (RP) a period of ischemia (I), followed by a period of reperfusion (R) occurs frequently, associated with the severity of vasculopathy. [1] Only in secondary RP digital ulcers develop. We hypothesized that I/R injury may play a role in the pathogenesis and could offer new therapeutic targets.

Objectives: To explore the course of oxidative stress in patients with SSc compared with primary RP and healthy controls.

Methods: A total of 30 patients were included: 10 with limited cutaneous SSc (age: 57 (53–61) yr, male/female 5/5), 10 with primary RP (age: 54 (41–58), 2/8), and 10 healthy controls (age: 29 (22–25), 3/7). A standardized cooling experiment was performed and digital perfusion was assessed in all 5 fingers using photo-electric plethysmography: at baseline (T=0) the dominant hand was submerged in water at 33°C, followed by cooling in steps of 3°C every 4 minutes, until 6°C or when pain became intolerable (T=1). Recording was continued 10 (T=2) and 30 (T=3) minutes of rewarming to ambient temperature (23°C). Blood was drawn from ipsilateral cubital vein at T0, 1, 2 and 3, markers for tissue injury (lactate, LDH, creatinine phosphokinase (CPK) [routine methods]), redox status ([N-2NO- [NO-R] were measured in plasma. [1–3] Numbers are in median (IQR).

Results: Baseline free thiols were significantly decreased in RP vs. controls (5.18 (4.79–5.63) vs 5.87 (5.41–5.99) umol/g, p=0.013), with no differences in lactate, LDH, CPK, and NO activity. Raynaud’s attack was induced in all RP patients but not in controls. Median duration of hypoperfusion was greater in SSc vs. PRP (30 (27-35) vs. 12 (9–14) min, p=0.010), with a considerably longer recovery time (8 (4–10) vs 9 (0–1) min, p=0.006). No changes were observed in lactate, LDH, and CPK levels. A rise in free thiols occurred at recovery (T4) in all 3 groups (figure 1). The concentrations of NO-related products did not change during cooling or recovery. No association was detected between the extent of I/R and plasma parameters.

Conclusions: In patients with RP free thiols were significantly reduced, indicating increased redox stress. During the cooling and rewarming experiment, a clear rise in free thiols was observed during rewarming, irrespective of the underlying disease or finger perfusion. Meanwhile, NO-related products remained stable.
Although these findings need further study, they may suggest activation of ubiquitous antioxidant defense mechanisms during cooling and/or rewarming and should be explored for future use as a potential therapeutic target in RP.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5972

FR0367 NEW AUTOIMMUNE TARGETS IN IDIOPATHIC INFLAMMATORY MYOPATHIES - AN AGENT BEAD ARRAY APPROACH

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Background: The Idiopathic Inflammatory Myopathies (IIM) is a group of rare systemic inflammatory diseases characterized by severe organ involvement and premature mortality. Several myositis specific auto-antibodies (MSAs) have been recognized and associated with specific clinical manifestations and prognosis, still many patients are autoantibody negative. Identification of new autoimmune targets will be helpful in improving diagnosis, better stratifying into subgroups, prediction of prognosis, tailoring treatment and to understand underlying biological pathways.

Objectives: To identify new autoimmune targets in IIM by antigen bead array (1).

Methods: A bead array with 354 antigens was used to explore the autoimmune reactivity in 881 plasma samples from patients with IIM (N=225), Systemic Lupus Erythematosus (SLE) (N=350) and population controls (N=350). The antigens were selected from initial screenings of 160 SLE-samples on a total of 5760 antigens on planar arrays, and a first verification bead array with 355 antigens. The IIM samples represented three groups of patients with distinct diagnoses: Dermatomyositis (DM, N=83), Polymyositis (PM, N=111) and Inclusion Body Myositis (IBM, N=21), who were regularly followed at the Rheumatology Unit of the Karolinska University Hospital from January 2003 until March 2014. Based on 2 possible levels of cutoff, each sample was classified as reactive to each single antigen (Ag) at low or high cut off or non-reactive.

Results: In general, depending on the cutoff stringency, 86–88% of the 354 selected antigens showed reactivity in at least one sample with no difference between IIM, SLE and controls. Comparing PM, DM according to the cut off was observed towards E3 ubiquitin protein ligase 2 (SIAH2), leiomodin 2 (LMO2) and RAD23 homolog A (RAD23A). In the group of IIM patients with extensive clinical and nailfold capillaroscopy (NFC) pattern assessment, as well as quantification of serum E-sel, ICAM-1, ET-1, vWF, IL-6 and C-reactive protein (CRP) were performed on all patients. Associations between vascular biomarkers and disease characteristics were evaluated by Mann-Whitney U-test and Spearman correlations.

Conclusions: Serum biomarkers reflecting endothelial cell activation and/or dysfunction are elevated in patients with more severe SSC-associated vasculopathy and correlate with serum CRP. Together with NFC data they might be used for assessing vasculopathy severity in SSC and identifying patients who would benefit from more aggressive vasoactive treatment.

Acknowledgements: This work was performed as part of the project “Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis” (QUANTICAP), financed by the UEFISCDI PN-IP JPT-PCCA-2013–4-1589 grant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5203

FR0358 NAILFOLD CAPILLAROSCOPY CHANGES REACT-ENDOTHELIAL ACTIVATION AND INJURY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a severe connective tissue disease characterized by vascular and fibrotic changes in the skin and various internal organs. Pathogenesis of SSc includes early-onset vasculopathy with endothelial cell activation, microvascular injury and impaired angiogenesis.

Objectives: We aimed to determine the association of several biological molecules reflecting endothelial cell activation or dysfunction: E- selectin (E-se1), inter-cellular adhesion molecule 1 (ICAM-1), endothelin 1 (ET-1), von Willebrand factor (vWF) and interleukin 6 (IL-6), with distinct capillaroscopic SSc patterns and with more severe disease.

Methods: Forty consecutive SSc patients attending our EUSTAR SSc clinic, aged [median (IQR)] 52 (18) years, male gender 4/40 (10%), diffuse cutaneous subset (dcSSc) 14/27 (35%) were enrolled in this study. Extensive clinical and nailfold capillaroscopy (NFC) pattern assessment, as well as quantification of serum E-sel, ICAM-1, ET-1, vWF, IL-6 and C-reactive protein (CRP) were performed on all patients. Associations between vascular biomarkers and disease characteristics were evaluated by Mann-Whitney U-test and Spearman correlations.

Conclusions: Serum biomarkers reflecting endothelial cell activation and/or dysfunction are elevated in patients with more severe SSc-associated vasculopathy and correlate with serum CRP. Together with NFC data they might be used for assessing vasculopathy severity in SSC and identifying patients who would benefit from more aggressive vasoactive treatment.

Acknowledgements: This work was performed as part of the project “Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis” (QUANTICAP), financed by the UEFISCDI PN-IP JPT-PCCA-2013–4-1589 grant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5863

FR0359 PROSPECTIVE EVALUATION OF THE CAPILLAROSCOPIC SKIN ULCER INDEX (CSURI) IN CLINICAL PRACTICE

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Background: Nailfold videocapillaroscopy (NVC) is an imaging technique representing a reliable tool for the classification, diagnosis and monitoring of systemic sclerosis (SSc) patients. The capillaroscopic skin ulcer index (CSURI) was suggested to identify patients at risk of developing digital ulcers (DU) [1].

Objectives: This study aims (1) to describe the practicality of the CSURI in clinical practice, (2) to describe the change of CSURI during follow-up, and (3) to assess associations between the change in CSURI and demographic and disease characteristics.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5972
Scleroderma: A Validation Study Using Nailfold Video-Capillaroscopy

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Background: Optical Coherence Tomography (OCT) of the skin has been proposed as imaging biomarker of fibrosis in Systemic Sclerosis (SSc) [1]. However, over the past few years, growing efforts have been made to enable OCT to the study of human skin microcirculation including human nailfold [2].

Dynamic OCT (D-OCT) is a newly developed OCT technology that allows detection of blood flow in vivo in addition to the images of traditional OCT scans [3].

Objectives: Aims of this study were: 1) to evaluate face/criterion validity and feasibility of nailfold capillary D-OCT imaging as compared with nailfold video-capillaroscopy (NVC) capillary patterns in SSc patients; 2) to investigate whether D-OCT could offer a complementary value to NVC through the 3-dimensional reconstruction and quantification of nailfold capillary abnormalities in SSc patients.

Methods: Fifty subjects including forty SSc patients all fulfilling 2013 EULAR/ACR classification criteria (10 with normal/non-specific, 10 with early, 10 with active, 10 with late capillary pattern respectively) and ten age/gender-matched healthy volunteers (HV) were enrolled in this study. All subjects had NVC done on 8 fingers and classified according to the capillary pattern. Nailfold of the finguer with the worst capillary score in SSc patients and the 4th finger (the most affected in the SSc groups) of the dominant hand in subjects with normal capillary pattern was subsequently scanned using Viviosight D-OCT (Michelson Diagnostics Ltd., Kent, UK). D-OCT images were analyzed using the proprietary software tool to extract a quantitative measure of the speckle variance (SV)-signal. Results were expressed as mean±standard error. Statistical analysis was performed using GraphPad Prism software V.7.0.

Results: The finger with the worst capillary score was the 4th (33%) in the SSc patients. The typical nailfold capillary features seen at NVC were visualized at D-OCT images. Representative images are shown in figure 1. Each nailfold D-OCT scan lasted 60 seconds, was well tolerated and did not require use of gel or immersion oil. OCT mean SV-signal measurements were significantly different between HV and SSc patients with any specific capillary pattern (0.14±0.01 vs 0.10±0.01, p=0.0028) and between SSc patients without and with specific capillary pattern (0.14±0.01 vs 0.10±0.01, p=0.02). The mean SV-signal was higher in HV than in SSc patients without specific capillary pattern however the difference was not statistically significant. When analyzing the three specific capillary patterns, SV-signal measurements were not significantly different. Interestingly, within the late capillary pattern, mean SV-signal was significantly lower in patients displaying capillary loss as main feature compared with those with remarkable neoangiogenesis (p=0.03).

Conclusions: D-OCT is a feasible technique able to reproduce the capillary changes seen at NVC in SSc patients. More importantly D-OCT could offer a complementary value to quantify peripheral blood flow at capillary level. Future longitudinal studies are needed to evaluate the sensitivity to change over time and the potential of D-OCT as quantitative outcome measure of microvasculopathy in SSc.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5598
Background: Interstitial lung disease (ILD) is currently the primary cause of death in systemic sclerosis (SSc). Thoracic high-resolution computed tomography (HRCT) is considered the gold standard for diagnosis. Recent studies have proposed several clinical algorithms to predict the diagnosis and prognosis of SSc-ILD.

Objectives: To test the clinical algorithms to predict the presence and prognosis of SSc-ILD, and to evaluate the association of extent of ILD with mortality in a cohort of SSc patients.

Methods: Prospective cohort study, including 177 SSc patients assessed by clinical evaluation, laboratory tests, pulmonary function tests, and HRCT. Three clinical algorithms, combining lung auscultation, chest radiography and % predicted forced vital capacity (FVC) [1], were applied for the diagnosis of different extents of ILD on HRCT. Univariate and multivariate Cox proportional models were used to analyze the association of algorithms [1,2] and the extent of ILD on HRCT with the risk of death using hazard ratios (HR).

Results: The prevalence of ILD on HRCT was 57.1% and 79 patients died (44.6%) in a median follow-up of 11.1 years. For identification of ILD with extent ≥ 10 and ≥ 20% on HRCT, all algorithms presented a high sensitivity (> 89%) and a very low negative likelihood ratio (< 0.16). For prognosis, survival was decreased for all algorithms, especially the algorithm C (HR 3.47, 95% CI 1.62–7.42), which identified the presence of ILD based on crackles on lung auscultation, findings on chest X-ray or FVC < 80%. Extensive disease as proposed by Goh and Wells (extent of ILD > 20% on HRCT or, in indeterminate cases, FVC < 70%) had a significantly higher risk of death (HR 3.42, 95% CI 2.12 to 5.52). Survival was not different between patients with extent of 10 or 20% of ILD on HRCT, and analysis of 10-year mortality suggested that a threshold of 10% may also have a good predictive value for mortality. However, there is no clear cutoff above which mortality is sharply increased.

Conclusions: Clinical algorithms had a good diagnostic performance for extents of SSc-ILD on HRCT with clinical and prognostic relevance (> 10 and > 20%), and were also strongly related to mortality. Therefore, they probably could be used to obviate the requirement of HRCT in some cases.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1448

The DUCAS: A PROPOSAL FOR A DIGITAL ULCER ASSESSMENT SCORE IN SCLERODERMA

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Background: No objective measure is presently available to assess digital ulcer (DU) in SSc patients apart from “healed/non healed” and experience-based clinical judgment.

Objectives: The aim of the current study is to propose a composite DU clinical assessment score (DUCAS) and, to lend it, test its face validity by correlating it with commonly used disease related patient-reported outcomes (PROs) and physician evaluation.

Methods: SSc patients presenting at least one DU and attending the Rheumatology Wound Care Clinic of the Florence University Hospital or the London Royal Free Hospital were enrolled. Patients were assessed with HAQ-DI, Cochin scale, Visual analogic scale (VAS) for DU-related pain (DU_pain, 0–100 mm), patient global assessment (P GA, 0–100 mm) as PROs and physician VAS for DU status (phyGDU, 0–100mm). The DUCAS included 7 DU related variables selected by a committee of 8 SSc DU experts - they are outlined in figure 1. Each variable was weighted on a clinical basis and the DUCAS score was the sum of the values for the 7 variables (max=19.5). Spearman’s correlation tests were calculated for to examine face validity. A linear regression model with forward and backward stepwise analysis was used to determine the relationship of individual variables with the primary clinical parameter, phyGDU.

Results: 44 SSc patients (9 males, mean age 54.3±15.8 years, mean disease duration 9.9±5.8 years) were enrolled in the study. Mean phyGDU was 44.3±23.9mm, mean pGDU was 54±30mm (Wilcoxon p=0.022, phyGDU VAS vs pGDU) and mean DUCAS score was 4.2±2. Overall DUCAS showed significant positive correlations with all PROs, but when all the individual clinician and patient’s variables were modelled, only the overall DUCAS significantly predicted PhyGDU; after backwards stepwise analysis overall DUCAS and phyGDU best predicted PhyGDU, with an adjusted R²=0.437 and AIC=380.3 (Table 2).

Table 1

<table>
<thead>
<tr>
<th>A</th>
<th>Linear Regression for DUCAS</th>
<th>B</th>
<th>Linear Model to PhyGDU</th>
<th>Linear Model to PhyGDU after backwards stepwise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spearman Correlation p</td>
<td>Estimate SE p</td>
<td>Estimate SE p</td>
<td>Estimate SE p</td>
<td></td>
</tr>
<tr>
<td>PtGA</td>
<td>0.56</td>
<td>&lt;0.001</td>
<td>0.12</td>
<td>0.019</td>
</tr>
<tr>
<td>P GDU</td>
<td>0.54</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.171</td>
</tr>
<tr>
<td>DU Pain</td>
<td>0.44</td>
<td>&lt;0.003</td>
<td>0.048</td>
<td>0.012</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.44</td>
<td>0.001</td>
<td>4.58</td>
<td>0.7563</td>
</tr>
<tr>
<td>COCHIN</td>
<td>0.51</td>
<td>&lt;0.001</td>
<td>0.035</td>
<td>0.252</td>
</tr>
<tr>
<td>PhyGDU</td>
<td>0.63</td>
<td>&lt;0.001</td>
<td>4.636</td>
<td>1.617</td>
</tr>
</tbody>
</table>

Conclusions: DUCAS is a newly proposed clinical score for SSc related DU which has face validity and which may reflect DU status as judged by SSc experts. Further validation of this score will be undertaken.

Acknowledgements: Cosimo Bruni received a EULAR travel bursary to run this project in the UK.

Disclosure of Interest: None declared


Clinical Algorithms for the Diagnosis and Prognosis of Interstitial Lung Disease in Systemic Sclerosis

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Background: Interstitial lung disease (ILD) is currently the primary cause of death in systemic sclerosis (SSc). Thoracic high-resolution computed tomography (HRCT) is considered the gold standard for diagnosis. Recent studies have proposed several clinical algorithms to predict the diagnosis and prognosis of SSc-ILD.

Objectives: To test the clinical algorithms to predict the presence and prognosis of SSc-ILD, and to evaluate the association of extents of ILD on HRCT with clinical and prognostic relevance (HRCT) is considered the gold standard for diagnosis. Recent studies have proposed several clinical algorithms to predict the diagnosis and prognosis of SSc-ILD.

Methods: Three clinical algorithms, combining lung auscultation, chest radiography and % predicted forced vital capacity (FVC) [1], were applied for the diagnosis of different extents of ILD on HRCT. Univariate and multivariate Cox proportional models were used to analyze the association of algorithms [1,2] and the extent of ILD on HRCT with the risk of death using hazard ratios (HR).

Results: The prevalence of ILD on HRCT was 57.1% and 79 patients died (44.6%) in a median follow-up of 11.1 years. For identification of ILD with extent ≥ 10 and ≥ 20% on HRCT, all algorithms presented a high sensitivity (> 89%) and a very low negative likelihood ratio (< 0.16). For prognosis, survival was decreased for all algorithms, especially the algorithm C (HR 3.47, 95% CI 1.62–7.42), which identified the presence of ILD based on crackles on lung auscultation, findings on chest X-ray or FVC < 80%. Extensive disease as proposed by Goh and Wells (extent of ILD > 20% on HRCT or, in indeterminate cases, FVC < 70%) had a significantly higher risk of death (HR 3.42, 95% CI 2.12 to 5.52). Survival was not different between patients with extent of 10 or 20% of ILD on HRCT, and analysis of 10-year mortality suggested that a threshold of 10% may also have a good predictive value for mortality. However, there is no clear cutoff above which mortality is sharply increased.

Conclusions: Clinical algorithms had a good diagnostic performance for extents of SSc-ILD on HRCT with clinical and prognostic relevance (≥ 10 and ≥ 20%), and were also strongly related to mortality. Therefore, they probably could be used to obviate the presence of HRCT in some cases.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1448
SUBSTANCE P AND VASCULAR ENDOTHELIAL GROWTH FACTOR PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS DERIVING FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Many cytokines may potentially play a relevant role in the pathogenesis of different aspects of SSC, particularly fibrosis and endothelial injury. Some data suggest that substance P (SP) may act in an autocrine/paracrine manner to regulate vasconstriction and/or immunologic and inflammatory responses. VEGF and MCP1, which are produced by inflammatory cells, may be involved in the pathogenesis of vascular changes and accumulation of extracellular matrix in SSc.

Objectives: The aim of this study was to determine the expression of Substance P (SP), Vascular Endothelial Growth Factor (VEGF), Monocyte Chemoattractant Protein-1 (MCP-1) in SSc patients and their relationship with the main clinical manifestations of disease.

Methods: 34 SSc patients fulfilling the 2013 ACR/EULAR criteria for SSc and classified according to Leroy as having limited cutaneous (ISSc) or diffuse cutaneous disease (dSSc) were recruited. 28 sex and age matched healthy subjects was used as control. For each recruited patient we analyzed the disease characteristic, including the extent of skin fibrosis, the pattern of internal organ involvement, degree of skin involvement (Rodnan Skin Score), bone mass index (BMI). For each recruited patient we analyzed the disease characteristic, including the extent of skin fibrosis, the pattern of internal organ involvement, degree of skin involvement (Rodnan Skin Score), bone mass index (BMI), and autoantibody profile was found.

Results: The results showed that the mRNA and the protein levels of SP and VEGF were significantly higher in SSc patients compared to controls (190.56±5.1pg/mL vs. 85.56±9.1pg/mL, p<0.05); further, SP and VEGF levels were higher in dSSc compared to ISSc and correlated to disease duration. No difference was detected in MCP1 synthesis and expression between SSc subjects and healthy controls (507.17±153.9pg/mL vs 481.21±19.2pg/mL, p>0.05). In SSc patients a slight increase was observed. VEGF production negatively correlated with the prevalence of DU. No correlation between cytokine production and clinical manifestations was evaluated.

Conclusions: The preliminary data of this study show that SP and VEGF are overproduced in PBMCs of SSc subjects and are related to the extent of skin involvement, whereas only VEGF production negatively correlates with the prevalence of DU. The exact role played by SP and VEGF in the pathogenesis of vascular injury and fibrosis in SSc and their relationship with the immune abnormalities observed in this disease is not completely clear and the available data are contrasting. Additional in vitro and in vivo studies are needed to better understand the role of SP and VEGF in the pathogenesis of SSc.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6887

BONE MINERAL DENSITY AND TRABECULAR BONE SCORE IN TWO SUBSETS OF SYSTEMIC SCLEROSIS PATIENTS

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Background: Data concerning the relationship between Systemic Sclerosis (SSc) and alterations of Bone Mineral Density (BMD) are very conflicting. The established standard for measuring BMD is Dual X-ray Absorptiometry (DXA), but other methods such as Peripheral Blood Mononuclear Cells (PBMCs) were isolated and cultured from both SSc patients and healthy controls. The expression of SP, VEGF, MCP1 was analyzed by real-time polymerase chain reaction (PCR) and their concentrations in supernatants of cultured PBMCs using enzyme-linked immunosorbent assay (ELISA). The correlation between cytokine expression and clinical manifestations was evaluated.

Results: The results showed that the mRNA and the protein levels of SP and VEGF were significantly higher in ISSc patients compared to controls (190.56±5.1pg/mL vs. 85.56±9.1pg/mL, p<0.05); further, SP and VEGF levels were higher in dSSc compared to ISSc and correlated to disease duration. No difference was detected in MCP1 synthesis and expression between SSc subjects and healthy controls (507.17±153.9pg/mL vs 481.21±19.2pg/mL, p>0.05). In dSSc patients a slight increase was observed. VEGF production negatively correlated with the prevalence of DU. The exact role played by SP and VEGF in the pathogenesis of vascular injury and fibrosis in SSc and their relationship with the immune abnormalities observed in this disease is not completely clear and the available data are contrasting. Additional in vitro and in vivo studies are needed to better understand the role of SP and VEGF in the pathogenesis of SSc.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5207

REAL-LIFE TREATMENT STRATEGIES FOR SYSTEMIC SCLEROSIS ACCORDING TO EXPERTS

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Background: Second line treatment options for Systemic Sclerosis (SSc) are limited, and scarce data are available for choosing the order of treatment.

Objectives: The aim of this study is to update the SSc treatment algorithms obtained in 2012, based on SSc experts’ daily practice.

Methods: An initial survey was designed based on the 2012 algorithms. The survey asked experts whether they agreed with the 2012 algorithms or not, and which changes should be considered. The questionnaire was completed by 62 of 168 surveyed (67% response) between August and October 2016.

Results: For scleroderma renal crisis (SRC), there was 65% to 69% agreement with the previous algorithms (1st line angiotensin converting enzyme inhibitors [ACE1], 2nd and 3rd adding: calcium channel blockers [CCB] or angiotensin receptor blockers [ARB], and 4th alpha-blocker). In mild pulmonary arterial hypertension (PAH), only 45% of the experts agreed with the old algorithm. The majority suggested first phosphodiesterase 5 inhibitors (PDE5i) or endotelin receptor antagonists (ERA) plus PDE5i, then prostanoids. In severe PAH, 65% agreed with the previous scheme (1st prostanoids, 2nd ERA plus PDE5i, 3rd ERA plus prostanoids). For mild Nailaoud's phenomenon (RP) 66% agreed with the previous algorithm (1st CCB, 2nd adding PDE5i, 3rd ARB or switching to another CCB, 4th prostanoids). Regarding severe RP, 52% agreed with previous (1st CCB, 2nd adding PDE5i, 3rd ERA, 4th prostanoids). Conversely, 60% of the experts did not agree with the prior active digital ulcer (DU) treatment, suggesting 1st CCB, 2nd PDE5i, 3rd prostanoids. For intestinal lung disease (ILD), for induction only 24% agreed with the older proposal. Experts suggested 1st periostitent myophenolate (MMF), 2nd intravenous (IV) cyclophosphamide (CYP), 3rd rituximab. There was a 65% agreement on ILD maintenance (1st MMF, 2nd azathioprine [AZA], 3rd IV CYP, 4th oral CYP). For skin involvement, agreement for patients with a modified Rodnan skin score (mRSS) of 10 was 57% (1st methotrexate [MTX]), 2nd MMF; if the mRSS was 24, 32% suggested 1st MTX, 2nd MMF, 3rd prostanoids. For severe Raynaud’s phenomenon (RP) 65% agreed with the previous algorithm, whereas others suggested 1st MTX, 2nd low dose steroids, 3rd hydroxychloroquine, 4th rituximab or tocilizumab.

Conclusions: There remains some disagreement for 2nd line treatment of SSc. Combination of PDE5i and ERA are prescribed now in mild PAH treatment.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1574
Differences in Right Ventricular Function and Morphology in SSC-PAH and IPAH Assessed by Right Heart Catheterization and Cardiac MRI

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Background: Systemic sclerosis (SSc) is a serious disorder with high mortality, mainly driven by cardiopulmonary pathologies including pulmonary arterial hypertension (PAH). Patients with SSC-PAH appear to have worse prognosis than idiopathic PAH (IPAH).

Objectives: (A) Compare cardiac magnetic resonance (CMR) of the right ventricle, hemodynamic parameters and immunological markers between patient cohorts with SSC-PAH, IPAH and without PAH, respectively. (B) Evaluate the impact of these variables on PAH-related heart morbidity and mortality.

Methods: The study cohort included SSC-PAH (n=16), IPAH (n=15) and SSc without PAH (n=20). At baseline, all patients were examined by ventricular volumes by short axis summation of cine CMR, echocardiography and right heart catheterization (RHC). Blood samples were analysed for immune-related factors. At a median follow up of 3 years, clinical data, and new onset of PAH and vital status were registered. A composite outcome for PAH related events was created including: PAH progression, end-stage PAH, hospitalization for PAH worsening and all-cause mortality. Association between parameters was assessed using ANOVA, Pearson Chi-square, Fishers exact, or independent sample t-test.

Results: Patients with SSC-PAH were significantly older at PAH onset, had lower 6MWD, DL60% and Hb than the IPAH patients. RHC results are shown in Table 1. CMR showed that SSC-PAH patients had lower right ventricular mass index (RVM), RV to left ventricular ratio and RV mass to volume ratio (Table 1). Multiple immune assays demonstrated higher serum levels of IP-10, VEGF and, IL12 in SSC-PAH than in IPAH. At the end of study, 12/15 SSC-PAH had developed a PAH-related event. Compared to event-free patients, they were marked by significant CMR changes including higher RVM (p=0.006) and RVMI (p=0.005).

In the IPAH subgroup, 7/16 patients developed an event. These patients were characterized by younger age at onset (p=0.001), higher NT-proBNP (p=0.017), lower 6MWD (p=0.034), higher RVM (p=0.010), RV-to-LV ratio (p=0.001) on CMR.

Conclusions: The CMR measures indicate that the RV adapts differently in IPAH and SSC-PAH; with more pronounced RV hypertrophy in IPAH patients. The mechanisms behind the differences in RV hypertrophy in SSC-PAH and IPAH are not known, but may involve microvascular changes and deregulated inflammatory cascades. This study indicates that CMR can predict PAH progression in SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1390

FRI0378 CARDIAC INVOLVEMENT IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE AT RISK FOR SYSTEMIC SCLEROSIS. A TISSUE DOPPLER IMAGING STUDY

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Background: Undifferentiated connective tissue disease at risk for Systemic Sclerosis (UCTD-risk SSCs), previously referred to as very early SSCs, is a condition characterized by Raynaud’s phenomenon (RP) with SSC marker autoantibodies and/or typical capillaroscopic findings and unsatisfying classification criteria for the disease (1). UCTD-risk SSCs patients have been reported to present, in about 40% of the cases, a preclinical vascular internal organ disease as detected by a diffusing lung capacity for CO <80% of the predicted value (lung involvement) and/or a low esophageal sphincter pressure <15 mmHg (oesophageal involvement) and/or a mitral E/A ratio <1 (heart involvement) (2, 3).

Methods: NCM was assessed in consecutive patients with RP (n=759) by widefield videocapillaroscopy, according to standardized procedures at a dedicated vascular laboratory by trained and experienced technicians. The pattern was classified as normal (n=325), non-specific (n=188) or SSc pattern (early (n=106), active (n=140) or late (n=0) based on the Cutolo patterns). Potential pulmonary involvement was defined as forced vital capacity or diffusion capacity <70%.

Gastro-intestinal involvement as scintigraphically (Tc-99M colloid) oesophageal dysmotility. Skin involvement as puffy fingers or sclerodactyly. Patients were classified as primary RP (normal NCM and negative serology, n=226) or secondary RP (abnormal NCM and/or serology) groups: early SSc (n=165), SSc (n=40), incomplete Sjogren’s syndrome (SSS, n=5), primary SS (pSS, n=30), incomplete systemic lupus erythematoses (ISLE, n=42), SLE (n=30), mixed CTD (MCTD, n=7), rheumatoid arthritis (RA, n=15) or when meeting criteria as other (n=169). None were diagnosed with polymyositis or dermatomyositis.

Results: SSc pattern was observed in 33% of patients with pSS, 17% SLE, 71% MCTD and 13% RA. Pulmonary, oesophageal and skin involvement was more frequent in secondary RP patients with an SSc pattern, even when analysing only those fulfilling definite criteria for CTD or after exclusion of early SSc and SSc patients. For secondary RP patients, absence of an SSc NCM pattern had a high negative predictive value for pulmonary (92%), oesophageal (91%) and skin (96%) involvement, while positive predictive values were low.

Table 1. NCM pattern in consecutive patients with Raynaud’s phenomenon

<table>
<thead>
<tr>
<th>NCM pattern</th>
<th>Primary Raynaud</th>
<th>Secondary Raynaud</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSc</td>
<td>pSS</td>
<td>SLE</td>
</tr>
<tr>
<td>Early</td>
<td>n=165</td>
<td>n=40</td>
</tr>
<tr>
<td>Early</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Active</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: SSc pattern on NCM is common in CTD patients and is associated with frequent prevalence of organ involvement, even in the absence of (early) SSc. Although this was a retrospective cohort, these data underline the importance of assessing NCM in RP patients to evaluate the risk for organ involvement in CTD other than SSc, already in early disease stages.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1390

FRI0376 ABNORMAL NAILFOLD CAPILLAROSCOPY PATTERN IS COMMON IN PATIENTS WITH CONNECTIVE TISSUE DISEASE AND ASSOCIATED WITH ORGAN INVOLVEMENT

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Background: Nailfold capillary microscopy (NCM) has been shown to be associated with disease severity and internal organ involvement in non-consecutive systemic sclerosis (SSc) cohorts. NCM may help in early recognition of connective tissue disease (CTD) but it is unclear to which extent NCM abnormalities occur in several CTD and whether these are associated with organ involvement.

Objectives: To assess NCM in consecutive patients with Raynaud’s phenomenon (RP) and whether these are associated with signs of organ involvement.

Methods: NCM was assessed in consecutive patients with RP (n=759) by wide-field videocapillaroscopy, according to standardized procedures at a dedicated vascular laboratory by trained and experienced technicians. The pattern was classified as normal (n=325), non-specific (n=188) or SSc pattern (early (n=106), active (n=140) or late (n=0) based on the Cutolo patterns). Potential pulmonary involvement was defined as forced vital capacity or diffusion capacity <70%.

Gastro-intestinal involvement as scintigraphically (Tc-99M colloid) oesophageal dysmotility. Skin involvement as puffy fingers or sclerodactyly. Patients were classified as primary RP (normal NCM and negative serology, n=226) or secondary RP (abnormal NCM and/or serology) groups: early SSc (n=165), SSc (n=40), incomplete Sjogren’s syndrome (SSS, n=5), primary SS (pSS, n=30), incomplete systemic lupus erythematoses (ISLE, n=42), SLE (n=30), mixed CTD (MCTD, n=7), rheumatoid arthritis (RA, n=15) or when meeting criteria as other (n=169). None were diagnosed with polymyositis or dermatomyositis.

Results: SSc pattern was observed in 33% of patients with pSS, 17% SLE, 71% MCTD and 13% RA. Pulmonary, oesophageal and skin involvement was more frequent in secondary RP patients with an SSc pattern, even when analysing only those fulfilling definite criteria for CTD or after exclusion of early SSc and SSc patients. For secondary RP patients, absence of an SSc NCM pattern had a high negative predictive value for pulmonary (92%), oesophageal (91%) and skin (96%) involvement, while positive predictive values were low.

Table 1. NCM pattern in consecutive patients with Raynaud’s phenomenon

<table>
<thead>
<tr>
<th>NCM pattern</th>
<th>Primary Raynaud</th>
<th>Secondary Raynaud</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSc</td>
<td>pSS</td>
<td>SLE</td>
</tr>
<tr>
<td>Early</td>
<td>n=165</td>
<td>n=40</td>
</tr>
<tr>
<td>Early</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Active</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: SSc pattern on NCM is common in CTD patients and is associated with frequent prevalence of organ involvement, even in the absence of (early) SSc. Although this was a retrospective cohort, these data underline the importance of assessing NCM in RP patients to evaluate the risk for organ involvement in CTD other than SSc, already in early disease stages.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1390
Objectives: Aim of the present study was to assess the prevalence of right (RV) or left ventricle (LV) systolic and/or diastolic dysfunction by standard echocardiography and tissue Doppler imaging (TDI).

Methods: Thirty patients with UCTD-risk-SSc (28 female, aged 47±13 years, range 21–70) and 30 age- and sex-matched controls underwent cardiac assessment by standard echocardiography and TDI.

Results: UCTD-risk-SSc patients and controls did not show any difference at standard echocardiographic evaluation. In particular, an inverted E/A ratio was pointed out in 10/30 patients and 7/30 controls (p=ns). TDI showed a mild impairment of LV and RV diastolic (Ea=15±4 vs 19±2, p<0.001; E/e= 6.1±7 vs 4.8±1.2, p=0.001; E: 14.5±3 vs 16.2±2, p=0.02; E/A:0.9±0.4 vs 1.30±3, p=0.002; increased pulmonary artery wedge pressure 9±2 vs 8±1, p=0.001) and systolic function (Smax 3.2±2 vs 5.2±2 cm/sec, p<0.0003; Ss 14±2 vs 16±3 cm/sec, p<0.0001) in UCTD-risk-SSc patients in comparison to controls.

Conclusions: Our study shows that UCTD-risk-SSc patients present a previously unrecognized, mild biventricular systolic and diastolic dysfunction as compared to controls. The pathophysiologic meaning (i.e.intramyocardial artery disease and/or patchy fibrosis) as well the predictive value of developing overt SSc should be elucidated.

Disclosure of Interest: None declared. DOI: 10.1136/annrheumdis-2017-eular.5080

FR10379 PREVALENCE OF FAM111 B GENE MUTATIONS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a prototypic systemic fibrotic disease with unclearly characterized genetic basis. Implicated genes have been associated with autoimmune dysregulation with relatively few variants associated with fibrosis [1]. We have discovered that mutations in FAM111 B gene cause hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis (POIKTMP)[2], a multisystem fibrotic condition with clinical aspects of SSc [3]. This observation has established FAM111B as a candidate gene for SSc.

Objectives: The objective is to investigate whether FAM111B gene mutations are present in SSc patients and further explore relationships between FAM111B mutations and clinical expression of SSc.

Methods: Patients with a definite diagnosis of SSc attending the Rheumatology outpatient departments at Groote Schuur Hospital, Cape Town, and Chris Hani Baragwanath Hospital, Johannesburg, were enrolled into the study. Physical examination assessing the extent of disease was done in all patients and the modified Rodnan skin score (mRSS) was used to determine the extent of the skin involvement. Blood samples were collected for DNA extraction and mutation screening using the high-resolution melt technology. Samples with abnormal electropherograms were selected for Sanger sequencing to identify mutations. Public databases were used to verify the frequency of variants in FAM111B.

Results: 131 patients were genotyped, 13 men and 118 women, with a mean age 57±6 years. The majority of patients were black (59.5%). 72% of patients had diffuse systemic sclerosis (DSSc) with a median mRSS of 11. Genetic analysis revealed seven rare genetic polymorphisms with no functional impact.

Conclusions: Rare genetic variants of unknown significance (GVUS) in FAM111 B gene were found in patients with SSc. It is possible that the GVUS may modify the function of FAM111B, and influence the pathogenesis of SSc or are rare polymorphisms with no functional impact.

Disclosure of Interest: None declared. DOI: 10.1136/annrheumdis-2017-eular.4320

FR10380 PATIENT PREFERENCES AND DIFFICULTIES CONCERNING THE HOME TREATMENT OPTIONS IN SYSTEMIC SCLEROSIS (SSC)

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Background: SSC patients suffer from Raynaud’s phenomenon, hand skin hardening and scarring, digital ulcers, esophagus/gastric dysmotility, dysphagia and mucosal dryness. These symptoms significantly reduce patient’s life autonomy and impair the capacity to handle their therapy usually made by different modalities of administration: oral, topical, inhalation, intramuscular, subcutaneous, intravenous, and rectal.

Objectives: to investigate the methods of administration used by SSC patients, their preferred methods, their compliance to pharmacological therapy, and the difficulties that are encountered by the patients during pharmacotherapy.

Methods: 2 questionnaires were prepared on an ad hoc basis. The first given to patients, the second to be filled out by the patient’s physician. The first questionnaire comprised 25 questions to investigate the problems the patients when taking their medications by correlating these with two validated activities indices: SHAQ-DI (activities of daily living) and the COCHIN scale (hand activities). The second questionnaire was composed of the standard SSC-related clinical information (eg.age, sex, disease duration, symptoms). 80 Ssc patients completed the questionnaires, maintaining anonymity. A “difficulty index” was also filled out, where: 0 = no difficulty to 4 = impossible to use or too difficult to use.

Results: In particular, the dimension of the pills is problematic, and has identified a paradoxical situation because large pills are difficult to swallow (41.25% patients who use pills) but at the same time small pills are difficult to pinch with the fingers (62.25% patients who use pills).

Conclusions: SSC patients experience significant problems in maintaining adherence to treatments due to difficulties in the use of blisters and bottles with children proof stoppers. Pills still remain the most preferred method of treatment. In conclusion, patients unanimously wished to avoid the use of blisters, definitively preferring bottles without the children proof stopper to make the treatment easier and provide a more independent life.

Disclosure of Interest: None declared. DOI: 10.1136/annrheumdis-2017-eular.4848

FR10381 INCREASED RISK OF OSTEOPOROTIC FRACTURES IN ADULT PATIENTS WITH POLYMYSITIS AND DERMATOMYOSITIS: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Background: Patients with polymyositis and dermatomyositis (PM/DM) are characterized by chronic muscle weakness due to autoimmune-mediated myositis and are usually treated with corticosteroids initially. PM/DM patients prone to develop osteoporosis and subsequent fractures but are rarely investigated.

Objectives: To explore the incidence rate (IR) and risk factors of osteoporotic fractures (OFs) among adult PM/DM patients.

Methods: We conducted a cohort study by utilizing the Taiwan National Health Insurance database. PM/DM patients and respective age- and gender-matched cohort without PM/DM were enrolled. The primary endpoint was the initial event of OFs. We used the Cox proportional hazard model to study the risk factors of OFs in the PM/DM cohort.

Results: Among 2391 PM/DM patients (67.8% female, mean age: 49.5 years) followed for a mean (SD) of 6.1 (5.0) years, 116 developed vertebral fractures, 32 had hip fractures, and 14 experienced radius fractures (IR: 8.18, 2.20, and 0.96 per 1000 person-years, respectively, Table 1). Compared with the matched cohort, the PM/DM patients had higher IR (RRs) (95% CIs) of OFs at all age groups at enrollment: 3.27 (2.19 to 4.81; p<0.0001) for people <50 years and 2.29 (1.85 to 2.82; p<0.0001) for those ≥50 years. The RRs were 2.39 (1.92

Table 1. Patient use of pharmacological therapies

<table>
<thead>
<tr>
<th>% Using</th>
<th>% Users preferring this method</th>
<th>Difficult index</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>100</td>
<td>91.25</td>
<td>0.83</td>
</tr>
<tr>
<td>Eye drops</td>
<td>52.5</td>
<td>2.5</td>
<td>0.77</td>
</tr>
<tr>
<td>Topicals</td>
<td>33.75</td>
<td>3.75</td>
<td>0.77</td>
</tr>
<tr>
<td>Injections</td>
<td>28.25</td>
<td>2.5</td>
<td>2.17</td>
</tr>
<tr>
<td>Inhaler</td>
<td>16.25</td>
<td>0</td>
<td>1.07</td>
</tr>
<tr>
<td>Vaginal/rectal</td>
<td>6.25</td>
<td>0</td>
<td>1.03</td>
</tr>
</tbody>
</table>

Table 2. Most frequent problems encountered

<table>
<thead>
<tr>
<th>% Using</th>
<th>Most frequent problems</th>
<th>% Users have these problems</th>
<th>Difficult index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>100</td>
<td>Blister: pushing out pills</td>
<td>73.75</td>
</tr>
<tr>
<td>Eye drops</td>
<td>52.5</td>
<td>Open thin stoppers</td>
<td>76.75</td>
</tr>
<tr>
<td>Topicals</td>
<td>33.75</td>
<td>Cannot open the top (safety lock)</td>
<td>70.5</td>
</tr>
<tr>
<td>Inhaler</td>
<td>16.25</td>
<td>Cannot spray/push the inhaler</td>
<td>85</td>
</tr>
</tbody>
</table>

*14 = most difficult.
to 2.94, p<0.0001) for vertebral fractures and 1.62 (1.07 to 2.38, p=0.0093) for hip fractures. PM/DM patients experienced vertebral fractures and hip fractures at younger ages (62.2 vs 68.4 and 66.0 vs 75.4 years, respectively; both p<0.001). Multivariable Cox regression analyses showed that being female gender, age ≥50 years, having hypertension, coronary artery disease, asthma, and using daily prednisolone equivalent to >5 mg are associated with rQS.

Table 1. IRs and IRRs of osteoporotic fractures: overall and subgroup analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>IRs</th>
<th>Control IR</th>
<th>IRR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall fracture</td>
<td>10.90</td>
<td>5.23</td>
<td>2.08 (1.73 to 2.49)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age &lt;50 year</td>
<td>4.51</td>
<td>1.38</td>
<td>3.27 (2.19 to 4.81)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age ≥50 year</td>
<td>22.59</td>
<td>9.85</td>
<td>2.29 (1.85 to 2.82)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vertebral fracture</td>
<td>8.18</td>
<td>3.43</td>
<td>2.39 (1.92 to 2.94)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age &lt;50 year</td>
<td>3.39</td>
<td>0.98</td>
<td>3.47 (2.17 to 5.44)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age ≥50 year</td>
<td>16.82</td>
<td>6.33</td>
<td>2.66 (2.07 to 3.39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>2.20</td>
<td>1.36</td>
<td>1.62 (1.07 to 2.38)</td>
<td>0.0093</td>
</tr>
<tr>
<td>Age &lt;50 year</td>
<td>0.65</td>
<td>0.10</td>
<td>6.56 (1.75 to 24.6)</td>
<td>0.0027</td>
</tr>
<tr>
<td>Age ≥50 year</td>
<td>4.87</td>
<td>2.83</td>
<td>2.72 (1.09 to 2.62)</td>
<td>0.0081</td>
</tr>
<tr>
<td>Radius fracture</td>
<td>0.96</td>
<td>0.83</td>
<td>1.15 (0.60 to 2.02)</td>
<td>0.3081</td>
</tr>
<tr>
<td>Age &lt;50 year</td>
<td>0.43</td>
<td>0.35</td>
<td>1.25 (0.31 to 2.63)</td>
<td>0.3289</td>
</tr>
<tr>
<td>Age ≥50 year</td>
<td>1.98</td>
<td>1.40</td>
<td>1.35 (0.62 to 2.63)</td>
<td>0.1857</td>
</tr>
</tbody>
</table>
| IR, incidence rate per 1000 person-year; IRR, incidence rate ratio; CI, confidence interval.

Conclusions: Implementation of DA in a largely asymptomatic non-selected SSc patient population is more sensitive for RHC referral than annual TTE screening. Recommendations for RHC per DETECT score are difficult to predict on symptom and other traditional clinical parameters. The use of DA will lead to increased RHC referrals. Cardiologists may need education on this new method for screening and although the ESC/ERS 2015 guidelines discuss DA, they conclude that its cost-effectiveness has not been clarified as compared with symptom-based detection.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5928

FR10382

USE OF THE DETECT ALGORITHM FOR EARLY PULMONARY ARTERY HYPERTENSION DIAGNOSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS IN EVERYDAY CLINICAL PRACTICE

C. Koutsianas, S. Subasinghe, K. Douglas. Department of Rheumatology, The Dudley Group NHS Foundation Trust, Dudley, United Kingdom

Background: The DETECT algorithm (DA)¹ provides a sensitive tool for early identification of patients with Systemic Sclerosis (SSc) at risk of Pulmonary Arterial Hypertension (PAH) and advocates evaluation with Right Heart Catheterisation (RHC). Few published data look into its implementation in everyday clinical practice and compare it to annual echocardiographic (TTE) screening.

Objectives: To compare DA and TTE screening of SSc patients for RHC referral rates and related patient characteristics.

Methods: Data on 57 consecutive patients with a diagnosis of SSc that had at least one visit to Russells Hall Hospital Scleroderma clinic from February to November 2016 was prospectively collected on Excel (clinical history, physical examination, immunological status, treatment, PFTs, NT-proBNP, urate, ECG, TTE, CXR and HRCT results). DETECT scores were calculated (www.detect-pah.com) and compared with the TTE probability for PAH as per the 2015 ESC/ERS Guidelines.²

Results: 31 patients with a full set of data were included in the final analysis. 93.5% were female with a mean age of 64.4±12.9 years, 87% had limited cutaneous (lc) SSc, 58.1% positive anticentromere antibody and mean time since diagnosis was 6.2±3.2 years. The majority of patients (80%) were asymptomatic for PAH. Mean DLCO was 60.9±18.3% predicted (the DETECT study included on patients with DLCO<60%). We did not exclude patients with renal insufficiency; mean eGFR was 74±17.7ml/min.

The implementation of DA recommended RHC in 18/31 patients (DETECT step 2 score >3.5, 58%, see table 1) compared to just 4/31 (13%) based on TTE by 2015 ESC/ERS guidelines. The additional 14 patients identified by DA were found to have no statistically significant differences in SSc type, dyspnea symptomatology, immunosuppressive treatment, presence of interstitial lung disease (ILD), age, time from diagnosis or symptom onset, eGFR and CRP compared to patients where RHC was not recommended. From the 18 patients identified by DA, only 4 reported shortness of breath. 2/18 had existing cardiac conditions (aortic stenosis, left ventricular hypertrophy), while 9/18 had ILD (5 mild, 2 moderate, 2 severe as per HRCT).

Table 1. DETECT step 2 score

<table>
<thead>
<tr>
<th>Age, years (median (IQR))</th>
<th>Disease duration, years (median (IQR))</th>
<th>eGFR, ml/min (median (IQR))</th>
<th>CRP, mg/L (median (IQR))</th>
<th>DLCO, % (median (IQR))</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>65.8 (26.9)</td>
<td>63.2 (22.3)</td>
<td>72.4 (25.1)</td>
<td>0.875</td>
</tr>
<tr>
<td>35–39</td>
<td>8 (4)</td>
<td>4 (7)</td>
<td>5 (9)</td>
<td>0.996</td>
</tr>
<tr>
<td>≥40</td>
<td>80 (28)</td>
<td>83 (17)</td>
<td>54.5 (47)</td>
<td>0.158</td>
</tr>
<tr>
<td>≥50</td>
<td>3.39</td>
<td>0.98</td>
<td>3.47 (2.17 to 5.44)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Overall fracture</td>
<td>10.90</td>
<td>5.23</td>
<td>2.08 (1.73 to 2.49)</td>
<td>&lt;0.0001</td>
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<td>Vertebral fracture</td>
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<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>2.20</td>
<td>1.36</td>
<td>1.62 (1.07 to 2.38)</td>
<td>0.0093</td>
</tr>
</tbody>
</table>

Conclusions: Adult PM/DM patients had a high IR of vertebral and hip fractures. Patients who were female, advanced age, having certain comorbidities, and exposed to corticosteroid exhibited a higher risk.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6043

FR10383

DETECT SCREENING FOR PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS: DATA FROM AN EUSTAR COHORT

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Background: Early documentation of pulmonary arterial hypertension (PAH) related to systemic sclerosis (SSc) remains a challenge in daily clinical practice, with major prognostic and therapeutic implications. Although several screening algorithms specifically designed to optimize the detection of secondary PAH have already been proposed (e.g., DETECT, REVEAL), no precise approach received complete validation, especially the use of invasive diagnostic right heart catheterization (RHC).

Objectives: Main objective was to assess the risk of PAH in patients with SSc and to compare with PAH screening promoted by European Society of Cardiology/European Respiratory Society (ESC/ERS) 2009 guidelines, while secondary one to identify predicting factors for developing PAH among clinical and immunological SSc variables.

Methods: Cross-sectional prospective single-center study, applying the DETECT calculator in patients with SSc recruited in EUSTAR 162 center cohort between January 2013- December 2016; all SSc completing at least two monitoring visits at 6 months were considered. Standard assessments included MEDS (minimal data set EUSTAR), annual echocardiography with systolic pulmonary artery pressure (sPAP), pulmonary function tests with forced vital capacity (FVC), percentage predicted/diffusing capacity for carbon monoxide (DLCO) % predicted, ECG, serum biomarkers (serum urate, NT-proBNP).

PAH risk calculator (http://detect-pah.com/pah-risk-calculator), a tool developed and validated in the DETECT study, is able to identify patients requiring echocardiography (STEP 1) respectively RHC (STEP 2), and was systematically applied in our cohort. All sPAP ≥45 mmHg or between 35–45 mmHg in the presence of dyspnea were proposed for invasive testing.

Statistical analysis was performed in IBM SPSS-19 version, p<0.05.

Results: 41 out 56 SSc in our database were recruited: mainly women (85.36%) with diffuse cutaneous SSc (63.41%), anti-topoisomerase (up to half) and anti-centromere (about one third) positive disease; one out of four SSc presented with digital ulcers and one of three with active capillaroscopic pattern.
Using the DETECT PAH calculator, 14/41 (34.14%) were recommended for RH as follows: an initial value above 300 points in STEP 1 (with further indication of echocardiographic assessment) and subsequent STEP 2 over 35 were recorded. On the other hand, only 9/41 (21.95%) cases met the ultrasound criteria to be addressed to an invasive assessment when applying the ESC/ERS 2009 guidelines, the difference being statistically significant as compared to DETECT (p<0.05).

PAH was finally confirmed in 8/41 (19.51%) cases, supporting our preliminary results in a pilot study on a limited number of patients.

**Conclusions:** DETECT is a reliable algorithm for early detection of PAH in patients with SSC, optimizing PAH screening and prompting the rheumatologist-cardiologist collaboration.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4053

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**FRI0384**

**A MINI-INVASIVE TECHNIQUE FOR HAEMODYNAMIC EVALUATION: NEW PERSPECTIVES FOR PULMONARY ARTERIAL HYPERTENSION (PAH) DIAGNOSIS IN SYSTEMIC SCLEROSIS (SSC)**

E. Bellucci 1, M.S. Romano 2, M. Chiostri 2, C. Bruni DLCO 0.94 0.87–1.01 0.072

Right stroke work index 1.12 1.03–1.21 0.007

DLCO 0.94 0.90–0.99 0.021

Right Cardiac Power index 1.11 1.04–1.18 0.002

Arterial Elastance 3.16 0.70–14.24 0.134

Dicrote Pressure 1.04 1.00–1.09 0.064

**Methods:** 40 ssc patients (35 women, mean age 60±9,3 years; mean disease duration 7.5 years) were evaluated with both RHC and PRAM on the same day. Mean pulmonary arterial pressure (mPAP), cardiac index (CI), systemic vascular resistances (SVR), right cardiac power index (RCPI, calculated with mPAP×CO/HR×451) were measured and concordance of the two methods was assessed through Bland-Altman analysis. Systolic pulmonary arterial pressure and TAPSE from echocardiography, forced vital capacity, total lung capacity, both absolute and alveolar volume adjusted Carbone oxide lung diffusion (DLCO and DLCO/VA) from pulmonary function tests, blood tests parameters, nailfold videocapillaroscopy scleroderma patterns were recorded. Univariate and multivariate logistic regression analysis identified variables correlating with RHC-diagnosed PAH: a scoring system was then created, giving 1 point for value satisfying cut-off level.

**Results:** PRAM showed concordance with RHC estimate of CI and SVR within 95% interval confidence; 14 patients were diagnosed with PAH (mean age 64.4±9.3, mean disease duration 10.5 years, IScE 61.5%). Multivariate logistic regression analysis showed DLCO (cut off value 47% obtained through ROC curve analysis, p=0.004) and RCPI (cut off value 0.12 Watt obtained through ROC curve analysis, p=0.001) as the most highly PAH-associated variables. When combining these two variables in the scoring system, patient with score=0 (DLCO<47% and RCPI<0.12 Watt), score=1 (DLCO≥47% or RCPI<0.12 Watt) and score=2 (DLCO<47% and RCPI≥0.12% were 0%, 21.4% and 78.6% of the PAH population respectively.

**Conclusions:** PRAM is comparable to RHC in detecting haemodynamic parameters such as SVR and CI. The scoring system combining DLCO and RCPI, obtained with non-invasive tools, could offer the possibility of detecting PAH patients with a high specificity.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5817

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**FRI0385**

**JOINT MANIFESTATIONS IN PATIENTS DIAGNOSED WITH IDIOPATHIC INFLAMMATORY MYOPATHY: MULTICENTER REGISTRY**


**Background:** Idiopathic inflammatory myopathies (IIM) comprise a heterogeneous group of autoimmune conditions. Joint involvement can be considered to be part of the IIM systemic manifestations, together with a possible gastrointestinal, cardiovascular or pulmonary involvement. Although articular involvement in the IIM has been described as variable and non-specific with a chronic course it might be an early symptom of dermatomyositis in up to 30% of cases and in those patients with overlap syndromes.

**Objectives:** To evaluate and to identify joint manifestations in IIM patients.

**Methods:** We evaluated a cohort of 479 patients that included 12 hospitals in the Community of Madrid belonging to the IIM registry of the Society of Rheumatology of Madrid (SORCOM-REMICA) with diagnosis from January 1980 to December 2014. All patients were diagnosed of IIM according to Bohan and Peter criteria (1). The presence of arthralgia and arthritis was considered. IIM were classified as dermatomyositis (primary and secondary dermatomatoses) (DM) and polymyositis (PM) including the rest of the patients (classification I). Also, IIM were classified (II) as primary polymiositis (PPM), primary dermatomatoses (PDM), overlap syndrome (OSd), juvenile myopathies (JM), cancer-associated myopathies (CAM), autoimmune necrotizing myopathy and inclusion body myositis (these were grouped as other myositis; OM).

**Results:** We found 70 (18%) patients with acute arthritis (<6 weeks), 74 (19%) patients with chronic arthritis (<6 weeks) and 245 (65%) patients without any joint manifestations. Using the Tanimoto et al. criteria (1), the presence of erosive arthritis was observed in 149/479 (38.3%) of the patients. When comparing the joint manifestations in the PM and DM groups (n=225; 52.2% vs. n=229; 47.8%) no statistically significant differences were observed. However, assessing joint manifestations according to classification II, we observed that the highest prevalence was found in the OSd group, followed by the PDM group (p<0.0001). The group with less joint manifestations was JM compared to OSd and PDM (Table 1).

**Conclusions:** The presence of joint manifestations associated with IIM in our cohort is higher compared to other studies described in the literature so far and

| Table 1: Joint manifestations in IIM according to classification II |
|--------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                          | PPM             | PM              | DM              | PM              | OSd             | CAM             | OSd             | CAM             | OSd             | CAM             | OSd             |
| Comparison between groups| vs.             | vs.             | vs.             | vs.             | vs.             | vs.             | vs.             | vs.             | vs.             | vs.             | vs.             |
| Frequency                | 90%             | 90%             | 90%             | 90%             | 90%             | 90%             | 90%             | 90%             | 90%             | 90%             | 90%             |
| P                        | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          | 0.0001          |

Note: The table above shows the frequency of joint manifestations in IIM according to classification II.
emphasize the importance of an accurate joint examination in these patients. The OSd group showed more joint manifestations which might be explained by the coexistence of SLE and MCTD patients in this group. Currently, no association between the clinical subtypes of IIM, overall, these results are encouraging and suggest that joint assessment in follow up may be helpful in differentiating subtypes of IIM.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7051

**FR01088** | LONG-TERM TREATMENT WITH RITUXIMAB IN SYSTEMIC SCLEROSIS PATIENTS: UPDATE OF OUR CLINICAL EXPERIENCE
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**Background:** Systemic sclerosis (SSc) is an immune-mediated disorder characterized by abnormal fibrosis and diffuse microangiopathy with skin and internal organ involvement. The treatment of SSc represents a great clinical challenge because of the complex disease pathogenesis including vascular, fibrotic, and immune T- and B-lymphocyte-mediated alterations. Therefore, SSc should be treated by combined or sequential therapies according to prevalent clinicopathogenic phenotypes. Some preliminary data suggest that rituximab (RTX) may be usefully employed in SSc patients.

**Objectives:** The present study aimed to evaluate the efficacy of RTX in our SSc population, concerning the time to rituximab response (TFRR) in various subsets of SSc.

**Methods:** A series of 15 SSc patients (MF 6/9, mean age 52.7±17.95 years, mean disease duration 10.3±7.15 years, L/D cutaneous subsets 5/10) were treated with one or more cycles of RTX (4 weekly infusions of 375 mg/m²). In all patients RTX was repeated every 6 months for a total of 2–6 cycles. Patients' clinical-serological evaluation, including the self-evaluation of quality of life by means of HAQ and visual analogical scale (VAS) assessment, was performed every 6 months for a mean follow-up period of 42±24SD months.

**Results:** After the first 6 months following RTX treatment the extent of skin sclerosis measured with Modified Rodnan Skin Score (mRSS) significantly improved (from 17.3±10.4 to 13.4±7.6; p<0.01), and remained stable at the end of the follow-up (13.3±8.1; p=0.009). The usefulness of RTX on skin sclerosis was more evident in patients with diffuse cutaneous SSc (n=10) showing a significant decrease of mRSS after the first 6 months (from 24.2±5.1 to 18.1±4.7; p=0.006) and at the end of the follow-up period (18.0±2.0; p=0.005). Similarly, a valuable improvement of other cutaneous manifestations, namely hyperelasticity (12/12 pts), pruritus (11/13 pts), and calcinosis (3/6 pts) was observed. Moreover, arthritis revealed particularly responsive to RTX treatment leading to a clear-cut reduction of swollen and tender joints in 12/13 patients; while lung fibrosis detected in...
FOOT INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS: A SINGLE-CENTRE REPORT

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Background: Foot involvement can be a source of morbidity and disability in patients with systemic sclerosis (SSc). Some studies have previously reported severity, echographic and radiographic manifestations of foot involvement in SSc.

Objectives: The aim of our study was to assess the nature and prevalence of foot problems in patients with SSc reporting a single centre experience.

Methods: A podiatrist and a rheumatologist assessed 81 (76 female) consecutive patients attending our SSc outpatient clinic. The mean age was 50 years (range 21–70). Thirteen (16%) had diffuse cutaneous SSc with a median disease duration from Raynaud’s Phenomenon of 5 years (range 3–19); 68 (84%) had limited cutaneous SSc with a median disease duration of 11.5 years (range 1–41). The overall median disease duration was 11 years (range 11–41). Thirty (37%) were anticientromere antibodies positive, thirty five (43%) anti-scl70 antibodies positive.

The two investigators evaluated the presence of the following features: colour changes, pain, previous ulceration, current ulceration, pre-ulceration (discoloration and thinning of the skin), toenail changes, hyperkeratosis, calcinosis, onychomycosis, dry skin, skin sclerosis, warts, scleredema, flatfoot. The presence of paresthesias, cramps, metatarsalgia were also investigated.

Results: The diagram reports the prevalence of foot manifestations in the 81 SSc patients. Most SSc patients suffer from symptoms related to their feet, particularly dry skin (70%), hyperkeratosis (plantar 58%, finger V 63%), Raynaud’s phenomenon (59%), cramps (55%). No statistically significant differences were found between diffuse and limited SSc groups.

Conclusions: Our study suggests that, in patients with SSc, foot problems are common and potentially disabling. A careful assessment of the feet should always be performed in these patients, in order to identify problems at an early stage.

References:

Disclosure of Interest: None declared

EUROPEAN MULTICENTRE STUDY VALIDATES ELF TEST AS BIOMARKER OF FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: The Enhanced Liver Fibrosis (ELF) test is a serum test including the serum concentrations of amino-terminal pro-peptide of procollagen type III (PIIINP), tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) and hyaluronic acid (HA). A recent single centre study showed that ELF score and its components are markers of overall fibrosis in systemic sclerosis (SSc) mainly reflecting skin and lung involvement (1).

Objectives: To determine the value of ELF score and its single analytes in an independent multicentre cohort of SSc patients.

Methods: 254 SSc patients from 6 European Rheumatology Centres were included in this study. Clinical data were collected at time of sampling. Serum samples were collected and stored according to EUSTAR biobanking recommendations (2). Sera were analysed employing a high-throughput in vitro diagnostic (Siemens Alpha-Centauro). Statistical analysis was performed with SPSS software V24.

Results: The 254 SSc patients had a mean age 55±13.8 years, and included 209 females and 80 patients with diffuse cutaneous SSc (dcSSc). ELF score was overall higher in males than in females (p=0.0236) as well as in dCSSc compared to limited cutaneous SSc patients (p=0.0015). ELF score and the single markers significantly correlated with the degree of skin involvement (mRSS) and inversely correlated with FVC%, TLC% and DLCO%. Concordancy all markers significantly correlated with skin and lung severity as assessed by the Medsger’s scale (Table 1). TIMP-1 and PIIINP levels were higher in patients with lung fibrosis assessed by chest HRCT scan (p=0.0126 and p=0.0338 respectively). Significant correlation (p<0.0001) was found between ELF score, TIMP-1, PIIINP, HA and total disease severity and activity. Multivariate analysis indicated that age (p<0.0001), mRSS (p<0.0001) and PIIINP (p=0.005) were independently associated with ELF score.

Table 1. Coefficient correlation (r) between ELF score, TIMP-1, PIIINP, HA and disease severity (mRSS, DLCO%, mRSS, Sev_lung, Sev_scl) and clinical variables

<table>
<thead>
<tr>
<th>Serum values (median, range)</th>
<th>ELF score</th>
<th>TIMP-1 (ng/mL)</th>
<th>PIIINP (ng/mL)</th>
<th>HA (ng/mL)</th>
</tr>
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<tbody>
<tr>
<td>r</td>
<td>r</td>
<td>r</td>
<td>r</td>
<td></td>
</tr>
<tr>
<td>Age 0.41***</td>
<td>0.06</td>
<td>0.26***</td>
<td>0.52***</td>
<td></td>
</tr>
<tr>
<td>mRSS 0.36***</td>
<td>0.29***</td>
<td>0.18**</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>DLCO% -0.12</td>
<td>-0.25***</td>
<td>-0.2*</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Sev_lung -0.25***</td>
<td>-0.39***</td>
<td>-0.30**</td>
<td>-0.18*</td>
<td></td>
</tr>
<tr>
<td>Sev_scl -0.28***</td>
<td>0.27***</td>
<td>0.22*</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>Sev_total -0.25**</td>
<td>0.29***</td>
<td>0.3***</td>
<td>0.18**</td>
<td></td>
</tr>
<tr>
<td>BscsGAl -0.32***</td>
<td>0.26***</td>
<td>0.27**</td>
<td>0.22**</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: The value of ELF score as independent marker of skin and lung involvement is confirmed in a second independent multicentre cohort of SSc patients. A longitudinal study paired with analysis of large cohort of healthy controls is currently on going to identify a SSc specific test with the highest predictive value for skin and lung progression independently of age and gender.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular3236

A PERFUSION-METABOLIC MISMATCH IN 99MTL AND 123I-BMIPP SCINTIGRAPHY PREDICTS WORSE PROGNOSIS IN SYSTEMIC SCLEROSIS PATIENTS WITH ASYMPTOMATIC CARDIAC INVOLVEMENT

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Background: Cardiac involvement is a manifestation of systemic sclerosis (SSc) that contributes to significant mortality and morbidity. Since many SSc patients with cardiac involvement are asymptomatic and it may progress silently, early diagnosis is still challenging. The perfusion-metabolic mismatch in cardiac scintigraphy indicates functional abnormality due to myocardial injury and has been expected to detect early cardiac involvement in various diseases. However, its clinical utility has been poorly evaluated in patients with SSc.
Objectives: To evaluate clinical utility of perfusion and myocardial fatty acid metabolism mismatch in SSC patients without cardiac failure.

Methods: All patients who visited St. Marianna University Hospital from 2009 to 2015 and performed cardiac scintigraphy using 99mTc and 123I-BMIPP were retrospectively evaluated. Patients who fulfilled American Collage of Rheumatology classification criteria of SSc and systemic lupus erythematosus (SLE) were selected. We subtracted %uptake of metabolism (123I-BMIPP) from that of perfusion (99mTc) on each 17 myocardial segments standardized by American Heart Association. We compared sum of all the scores and each score in 3 coronary artery regions between patients with SSc and SLE. Furthermore, we evaluated incidence of cardiac death or cardiac failure depending on the scores of each coronary artery regions.

Results: Among 177 patients, we analyzed the data in 22 cases with SSc and 23 with SLE. The sum of all mismatch scores was not significantly different between the 2 groups (p=0.05). The mismatch score of left anterior descending coronary artery (LAD) region was significantly higher in SSc than SLE (p=0.05) (Figure 1A). We next divided SSC patients into 2 groups depending on degree of the LAD mismatch score and found the group with low score had higher incidence of cardiac death or cardiac failure (p=0.04) than that with high score (Figure 1B).

Conclusions: The low mismatch score in LAD region of cardiac scintigraphy could be associated with cardiac death or cardiac failure in SSC patients. Since myocardial fibrosis might replace viable cardiomyocytes leading to loss of ventricular volume metabolic mismatch detected by scintigraphy might be less detectable.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4829

FR10392 OPPORTUNISTIC INFECTIONS IN PATIENTS WITH MYOSITIS. A RETROSPECTIVE COHORT STUDY

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Background: Idiopathic inflammatory myopathies, also known as myositis, are a heterogeneous group of acquired diseases of probable autoimmune origin, characterized by the presence of inflammatory muscle infiltrates. Infectious complications are not uncommon in myositis, and some predisposing factors, such as upper esophageal involvement, calcinosis cutis, ventilatory insufficiency due to diaphragm involvement, calcification cuts, ventilatory insufficiency due to diaphragm involvement, and immunosuppressive drug therapies, seem to be implicated.

Objectives: To describe the prevalence, clinical characteristics, and risk factors for opportunistic infection (OI) in a cohort of patients with inflammatory myopathies, and compare mortality rates between those with and without OIs.

Methods: In total, 204 patients from our myositis cohort were reviewed to identify patients who had experienced an OI during the period 1986–2014. The onset of the myositis and OIs were systematically recorded. Disease activity at the OI diagnosis and cumulative doses of immunosuppressive drugs were analyzed, as well as the specific pathogens involved and affected organs.

Results: The prevalence of OI in the total cohort, was 6.4%: viruses, 44.4% (varicella-zoster virus, cytomegalovirus); bacteria, 22.2% (Salmonella sp., Mycobacterium tuberculosis, M. chelonae); fungi, 16.7% (Candida albicans, Pneumocystis jirovecii); and parasites, 16.7% (Toxoplamosis gondii, Leishmania spp.) were the pathogens detected. Lung and skin/soft tissues were the organs most commonly affected (27.8%). Overall, 55.6% of OIs developed during the first year after the myositis diagnosis and were significantly associated with administration of high-dose glucocorticoids (p=0.0148). Fever at onset of myositis (p=0.0317), biological therapy (p=0.001) and sequential administration of 4 or more immunosuppressive agents during myositis evolution (p=0.0032) were significantly associated with OI. All-cause mortality in the OI group was 3.69 deaths per 100 patients/year versus 3.40 in the remainder of the cohort (p=0.096).

Conclusions: The prevalence of OI was 6.4% in our myositis cohort. High-dose glucocorticoids at disease onset and severe immunosuppression are implicated in the development of these complications. Mortality did not differ from the remainder of the cohort.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4590

FR10393 PREVALENCE OF MYOSITIS-SPECIFIC ANTIBODIES IN IDIOPATHIC INFLAMMATORY MYOPATHY COMPARED TO DISEASE AND HEALTHY CONTROLS

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Background: Myositis-specific autoantibodies (MSA) are increasingly recognized as important diagnostic and prognostic markers in idiopathic inflammatory myopathies (IIM) (polymyositis, dermatomyositis, sporadic inclusion body myositis and necrotizing autoimmune myositis). The prevalence of these MSAs in other systemic autoimmune rheumatic diseases and neuromuscular diseases is unclear.

Objectives: To compare positivity of MSA in a cohort of IIM patients to positivity in healthy controls and different systemic autoimmune rheumatic diseases (SARD) or chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: A line immunoassay (Myositis 12 IgG DOT for BlueDiver) for IgG autoantibodies against Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1-Y, HMGCR, SSA/Ro52kD, SAE1/2 and NXP-2 antigens was performed in patients with IIM (n=146), healthy controls (blood donors, n=40) and disease controls (n=200). The disease control group consisted of patients with other SARD (rheumatoid arthritis, RA; systemic sclerosis, Ssc; Sjogren’s syndrome, SJ; and systemic lupus erythematosus, SLE) (n=40 for each disease group) and CIDP (n=40).

Results: 50% of 146 patients with IIM tested positive for an MSA (table 1), compared to 3.5% of 200 disease controls (table 1). 1 SSC patient was positive for Jo-1, 1 CIDP patient was positive for PL12, 2 SSc patients were positive for TIF1-Y and a RA patient was positive for SAE1/2 and Mi-2. 10 AU MSA detected 68 (47%) 7 (3,5%) 0 (0%) Jo-1 28 (19%) 1 (0,4%) 0 (0%) PL12 3 (2%) 1 (0,4%) 0 (0%) PL7 1 (1%) 0 (0%) 0 (0%) EJ 2 (1%) 0 (0%) 0 (0%) Mi-2 7 (5%) 0 (0%) 0 (0%) MDA-5 7 (5%) 0 (0%) 0 (0%) SRP 3 (2%) 0 (0%) 0 (0%) HMGCR 7 (5%) 0 (0%) 0 (0%) SAE1/2 3 (2%) 2 (0,8%) 0 (0%) TIF1-gamma 3 (2%) 2 (0,8%) 0 (0%) NXP2 5 (3%) 1 (0,4%) 0 (0%) SAE1/2 and NXP2 4 (3%) 0 (0%) 0 (0%) Jo-1 + EJ 1 1 CIDP patient was positive for PL12, 2 SSc patients were positive for TIF1-Y and a RA patient was positive for SAE1/2 and Mi-2.

Conclusions: MSA positivity in patients with a clinical non-IIM diagnosis (other SARD or CIDP) is infrequent compared to positivity in the IIM group. For MSA positivity in patients with a clinical non-IIM diagnosis (other SARD or CIDP) is infrequent compared to positivity in the IIM group. For MSA positivity in patients with a clinical non-IIM diagnosis (other SARD or CIDP) is infrequent compared to positivity in the IIM group. For MSA positivity in patients with a clinical non-IIM diagnosis (other SARD or CIDP) is infrequent compared to positivity in the IIM group. For MSA positivity in patients with a clinical non-IIM diagnosis (other SARD or CIDP) is infrequent compared to positivity in the IIM group.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4829
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5143

FR0394 NEUROPATHIC PAIN IS ASSOCIATED WITH SKIN THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS
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Background: Systemic Sclerosis (SSc) is a connective tissue disorder characterized by fibrosis of skin and internal organs, vasculopathy and systemic inflammation. To date, few studies assessed pain in SSc patients, (1) namely the neuropathic component. Data is also scarce on defining possible neuropathic pain (NP) predictors in these patients.

Objectives: To determine if patients with SSc have a higher prevalence of NP compared with a group of age and sex matched controls and study possible associations between NP and SSc clinical variables.

Methods: The study evaluated patients diagnosed with SSc fulfilling the SSc classification criteria of the American College of Rheumatology (ACR), older than 18 years old and followed up at our Rheumatology Unit. Forty-eight patients with mean age of 56.98±12.73 years and mean disease duration of 9.77±6.12 years were included. Comparison group comprised 45 age and sex matched controls. Patients and controls were consecutively evaluated at our Unit and NP in 4 questions questionnaire (DN4) was used for assessing the presence of NP. In SSc patients, skin involvement was also evaluated clinically by the modified Rodnan skin thickness score (mRSS) ranging from 0 to 51. Hand mobility (HAMIS) and relevant clinical variables were also calculated and relevant clinical variables associations between NP and SSc clinical variables.

Results: In our study, prevalence of NP assessed by DN4 was significantly higher in SSc patients compared to controls (56.2% versus 13.3%, p<0.001). In addition to age and sex, presence of diabetes (p=0.041) was also similar in both groups. In SSc group, patients with and without NP showed some statistically significant differences (table 1).

Table 1. Comparative analysis between SSc patients with and without NP

<table>
<thead>
<tr>
<th>NP positive patients (n=27)</th>
<th>No-NP patients (n=21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (IQR)</td>
<td>61 (57–69)</td>
<td>52.38 (42.5–63.5)</td>
</tr>
<tr>
<td>Mean disease duration (years)</td>
<td>11.36±6.55</td>
<td>7.73±4.93</td>
</tr>
<tr>
<td>Diffuse/subcutaneous subtype</td>
<td>6/21</td>
<td>0/21</td>
</tr>
<tr>
<td>Mean mRSS</td>
<td>22.8±11.84</td>
<td>7.5±3.16</td>
</tr>
<tr>
<td>Mean HAMIS</td>
<td>10.4±4.16</td>
<td>6.1±3.99</td>
</tr>
<tr>
<td>Mean SScSS</td>
<td>10.0±2.43</td>
<td>9.3±2.07</td>
</tr>
<tr>
<td>Digital ulcers (%)</td>
<td>17 (63.0)</td>
<td>6 (26.6)</td>
</tr>
<tr>
<td>Calcinosis (%)</td>
<td>15 (55.5)</td>
<td>6 (26.6)</td>
</tr>
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</table>

Multivariate logistic regression revealed that only mean mRSS (odds ratio [OR] =1.90, 95% confidence interval [CI] 1.01 to 3.55, p=0.045) was independently associated with the presence of NP.

Conclusions: To the best of our knowledge, this is the first study evaluating the prevalence of NP in SSc patients in comparison with age and sex matched controls. NP was significantly more prevalent in patients with SSc. Skin thickness assessed by mRSS was independently associated with the presence of NP.

References:

FR0336 LEVELS PENTRAOXIN 3 AND C1Q IN SYSTEMIC SCLEROSIS: ASSOCIATION WITH PULMONARY ARTERIAL HYPERTENSION AND CLINICAL FINDINGS
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Background: Systemic sclerosis (SSc) is an autoimmune rheumatic disease with unknown etiology that characterized fibrosis and vascular endothelial damage with obliteration of the microvasculature caused from exaggerated synergy of collagen and extracellular matrix deposition in skin and internal organs. Pentraxin 3 (PTX3) accepted as a vascular inflammatory marker which secreted in early stage of endothelial dysfunction.

Objectives: In this study, we aimed to investigate plasma PTX3 and serum complement C1q levels and their relations with cytokines and pulmonary arterial pressure in SSc.

Methods: Fifty nine patients diagnosed with SSc and 28 subjects without inflammatory rheumatic disease recruited to the study. Plasma PTX3 and serum TNF-α, IL-1α, IL-4, IL-10, INF-γ, TGF-β and complement C1q measured in both groups. Clinical findings and pulmonary arterial pressure of the SSc patients assessed.

Results: Ages of fifty nine with SSc (54 female and 5 male) and 28 control subjects (23 female and 5 male) were 48,47±12.74 and 43,07±13,71 respectively. PTX3 (IL-1α and IL-4 levels) were increased in SSc patients. There were no differentiations between limited and diffuse cutaneous SSc subgroups in terms of PTX3, cytokines and C1q levels. Plasma PTX3 and serum IL-1α levels found decreased only limited cutaneous SSc subgroup comparing controls. According to the immunosuppressive drugs use; PTX3 levels found decreased in using group and TNF-α ve IL-1α levels found decreased in not using group comparing controls. Significant positive association found between PTX3 and C1q and all cytokines except TGF-β.

Conclusions: PTX3 suggested to be used in the pathogenesis and assessment of disease treatment efficacy of SSc, because of found decreased in SSc patients especially in limited cutaneous and immunosuppressive drugs using subgroups. Associations between C1q, and PTX3 and pulmonary artery pressure highlighted possible roles of both parameters in development of pulmonary hypertension. It is possible to develop preventive treatment strategies with better understanding of these associations. Advanced studies should be carried out for clarifying this condition.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2239

FR0395 INCIDENCE OF MYOSITIS-SPECIFIC AUTOANTIBODY (MSA) SPECIFICITIES IN SSc REFERRED TO NEW ZEALAND (NZ) MEDICAL LABORATORIES
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Background: Idiopathic inflammatory myopathies can be classified by clinico-pathological phenotype into four major groups: overlap myositis (OM), dermatomyositis (DM), polymyositis (PM) and inclusion body myositis (IBM). The different phenotypes associate with distinct MSA specificities although a variable percentage within each group are seronegative and the majority of IBM patients are seronegative. No commercial assay for the IBM associated specificity, n.lA is available. In NZ testing for MSA is restricted to two laboratories: Waikato Hospital (WHL) and Canterbury Health Laboratories (CHL). Both laboratories use the commercial Euroimmun Euroline assay. In addition CHL has developed an ELISA for anti HMGCR autoantibodies and receives referrals from throughout NZ.

Objectives: To define the incidence and specificities of MSA in serum samples referred for testing in New Zealand.

Methods: For the period 3 November 2015 to 2 November 2016 each laboratory information system (LIS) was interrogated for requests for MSA. For the purposes of this report positive results were grouped into the specificities associated with each of the defined clinicopathological phenotypes.

Results: 3 Department of Clinical Biochemistry, Numune Education and Research Hospital; 2Department of Internal Medicine Division of Rheumatology, Hacettepe University Faculty of Medicine; 3Department of Biochemistry, Numune Education and Research Hospital, Ankara, Turkey

FR0397 EVALUATION OF VITAMIN B12 DEFICIENCY AND ASSOCIATED FACTORS IN PATIENTS WITH SYSTEMIC SCLEROSIS
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Background: Vitamin B12 (Vit B12) deficiency is a common condition, which can be manifested with non-specific clinical features or with neurological and/or haematological abnormalities in severe cases. In systemic sclerosis (SSc)
to the ENMC classification, non-specific myositis was the most frequent finding on muscle biopsy (n=5/15, 30% vs. n=1/24, 4% in the non-axial group, p<0.05) and dermatomyositis (DM) pattern tended to be less frequent in axial-IM patients (3/12 20% vs. 11/24, 46%, p=0.10).

Most of the patients (75%) had also extra muscular involvement including acrosclerosis (45%), interstitial lung disease (35%), sclerodactyly (30%), telangiectasia (25%), digital tip ulcers (10%), sclerodermy (5%). By contrast, no patient had polyarthritis (vs. 20% in the controls, p<0.05). DM rash was hardly threefold less frequent in axial IM patients (15% vs. 42%, p<0.05).

Auto-antibodies associated with scleromyositis were the most frequent in axial-IM patients (30%, 25% ant-PM/Scl, 10% anti-RA, 15% anti-Scl-70). One patient (5%) had cancer within the 3 years before or after IM diagnosis (NS vs. controls).

Thus, most frequent diagnosis in axial-IM patients were scleromyositis (35% vs. 5% in the controls, p<0.05) and inclusion body myositis (20% vs. 2.6% in the controls, p<0.05). DM was twofold less frequent than in control (10% vs. 41%, p<0.05). Other IM subtypes were not statistically different from the control groups. Except with patients diagnosed of sIBM, all axial IM-patients received corticosteroids with another immunomodulatory drugs (median number 2, range 1–5). Half of the axial-IM patients received intravenous immunoglobulin. After a mean follow up of 68.4±3.76 months all patients had improvement, including in axial weakness, except in patients with sIBM. One patient died from ischemic cardiomyopathy.

Conclusions: In IM, camptocormia and dropped head syndrome are associated with late onset scleromyositis and sIBM with delayed diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6564

**FR10399**

**EFFICACY OF AN INTENSIVE 24-WEEK PHYSIOTHERAPY PROGRAMME IN PATIENTS WITH SYSTEMIC SCLEROSIS - PRELIMINARY DATA FROM A SINGLE-CENTER CONTROLLED STUDY**

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**Background:** Involvement of skin and musculoskeletal system in systemic sclerosis (SSc) leads to loss of function, disability and reduced quality of life. Data on efficacy of non-pharmacologic care in SSc is very limited due to variety in studied interventions/outcomes.

**Objectives:** To address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24-week intervention, 24-week follow-up), intensive 1h physiotherapy + 0.5h occupational therapy twice weekly, and home-exercise for 0.5h 5x weekly), tailored physiotherapy programme on function/impairment of hands/faces, and quality of life/disability in cohorts with a substantial number of SSc patients.

**Methods:** All patients fulfilled ACR/EULAR 2013 criteria, had skin involvement of hands/mouth, and were consecutively recruited from 2014 to 2016 at the Institute of Rheumatology in Prague. Both groups received educational materials and instructions for home exercise at baseline, however, only intervention group underwent the intensive physiotherapy programme. At months 3,6,12 all patients were assessed by a physician (physical examination, mRSS-Modified Rodman’s skin score, EUSTAR SSc activity score, Medsger SSc severity score), and a physiotherapist blinded to intervention [validated measurements (dFTP-digital footprint area, grip strength, goniometry, dFTP using Baseline dynamometer); tests (HAMIS-Hand Mobility In Scleroderma)], patients filled out patient reported outcomes/questionnaires (CHFS-Cochin Hand Function Scale, MHISS-Mouth Handicap in SSc Scale, HQA, SHAQ, SF-36) and provided blood for routine laboratory analysis and biobanking. Normality of data was tested, inter-group analysis was performed with 2-way ANOVA, and intra-group analysis by Friedman’s test with Dunn’s post hoc test.

**Results:** 25 SSc patients (22 female/3 male, 14 limited cutaneous (lc)SSc/11 diffuse cutaneous (dc)SSc, median of age 54.0 and disease duration 7.0 years, with 30% in the intervention group (IG) and 29 patients into the control group (CG) (25 female/4 male, 16 lcSSc/15 dcSSc, median of age 49.0 and disease duration 5.0 years, mRSS 11). Compared to observed statistically significant deterioration in CG over the period of m0-m6, we found statistically significant improvement in dFTP, grip strength, HAMIS, inter-incisor and inter-lip
Efficacy of Intravenous Immunoglobulin Therapy in Refractory Dysphagia in Patients with Idiopathic Inflammatory Myopathies


Objectives: To assess the efficacy and safety of intravenous immunoglobulins (IVIg) as therapy of refractory dysphagia (1) in patients affected with PM/DM who have received conventional treatments for at least three months. These are the extended data of a previous abstract entitled “Improvement of refractory dysphagia (1) in patients affected with PM/DM who received IVIg standard dose (2 g/kg in a day) every two months for 3 cycles. In all patients, MMT12 score was 4.45±0.35. Following IVIg therapy we observed a significant improvement of EAT score after the first dose (9±8, p=0.006) with a further reduction after the second dose (7±4, p=0.007) and stability after the third one (7±3, p=0.008). An improvement of pharyngeal muscle propulsation, with a significant resolution of solid stasis and a partial resolution of liquid stasis were observed. In addition, MMT12 score progressively improved after each dose, increasing at 4.65±0.16 after the third dose (p<0.001). Notwithstanding, the third IVIg dose, three patients reported the steroids and the remaining 12 were treated with a significant lower dose of 5 mg/day of prednisone (p=0.04).

Conclusions: According to literature, our findings provided evidence that IgG-induced a meaningful improvement of dysphagia, also having a steroid-sparing effect. An improvement of muscle strength was also detected. Although further studies of larger cohort of patients and a longer follow-up time are needed, our findings corroborate the utility of IgG in the treatment of more resistant idiopathic inflammatory myositis related dysphagia.

Disclosure of Interest: None declared

DOI: 10.1136/eann-rheumdis-2017-eular.5049

References:


Disclosure of Interest: None declared

DOI: 10.1136/eann-rheumdis-2017-eular.5692

Systemic Sclerosis

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Background: In most patients with SSC, the onset is in the form of Raynaud’s phenomenon (RP), but in a few is in the form of visceral or musculoskeletal involvement or skin sclerosis. Several risk factors are related to poor outcome in patients with SSC, but never before has the mode of onset been described as one of them.

Objectives: To assess the mode of onset as prognostic factor in patients with SSC.

Methods: A retrospective and multicentre cohort study including 1625 patients with SSC, based on the National Spanish Scleroderma Registry (RESCLE) which includes 28 referral centres.

Results: RP, puffy hands, arthralgia/arthritis, skin sclerosis, interstitial lung disease (ILD), pulmonary arterial hypertension (PAH) and esophageal hypomotility where (p<0.01) stopped clinical modes of onset.

Conclusions: The cohort was split up in two groups: 1342 patients (83%) presented as RP and 283 (17%) presented as non-RP (see graphic below) Non-RP patients where younger at onset of disease (44.7±15.6 vs 49±15.6 years, p<0.001). showed higher percentage of diffuse subtype (36% vs 19%, p<0.001), developed more visceral involvement during the course of the illness and where more frequently anti-RNAPIII positive (29 vs 10%, p<0.001). Overall mortality was 16% in patients presented as RP vs 23% in non-RP patients (p=0.003). Few differences where noted among causes of death related to SSC, but other mortality was observed in RP group due to SSc-RV (19% vs 8.1%, p=0.05) and due to ILD in non-RP group (24% vs 8.3%, p=0.002).

Survival of patients with RP at onset was better at anytime than those with a non-RP onset: 0.97 vs. 0.89 at 5 years, 0.93 vs. 0.82 at 10 years, 0.83 vs. 0.63 at 20 years and 0.71 vs. 0.51 at 30 years from onset (p<0.001).
Conclusions: The mode of onset can be considered as independent prognostic factor, and specifically non-RP onset can be considered as a risk factor related to poorer outcome and RP onset and arthralgias can be considered as protector factors.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1675

FR10404 | THE EFFECT OF A HOME-BASED OROFACIAL EXERCISE PROGRAM ON ORAL APERTURE OF SYSTEMIC SCLEROSIS PATIENTS

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Background: Microstomia is one of the major problems that causes multiple dysfunctions and affects quality of life in systemic sclerosis (SSc).

Objectives: The purpose of this study is to evaluate the effect of a home-based orofacial exercise program on the oral aperture (OA) of SSc patients.

Methods: In this study, patients with systemic sclerosis (SSc) fulfilled the American College of Rheumatology (ACR) 2013 criteria with an OA of <40mm were included in the study. Patients were randomly divided into two groups. Group 1 was given oral augmentation and mouth stretching exercises with combination of strengthening exercise to masseter muscle twice a day for one month in addition to oral hygiene care advice; followed by no activity but oral hygiene care for the next four months. Group 2 received oral hygiene care advice for the first one month followed by the same orofacial exercise program twice a day for the next four weeks.

Results: A total of 52 patients were included in the study. Twenty-seven patients were assigned to group 1 (mean age 53.70±9.79 years; 90.4% female) and twenty-five to group 2 (mean age 50.68±11.93 years; 96.0% female). A total of 28 patients (group 1, n=18; group 2, n=10) completed the study. After four weeks period, OA increased in group 1 (P<0.001), whereas no change was observed in group 2 (P=0.906). At the end of 2 months the intragroup analysis showed no additional increase in group 1 (P=0.283), but a statistically significant increase in group 2, regarding the measurement of OA (P<0.010). We didn’t find any statistically significant difference between OA measurements of the groups 1 and 2 at the end of the trial (P=0.830).

Conclusions: The results of this pilot study suggested that an intervention of combined home-based orofacial exercise program might improve oral aperture of SSc patients. Future studies with longer follow-up period and higher number of patients are needed to observe the long-term benefits of the presented home-based exercise program.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6274

FR10405 | PREVALENCE, CLINICAL CORRELATES AND POSSIBLE CAUSES OF NEUROPATHIC PAIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Objectives: To assess prevalence, possible causes and clinical correlates of neuropathic pain (NP) in patients with systemic sclerosis (SSc).

Methods: In 42 patients with SSc, presence of NP was assessed using the PainDetect questionnaire and subsequently confirmed by neurological evaluation. Patients with previously diagnosed neurological disorders and diabetes were excluded. Relationship between NP and disease status, symptoms of depression and quality of life was investigated. Index of disease status (IDS) was assessed using the Scleroderma Assessment Questionnaire (SAQ), occurrence of depressive symptoms using the Beck’s Inventory (BDI), and quality of life was evaluated using the EQ-SD index. In order to evaluate possible causes of NP in SSc, all patients with NP, except one (who did not agree with further assessments) underwent detailed neurological and electroneurography (ENG) examination, as well as HgbA1C and vitamin B12 level testing.

Results: 12/42 (28.6%) of patients were found to have NP. Patients with and without NP were similar in age and disease duration. NP was found more frequently in patients with IcSSc (32.3%), than in dcSSc (18.2%), as well as in patients with ACA (46.7%) compared to patients with ATA (17.6%) and both ACA and Anti-RNA polymerase antibodies, but the differences were not statistically significant. Patients with NP had significantly higher mean values of IDS (1.28 vs 0.66) and BDI (18.3 vs 9.9) than patients without NP (p<0.01). Mean value of the EQ-SD index was significantly lower in patients with NP (0.39 vs 0.79, p<0.01).

Conclusion: The presence of NP was significantly associated with the presence of SSc. There was a significant decrease in EQ-SD and scores of Beck’s Inventory and present higher level of depression in patients with NP. The findings are consistent with previous studies. Further studies are needed to better understand the complex mechanisms underlying the development of this frequently occurring NP.
MORTALITY PROFILE IN SYSTEMIC SCLEROSIS: A LARGE RETROSPUNCTIVE POPULATION-BASED STUDY FROM BRAZIL

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Background: Systemic sclerosis (SSc) is an uncommon autoimmune multisystem disease associated with reduced life expectancy compared with the general population.1 In order to prolong survival of this patient population, clear information on the most important death-related conditions is undoubtedly necessary. No mortality data in SSc, however, are available from Latin America, as well as few large series studies have been done at the mortality profile in SSc.

Objectives: We aimed to describe the causes of death in SSc occurred in the state of Rio de Janeiro, Brazil, from 2006–2015, and also to compare the data gathered with the general population mortality.

Methods: All death certificates issued in the state of Rio de Janeiro, Brazil, from 2006–2015 were screened for the code attributed to SSc according to the tenth revision of the International Classification of Diseases (ICD-10), either as an underlying (UD) cause of death (also referred to as basic cause of death) or a non-underlying (non-UD) cause. In addition to compiling the causes of death in both settings, we also non-adjusted as well as the age bracket-adjusted (age at death ≤50 years and ≥50 years) mortality ratio against the general population for each cause of death when SSc was listed as a non-UD cause.

Results: Of 1,294.491 fatalities recorded over the study period, ICD-10 code for SSc was listed on 374 (0.02%) death certificates, being a basic cause of death on 223 occasions and a non-UD cause on 151 occasions. The overall mean (SD) age at death in SSc was 58.7 (15.6) years, with men (n=56) having an earlier mean age at death than women (n=318) [53.5 vs 59.6 years, respectively; p<0.004]. For SSc as a basic cause of death, the main non-UD causes were respiratory system diseases had a strong impact on mortality, as evidenced by previous publications.1 Although microvascular and macrovascular abnormalities frequently coexist in disease such as diabetes mellitus and other vascular diseases, the possible association between microvascular failure and macrovascularopathy in SSc patients have been only recently described.2

Objective: The aim of the study was to estimate in SSc patients the relationship between the function by serum enzyme-linked immunosorbent assay. We serially measured serum anti-MDA5 antibody, and neopterin and IL-18 as markers of activated macrophage by serum enzyme-linked immunosorbent assay. We tracked them at three points in each patients: before treatment, soon after a series of intravenous cyclophosphamide pulse therapy (about 3 months later after onset) and the remission status (about one year later after onset).

Methods: Thirteen anti-MDA5 positive CADM patients were enrolled. We measured serum anti-MDA5 antibody, and neopterin and IL-18 as markers of activated macrophage by serum enzyme-linked immunosorbent assay. We tracked them at three points in each patients: before treatment, soon after a series of intravenous cyclophosphamide pulse therapy (about 3 months later after onset) and the remission status (about one year later after onset).

Results: Four patients died soon after the initial treatment because of the deterioration of RPILD. At onset of the disease, the levels of serum anti-MDA5 antibody and neopterin were extremely high (169.75±24.3 index and 27.6±24.1 nmol/l) in all patients. However serum IL-18 level was almost normal (479.3±501.4 pg/ml). Among the 9 surviving patients, it took about one year for anti-MDA5 antibody level to decrease to the normal range. On the other hand, neopterin level decreased quickly after the initial treatment. The level of anti-MDA5 antibody transitioned from 169.75±24.3 index to 93.1±50.1 index, and then to 44.8±54.5 index (P<0.003). Neopterin level transitioned from 27.6±24.1 nmol/l to 9.1±6.5 nmol/l, and then to 6.4±5.0 nmol/l (P<0.006). IL-18 level transitioned from 479.3±501.4 pg/ml to 246.0±175.8 pg/ml, and then to 233.2±180.1 pg/ml (P<0.02). The level of anti-MDA5 didn’t correlate with the level of ferritin (r=0.28), neopterin (r=-0.16), IL-18 (r<0.08) and soluble IL-2 receptor (r<0.27), but the level of anti-MDA5 antibody decreased quickly after the initial treatment.
of neopterin was well correlated with the level of ferritin (r=0.95), IL-18 (r=0.77) and soluble IL-2 receptor (r=0.75).

Conclusions: Anti-MDA5 antibody titer is useful if the patients could reach and maintain the remission or not. Serum neopterin level is useful to predict the clinical status at present for therapeutic indication.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4880

Osteonecrosis of the Lunate Bone Associated to Systemic Sclerosis

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Background: Osteonecrosis of the lunate bone (OLB), also known as Kienböck’s disease, is a rare disorder that has been recently reported in several patients with systemic sclerosis (SSc).1, but still it is not clear if this is only a coincidence of 2 rare disorders or whether OLB is a potentially under-recognized manifestation of SSc.

Objectives: To describe the clinical features of patients with SSc seen in a Spanish tertiary care center, who develop OLB.

Methods: We performed a retrospective observational study that included patients followed in our center between January 2010 to December 2015. Demographic data, clinical and laboratory features, risk factors for osteonecrosis, imaging, treatment and outcome were collected.

Results: A total of 115 SSc patients were identified and 4 of them (3.47%) developed OLB. Mean age of these patients was 58.5 (range: 52–73), being all women. 2 cases were limited cutaneous SSc ( lcSSc) and 2 cutaneous diffuse SSc. 3 cases showed antitopoisomerase I antibodies, but none presented anticitodiolipin antibodies nor had previous thrombotic events. Mean disease duration was 13.5 years (range: 7–17). One patient was ex-smoker, but none had alcohol consumption, and one case was hypertensive. All patients had vascular manifestations (severe Raynaud phenomenon, digital ulcers in treatment with endothelin antagonists and perfusion of iv prostaglandins, and one case had critical digital ischemia); all the patients showed calcinosis in the upper limbs, and they also had joint involvement (50%), gastrointestinal (100%), and pulmonary (50%) manifestations. History of reloged corticosteroid therapy at low doses (prednisone 5–10 mg/day) was present in all cases and was discontinued one year before the onset of osteonecrosis in one case. OLB was unilateral right in 3 cases and bilateral in one case. The patients presented with clinical pain and/or swelling in the affected wrist in the months prior to diagnosis of OLB, which was evidenced by simple radiography, MRI and bone scintigraphy. One of the cases also showed extensive synovitis in the affected wrist and another one developed collapse of the lunate bone with displaced fragment and edema. Treatment was surgical in 25% of the cases (proximal carpectomy), and conservativin in the rest. Among the total SSc population studied there was another case of lcSSc presenting osteonecrosis of the left talar scaphoid bone.

Conclusions: A total of 15 cases of OLB associated to SSc have been reported to date, so it could be an underestimated disease-associated feature of SSc. It has been suggested that its etiology is linked to SSc-related vasculopathy and all our cases had evidence of severe vasculopathy. The location and vascularization of the lunate bone should be taken into account, since no case developed osteonecrosis in other common locations despite corticotherapy, and complete occlusion of the distal ulnar artery has been reported in 3 cases of the literature. The presence of pain, with or without wrist inflammation in SSc patients should make us consider OLB, which is probably more frequent than expected, especially when there is evidence of severe SSc-related vasculopathy.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5965

Predictors of Morbidity and Mortality in Patients with Early Systemic Sclerosis: Long-Term Follow-Up from a Single Centre Inception Cohort Study

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Background: Several studies have investigated the predictors of morbidity and mortality in Systemic sclerosis (SSc). However long-term follow-up data from inception cohorts of early SSc patients are limited.

Objectives: To identify predictors of morbidity and mortality in a single centre inception cohort of early SSc patients at long-term follow-up.

Methods: Our inception cohort comprised SSc patients who fulfilled the American College of Rheumatology criteria, were recruited within 12 months of disease onset and followed prospectively for at least 3 years. Clinical manifestations, laboratory and lung function tests were recorded for each patient at baseline and at 3rd and 6th years of follow up. Multivariate regression analysis and Cox proportional hazard models were used to identify predictors (clinical manifestations, laboratory and lung function tests at baseline) of morbidity and mortality in SSc, respectively.

Results: A total of 114 patients (96 female, mean age at diagnosis 48.1±13.5 years, 53 diffuse SSc subtype) were included in the study, from January 1997 to December 2012. All patients were followed for at least 3 years and 84 patients for at least 6 years. Twenty (17.5%) of 114 patients died during a mean follow up of 101.8±48.5 months. In multivariate regression analysis predictors for major SSc manifestations at 6 years were: diffuse subtype (OR: 6.2, p=0.015); anti-Scl-70 positivity (OR: 3.9, p=0.05), esophageal involvement (OR: 6.5, p=0.017) and digital ulcers (OR: 8.6, p=0.003) at baseline for the development of pulmonary fibrosis (PF). The presence of digital ulcers at baseline was a predictor for the development of arthritisms (OR: 3.7, p=0.05) and the presence of arthritisms at baseline for the development of pulmonary hypertension (PH) (OR: 5.4, p=0.039). Cox proportional hazard models multivariate analysis revealed that independent predictors of mortality were: male gender (HR: 3.3, p=0.023), diffuse type (HR: 8.7, p=0.004), PF at baseline (HR: 2.7, p=0.05), PH based on echocardiography at baseline (HR: 12.7, p=0.001) FVC <80% (HR: 2.74, p=0.042) and DLCO <60% of predicted value at baseline (HR: 2.97, p=0.016).

Conclusions: Results from long-term follow-up data from a single centre inception cohort indicate that diffuse SSc subtype, anti-Scl-70 positivity, esophageal involvement and digital ulcers at baseline are independent predictors for the development of PF. Male gender, diffuse subtype, PF, PH and decreased FVC and DLCO at baseline are prognostic factors of mortality.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6656

Coadministration of Bosentan Has No Effect on the Pharmacokinetics of Nintedanib

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Background: Nintedanib is a potent intracellular inhibitor of tyrosine kinases that has been approved for the treatment of idiopathic pulmonary fibrosis and is being investigated as a treatment for interstitial lung disease associated with systemic sclerosis (SSc-ILD). Bosentan is a dual endothelin receptor antagonist used in the treatment of pulmonary arterional hypertension, which is a common comorbidity of SSc-ILD.

Objectives: To ascertain the effect of bosentan on the pharmacokinetics of nintedanib.

Methods: In an open-label, single-centre study, healthy male subjects aged ≥18 and ≤56 years with a body mass index (BMI) =18.5 and ≤29.9 kg/m2 received a single dose of nintedanib 150 mg alone (period 1) followed by bosentan 125 mg twice daily (bid) for 8 days (bosentan loading dose phase on days 1–6) with a single dose of nintedanib 150 mg on day 7 (period 2). The primary endpoints were the maximum plasma concentration (Cmax) of nintedanib and the area under the plasma concentration-time curve from time 0 to the last quantifiable concentration (AUC0-∞) of nintedanib. The secondary endpoint was the AUC from time 0 extrapolated to infinity (AUC0-∞) for nintedanib.

Results: Thirteen subjects (12 White; mean [SD] age 35.0 [9.8] years and BMI 24.5 [2.5] kg/m2) were treated. All subjects completed the planned observation period. Based on Cmax, AUC0-∞ and AUC0-∞ exposure to nintedanib was similar after a single dose of nintedanib given alone or in combination with multiple doses of bosentan 125 mg bid (Table). Adverse events were reported in 4 subjects (30.8%) on nintedanib alone (period 1), 4 subjects (30.8%) on bosentan 125 mg bid (period 1–6 of period 2) and 2 subjects (15.4%) after administration of bosentan with nintedanib (days 7 and 8 of period 2). All adverse events were mild in intensity.

Conclusions: Coadministration of bosentan 125 mg bid had no effect on the pharmacokinetics of a single dose of nintedanib 150 mg.

Disclosure of Interest: None declared

Nintedanib 150 mg alone Nintedanib 150 mg coadministered with multiple doses of bosentan 125 mg bid Adjusted geometric mean ratio (90% CI)

Cmax (ng/mL)
21.9
22.7
103.4 (98.1, 124.0)

AUC0-∞ (ng h/mL)
104.9
192.6
98.9 (91.3, 107.0)

AUC0-∞ (ng h/mL)
204.3
208.3
102.0 (94.9, 109.6)
Disclosure of Interest: S. Wind Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, G. Simons Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, J. Bertulis Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, C. Cocek Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG
DOI: 10.1136/annrheumdis-2017-eular.5849

**FR0412 THE POSITIVE EFFECT OF RITUXIMAB IN PULMONARY FIBROSIS OF SYSTEMIC SCLEROSIS**

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**Background:** Pulmonary fibrosis is one of the graven manifestations of Systemic Sclerosis (SSc) and conventional DMARDs therapy has not shown any particular positive effect.

**Objectives:** Our goal was to see whether the elimination of B - lymphocytes through use of anti – CD20 Mab, Rituximab (RTX) would offer to the improvement of the pulmonary function of SSc patients.

**Methods:** We studied 23 SSc patients with pulmonary fibrosis, who received treatment with RTX (n=12) or DMARDs treatment (n=11) for 1 to 3 years (1.9 years). Conventional therapy included azathioprine (n=4), mycophenolate mofetil (n=5), and DMARDs treatment was recorded with FVC improvement in the first year of treatment (FVC 81.3 +/- 12.6 vs FVC 87.4 +/- 11.3 out on the onset of the study and at the first year respectively, p=0.02) when on the other hand DMARDs treated patients didn’t show any FVC improvement at all.

**Results:** All RTX – treated patients did not present any lung HRCT deterioration imaging, in contrast to DMARDS – treated patients who were also submitted to lung HRCT each year of the study, all showing signs of CT imaging deterioration. Similar findings, as far as FVC was concerned, were recorded at the 3rd year of the study (RTX patients, n=6 and DMARDs patients, n=11). 3rd year RTX FVC deterioration of the interstitial pulmonary fibrosis of Systemic Sclerosis. The pathophysiology of this particular fibrosis and the possible molecular role of B-lymphocytes in the inversion of this procedure need yet to be furtherly explored.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5849

**FR0413 ACUTE EFFECT OF ILOPROST ON PERIPHERAL CIRCULATION AS ASSESSED BY VIDEOCAPILLAROSCOPY AND 22-MHZ POWER DOPPLER ULTRASONOGRAPHY**

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**Background:** Vascular involvement is a hallmark of systemic sclerosis (SSc) and it is responsible for some of the most common complications of the disease such as Raynaud’s phenomenon (Rp), digital ulcers (DUs) and pulmonary arterial hypertension. I.V. iloprost (ILO), a prostacyclin analogue, has been shown to be effective in reducing Rp severity, DUs healing and preventing [1].

**Objectives:** To assess the acute effect of ILO on acral circulation as assessed by videocephaloscopy and 22-MHz Power Doppler ultrasonography (PDUS).

**Methods:** 44 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. Each patient was evaluated before and immediately after I.V. ILO administration (0.5–2.0 ng/Kg/min for 6 consecutive hours). PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 VVG by means of linear array transducer (10–22 MHz). Power Doppler settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PRF 750 Hz). PDUS measurements included sagittal scan of nailbed and fingertip perfusion score of sagittal scan of nailbed and fingertip pre- and post-therapy are shown in Table 1.

**Results:** The study population included 44 SSc patients, 40 (90.9%) women, 35 (79.5%) limited cutaneous SSc, median age 60.2 years old and median disease duration 8 years. 19 (43.2%) had history of DUs, among them 15 had experienced more than one DUs and 1 had active DU at the moment of evaluation. In a study where operator-dependent methodological errors are limited we found that the majority of connective tissue disease patients with PAH showed no difference between baseline RHC-derived PASP or PVR could be predicted by the corresponding changes from baseline in follow-up TTE. RHC and TTE were always performed, each, by the same examiner.

**Conclusions:** In a study where operator-dependent methodological errors are limited we found that the majority of connective tissue disease patients with PAH showed no difference between baseline RHC-derived PASP or PVR could be predicted by the corresponding changes from baseline in follow-up TTE. RHC and TTE were always performed, each, by the same examiner.

**References:**

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6398

**FR0414 CAN ECHOCARDIOGRAPHY REPLACE FOLLOW-UP CARDIAC CATHETERIZATION IN RE-EVALUATION OF PULMONARY ARTERIAL HYPERTENSION? A LONGITUDINAL SINGLE-CENTER STUDY OF 30 CONNECTIVE TISSUE DISEASE PATIENTS**

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**Background:** Transthoracic echocardiography (TTE) is well validated for initial assessment of connective tissue disease patients with suspected pulmonary arterial hypertension (PAH). However, in patients with PAH confirmed by the gold-standard method of right heart catheterization (RHC) the role of TTE in their follow-up is less known.

**Objectives:** To test the hypothesis that TTE can replace follow-up RHC in connective tissue disease-associated PAH.

**Methods:** This retrospective study included 30 consecutive patients with systemic sclerosis (n=24) and mixed connective tissue disease (n=6) (mean age±SD: 60±12 years, 87% women), in whom PAH was suggested by TTE and further confirmed by a baseline RHC (pulmonary artery systolic pressure (PASP): 56±19.1, range 25–90mmHg; pulmonary vascular resistance (PVR): 5.9±3.6, range 0.7–14.5). The cohort excluded patients: diabetic cardiopathy (n=4), range 2–7 (L/m²/m²). All 30 patients underwent a second RHC and TTE at follow-up, after 11±6 (range 4–29) months. Ten patients had a 3rd follow-up RHC and TTE 22±7 (range 15–37) months from baseline, thus producing in all 50 pairs of baseline and follow-up measurements. By considering follow-up RHC as the gold-standard, we examined whether clinically meaningful hemodynamic changes (i.e.<15% change from baseline) in either RHC-derived PASP or PVR could be predicted by the corresponding changes from baseline in follow-up TTE. RHC and TTE were always performed, each, by the same examiner.

**Results:** In 68% of comparisons between baseline and follow-up, the latter TTE measurements could safely replace RHC in terms of PASP estimation. Using McNemars test we confirmed that the two methods did not differ significantly (Table 1). When in addition to changes in PASP, PVR changes were also considered, follow-up TTE could again safely replace the second RHC in 70% patient retests (Table 2). Of note, baseline hemodynamic values or TTE measurements did not differ between patients in whom TTE could replace RHC and those in whom the results of the two methods at follow-up were divergent.

**Table 1. McNemars test comparing PASP estimated by repeat TTE to that measured by repeat RHC shows no difference between the two methods**

<table>
<thead>
<tr>
<th>Repeat TTE</th>
<th>Repeat RHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable or improved PASP</td>
<td>Deteriorated PASP (&gt;15%)</td>
</tr>
<tr>
<td>Stable or improved PASP</td>
<td>25</td>
</tr>
<tr>
<td>Deteriorated PASP (&lt;15%)</td>
<td>7</td>
</tr>
</tbody>
</table>

**Table 2.**

<table>
<thead>
<tr>
<th>Pre-infusion</th>
<th>Post-infusion</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistivity index</td>
<td>0.773</td>
<td>0.794</td>
</tr>
<tr>
<td>Capillary width</td>
<td>247.5</td>
<td>257.9</td>
</tr>
</tbody>
</table>

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5849
capillary abnormalities correlate with organ damage in Chinese patients with systemic sclerosis

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Objectives: To study the nailfold capillaroscopic patterns and microangiopathy evolution score (MES) and correlate with the severity of organ damage in Chinese patients with systemic sclerosis (SSc).

Methods: Patients who fulfilled the 2013 ACR criteria for SSC were studied. A full physical examination was performed. Blood was taken for SSC autoantibodies, along with a full lung function test and echocardiogram. The extent of skin involvement was assessed by the modified Rodnan skin score (mRSS). Organ damage of SSc was assessed by the Medsger disease severity scale. A Nailfold capillaroscopic examination was performed by a trained nurse blinded to the medical history of the patients. The following parameters were obtained: (1) capillaroscopic patterns (early, active and late); (2) Degree of enlarged capillaries, giant capillaries, capillary haemorrhages, capillary density, disorganization of vascular array and capillary ramification assessed by a semi-quantitative method; and (3) MES score (sum of capillary density, disorganization of vascular array and capillary ramification). Correlation among the capillaroscopic patterns, individual capillaroscopic parameters and the MES with organ damage was performed by the Spearman’s rank correlation test.

Results: A total of 138 Chinese patients were studied (91.3% women; age 58.36±11.81 years). The median disease duration was 8.14±6.21 years. 39 (28.3%) patients had DcSSc and 99 (71.7%) had LcSSc. Anti-centromere, anti-Scl 70 and anti-RNA polymerase III antibodies were present in 28.6%, 28.5% and 5.6% of the patients respectively. Organ damage was present in all patients, most common being skin (84%), lung (79%), peripheral vascular (74%) and GI tract (46%). The median mRSS was 6 (ICR 2–12). A total of 27 patients (19.7%) had early SSc pattern on capillaroscopy, 40 (29.2%) had active pattern and 68 (49.6%) had late pattern. The median MES score was 3.02 (ICR 1.76–5.25). Patients with late SSc pattern on capillaroscopy had significantly longer disease duration and were more likely to have organ damage in the general, peripheral vascular and lung domains compared to those not having late SSc patterns. The total MES score correlated significantly with organ damage scores in the muscle (Rho 0.188; p=0.029), GI tract (Rho 0.189; p=0.048) and lung (Rho 0.265; p=0.006) domains. Regarding individual components of the MES score, capillary density correlated significantly with scores in the peripheral vascular (Rho 0.460; p<0.001), skin (Rho 0.343; p<0.001), joint/tendon (Rho 0.290; p<0.01), muscle (Rho 0.295; p<0.001) and GI tract (Rho 0.188; p=0.028) and lung (Rho 0.238; p=0.015) damage domains. Enlarged capillaries correlated significantly with scores in the muscles (Rho -0.205; p=0.017) and lung (Rho -0.213; p=0.029) damage domains. Giant capillaries and microhaemorrhages correlated significantly with scores in the peripheral vascular (Rho 0.239; p<0.005 and Rho 0.228; p=0.007) respectively damage domains. Disorganization of capillary array correlated significantly with scores in the lung (Rho 0.253; p=0.009) damage domain. Capillary ramifications correlated significantly with the scores in the kidney (Rho 0.171; p=0.048) damage domains.

Conclusions: In Chinese patients with SSC, capillaroscopic patterns and components of the microangiopathy evolution score were associated with severity of organ damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5548
Hg. For transcriptome analysis, total RNAs from whole peripheral blood cells were extracted with using PAXgene miRNA kit. After constructing single-stranded, strand-specific libraries, multiplex sequencing was done. After quantifying the expressions of transcripts, differentially expressed genes (DEGs) between exPH and exN group were selected by paired T-test (P < 0.05). And then, hierarchical clustering analysis and pathway enrichment analysis (PathVisio) were performed.

Results: There were no significant differences between exPH and exN group in the result of total skin score, serum BNP, tests of pulmonary function and thermography after 0°C-stress. Positive SSc-related autoantibody was a risk factor for exPH (odds ratio, 1.41); especially, positive anti-RNP seemed to be prominent (odds ratio, 3.21). Based on the 817 DEGs between exPH and exN group, the hierarchical clustering showed major 4 clusters, and one of them consisted of only cases in exPH group. When we focused on 117 genes reported to be for exPH, it is noteworthy that 4 of them including TGF-β induced protein were differentially expressed. Pathway analysis of transcriptome revealed that 22 pathways, such as the hypertrophy model, lung fibrosis and Wnt/B-catenin signaling, were differentially enriched between exPH and exN group.

Conclusions: The paradigm of SSc-PAH management should ideally be aimed at detecting early PVD and starting treatment prior to fulfilling the criteria for PAH. Although detection of early PVD in SSc patients remains a major challenge, exercise DE seemed to be a good, non-invasive method for screening. It is noteworthy that expression changes in some of known PAH-related genes were detected from peripheral blood of exPH patients. It shows the possibility that the therapeutic intervention at early stage of the disease may alter the clinical course.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3627

FRI0419 FACTORS ASSOCIATED WITH STEROID-FREE REMISSION IN PATIENTS WITH INFLAMMATORY MYOPATHIES. A RETROSPECTIVE ANALYSIS OF A SINGLE-CENTER COHORT

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Background: The inflammatory myopathies are a heterogeneous group of connective tissue diseases characterized by muscle weakness and inflammation. Corticosteroids are the standard main treatment for inflammatory myopathies. However, steroid therapy often causes a wide range of side effects. Although immunosuppressive drugs are used as steroid-sparing agents in an effort to prevent disease recurrence, the appropriate duration of steroid use remains unclear.

Objectives: We investigated whether steroid therapy can be safely withdrawn in patients with inflammatory myopathies followed in a single center.

Methods: We retrospectively reviewed clinical charts of 71 consecutive patients (age 51±15.7 y.o., female 69%) who met Bohan and Peter criteria for polymyositis (PM)/dermatomyositis (DM) and modified Sontheimer’s criteria for clinically amyopathic dermatomyositis (ADM), respectively. Steroid-free remission was defined as a 3-month consecutive period of no disease activity without corticosteroid treatment. Factors associated with steroid-free remission were examined.

Results: Of 71 identified patients, 29 patients (40%) were DM, 15 patients (21%) were PM, 9 patients (13%) were overlap myositis, and 18 patients (25%) were ADM. Thirty-seven patients (52%) had muscle weakness, 5 patients (7%) had malignancies and 43 patients (61%) had signs of interstitial lung disease. With a mean follow-up of 6.6±5.0 years, 9 patients (13%) died during follow-up period. The remaining 62 patients were treated with corticosteroids alone or in combination with immunosuppressants. Steroid-free remission was achieved in 21 of 62 patients (34%) patients with a mean time to steroid withdrawal of 5.5±4.0 years. Six of 21 patients (29%) relapsed 1.7±1.7 years after steroid withdrawal. There were no differences in onset of age, disease duration, positive ANA, positive Anti-Jo-1 antibodies, serum creatine kinase levels, maximum dose of corticosteroids, skin, joint and lung involvement between steroid-free group and non-steroid-free group. Elevated inflammatory markers were associated with long-term steroid use (p < 0.038). Concomitant immunosuppressants were more frequently used in non-steroid-free group than steroid-free group (p < 0.002).

Conclusions: Steroid-free remission might be achieved in some patients with inflammatory myopathies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3627

FRI0418 THE PREDICTIVE PROGNOSTIC FACTORS FOR CLINICAL COURSE OF POLYMYSITIS/DERMATOMYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) and concomitant infectious diseases are the predominant causes of death in polymyositis/dermatomyositis (PM/DM). We have already reported that hypocapnea and ILD lesion in upper lung fields are independent prognostic factors. Micro RNA is a non-coding RNA, which has a certain function such as transcriptional regulation. miR-1 has been reported to be associated with myocyte differentiation and to decrease in muscle tissue from patients with inflammatory myopathies.

Objectives: Here we investigated the association of serum miR-1 level with clinical course of PM/DM-associated ILD (PM/DM-ILD).

Methods: We retrospectively analyzed clinical baseline, serum miR-1 level, initial therapeutic regimens, total amounts of PSL, clinical outcomes, and episode of infection of patient with PM/DM-ILD who had received initial treatment at six hospitals associated with Yokohama City University from 2003 to 2016. The serum miR-1 level was measured by quantitative real-time PCR.

Results: One hundred sixty patients (PM 22, DM 51, and clinically amyopathic DM 43) patients were included. The mean age was 56±15 years and 83 were female. As initial therapies, oral PSL, methylprednisolone (mPSL) pulse, intravenous cyclophosphamide (IVCY), and oral calcineurin inhibitor therapies were performed in 113 (97%), 80 (69%), 48 (41%), and 58 (48%) patients, respectively. Forty-one patients had a serious infection at 51±38 days from initiation of immunosuppressants and 10 died of infections. Old age, low PaCO2 and albumin, high LDH and K, high score of ILD, high initial dose of PSL, mPSL pulse, IVCY, calcineurin inhibitor and combination therapy were extracted as risk factors for infection by univariate analyses. A multivariate logistic regression analysis revealed that combination therapy (p = 0.012, OR 2.83), old age (p = 0.024, OR 2.12), high initial dose of PSL (p = 0.024, OR 2.69), low albumin (p = 0.031, OR 3.56), and low PaCO2 (p = 0.038, OR 2.67) were independent risk factors for infection. Serum samples were obtained from total of 14 patients and 13 healthy controls. Serum miR-1 levels in PM/DM-ILD patients before treatment were significantly higher than those in healthy controls (p = 0.047). Also serum miR-1 levels were significantly higher in PM/DM-ILD patients with concomitant infectious diseases as compared to patients without infectious diseases (p = 0.043). We further divided the PM/DM-ILD cases into two groups by the serum miR-1 level. The higher miR-1 group showed poorer effectiveness of ILD treatment (p = 0.040), and lower lymphocyte count (p = 0.013) as compared to the lower miR-1 group.

Conclusions: Appropriate monitoring is important for PM/DM-ILD, especially in older patients with malnutrition or decreased respiratory function. miR-1 can be a new biomarker for predicting treatment response and concomitant infectious diseases during treatment for PM/DM-ILD.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3168

FRIDAY, 16 JUNE 2017

Spondyloarthropathy - etiology, pathogenesis and animal models

FRI0420 ASSOCIATION OF SUPPRESSOR OF CYTOKINE SIGNALING -3 (SOCS-3) EXPRESSION WITH INTERLEUKIN-23 RECEPTOR (IL-23R) SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN ANKYLOSING SPONDYLITIS (AS)

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Background: Nowadays genetic-association studies have discovered new genes, other than HLA-B27, as IL-23R associated with AS. The signalling pathway through IL-23R is negatively regulated by the SOCS proteins. However, the reports regarding the roles of SOCS in AS are very rare at present.1,2

Objectives: The aim of this study is to assess the gene expression of SOCS-1,
Dysregulated miR-125 promotes joint angiogenesis

Methods: We studied 74 patients (64.8% males) recruited from the Rheumatology Unit of the Puerta de Hierro Hospital diagnosed of AS following the Modified New York Criteria. The study cohort included patients with a mean age of 55.2±11, 2 years of follow-up (Statistical analysis: Kruskal-Wallis and reverse transcribed into cDNA. mRNA expression was assessed by real-time quantitative RT-PCR using specific primers and Power SYBR Green PCR Master Mix (Applied Biosystems). SNP genotyping [rs1129026 (G/A), rs10489629 (T/C), rs1343151 (G/A) rs2201841 (C/T), rs1004819 (C/T) y rs11209032 (A/G)] was performed using the Sequenom MassARRAY platform. In 17 cases there were two samples from the same patient. These samples were obtained from two scheduled visits and 99 samples were analyzed. To determine the effect of independent variables on levels of SOCS genes expression, we fitted population-averaged mixed-effects linear regression models, nested in a random intercept, using the xtgee command of Stata v12. P-values of <0.05 were considered statistically significant.

Results: Cellular SOCS-1, -2 and -6 expression did not show significant differences between the risk alleles carriers and the protective alleles carriers in any of the IL-23R SNP studied. SOCS-3 increased significantly in protective alleles carriers of the IL-23R intronic SNP rs10489629-G (CC-CT-CT, P=0.029), the IL-23R non-synonymous SNP (Arg381Gln) rs11209026-A (AA-GG-GG, P=0.047) and the IL-23R intronic SNP rs1343151-1 (AA-AG-GG, P=0.005).

Conclusions: Higher SOCS-3 expression levels for AS patients carriers of protective alleles of the IL-23R rs10489629-G, rs11209026-A and rs1343151-1 as compared to carriers of risk genotypes could influence the pathogenesis of this disease.

References:

Acknowledgements: This work have been supported by Fondo de Investigación Sanitaria (PI11/00400) and by RETIC Programs, RD08/0075 (RIER) from Instituto de Salud Carlos III (ISCIII), within the VI PN de I+D+I 2008–2011, (FEDER).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3832

FRI0421 | DYSREGULATED MIR-125 PROMOTES JOINT ANGIOGENESIS IN PSA THROUGH ALTERED BIOENERGETICS

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Background: Psoriatic arthritis (PsA) is characterised by an early vascular phase which is essential in perpetuating pannus growth, immune responses and disease progression. Recently, numerous studies have highlighted the emerging importance of endothelial cell metabolism in controlling angiogenesis. Herein, we propose microRNA, miR-125, modulates EC bioenergetics and orchestrates joint angiogenesis as characterised using ex vivo and in vivo tissue/cell assays and a novel in vivo model.

Objectives: To examine the relationship between miR-125, angiogenesis and cellular metabolism in the PsA synovium.

Methods: Primary PsA synovial fibroblasts (PsA FLS) and microvascular endothelial cells (HMVEC) were transfected with anti-miR-125a. Angiogenic mechanisms were quantified using tube formation assays, invasion by Transwell Matrigel chambers, migration by wound repair and metabolic gene expression by RT-PCR. Real-time analysis of extracellular acidification rates (ECAR) and oxygen consumption rates (OCR) of anti-125 treated HMVEC was assessed using the XF-24 Flux Analyzer (Seahorse Bioscience). To determine if altered metabolic gene expression was associated with microRNA expression, the IL-23R and the IL-23R gene expression levels were assessed in early undifferentiated arthritis (EUA) and PsA patients.

Results: In vivo angiogenic effects of miR-125 were assessed using the Zebrafish model. A significant increase in tube formation, cellular invasion and/or migration was observed in anti-miR-125a morpholinos treated Zebrafish as compared to control. miR-125 significantly decreased basal, maximal and stimulated glycolysis as characterised using the XF-24 Flux Analyzer (Seahorse Bioscience).

Conclusions: Our data demonstrates decreased expression of miR-125 in PsA synovium and in vivo models was strongly associated pro-angiogenic mechanisms. Elevated glycolysis following miR-125 inhibition may enables endothelial cells to meet the increased energy and biosynthetic demands for new vessel formation. Correcting these deficiencies and their resulting metabolic shift, either by using a novel drug target, may provide therapeutic benefit, especially in early disease.

Disclosure of Interest: None declared


FRI0422 | ESTROGEN ATTENUATES THE DISEASE ACTIVITY OF SPONDYLOARTHRITIS IN SKG MICE

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Background: Ankylosing spondylitis is a male-predominant disease, and the male gender is also associated with more severe radiographic damage. Estrogen modulates immune-related processes such as T cell differentiation and cytokine production.

Objectives: This study aimed to evaluate the role of estrogen in the disease activity of spondyloarthritis (SpA).

Methods: The effects of estrogen on the development of arthritis were evaluated by performing an ovariectomy and E2 pellet implantation in the zymosan-treated SKG mouse. Clinical arthritis scores were measured and PET-CT was performed to quantify joint inflammation. Total RNA was extracted from the hindpaws and perepaws and the expression of TNFα, IL-6, IFNγ, IL-4, IL-17A, IL-23, Dkk1, and SOST was measured by Quantigenie 2.0 plex assay. Results: Zymosan exposure triggered SpA-like diseases in SKG mice, including peripheral arthritis, spondylitis, dactylitis, enthesitis, and psoriatic skin lesions. E2-treated mice showed remarkable suppression of arthritis clinically and little infiltration of inflammatory cells in the Achilles tendon and intervertebral disc.

Conclusion: Estrogen suppressed arthritis development in SpA model of SKG mouse. Results of the study suggest that estrogen may have an anti-inflammatory effect on the disease activity of SpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3341

FRI0423 | ANTIBODIES TO TYPE II COLLAGEN: A NOVEL TOOL FOR THE SPONDYLOARTHRITIS DIAGNOSIS?

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Background: Spondyloarthritis (SpA) is an inflammatory joint disease with chronic, progressive, axial inflammation of the spine and the sacroiliac joints. Diagnosis of SpA is done criteria by clinical symptoms, radiology and MRI or ultrasound following ASAS criteria. AS is similar to rheumatoid arthritis (RA) and psoriatic arthritis (PsA) as they are all inflammatory joint disease. Nevertheless they show considerable different pathology.

Objectives: The aim of our study is to test whether a novel assay that we developed for RA can be used for SpA diagnosis. We have previously showed that antibodies to oxidative post-translational modified collagen type II (oxPTM-CII) are present specifically in RA patients whether ACPA positive or negative. [2] Our study intends to investigate the reactivity to oxPTM-CII in SpA patients in comparison to other inflammatory diseases (PsA, EUA) and newly diagnosed SpA.

Methods: oxPTM-CII were generated using ribose and various reactive oxidants, and then they were analysed by SDS-PAGE. Binding to native and oxPTM-CII was evaluated by ELISA and Western Blotting. We used a cohort of sera from 67 patients with SpA, 54 patients with PsA, 49 patients with EUA. As control we used 80 patients with fibromyalgia (FM) and 70 healthy subjects. The specificity of the binding was further assessed by competitive ELISA and western blot.

Results: We detected stronger reactivity to SpA compared to PsA and even EUA serum samples. Hence specific binding to oxPTM-CII was seen in the 52% of SpA sera compared to 12% in PsA and 10% in EUA. There was no binding in samples from FM and healthy individuals. A group of the most reactive SpA samples was evaluated by western blot confirming a strong binding to several fragments or aggregates of oxPTM-CII.

Conclusion: For the first time we demonstrated that anti-ROS-CII may become a novel biomarker for SpA diagnosis.

References:
Background: Previous studies indicated a potential role for mucosal-associated invariant T (MAIT) cells in the pathogenesis of ankylosing spondylitis (AS)\(^1\),\(^2\). Active peripheral arthritis and extra-articular manifestations may influence the presence of circulating MAIT cells in AS.

Objectives: To investigate circulating MAIT cells in a homogeneous group of axial spondyloarthritis (SpA) patients with only axial involvement in comparison to age- and sex-matched healthy controls (HC). Secondly, to explore the association of MAIT cells with symptom duration and disease activity.

Methods: Consecutive axial SpA patients from the Groningen Leeuwarden axial SpA (GLAS) cohort without active peripheral arthritis, inflammatory bowel disease, psoriasis or uveitis were included. Patients with active infections or current use of biologics were excluded to rule out possible influence on the presence of circulating MAIT cells. Disease activity was assessed using ASDAS, BASDAI, and serum CRP levels.

The frequencies and absolute numbers of circulating MAIT cells were examined in peripheral blood of all studied patients by 5-color flow cytometry. Immediately after sampling, EDTA-blood was stained with anti-CD3, anti-CD8, anti-TCRVa7.2, anti-CD161, and anti-TCR\(\gamma\)\(\delta\). After staining, the cells were washed, fixed, and analyzes immediately on FACS. MAIT cells were identified phenotypically as CD3\(^+\)CD8\(^+\)TCRVa7.2\(^+\)CD161\(^{high}\) cells.

Results: Of the 41 included axial SpA patients, mean age was 46±16 years, 73% were male, mean symptom duration was 23±14 years, and 78% were HLA-B27 positive. Mean ASDAS was 2.6±1.0, mean BASDAI was 4.4±2.5, and median CRP was 3 (range 2–30). 70%, 54% and 37% of axial SpA patients had ASDAS ≥2.1, BASDAI≥4 or CRP≥5, respectively. HC had exactly the same age and sex distribution.

Both the percentages and absolute numbers of circulating MAIT cells were comparable between axial SpA patients and HC (Figure 1). In axial SpA patients, absolute numbers of MAIT cells correlated negatively (rho=-0.339) with symptom duration. No significant associations were found between MAIT cells and disease activity, except for a negative correlation (rho=-0.332) between frequency of MAIT cells and BASDAI (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Association of percentages and absolute numbers of MAIT cells with symptom duration and assessments of disease activity in axial SpA patients (n=41), Spearman correlation coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom duration (yrs)</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>-0.248</td>
</tr>
<tr>
<td>-0.137</td>
</tr>
</tbody>
</table>

*P-value < 0.05.

Conclusions: In this homogeneous group of axial SpA patients with only axial disease, the presence of circulating MAIT cells did not differ from age- and sex-matched HC. No strong association was found between circulating MAIT cells and symptom duration or disease activity.

References:

Acknowledgements: Funding: This research project was supported by an unrestricted grant from Janssen. Janssen had no role in the design, conduct, interpretation, or publication of this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3498
regarding IL23 (276 vs 262 pg/ml, p<0.05) and IL17 levels (184 vs 223 pg/ml, p<0.02). Only 22 (6.6%) AS patients carried the protective rs11209026 A allele, while 206 (61.7%) carried the rs11209023 A risk allele (p=0.003). There was no demonstrable influence of individual genotypes (A vs G, AA vs AG vs GG) or haplotypic combinations on BASFI, spinal function tests, CRP, ESR, IL-23 or IL-17 levels (all p>0.05).

Conclusions: While there is a high prevalence of the IL-23R rs11209023 A risk allele in Caucasian AS patients, this has no demonstrable bearing on clinical disease measures or serum IL-23 and IL-17 levels.

Acknowledgements: The authors wish to acknowledge the technical assistance by Mr K Nielsen and the financial support of the North Norwegian Health Authority Research Fund

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5882

FRIO429

**DYSREGULATION OF THE SPICING MACHINERY IN LEUKOCYTES FROM ANKYLOSING Spondylitis PATIENTS IS ASSOCIATED TO DISEASE PATHOGENESIS**

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, of unknown aetiology, associated to the development of several comorbidities such as atherosclerosis. Splicing is a post-transcriptional process involved in the RNA maturation. Recent studies have revealed that a pathological dysregulation of the splicing machinery or splicosome is associated to several human diseases. Yet, the splicing alterations have not been described in AS.

Objectives: To analyze the dysregulation of the splicing machinery in patients with AS. To evaluate the association between the alteration of this process and the clinical, inflammatory, oxidative, and atherogenic profiles present in this pathology.

Methods: Fourteen AS patients and 14 healthy donors (HDs) were included in the study. Disease function and activity status were analyzed using the BASFI and BASDAI. The expression of selected components of the major (n=12) and minor-spoolosome (n=4), and splicing factors (n=28) was evaluated in purified monocytes, lymphocytes and neutrophils from patients and HDs (n=14 each) by Fluidigm methodology. Oxidative stress, inflammation and atherogenicity were evaluated by flow cytometry and ELISA. Endothelial function was determined by the post occlusive hyperaemia test using Laser-Doppler.

Results: Compared to HDs, a significant dysregulation in the expression of relevant splicing factors and splicosome components was found in all the leukocyte subtypes from AS patients, being neutrophils which displayed higher numerical differences, particularly in a specific subset of monocytes and minor-spoolosome members, and splicing factors was observed when compared lymphocytes (U4, U6, NOA1, RMB17), monocytes (PRP8, SF3B2 TV2, CELF4, ESRR2, RBM3, SAM68 TV1, SRSF10, TIA1) and neutrophils (U11, U2, U2AF2, U11, CA 150, ESRR1, PSF, PTB, SRM160).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4911

FRIO428

**THE JAK1-SELECTIVE INHIBITOR, FILGOTINIB, INHIBITS INFLAMMATION PATHWAYS OBSERVED IN AN IL-23-INDUCED PSORIATIC ARTHRITIS MURINE MODEL**

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Background: JAK1-selective inhibitor filgotinib (GLPG0634, GS-6034) has shown efficacy in PsA but not in Psoriasis, and it has no impact on psoriatic lesions. In this study, we demonstrate the anti-inflammatory activity of filgotinib (4 mg/kg) in an IL-23-induced murine CIA model, which is significant over placebo and results in a significant improvement of the clinical, inflammatory, oxidative, and atherogenic profiles present in this pathology.

Objectives: To evaluate the efficacy of filgotinib in an IL-23-induced murine CIA model.

Methods: Three-week-old C57BL/6 male mice were injected intradermally with 50μg of IL-23 enhanced Episomal Expression Vector (EVE) and treated with filgotinib or vehicle from day 10 (therapeutic mode) and sacrificed after 16 days of treatment. TNFα, IL-19, Mip1 and Tnf were used to determine the proportion of B-cells (CD45+, CD19+) NK cells (CD11b+, CD3+, CD19+) among CD3+ T-cells and T-cells expressing CCR6, a functional marker for IL-17 production, as was observed in mice (2). This is the first report of filgotinib targeting IL-23, as was observed in previous studies.

Results: Sixteen days after treatment, the proportion of T-cells was 26% and 34% in PEB and peripheral blood respectively.

Conclusions: Systemic expression of IL-23 in mice generated a PsA phenotype that was associated with altered gene expression in diseases. A strong interferon signature was reversed by filgotinib as were several inflammatory and disease markers. Together with the stage 2 clinical results in RA and CD, these data support the study of filgotinib for the treatment of PsA patients.
Correlation studies revealed that disease activity (CRP, ESR, BASDAI) was associated to the alteration of a vast number of spliceosome components in the three subtypes of analyzed leukocytes. In addition, the BASFI index correlated with the expression of splicing factors ESPR1, SRSF1 and TRA2B in neutrophils. The inflammatory, athrogenic and oxidative profile of AS leukocytes was related to the expression of a number of spliceosome molecules in the three leukocyte subsets, although neutrophils exhibited the highest number of deregulated spliceosome components related to inflammation (STAT3, TNF-α, IL-1α, IL-1β, IL-5) and cell adhesion (ICAM-1, SELLS, THBS4, CD45). Finally, endothelial dysfunction correlated with the expression of several components of the spliceosome-generating factors in monocytes and neutrophils.

Conclusions: 1) AS patients display a dysregulation of the splicing machinery components associated to disease function and activity. 2) The expression of spliceosome members in the different leukocyte subsets is related to the inflammatory, oxidative and proatherogenic profile of AS patients.

Alteration of the spliceosome may provide new biomarkers for diagnosis and clinical monitoring of AS.


Disclosure of Interest: None declared


Abstract FRIO431 – Table 1. Baseline characteristics of patients within each ASQoL-ASDAS trajectory

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Trajectory 1 (N=55)</th>
<th>Trajectory 2 (N=105)</th>
<th>Trajectory 3 (N=86)</th>
<th>Trajectory 4 (N=124)</th>
<th>Trajectory 5 (N=55)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>43.9±12.4</td>
<td>46.0±12.7</td>
<td>40.9±10.7</td>
<td>47.9±11.3</td>
<td>45.1±11.7</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>46 (83.6)</td>
<td>71 (67.6)</td>
<td>62 (72.1)</td>
<td>83 (66.9)</td>
<td>29 (52.7)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Smoking smoking (%)</td>
<td>28.9 (27.1)</td>
<td>23.85 (27.1)</td>
<td>2674 (35.1)</td>
<td>4498 (41.6)</td>
<td>2046 (43.5)</td>
<td>0.13</td>
</tr>
<tr>
<td>HLAB27 – positive (%)</td>
<td>50 (92.6)</td>
<td>73 (103.0)</td>
<td>94119 (79.0)</td>
<td>45588 (80.0)</td>
<td>0.01*</td>
<td></td>
</tr>
<tr>
<td>Symptom duration (yr)</td>
<td>20.3±10.9</td>
<td>21.4±12.1</td>
<td>17.0±10.9</td>
<td>22.2±13.1</td>
<td>21.3±12.6</td>
<td>0.04*</td>
</tr>
<tr>
<td>(Bridging) syndromes present (%)</td>
<td>16 (30.4)</td>
<td>45 (61.6)</td>
<td>38 (54.5)</td>
<td>64 (50.1)</td>
<td>18 (34.9)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Start disclosure of biological</td>
<td>15 (27.8)</td>
<td>41 (101.0)</td>
<td>81 (94.2)</td>
<td>85 (120.7)</td>
<td>35 (63.6)</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

FRIO430 | DUAL TREATMENT OF DISEASE ACTIVITY AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The ultimate goal of managing Ankylosing Spondylitis (AS) is to improve and maintain the patient’s health-related quality of life (HRQoL). To reach this goal, rheumatologists target towards low disease activity, as this is the main modifiable factor. To date, there is insufficient insight into (1) the co-evolution of disease activity and HRQoL, and (2) the heterogeneity in such trajectories among patients.

Objectives: To explore the heterogeneity of AS by identifying different temporal patterns of co-dependence between disease activity and HRQoL over 8 years follow-up.

Methods: Data from Outcome in AS International Study (OASIS; n=161) and Groningen Leeuwarden AS (GLAS; n=264) cohorts were used. All patients had an established diagnosis of AS. In GLAS, all patients started a biological. HRQoL and disease activity were measured bi-annually using ASQoL and ASDAS-CRP
respectively. Patients were classified into latent groups with individuals following a similar course of disease activity and HRQoL. These trajectories were estimated by Group-Based Trajectory Modelling. Next, the trajectories were profiled by Group-Based Trajectory Modelling. Finally, multivariate linear regression showed that 61.1% of the variability of HRQoL was mainly characterized by male gender and HLA-B27; improving impact by higher age, younger age, short symptom duration, and biological intake; high impact by higher age, long symptom duration, and (bridging) syndesmophytes (Table). 

Conclusions: We identified five dual trajectories of disease activity and HRQoL, each demonstrating a clear mutual relationship. These trajectories and their profiles provide insight into the heterogeneity of the impact of AS on patients’ health and overall functioning.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3802

FRIO0432

CLINICAL WORSENING ACCORDING TO THE PATIENT IS INFLUENCED BY AXIAL SPONDYLOARTHRITIS: RESULTS OF THE ASAS-FLARE STUDY IN 1169 PATIENTS
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Methods:
Prevalence of flares/worsening of the disease in axSpA is not well known, with prevalences ranging from 10 to 40%.

Objectives:
To evaluate the prevalence of disease worsening according to the patient’s perception in an axSpA population with stable disease and its correlation with disease activity parameters.

Methods: Study: International multicentric (20 countries) longitudinal (2 visits: 1 week – 6 months) observational in 2016, under the guidance of ASAS. Patients: axSpA patients with stable disease according to the rheumatologist. Data on disease characteristics were collected at baseline, and data on disease activity were collected at both visits. Disease worsening was defined at the follow-up visit by the patient using the MCID question (“Think about all the ways your spondyloarthritis has affected you during the last 48 hours. Compared to the last visit how did you feel during the last 48 hours? Improved/No change/Worse”). If patients answered “worse”, they marked if they considered themselves in an acceptable symptoms state (PASS) and whether they considered treatment intensification was necessary. Analyses were descriptive and changes in disease activity were calculated according to patient-reported worsening.

Results: Among the 191 patients included, 1169 patients had complete data. Patients were predominantly males (64.8%), had a mean age and disease duration of 41.7 (SD 12.4) and 12.6 (9.9) years, respectively. History of X-ray sacroiliitis, MRI sacroiliitis and HLAB27+ were present in 944 (80.6%), 471 (40.6%) and 807 (69.0%) patients, respectively. 56% (n=655) patients were receiving a biologic treatment. At the baseline visit, mean BASDAI (0–10) was 1.2, and CRP significantly increased in patients considering themselves worsening, not changed and worsened, respectively. Among the 1639 patients included, 1169 patients had complete data.

Results:
Among the 1169 patients with complete data, 116 patients had stable disease according to the rheumatologist. Data on disease-related factors and disease activity. Univariate logistic regressions and a logistic regression (with a categorical variable respectively) were performed to relate QoL with the studied covariates.

Background: Axial spondyloarthritis (SpA) is associated with several extra-articular manifestations such as the skin disease psoriasis. On the other hand, SpA was found to be more prevalent (3–4%) in patients with another skin disease: hidradenitis suppurativa (HS). HS is a chronic, recurrent, debilitating inflammatory skin disease that involves deep-seated painful nodules in the inverse body regions, with an average prevalence of 1% in the European population and a female predominance (ratio 3:1). Thus far, the prevalence of HS in axial SpA is not exactly known.

Objectives: To investigate the prevalence of HS in patients with axial SpA.

Methods: A self-screening questionnaire with validated questions concerning HS symptoms and signs including prototypical pictures was send to all participating patients from the Groningen Leeuwarden axial SpA (GLAS) cohort in 2016. All patients fulfilled the ASAS axial SpA criteria. Self-reported HS symptoms were verified by checking medical records and/or verification by phone, as defined by HS of a dermatologist.

Results: In total, 588 questionnaires were send to the GLAS patients, of which 459 were returned and could be included in the final analysis (response rate 78%). Of the included patients, mean age was 42±13 years, 63% were male, mean symptom duration was 23±13 years, and 78% were HLA-B27 positive. The questionnaire data showed a high self-reported HS prevalence of 11%. HS symptoms were confirmed by doctor’s diagnosis in the large majority of these patients (45% (51/225), respectively. The next step will be the comparison of patient characteristics and clinical assessments between axial SpA patients with and without HS.

Conclusions: The present observational cohort study shows that HS is a common skin disease in patients with axial SpA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6120

FRIO0434

POOR QUALITY OF LIFE IN PATIENTS WITH SPONDYLOARTHRITIS IS NOT EXPLAINED BY STRUCTURAL DAMAGE. DATA FROM REGISPONSER

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Background: In recent years it has become increasingly important the evaluation of the global impact of the disease in patients with Spondyloarthritides (SpA) through the use of the Patient-reported Outcomes (PROs) (1). One of the most used PROs is the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire, which refers to Health-Related Quality of Life (HRQoL). Since this is a subjective and multifactorial outcome (2), our goal is to detail the most important factors which are related in these patients.

Objectives: To evaluate QoL in patients with SpA and to define its association with disease-related factors and patient’s features.

Methods: A cross-sectional multicenter study which includes 2229 patients with SpA selected from the national Spondyloarthritides Spanish Registry (REGISPONSER). The main outcome was the assessment of QoL performed through the ASQoL questionnaire. Subsequently, we studied its relation with different factors organized into 5 groups: sociodemographics, emotional, functionality, disease-related factors and disease activity. Univariate logistic regressions and a multiple linear regression (considering ASQoL as a qualitative variable and quantitative variable respectively) were performed to relate QoL with the studied covariates.

Results: The mean ASQoL score in the entire population studied was 6.09±5.12. The average age was 47.7±13.26 years old and 698 (31.31%) were women. In univariate logistic regressions, significant differences (p<0.05) were seen in many variables included in the 5 groups: poor QoL (ASQoL<9) is related with gender (female), age, mental and physical component from SF-12 questionnaire, disease duration, inflammatory back pain (IBP), alternating buttock pain, BASFI (Bath Ankylosing Spondylitis Functional Index), BASDAI (Bath Ankylosing Spondylitis Functional Index), BASDI (Bath Ankylosing Spondylitis Disease Activity Index), ESR (Erythrocyte Sedimentation Rate) and global patient’s VAS (Visual Analogue Scale), among others.

Finally, multivariate linear regression showed that 61.1% of the variability of ASQoL (R² =0.611, p<0.001) is explained by sex (female), physical component and 2nd item form SF-12 questionnaire (related to functionality), 6th and 7th items form SF-12 (both related to mental status), global patient’s VAS, BASFI and BASDAI.

Conclusions: Poor QoL in SpA patients can be explained by high disease activity
and by a deterioration in functionality and mental status. However, clinical form of SpA, disease duration and structural damage in spine do not explain this decrease of QoL.

References:

Disclosure of Interest: None declared

[41x546]None declared

[41x693]


Scientific Abstracts
Friday, 16 June 2017 651

COMPARISON BETWEEN CENTRAL AND LOCAL ASSESSMENT OF RADIOGRAPHIC SACROILIACITIS IN PATIENTS WITH RECENTLY DIAGNOSED AXIAL SPONDYLODIRARTHROPATHY IN PROOF STUDY
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Background: High inter-reader variability of radiographic sacroiliitis assessment has been reported in a number of previous studies, suggesting its low reliability for the diagnosing and classification of axial spondylodirarthropathy (axSpA).

Objectives: To compare the results of local versus central scoring of radiographic sacroiliitis in a large multinational cohort of patients (pts) with recently diagnosed axSpA.

Methods: PROOF is a prospective observational study evaluating clinical and radiographic outcomes in axSpA pts in rheumatology clinical practice in 29 countries. Pts with axSpA fulfilling ASAS classification criteria were eligible if diagnosed ≤1 year prior to study enrolment. Radiographs of sacroiliac joints (SJ) collected at baseline were graded according to the modified New York (mNY) criteria (0–4 for each SJ). Pts with sacroiliitis of grade ≥2 bilaterally or grade ≥3 unilaterally were classified as ankylosing spondylitis (AS); otherwise pts were classified as non-radiographic axSpA (nr-axSpA). All available radiographs were assessed first by a local reader (LR) and then by a central reader (CR1), who was blinded to the results of the LR. In the case of a disagreement in the classification (AS or nr-axSpA), the radiograph was evaluated by the 2nd central reader (CR2), who was blinded to the previous assessments and the final classification was made based on the decision of 2 out of 3 readers.

Results: Of the 2126 pts enrolled in PROOF, 1583 were included in this analysis based on available radiographs of the SJ. Based on the LR judgment, 987 pts were classified as AS and 596 as nr-axSpA, while 1158 were classified as AS and 425 as nr-axSpA according to CR1. Following CR1 assessment, 1146 (72.4%) pts retained their LR classification, while 437 (27.6%) pts were classified differently. Of the 437 pts with discrepant classification assessed by CR2, 175 (72.4%) pts retained their LR classification, while 437 (27.6%) pts were classified as non-radiographic axSpA (nr-axSpA). All available radiographs were assessed first by a local reader (LR) and then by a central reader (CR1), who was blinded to the previous assessments and the final classification was made based on the decision of 2 out of 3 readers.

Conclusions: In the PROOF study, the agreement between local and central classification of pts with nr-axSpA vs AS was significant. Pts classified as nr-axSpA by LR were three times more likely to be re-classified compared with AS pts, which may be related to difficulty in the assessment of less advanced structural changes.

Acknowledgements: AbbVie funded the PROOF study, contributed to its design and implementation in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

Disclosure of Interest: D. Poddubnyy Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, BMS, Boehringer, MSD, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, R. Inman Grant/research support from: AbbVie, Agen, and Janssen, Consultant for: AbbVie, Agen, Janssen, Lilly, Novartis, and Pfizer, J. Sieper Grant/research support from: AbbVie, Merck, and Pfizer. Conflince of Interest: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Janssen, Merck, Novartis, Pfizer, Roche, and UCB, H. Haibel Consultant for: Boehringer, MSD, and Novartis, Speakers bureau: AbbVie, MSD, and Pfizer., M. Hoijnik Shareholder of: AbbVie, Employee of AbbVie


FR0436 | CHRONIC PAIN IN PATIENTS WITH ESTABLISHED AXIAL SPONDYLODIRARTHROPATHY AND ASSESSMENT OF PAIN SENSITIVITY BY COMPUTERIZED PNEUMATIC CUFF PRESSURE ALGOMETRY: RESULTS FROM THE SPARTAKUS COHORT
E. Mogard1, T. Olofsson1, A. Breemander2, S. Bergman3, L. E. Kristensen4, J. Kvistgaard Olsen5, J.K. Wallman1, E. Lindqvist1, 1IKVL, Department of Rheumatology, Lund University, Lund; 2School of Business, Engineering and Medicine, Halmstad University, Halmstad; 3Primary health care unit, Department of Public Health and Community Medicine, Institute of Public Health and Community Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; 4The Parker Institute Department of Rheumatology, Copenhagen University Hospital Fredriksberg and Bispebjerg, Copenhagen, Denmark

Background: Pain is a common symptom in all arthritides, and remains a problem also with better treatment options. In axial spondylodirarthropathy (axSpA), data on chronic pain remain scarce.

Objectives: To study pain distribution, duration and intensity in axSpA, and relate this to disease status and measurement of pressure pain sensitivity.

Methods: Consecutive patients (n=115) with clinical axSpA diagnoses (ankylosing spondylitis (AS) or undifferentiated axial spondylodirarthropathy (USpA)) were examined and answered a questionnaire. Patients were categorised as having no chronic pain (NCP), chronic regional pain (CRP) or chronic widespread pain (CWP). Pressure pain sensitivity was assessed by computerized pneumatic cuff pressure algometry (CPA) on the dominant lower leg, and pain threshold, pain tolerance and temporal summation (assessed by the temporal summation index, TSI) were recorded. Differences in disease status and pressure pain sensitivity between patients with CWP versus NCP were assessed (Chi-square or Mann-Whitney U-test).

Results: Fifty percent of patients reported CWP, irrespective of clinical diagnosis (AS 47%, USpA 53%), and more men than women reported CWP (59% versus 37%, p<0.001). Only 18% of all patients reported NCP. Overall, higher disease

Table: Comparison of Mean SD (SD) between All Cases, Non Chronic Pain, Chronic Regional Pain, Chronic Widespread Pain and NCP versus CWP.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Cases (n=115)</th>
<th>Non Chronic Pain (n=57)</th>
<th>Chronic Regional Pain (n=38)</th>
<th>Chronic Widespread Pain (n=20)</th>
<th>NCP versus CWP p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, n (%)</td>
<td>66 (57)</td>
<td>6 (30)</td>
<td>21 (37)</td>
<td>38 (68)</td>
<td>0.004</td>
</tr>
<tr>
<td>Age, years, years</td>
<td>53 (13)</td>
<td>52 (16)</td>
<td>49 (13)</td>
<td>55 (12)</td>
<td>0.384</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>25 (14)</td>
<td>24 (14)</td>
<td>22 (13)</td>
<td>29 (14)</td>
<td>0.148</td>
</tr>
<tr>
<td>HLA-B27, positive, yes (%)</td>
<td>63 (74)</td>
<td>14 (78)</td>
<td>30 (79)</td>
<td>39 (68)</td>
<td>0.560</td>
</tr>
<tr>
<td>AS/USpA (ICD-10)</td>
<td>60 (55)</td>
<td>13 (7)</td>
<td>19 (19)</td>
<td>28 (29)</td>
<td>0.299</td>
</tr>
<tr>
<td>VAS pain, 0–100</td>
<td>37 (27)</td>
<td>15 (18)</td>
<td>26 (36)</td>
<td>49 (24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAS global</td>
<td>38 (26)</td>
<td>19 (22)</td>
<td>32 (46)</td>
<td>48 (22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAS fatigue</td>
<td>40 (26)</td>
<td>23 (23)</td>
<td>33 (28)</td>
<td>51 (26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.5 (2.3)</td>
<td>1.6 (1.6)</td>
<td>3.0 (2.0)</td>
<td>4.9 (2.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASFI</td>
<td>2.5 (2.4)</td>
<td>1.1 (1.4)</td>
<td>1.8 (2.3)</td>
<td>3.7 (2.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BAI</td>
<td>3.1 (1.6)</td>
<td>2.9 (1.6)</td>
<td>2.9 (1.3)</td>
<td>3.3 (1.4)</td>
<td>0.255</td>
</tr>
<tr>
<td>ASDAS-SPR</td>
<td>2.1 (1.0)</td>
<td>1.2 (0.7)</td>
<td>1.8 (0.9)</td>
<td>2.7 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain threshold kPa</td>
<td>30.1 (14.4)</td>
<td>33.7 (18.7)</td>
<td>30.7 (11.5)</td>
<td>27.8 (14.8)</td>
<td>0.216</td>
</tr>
<tr>
<td>Pain tolerance kPa</td>
<td>62.2 (26.5)</td>
<td>71.6 (28.5)</td>
<td>63.0 (25.3)</td>
<td>56.8 (25.6)</td>
<td>0.069</td>
</tr>
<tr>
<td>TSI</td>
<td>0.6 (0.59)</td>
<td>0.53 (0.46)</td>
<td>0.60 (0.57)</td>
<td>0.63 (0.66)</td>
<td>0.189</td>
</tr>
</tbody>
</table>

AS = ankylosing spondylitis; nr-axSpA = non-radiographic axial spondylodirarthropathy.
activity, pain intensity, worse fatigue, global health and function were observed among patients with CWP compared to those with NCP. There was a trend towards lower pain tolerance in patients with CWP compared to NCP (Table). Lower pain tolerance and higher TSI scores were observed among patients reportingVAS pain >40 versus those with VAS pain scores <40 (mean (SD) 51.9 (21.2) versus 68.1 (28.1), p=0.007; 0.73 (0.60) versus 0.55 (0.59), p<0.045).

Conclusions: In this population-based, cross-sectional study of established axSpA, chronic widespread pain was common, affecting 50% of the patients and generally associated with higher disease activity and worse function. CPA shows promising results regarding assessment of pain sensitivity, although larger studies are needed for more conclusive results.

Acknowledgements: Miriam Walsh-Ingelström performing all CPA assessments

Disclosure of Interest: E. Mogard: None declared, T. Olofsson: None declared, A. Bremerander: None declared, S. Bergman: None declared, L.-E. Kristensen Grant/research support from: Oak Foundation, Consultant for: Celgene, BMS, MSD, Novartis, Pfizer, UCB, J. Kvistgaard Olsen: None declared, J. Wallman Consultant for: Celgene, Novartis, UCB, E. Lindqvist: None declared

DOI: 10.1136/annrheumdis-2017-eular.4626

FRIO437 EFFECTS OF ANKYLOSING SPONDYLITIS ON PLANTAR PRESSURE DISTRIBUTION

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1Physical Therapy and Rehabilitation, İstanbul Medeniyet University Göztepe Education and Research Hospital; 2Physical Therapy and Rehabilitation, Haydarpaşa Numune Education and Research Hospital, İstanbul, Turkey

Background: It is considered that postural changes that occur in patients with ankylosing spondylitis (AS) are biomechanically compensated for by contribution from movements of hip, knee and ankle joints [1]. The effects of this phenomenon on the foot, the most distant segment of the kinetic chain, have not been fully elucidated.

Objectives: In the present study, our aim was to investigate possible changes in plantar load distribution in AS patients.

Methods: The study enrolled 30 AS patients diagnosed as per modified New York criteria and 30 healthy controls matched for age, gender and body mass index. Bath Ankylosing Spondylitis Metrorolgy Index (BASMI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) scores were obtained for all patients. Using a foot pressure platform, the distance from the center of pressure (CoP) to the posterior heel line was measured in centimeters (cm) in both groups (DCoP) (figure 1). Percent total plantar load distribution over the proximal half and distal half of the foot was calculated.

Results: Mean DCoP distance was significantly shorter in AS patients 9.65±0.96 cm in comparison to that of control group (10.41±0.89 cm) (p=0.011). While the percent total plantar pressure applied on proximal half of the foot was 60.46±7.82% in AS patients, it was only 55.96±6.21% in the control group (p=0.031). However, AS patients had less percent pressure applied on the distal half of the foot (39.53±7.62%) versus control patients (44.04±6.21%) (p=0.031), The mean ratio of the percent pressure distribution over the proximal half of the foot, the most distal segment of the kinetic chain, have not been fully elucidated.

Conclusions: Plantar pressure distribution seems to be displaced towards the hindfoot in sagittal plane due to biomechanical changes in patients with ankylosing spondylitis. This points out to the significance of the lower extremities in the compensation of postural changes in AS patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6241

FRIO438 RISK FACTORS FOR UVEITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A RETROSPECTIVE COHORT STUDY

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Background: The uveitis is one of the most common extra-articular manifestation of ankylosing spondylitis (AS), occurring in 20–30% of the patients with AS. But it is not clear which factors are associated with the occurrence of uveitis in patients with AS.

Objectives: To evaluate the risk factors for uveitis in patients with AS.

Methods: A total of 1061 Korean patients who were diagnosed with AS at Seoul National University Hospital between January 2004 and December 2015 were evaluated in this study. Using electronic medical record review, the information on the occurrence of uveitis after AS diagnosis and the other demographic and clinical characteristic were obtained, which included, age, gender, disease duration, previous history of uveitis, smoking status, Bath ankylosing spondylitis activity index, HLA-B27 positivity and level of serum inflammatory markers. After dividing the patients into those who experienced uveitis after AS diagnosis (uveitis group) and those who did not (non-uveitis group), the potential risk factors for the occurrence of uveitis were evaluated using univariable and multivariable logistic regression analysis. Receiver operating curve analysis was performed.

Results: Among the 1061 patients, 837 (78.9%) were male and their mean (SD) age was 27.9 (6.2) years. During the observation of 4231 patient-year, uveitis occurred in 142 (13.4%) patients (uveitis group). Patients in the uveitis group had longer disease duration than those in the non-uveitis group (10.0±6.6 vs. 8.2±6.2 years, p=0.003). The proportion of the patients with prior uveitis before diagnosis of AS or HLA-B27 positivity were higher in the uveitis group than those in the non-uveitis group. (58.5% vs. 12.1%, 95.7% vs.83.7%, respectively) There were no significant differences in ESR and CRP between the two groups. In the multivariable analysis, two most significant risk factors for new-onset uveitis was the prior uveitis before the diagnosis of AS (OR=11.18 [95% confidence interval (CI): 7.09–17.63]) and HLA-B27 positivity (OR=9.15 [95% CI: 1.23–68.41]). The area under the curve (AUC) of the final multivariable model was 0.809 (95% CI: 0.77–0.85).

Table 1. Risk factors for uveitis in patients with AS (n=1061)

<table>
<thead>
<tr>
<th>Uveitis group (n=142)</th>
<th>Non-uveitis group (n=919)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>104 (73.2)</td>
<td>733 (79.8)</td>
</tr>
<tr>
<td>Age on symptom onset (years)</td>
<td>28.51±11.56</td>
<td>27.82±11.95</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>10.03±6.60</td>
<td>8.2±6.21</td>
</tr>
<tr>
<td>History of uveitis, n (%)</td>
<td>83 (58.5)</td>
<td>111 (12.1)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>35 (25.0)</td>
<td>184 (20.3)</td>
</tr>
<tr>
<td>ESR (mm)</td>
<td>28.1±10.77</td>
<td>28.1±10.77</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>1.93±2.70</td>
<td>1.6±0.61</td>
</tr>
<tr>
<td>HLA-B27, n (%)</td>
<td>135 (95.7)</td>
<td>764 (83.7)</td>
</tr>
<tr>
<td>BASDAI in n (%)</td>
<td>6.4±1.71</td>
<td>6.59±1.68</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2943

FRIO439 PSYCHIATRIC DISORDERS ASSOCIATED WITH ANKYLOSING SPONDYLITIS


Background: Ankylosing spondylitis (AS) is an inflammatory rheumatic disease characterized by spinal and/or peripheral involvement, enthesitis, dactylitis, and several extra-articular manifestations. Chronic inflammation often leads to reduced spinal mobility and functional disability. The frequency of fatigue, sleep disturbances, and psychological problems has increased in patients with AS.1

Objectives: Although there are studies investigating depression and anxiety frequency in AS patients, different psychiatric disorders such as impulsivity, alexithymia and eating disorders have not been evaluated. The aim of this study is to investigate the frequency of different psychiatric disorders in AS patients, and to evaluate the relationship between these disorders with disease activity and functional status.

Methods: Patients with AS (n=70) and healthy controls (n=56) were included in the study. The Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Functional Index, Bath Ankylosing Spondylitis Metrology

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6241
Index (BASMI), pain visual analog scale, Beck depression scale, Beck anxiety scale, Barratt impulsiveness scale, Toronto alexithymia scale, Eating attitude test, fatigue, Ankylosing spondylitis quality of life, and Nothingam health profile were administered.

Results: The frequency of depression, anxiety and non planning impulsiveness were higher in patients with AS than in healthy controls (p<0.05), although no difference was found in terms of alexithymia, fatigue, and eating attitude. Depression and anxiety were correlated with high disease activity, fatigue, impaired physical functioning, and lower quality of life in the patients with AS. Non planning impulsiveness was correlated with fatigue and lower quality of life while there was no correlation with disease activity and functional impairment. BASMI scores were not associated with psychiatric disorders.

Table 1. Demographic characteristics and Psychiatric disorders in Ankylosing spondylitis and healthy controls

<table>
<thead>
<tr>
<th>Ankylosing spondylitis patients</th>
<th>Healthy controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>42.8±10.46</td>
<td>44.7±10.04</td>
</tr>
<tr>
<td>Male (%)</td>
<td>57.14%</td>
<td>51.78%</td>
</tr>
<tr>
<td>Beck depression score</td>
<td>13.8±8.99</td>
<td>9.8±38.34</td>
</tr>
<tr>
<td>Beck anxiety score</td>
<td>14.5±10.02</td>
<td>10.5±38.99</td>
</tr>
<tr>
<td>Barratt impulsiveness - score</td>
<td>15.6±8.15</td>
<td>15.2±72.72</td>
</tr>
<tr>
<td>Barratt impulsiveness - motor</td>
<td>19.6±2.29</td>
<td>18.6±2.23</td>
</tr>
<tr>
<td>Barratt impulsiveness - non planning score</td>
<td>26.0±4.57</td>
<td>24.7±3.77</td>
</tr>
<tr>
<td>Toronto alexithymia score</td>
<td>54.8±12.86</td>
<td>54.3±11.12</td>
</tr>
<tr>
<td>Eating attitude score</td>
<td>21.7±31.18</td>
<td>22.0±13.24</td>
</tr>
</tbody>
</table>

Conclusions: Depression and anxiety were associated with disease activation, while impulsivity frequency was increased independently of disease activity. Reducing in the quality of life and functional competence due to the psychiatric disorders indicates that, AS patients may require a psychological care approach during the follow up.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5947

FR0441 | NECK PAIN IN ANKYLOSING SPONDYLITIS: FOCUS ON ACTIVE INFLAMMATORY AT THE CRANIOCEWAL JUNCTION ON MRI

G. Slobodin 1, I. Rosner 1, A. Avisiat 1, D. Rimar 1, A. Shigpelman 2, D. Militianu 3, 1Rheumatology; 2Orthopedic Surgery, Bni Zon Medical Center; 3Radiology/Musculoskeletal Imaging, Rambam Medical Center, hails, Israel

Background: A wide spectrum of structural changes in the elements of cranio cervical junction in patients with ankylosing spondylitis (AS) has been recently described in a retrospective study using computed tomography [1]. The clinical significance of those findings requires further elaboration.

Objectives: To explore and describe inflammatory MR imaging findings in the cranio cervical junction in patients with AS and neck pain.

Methods: Eighteen patients with AS and continuing neck pain, as well as 9 patients with fibromyalgia of the same age and similar level of severity of neck pain, were recruited as a control group, underwent relevant rheumatologic examination. X-ray of cervical spine and MRI study, which included STIR, CUBE T2, FSE and FSE FAT SAT sequences before and after administration of gadolinium.

Results: In the AS group, 12 males and 6 females diagnosed by 1984 New York criteria, of median age 40.5 years (range 31–61 years) and median disease duration of 8 (range 1–35) years, with 13 under treatment with anti-TNF agents were studied. All patients suffered from neck pain, with median VAS of 7 (range 2.5–10). Range of neck spine motion was limited in all but 3 patients. Seven of 18 patients had evidence of cervical syndesmophytes on X-Ray. In addition to expected findings of syndesmophytes, active inflammatory phenomena were seen in MR imaging in two of 18 patients with AS and in none with fibromyalgia (Fig. 1). Both AS patients with positive MRI were on anti-TNF therapy during the study and did not have syndesmophytes at the cervical spine as also by X-ray films.

Conclusions: Active inflammation of both entheses and joints of the cranio cervical junction was demonstrated by MRI in some patients with AS and persistent neck pain. Active lesions at the cranio cervical junction should be included in the differential diagnosis of neck pain in AS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2629

FR0440 | PRESENCE OF BONE MARROW EDEMA ON MAGNETIC RESONANCE IMAGING OF THE SACROLIAC JOINTS IN MILITARY RECRUITS BEFORE AND AFTER 6 WEEKS OF INTENSIVE PHYSICAL TRAINING

G. Varkas 1,2, M. de Hooge 1, T. Renson 1,2, F. Van den Bosch 1,2, M. de Hooge 1, T. Renson 1,2, P. Carron 1,2, S. De Mits 3, M. de Hooge 1, T. Renson 1,2, P. Carron 1,2, S. De Mits 3, I. Sung 4, S.-J. Kim. 1Department of Rheumatology, Ghent University Hospital; 2VIB Inflammation Research Centre; 3Department of Rehabilitation Sciences and Physical Therapy, Ghent University, Gent; 4Department of Radiology, Jessa ziekenhuis, Hasselt, Belgium

Background: Studies have shown an increase of bone marrow edema (BME) on magnetic resonance imaging (MRI), especially in feet and ankles of professional athletes and in minimally active healthy controls after mechanical stress [1]. Although this has been described for several joints and across different sport activities, information concerning BME in the sacroiliac joints (SIJ) has not been studied. In axial spondyloarthritis (AxSpA), the presence of 1 BME lesion is expected findings of syndesmophytes, active inflammatory phenomena were seen in MR imaging in two of 18 patients with AS and in none with fibromyalgia (Fig. 1). Both AS patients with positive MRI were on anti-TNF therapy during the study and did not have syndesmophytes at the cervical spine as also by X-ray films.

Objectives: To explore and describe inflammatory MR imaging findings in the cranio cervical junction in patients with AS and neck pain.

Methods: Eighteen patients with AS and continuing neck pain, as well as 9 patients with fibromyalgia of the same age and similar level of severity of neck pain, were recruited as a control group, underwent relevant rheumatologic examination. X-ray of cervical spine and MRI study, which included STIR, CUBE T2, FSE and FSE FAT SAT sequences before and after administration of gadolinium.

Results: In the AS group, 12 males and 6 females diagnosed by 1984 New York criteria, of median age 40.5 years (range 31–61 years) and median disease duration of 8 (range 1–35) years, with 13 under treatment with anti-TNF agents were studied. All patients suffered from neck pain, with median VAS of 7 (range 2.5–10). Range of neck spine motion was limited in all but 3 patients. Seven of 18 patients had evidence of cervical syndesmophytes on X-Ray. In addition to expected findings of syndesmophytes, active inflammatory phenomena were seen in MR imaging in two of 18 patients with AS and in none with fibromyalgia (Fig. 1). Both AS patients with positive MRI were on anti-TNF therapy during the study and did not have syndesmophytes at the cervical spine as also by X-ray films.

Conclusions: Active inflammation of both entheses and joints of the cranio cervical junction was demonstrated by MRI in some patients with AS and persistent neck pain. Active lesions at the cranio cervical junction should be included in the differential diagnosis of neck pain in AS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2629

FR0442 | IDENTIFICATION OF ENTHESITIS AT THE ACHILLES TENDON INSERTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS USING DIGITAL RADIOGRAPHY

I. Sung, S.-J. Kim. Orthopedic Department, Hanyang University Medical Center, SEOUL, KOREA, Seoul, Korea, Republic Of

Background: Posterior heel pain is a common symptom in the foot and ankle region, with many different causes that need to be distinguished by differential diagnosis. Among them is ankylosing spondylitis (AS), in which enthesitis of
the heel is common and occasionally is responsible for their initial symptom to seek clinics. An early or timely recognition of active enthesitis of AS from simple radiographs comes to be relevant issue.

**Objectives:** The purpose of current study is to assess measurement reliability and diagnostic validity for detecting the digital radiographic findings of enthesitis at the Achilles tendon insertion in patients with AS.

**Methods:** Current study is a blinded, matched, cross-sectional study with 44 patients (65 feet) having clinical enthesitis at the Achilles tendon insertion (Group I), and 44 healthy controls (65 feet) (Group II). Suggested findings of enthesitis including retrocalcaneal recess obliterations from retrocalcaneal bursitis, increased thickening in shadow of the Achilles tendon and posterior soft tissue at its insertion from the swellings of those soft tissues were assessed on digital radiographs of standing hindfoot lateral view, and their measurement reliabilities were determined. To investigate diagnostic validities, diagnostic odds ratios (DOR), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were estimated for radiographic findings of retrocalcaneal recess obliterations (RRO). For the thickness of the Achilles at its insertion (TAI) and swollen posterior soft tissue, the receiver operating characteristic (ROC) curve analysis was done.

**Results:** There were no significant differences between two groups in mean age, BMI and sex ratio. Intra- and inter-observer reliability of all measurements showed high degree of agreements (0.786 to 0.941). The diagnostic odds ratio of RRO for detecting enthesitis was 66.0. The sensitivity, specificity were 92.7%, 66.9%, and PLR, NLR were 8.00, 2.33, respectively. The mean TAI of Group I and II were 4.57mm±2.29, 3.87mm±1.57, respectively (p-value < 0.001). An under the ROC curve of TAI was 0.806, and the optimal cut-off value predicting enthesitis was 5.47mm, and its sensitivity and specificity were both 72.3%

**Conclusions:** Retrocalcaneal recess obliteration and thickened shadow of Achilles tendon at its insertion and swollen posterior soft tissue on digital radiographs of standing hindfoot lateral view are regarded as the easy and useful findings for enthesitis of the posterior heel. For searching enthesitis at the Achilles insertion in patients with AS, such findings from simple radiographs showed high measurement reliability and validity.

**References:**

**Disclosure of Interest:** None declared.

**Disclosure of Interest:**
[3] Freedman M, Steller D. Digital radiography of the musculoskeletal system: the radiographs of standing hindfoot lateral view are regarded as the easy and useful tool to both scores was higher in patients with AS+FM. According to the BASDAI in this analysis was 0.1/100PY (Table). The rates of IBD events varied across trials in early ankylosing spondylitis: do we need new criteria? Arthritis and Rheumatism 2005;52(4):1000–1008.

**Background:** Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that affects the axial skeleton and characterized by pain, stiffness and fatigue [4]. One of the frequent concomitant condition in patients with AS is fibromyalgia (FM), FM shares some common symptoms with AS. According to the many reports concurrent FM in patients with AS has been found in 5.7 - 41.3% cases [1, 2, 3, 5]. Due to the fact that pain is a major component of the disease activity scores of the AS (Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS)), concomitant FM can significantly modify the disease activity in patients with AS.

**Objectives:** The aim of this study was to evaluate the effect of FM on disease activity in patients with AS.

**Methods:** Diagnosis of AS was identified according to the modified New York criteria (1984). FM was diagnosed by ACR criteria (1990). Disease activity was assessed by BASDAI and ASDAS.

**Results:** 80 patients with AS were included into study (15 females and 65 males), age (M ± SD) 41.64±11.4 years. Nineteen patients (23.8%) met the criteria for FM. In both groups, ESR (37.7±18.8 and 39.00±19.6 mm/h) was comparable, while CRP in Group I and II were 4.52±2.11, 3.07±1.56, respectively (p-value < 0.001). Ankylosing spondylitis functional and activity indices in clinical practice. Alan G. MacDonald et al. Rheumatology 2014;53:650–657.

**Introduction**

**Background:** The incidence rates of IBD AEs in ADA clinical trials were generally low (12.7/100 pt-years). The rates of IBD events in patients with AS+FM (patients (pts) who are at higher risk of IBD as a feature of SpA).

**Objectives:** The purpose of this analysis was to determine the rates of IBD adverse events (AEs) in ADA clinical trials, particularly in spondyloarthritis (SpA) patients (pts) who are at higher risk of IBD as a feature of SpA.

**Methods:** The rates of IBD AEs in 73 phase 2–4 interventional ADA clinical trials in rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA), pediatric enthesitis-related arthritis, uveitis (non-infectious intermediate, posterior, or pan-uveitis), hidradenitis suppurativa (HS), adult and pediatric psoriasis (Ps), psoriatic arthritis (PsA), non-PsA peripheral SpA, non-IBD indications.

**Results:** ADA was administered to 23735 pts, representing 36404.6 PY of exposure. Overall, the IR for IBD events in all interventional ADA trials included in this analysis was 0.1/100PY (Table). The rates of IBD events varied across therapeutic interventions from <0.1 to 0.8/100PY. There were no reports of IBD events in pediatric pts. The IR for IBD events in RA, uveitis, HS, and PsA were <0.1, 0.2, 0.4, and <0.1/100 PY. In SpA, the overall rates of IBD were 0.5/100 PY, while the rates were 0.8, 0.5, and 0.7/100 PY in PsA, non-PsA pSpA, nr-axSpA, and AS, respectively. 2216 pts with axSpA (AS: 2026, nr-axSpA: 190) were exposed to ADA: in AS, 14 IBD events (7 new onset and 7 flares) were reported in 12 pts (7 new onset and 5 flares), while in nr-axSpA, 2 IBD events were reported in 1 pt (2 flares).

**Table. Incidence of IBD events in patients from ADA clinical trials.**

<table>
<thead>
<tr>
<th>Indication</th>
<th>N (PY)</th>
<th>All IBD AEs</th>
<th>n</th>
<th>(100 PY) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ARA 1</td>
<td>23735</td>
<td>40</td>
<td>0.1 (0.1–0.2)</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>15153</td>
<td>16</td>
<td>&lt;0.1 (0.0–0.1)</td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td>387 (538.8)</td>
<td>1</td>
<td>0.2 (0.1–0.3)</td>
<td></td>
</tr>
<tr>
<td>Hidradenitis suppurativa</td>
<td>733 (863.3)</td>
<td>3</td>
<td>0.4 (0.1–1.1)</td>
<td></td>
</tr>
<tr>
<td>Psoasitis</td>
<td>3500 (526.8)</td>
<td>1</td>
<td>&lt;0.1 (0.0–0.1)</td>
<td></td>
</tr>
<tr>
<td>All SpA</td>
<td>3216 (519.9)</td>
<td>19</td>
<td>0.5 (0.3–0.6)</td>
<td></td>
</tr>
<tr>
<td>Non-PsA pSpA</td>
<td>165 (290.7)</td>
<td>3</td>
<td>0.0 (0.0–0.3)</td>
<td></td>
</tr>
<tr>
<td>All nr-axSpA</td>
<td>2216 (2531.7)</td>
<td>16</td>
<td>0.4 (0.1–0.4)</td>
<td></td>
</tr>
<tr>
<td>nr-axSpA</td>
<td>190 (412.7)</td>
<td>2</td>
<td>0.5 (0.1–1.0)</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>2020 (2119.9)</td>
<td>14</td>
<td>0.7 (0.4–1.1)</td>
<td></td>
</tr>
</tbody>
</table>

**Table. Incidence of IBD events in patients from ADA clinical trials.**

<table>
<thead>
<tr>
<th>Indication</th>
<th>N (PY)</th>
<th>All IBD AEs</th>
<th>n</th>
<th>(100 PY) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ARA 1</td>
<td>23735</td>
<td>40</td>
<td>0.1 (0.1–0.2)</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>15153</td>
<td>16</td>
<td>&lt;0.1 (0.0–0.1)</td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td>387 (538.8)</td>
<td>1</td>
<td>0.2 (0.1–0.3)</td>
<td></td>
</tr>
<tr>
<td>Hidradenitis suppurativa</td>
<td>733 (863.3)</td>
<td>3</td>
<td>0.4 (0.1–1.1)</td>
<td></td>
</tr>
<tr>
<td>Psoasitis</td>
<td>3500 (526.8)</td>
<td>1</td>
<td>&lt;0.1 (0.0–0.1)</td>
<td></td>
</tr>
<tr>
<td>All SpA</td>
<td>3216 (519.9)</td>
<td>19</td>
<td>0.5 (0.3–0.6)</td>
<td></td>
</tr>
<tr>
<td>Non-PsA pSpA</td>
<td>165 (290.7)</td>
<td>3</td>
<td>0.0 (0.0–0.3)</td>
<td></td>
</tr>
<tr>
<td>All nr-axSpA</td>
<td>2216 (2531.7)</td>
<td>16</td>
<td>0.4 (0.1–0.4)</td>
<td></td>
</tr>
<tr>
<td>nr-axSpA</td>
<td>190 (412.7)</td>
<td>2</td>
<td>0.5 (0.1–1.0)</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>2020 (2119.9)</td>
<td>14</td>
<td>0.7 (0.4–1.1)</td>
<td></td>
</tr>
</tbody>
</table>

**Table. Incidence of IBD events in patients from ADA clinical trials.**

**No IBD events were reported in pediatric patients.**

| Age | ARA Adult and pediatric patients in all interventional studies excluding Crohn's disease, ulcerative colitis, and intestinal Behcet's disease.
|---|---|
| All ARA patients in all interventional studies of nr-axSpA, psA, non-PsA pSpA, nr-axSpA, and AS.
| All ARA patients in all interventional studies of nr-axSpA and AS.

**Abbreviations:** IBD = inflammatory bowel disease; ADA = adalimumab; PY = patient-years; SpA = spondyloarthritis; Wm = weight; CFRD = concomitant FM and AS.

**Conclusions:** The rates of IBD AEs in ADA clinical trials were generally low across all indications, with all events occurring in adult pts. In AS pts, who are at increased risk of manifesting IBD, the rates of IBD for pts treated with ADA (0.7/100 PY [95% CI, 0.4–1.1]) were similar to published placebo rates pooled
FAecal calprotectin, but not anti-saccharomyces cerevisiae antibodies, is linked to worse disease status in axial spondyloarthritis patients without inflammatory bowel disease: results from the spartakus cohort

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4The Parker Institute, Department of Rheumatology, Copenhagen University Hospital, Frederiksberg and Bispebjerg, Copenhagen, Denmark

Background: Inflammatory bowel disease (IBD) is a common comorbidity in axial spondyloarthritis.

Objectives: To study faecal calprotectin (F-calprotectin) levels and anti-Saccharomyces cerevisiae antibodies (ASCA) and their associations with disease status and gastrointestinal (GI) symptoms in axial spondyloarthritis.

Methods: Consecutive patients with a clinical axial spondyloarthritis diagnosis were examined and classified as non-radiographic axial spondyloarthritis (nr-axSpA) or ankylosing spondylitis (AS; modified New York criteria; n=48). Only patients without known IBD were included. F-calprotectin and ASCA IgA and IgG antibodies in serum were measured by commercially available enzyme-linked immunosorbent assay kits (Calpro AS; ORGENTEC Diagnostika).

Results: Elevated levels of F-calprotectin (>50 mg/kg) were observed in 15% of nr-axSpA and 40% of AS patients (non-significant difference, with reservation for small groups). Overall, worse mean disease activity/disability scores were observed among patients with elevated versus normal F-calprotectin levels (Table), whereas no association was seen between F-calprotectin and GI symptoms. Similar results remained after exclusion of patients with mononuclear type anti-tissue transglutaminase IgA. Elevated levels of ASCA IgA were observed in 8%/2% of nr-axSpA/AS patients, and IgG in 28%/26%. Only 2 subjects were ASCA double positive. Neither disease activity/disability measures nor GI symptoms were associated with ASCA status.

Disclosure of Interest: K. Andréasson Shareholder of: AbbVie, Employee of: AbbVie, F. Faustini 1, D. Simon 1, C.P. Figureido 1, A. Cavallaro 1,4, C. Muschitz 2, R. Kocian 3, H. Resch 2, R. Areya 2, J. Rech 1, M.F. Neurath 1, G. Schett 1, Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany; 2Medical Department 2, St. Vincent Hospital, The VINFORCE Study Group, Vienna, Austria; 3Department of Internal Medicine 1, University of Erlangen-Nuremberg, Erlangen, Germany; 4Div. of Rheumatology, Facultade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Background: Musculoskeletal symptoms are considered as one of the most frequent extra-intestinal manifestation in Inflammatory Bowel Disease (IBD) patients with a prevalence of up to 40% involving axial and/or peripheral joints. Data on the prevalence of musculoskeletal disease, in particular of SpA are limited and vary considerably due to different criteria the studies have used to define musculoskeletal disease in IBD patients.

Objectives: To define the prevalence of axial and peripheral spondyloarthritides (SpA) according to Assessment of Spondyloarthritis International Society (ASAS) criteria in patients with Crohn’s disease (CD) and ulcerative colitis (UC).

Methods: The SPICE cohort (Spondyloarthritis in IBD patients) enrolled 102 IBD patients (62 with CD and 40 with UC) with a median (IQR) disease of 11.0 (18.0) years were assessed. 38.2% fulfilled ASAS criteria for SpA with no difference between CD and UC. ASAS axial SpA criteria were fulfilled by 12%, ASAS peripheral SpA criteria by 31.4% of the IBD patients. Inflammatory back pain was present in 24.5% with MRI signs of sacroiliitis in 48% of IBD patients with inflammatory back pain. Disease activity according to ASDAS-CRP was moderate to high in 91% of the patients with axial SpA. Peripheral arthritis was present in 71.6%, while arthritis was found in 71.6% of the IBD patients.

Conclusions: Both major forms of IBD show a similar burden of musculoskeletal disease. More than one third of inflammatory bowel disease patients show axial or peripheral SpA according to ASAS criteria. Peripheral SpA is more commonly found than axial SpA.

References:

The prevalence and incidence of axial and peripheral spondyloarthritides in inflammatory bowel disease: a systematic literature review and meta-analysis. J Crohn Colitis 2016; 1–12.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular2393

PREVALENCE AND CHARACTERISTICS OF SPONDYLOARTHRITIS ACCORDING TO ASAS CRITERIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE – RESULTS FROM THE SPICE COHORT

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Conclusions: Both major forms of IBD show a similar burden of musculoskeletal disease. More than one third of inflammatory bowel disease patients show axial or peripheral SpA according to ASAS criteria. Peripheral SpA is more commonly found than axial SpA.

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The prevalence and incidence of axial and peripheral spondyloarthritides in inflammatory bowel disease: a systematic literature review and meta-analysis. J Crohn Colitis 2016; 1–12.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular2393
EVALUATION OF SUPPURATIVE HIDRADENITIS IN PATIENTS WITH CHRONIC ARTHRITIS TREATED WITH FULL AND TAPERED BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS


Background: Suppurative Hidradenitis (SH) is an inflammatory skin disease which often presents a poor prognosis to treatment. It is a disorder of the apocrine glands (axillary, inguinal and analgenial regions) that can result in infection, inflamed nodules, cysts, abscesses and sinus tracts. There is a 1–4% incidence of SH in patients with spondyloarthropathies and inflammatory bowel disease, possibly due to innate immune system deregulation. The use of biological disease-modifying anti-rheumatic drugs (bDMARD), specifically tumor necrosis factor inhibitors, has been useful in cases when other therapies fail.

Objectives: To evaluate the prevalence of SH using the SH-questionnaire in bDMARD-treated chronic arthritis patients.

Methods: This cross-sectional study included 325 patients diagnosed with chronic arthritis. Patients were recruited consecutively from the Biological Therapy Unit of the Hospital General Universitario Gregorio Marañon and evaluated from January to March of 2015. All patients had been undergoing full or tapered bDMARD treatment for at least 1 year and none had any history of SH. Those patients deemed to be in clinical remission were on tapered bDMARD dosage. All patients self-selected the validated SH-questionnaire (1) which was considered positive when one answer was affirmative and when lesions presented in >1 anatomical location. Patient pathologies were subclassified into 2 groups: i) peripheral arthritis (PerAR) which includes rheumatoid arthritis (RA), psoriatic arthritis (PsA) and peripheral spondyloarthropathies (PerSpA); ii) axial spondyloarthopathies (AxSpA). Clinical evaluation was performed by the same physician for all patients. Demographic, clinical and laboratory variables were recorded and disease status was assessed through the relevant clinical index, i.e.DAS28-ESR, DAS28-CRP, SDAI, CDAI, BASDAI, BASFI, ASDAS-CRP.

Results: SH-positive was observed in 25/325 (7.7% vs. 92.3%) patients. Of these 25 patients, 12 (48%) were female and 13 (52%) male. Mean age was 52 years (SD±12.9) and mean time since diagnosis was 14 years (SD±9.3). Twenty-four out of 25 patients were undergoing anti-TNF treatment (ETN=10, GOL=7, ADL=4, CTZ=1). Eighty-four percent of patients were undergoing full bDMARD dosage with the remaining 16% tapered. By subset pathology, 13 SH positives were PerAR type and 12 were AxSpA (5.8% vs. 11.8%, p=0.062). On analysis of PerAR subtypes, we found 6 patients had PsA and 9 RA. Evaluating clinical disease activity, we found 9/13 patients in the PerAR group to be in clinical remission according to DAS28-ESR and CDAI (p=0.02 for both). Additionally, we found only 4/12 patients in remission in the AxSpA group as defined under BASDAI, BASFI and ASDAS-CRP (p=0.006, p=0.005, p=0.004, respectively).

Conclusions: SH-positive was more common in the AxSpA than in the PerAR group, which is consistent with published data. A bDMARD tapered dosage was related to SH-positive which might be linked to persistent and undetectable chronic inflammation.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1254
Sex differences in disease activity according to composite indices in spondyloarthritis: a systematic review and meta-analysis

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1Public Health, University of Alicante, Alicante, Spain; 2Rheumatology, Rush University Medical Center, Chicago, United States; 3Rheumatology, Alicante University General Hospital; 4Rheumatology, Miguel Hernández University; 5Clinical Epidemiology, University of Alicante, Spain

Background: The Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI), an index of only patient-self-report measures, and AS Disease Activity Score (ASDAS)1, which adds patient global estimate and laboratory tests to BASDAI elements are widely used in Spondyloarthritis (SpA). Both indices are specifically designed to evaluate disease activity AS patients. Some studies have shown worse BASDAI in women, but sex-related differences by ASDAS remain unclear2,3.

Objectives: To analyze reports of sex-stratified disease activity measures -BASDAI and ASDAS- in patients with SpA.

Methods: Data sources included PubMed (1950 to December 2016), Embase, Web Of Science, and manual searches of references lists. We included observational studies and randomized trials comparing disease activity scores, specifically BASDAI and ASDAS, between men and women with SpA. Studies quality was determined in line with the STROBE statement for observational studies and CONSORT statement for RCT, considering ≥50% positive items as low quality. Randomized effects were performed to report the mean difference (95% confidence interval) by gender, and heterogeneity was measured via I2 statistic in order to check the results robustness.

Results: From 672 identified studies 18 cross-sectional studies, 3 cohort, 2 case-control studies, and 1 RTC reported sex-stratified BASDAI and ASDAS. ASDAS was evaluated in 3,758 patients (36.5% women) in 9 studies, and BASDAI included 12,329 patients (34.3% women) in 24 studies. In a meta-analysis of mean difference BASDAI including 19 studies the mean difference was 0.56 (95% CI: 0.47, 0.66) and I2=43%, indicating a significantly higher disease activity in women (Figure). In a meta-analysis of 7 studies ASDAS the mean difference was 0.06 (95% CI: -0.04, 0.16) and I2=41%, not showing statistically significant differences.

Conclusions: We identified relevant sex differences in disease activity according to BASDAI with higher disease activity in women, but not according to ASDAS. In SpA, women present more peripheral arthritis and higher pain, which may influence the BASDAI score, mainly based on patient-self-report measures. It is important to recognize these differences that may influence management decisions based on disease activity measures.

References:
**FR0452** IMPACT OF A TRAINING PROGRAM AND EARLY REFERRAL ON DIAGNOSTIC DELAY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbraa1, D. Galvez-Ruiza1, J. Gratacos-Masmiglia1, C. Blanch Mur1, E. Collantes-Estevez1, P. Zarcoc-Montejo1, O. Braco1, I. Universidad de Sevilla, Seville, Spain; 2. La Paz, Madrid; 3. Par Tauli, Sabadell; 4. L'Hospitalet de Llobregat, Barcelona; 5. Universidad de Cordoba, Cordova; 6. Fundación Alarcón, Madrid, Spain

**Background:** In patients with axial spondyloarthritis (axSpA), diagnosis delay (DD) postpones the initiation of the most appropriate treatment with irreversible consequences on physical function, mobility and quality of life of patients. DD is also responsible for increased health costs resulting from incorrect referrals, visits to inappropriate health professionals and poorly planned diagnostic tests. Many initiatives have been undertaken in recent years in an attempt to reduce DD but their influence is still unknown.

**Objectives:** i) To determine diagnosis delay in patients with axSpA in Spain; ii) To assess the pre-diagnosis care process; iii) To analyse the possible beneficial effects on DD of a training programme for primary care physicians and early referral to rheumatology units.

**Methods:** A sample of 680 patients diagnosed with axSpA was interviewed during 2016 as part of the SPANISH ATLAS in Spain. This project aims to improve early diagnosis and to promote the use of effective treatments in axSpA patients. Collected data included: socio-demographics, medical visits prior to diagnosis, date for first symptoms and diagnosis and disease characteristics. This information was used to determine the DD and the possible beneficial effects on DD of a training programme, in terms of health care visits and early referral to rheumatology units. A descriptive analysis was performed, stratifying the results according to the start of the symptoms (before and after 2009). The ESPERanza Program (a Spanish prospective multicenter national health programme aimed at facilitating early diagnosis of patients with axSpA) started in 2009.

**Results:** 53% of the patients included were females. Mean scores (standard deviation) were 45.7 (10.8) years for age and 12.4 (11.2) for disease duration. 77.1% were HLA-B27+. Visits to health professionals prior to diagnosis included: primary care physicians (88.5%), orthopaedic surgeons (71.7%), rheumatologists (70.4%), and physiotherapists (47.6%). The mean number of consultations prior to diagnosis was 2.6; 3.0; 2.0 and 3.4, respectively. Patients stated the onset of the first ax-SpA symptoms was at mean 24.4 years of age, with diagnosis at mean 32.9 years of age, translating into a mean DD of 8.5 years. For 25% of patients DD was >12 years, whereas a DD of >2 years was found in only 25% of respondents. Mean DD for patients whose first symptoms appeared before 2009 was 9.5 years, whereas for patients whose first symptoms appeared after that date it was significantly reduced to 2.5 years.

**Conclusions:** The mean delay in diagnosis axSpA in Spain is above 8 years. Patients make a longer number of visits to a wider variety of specialist physicians before they are diagnosed, which could point to proof of wrong referrals by primary care. However, DD has fallen drastically (to a mean 2.5 years) since the implementation of the ESPERanza Program in 2009, suggesting that training primary care physicians has substantial beneficial effects on patients with axSpA and the care process.

**Acknowledgements:** This project has been supported by Novartis.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.4090

**FR0454** M-SASSS AND CERVICAL SEGMENT C7-D1. SHOULD THE ORIGINAL SCORE BE MODIFIED?

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**Background:** Spondyloarthritis (SpA) is considered a chronic inflammatory condition. Spondylitis affects the junction of vertebrae, but with x-rays in special positions. Theoretically, the C7-D1 intervertebral segment should not be evaluated through a simple lateral radiograph, but with x-rays in special positions.

**Objectives:** To evaluate the importance of the assessment of the C7-D1 intervertebral segment in patients with Ankylosing Spondylitis.

**Methods:** The patients come from a Spondyloarthropathies Unit (Hospital Virgen of the Arrixaca, Murcia, Spain). All patients are diagnosed with Ankylosing Spondylitis (New York Modified Criteria)

The usual radiographic study was performed to calculate the m-SASSS (lateral cervical and lumbar) at level C7-D1 of patients with axSpA and control patients.

**Results:** We included 47 patients (81% male and 19% female) with a mean age of 48 (± 8) years and a mean duration of symptoms of 18 (± 5) years. The mean time between the two radiographic studies was 3 (± 1) years. The control group was made up of 61 people (40, 7% men) with a mean age of 50 years (± 11).

The mean age of the control group was higher than patients (p < 0.001).

The C6-C7 intervertebral level could be assessed radiographically with the lateral cervical radiograph in 93% of the patients and in 85, 2% of controls, and the C7-D1 level was only assessed in 22, 7% of the patients and 50% of the controls.

We analyzed whether the assessment of intervertebral level C7-D1 could be influenced by other variables such as sex, age or duration from the symptoms without finding a statistical result.

The 88, 5% of patients had a lower border of C7 normal or with squaring, erosion or sclerosis. Only 1 patient had syndesmophyte and 2 patients had a bridge between vertebrae. On the upper border of D1, 85, 5% of patients had normal or type-1 lesions (squaring, sclerosis or erosion), there wasn’t syndesmophytes and 2 patients had a bridge (Table)
Conclusions:

- The cervical segment C7-D1 is not usually valuable through a lateral cervical radiograph.
- Most of our patients with Spondylitis have no significant lesions in this segment.
- It is recommended to modify the m-SASSS index by removing the assessment of the cervical segment C7-D1.

References:


Disclosure of Interest: None declared


FR0455 | RADIOGRAPHIC PROGRESSION OF HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF INHIBITORS

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Background: Although there is debate whether treatment with TNF inhibitors (TNFi) in AS may not inhibit spinal radiographic progression, the effect on hip involvement may be different (1,2).

Objectives: To estimate the impact of long-term TNFi treatment on radiographic progression of hip arthritis in AS, by adding a quantitative scoring method, previously applied in hip osteoarthritis, to the BASRI-hip score.

Methods: Consecutive TNFi-naïve AS patients (fulfilling the modified New York criteria) who were eligible for TNFi treatment were included. Hip involvement was assessed clinically (pain, reduced range of motion and intermalleolar distance) and radiographically. X-rays of the pelvis and lateral cervical and lumbar spine were obtained at 3 time points: at baseline two and seven years after the start of TNFi. Both hips were scored using: a) BASRI-hip score (BASRI-h score ≥2 is classified as definitive hip involvement), b) mean joint space width (MJSW), c) vertical span of bridging syndesmophyte.

Results: 262 AS patients (188 men, age: 49.6±12 years, disease duration: 24.4±12 years) under TNFi treatment were included. Definite hip involvement at baseline was detected in 95/262 (36%) patients, who had significantly higher BASRI-hip score [2 (2-2.5) median (IQR) vs. 0.5 (0-1) p<0.0001] and lower MJSW (3.6±0.7 vs. 4.5±0.7, p<0.0001), compared to those without. In patients with hip arthritis at baseline, both BASRI-h score and MJSW remained unchanged during follow up. In patients without hip arthritis, the BASRI-hip score remained unchanged after 2.5±0.7 years, but increased significantly after 7±2.3 years compared to baseline. In contrast, the MJSW in patients without hip arthritis remained unchanged at the three time points. The MJSASSS raised significantly during the follow-up period, regardless of hip involvement (see table).

Conclusions: One third of the AS patients suffer from radiographic hip involvement, which seems to stabilize during long-term anti-TNF treatment. Assessment of MJSW may contribute to detect minor changes in contrast to BASRI-hip score’ rough estimation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6733

FR0456 | AGE AT SPONDYLOARTHRITIS DIAGNOSIS AND RISK OF CARDIOVASCULAR COMORBIDITY: RESULTS FROM THE COMOSPA STUDY

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Background: Spondyloarthritis (SpA) and chronic inflammatory diseases are associated with a number of cardiovascular comorbidities. It is unknown whether age at SpA diagnosis is associated with cardiovascular outcomes in later life.

Objectives: To examine the relationship between “younger age at SpA diagnosis” and risk of various cardiovascular comorbidities.

Methods: COMOSPA is a large worldwide cross-sectional study comprising 3984 patients from 23 countries evaluating comorbidities in patients with SpA (1). We evaluated the association between “younger age at SpA diagnosis” (defined in 5-year blocks) and cardiovascular comorbidities using uni-variable and multi-variable logistic regression. Each model comprised one cardiovascular co-morbidity as dependent and “age at SpA diagnosis” as predictor adjusted for age, sex, BMI, history of smoking, alcohol, NSAIDs, DMARDs, biologics, steroids and other relevant factors.

Results: The data of 3923 patients (64% male) were available for analysis. Current age ranged from 18 to 100 with median (IQR) of 42 (32–53) years. The median (IQR) age at SpA diagnosis was 33 (25–43) years. Main reported cardiovascular-related comorbidities were hypertension (22.4%), ischemic heart disease (IHD) (6.2%), stroke (1.3%) and diabetes mellitus (5.5%). The risk of hypertension, after adjustment for potential confounding factors was associated with younger age at SpA diagnosis (OR=1.10, 95% CI: 1.05 -1.16), indicating 10% higher risk of hypertension for each 5 year younger age at time of SpA diagnosis (Table). Confounding variables showing significant association with hypertension were current smoking (OR=1.12, 95% CI: 1.10–1.13, p<0.001), male gender (OR=1.47, 95% CI: 1.20–1.80, p<0.001), current BMI (OR=1.09, 95% CI: 1.07–1.11, p<0.001), ever use of steroids (OR=1.24, 95% CI: 1.03–1.50, p=0.027) and ever use of synthetic DMARDs (OR=1.28, 95% CI: 1.05–1.57, p=0.017), but not ever use of NSAIDs or biologic DMARDs.

Conclusions: Younger age of SpA diagnosis is associated with increased risk of developing hypertension but not other cardiovascular comorbidities in this study. The explanation for this association is not clear and does not appear to be due to increased NSAID exposure.


Disclosure of Interest: None declared


FR0457 | THE ROLE OF SERUM HMBG1 IN BONE REMODELING AND OSTEOPOOROSIS IN A GROUP OF ANKYLOSING SPONDYLITIS PATIENTS

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Background: Ankylosing spondylitis is characterized by new bone formation and bone loss, associated with inflammation, which are mediated by cytokine-signaling pathways. High mobility group box 1 (HMBG1) protein, is a nonhistone nuclear protein, which is secreted by inflammatory cells, is also defined as a bone-active

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6733
cytokine. Recent studies have shown that RANKL induces HMGB1 release and it is required for RANKL-induced osteoclastogenesis in vitro and in vivo.

**Objectives:** To investigate the relationship of serum HMGB1 levels with RANKL/Osteoprotegerin (OPG) axis and clinical and radiographic parameters in patients with AS.

**Methods:** In this cross-sectional study, serum samples for total HMGB1, sRANKL and OPG were detected from 54 tumour necrosis factor (TNF) inhibitor naive patients with AS according to the modified New York criteria [mean age 34.9 years (S.D. 7.1); duration of symptoms 8.6 years (S.D. 4.2); male gender 38 patients (70.4%) and 26 healthy controls. ESR, CRP, Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASI) were assessed for each patient.

**Results:** Baseline HMGB1 levels were relatively higher in patients with AS than HC, however no statistically significant in other. Serum HMGB1 levels correlated with CRP (rho=0.368 and P=0.006), ASDAS-CRP (rho=0.358 and P=0.008) and BASDAI (rho=0.334 and P=0.014) and BASFI (rho=0.355 and P=0.014) in patients with AS. CRP and ASDAS-CRP showed more correlation to HMGB1 levels than BASDAI. There was no significant correlation between HMGB1 levels with sRANKL, OPG, mSASSS and spine or femur BMD values. In addition, serum OPG levels and the ratio of sRANKL to OPG from AS patients were significantly higher than those of HC.

**Conclusions:** The studied levels of HMGB1 in the sera of AS patients, are increased compared to healthy controls. Serum HMGB1 levels are related to BASDAI, ASDAS-CRP BASFI and CRP in patients with AS. Different results in the literature on serum HMGB1 levels as well as our results support the hypothesis that HMGB1 plays a role in the pathogenesis of AS. According to our knowledge, it is the first trial evaluating association between serum HMGB1 levels with sRANKL-OPG axis, bone mineral density and new bone formation in AS patients and it seems not to be related for these conditions.

**References:**


**Acknowledgements:** Grant Support: by Erciyes University Council of Scientific Research Committee.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4033

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**Table 1.** BMD at baseline and after 1 and 2 years follow up

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Body mass index (kg/m²)</th>
<th>Disease duration (yrs)</th>
<th>ESR (mm/hr)</th>
<th>CRP (mg/L)</th>
<th>HMGB1 (ng/ml)</th>
<th>sRANKL (ng/ml)</th>
<th>OPG (ng/ml)</th>
<th>CRP vs HMGB1</th>
<th>OPG vs HMGB1</th>
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<tr>
<td>35.9±7.1</td>
<td>24.0±4.7</td>
<td>6.8±1.4</td>
<td>23.8±5.6</td>
<td>11.5±6.9</td>
<td>337.1±166.1</td>
<td>148.6±11.4</td>
<td>285.6±6.9</td>
<td>0.02</td>
<td>0.02</td>
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<tr>
<td>33.4±4.0</td>
<td>25.1±6.4</td>
<td>8.6±1.4</td>
<td>22.0±8.5</td>
<td>11.5±6.9</td>
<td>337.1±166.1</td>
<td>148.6±11.4</td>
<td>285.6±6.9</td>
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**FR0458**

**ASSESSMENT OF BONE MINERAL DENSITY IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHROPSIS FROM CORSOR COHORT: 2 YEARS FOLLOW UP**


**Background:** Bone loss in patients (pts) with early axial spondylarthropathy (axSpA) is insufficiently studied and may be associated with disease activity. Objective: To assess the bone mineral density (BMD) in pts with early axSpA base on data from 2 years follow up of CORSAR cohort.

**Methods:** The research included 65 pts with axSpA (criteria ASAS 2009) with disease duration <5 years and age at onset <45 years. Pts at least 2 years follow up, 32 (49.2%) male, pts mean age was 25.8 (5.6) y., average disease duration 2.1 (15.4) mo, 60 (92.3%) pts were HLA-B27 positive. At baseline all pts were NSAID-naive, DMARD-naive, anti-TNF-naive. For 2 years all pts taking NSAIDs at therapeutic doses, part of the pts received sulfasalazine and anti-TNF. BMD was measured using dual energy x-ray absorptiometry (DXA) of the femoral neck (FN) and lumbar spine (LS) (L2–4) at baseline and after 1 year, and 2 years follow up. BMD reduction was defined as Z score < -2 (at least one site).

**Results:** Low BMD at baseline followed in 9 (13.8%) pts, in 10 (15.3%) pts after 1 year and in 5 (7.7%) pts after 2 years follow up. There were no significantly differences between the mean values of BMD at baseline and after 2 year, data are shown in the Table.

**Conclusions:** Low BMD was quite rare (14%) in patients with early axSpA. Small frequency of BMD reduction in the Russian cohort of axSpA patients after 2 years of study is probably due to disease activity decrease on anti-inflammatory therapy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3209

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**FR0459**

**DEVELOPMENT AND VALIDATION OF A SPANISH TOOL FOR SEMI-AUTOGRAPHIC QUANTIFICATION OF SACRIOCILIAC INFLAMMATION BY MAGNETIC RESONANCE IN SPONDYLOARTHROPSIS (SCAIS)**

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**Background:** Different systems to quantify inflammatory changes in sacroiliac MRI have been developed [1, 2] These systems include the Spondyloarthropathy Research Consortium of Canada (SPARCC), the Berlin, the Aarhus-Puhakka, and Aarhus-Madsen, the Leeds, the MR Imaging of Seronegative SpA (MSS), Leeds, Sieper/Rudwaleit and Hermann/Bollow scoring systems. In addition, the use of these quantification methods is restricted to clinical trials, since their use in clinical practice is limited due to their complexity, need for trained personnel, and prolonged procedural time. The development of computer-aided systems that make it closer to the developed technique, the authors modified the SPARCC method by using a single coronal section instead of the standard six consecutive ones.

**Results:** The interobserver reliability was high, with intraclass correlation coefficients for global score of 0.81 (95% CI: 0.59–0.94). Convergent validity was good, with high correlation with the Berlin (rho between 0.797 and 0.913) and the SPARCC methods (rho between 0.566 and 0.897). Mean time employed in the reading procedure was 30 seconds.

**Conclusions:** The developed semi-automatic technique permits a fast and valid calculation of overall BME lesion at the SI joint on MRI images.

**Disclosure of Interest:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1281

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**FR0460**

**EXTRA-ARTICULAR MANIFESTATIONS IN PATIENTS WITH AXIAL SPONDYLOARTHROPSIS: A CROSS SECTIONAL STUDY FROM SOUTHERN DENMARK**

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1Unit Rheumatology; 2Department of Clinical Research, Odense University Hospital, Svendborg; 3Rheumatology; 4Patient data Explorative Network, H.C. Horn 3, I.M.J. Hansen2,5.

**Objectives:** To compare patients with AS and articular symptoms, many patients with SpA also have extra-articular manifestations (EAM) which contribute to reduced quality of life. SpA appears to the prototype of the disorder, AS, three male cases are documented for every female case.

**Background:** Axial (ax) spondylarthropathy (SpA) is a heterogeneous group of chronic inflammatory diseases. In SpA, extra-articular disease is subdivided into two groups referred to as nonradiographic and radiographic (i.e. AS) respectively. Next to the spinal and articular symptoms, many patients with SpA also have extra-articular manifestations (EAM) which contribute to reduced quality of life. SpA appears to be more frequent in men than women in its axial presentations, and in reference to the differential expression of the disorder, AS, three male cases are documented for every female case. However, since the introduction of the new ASAS criteria for axSpA these differences are no longer so apparent. Nevertheless, little is known of the differential clinical expression of SpA between males and females.

**Objectives:** The objective of this study was to compare patients with AS and...
nr-axSpA stratified by gender, using standardized clinical tools (including patient-reported outcomes (P-ROs)) and C-reactive protein (CRP) level as a biomarker for inflammation.

**Methods:** AxSpA patients were included prospectively and underwent an examination program at one visit. We used ASAS criteria and the modified New York criteria for classification. Information on demography and P-ROs was obtained. A trained physician performed a clinical examination, and BASMI and the Spondyloarthropathy Research Consortium of Canada Enthesitis Index (SPARCC) was used to enthesis count. Chi-square and t-tests were used for categorical and continuous variables respectively to test the null hypothesis.

**Results:** Eighty patients with axSpA were included. Table 1 shows the results (mean ± SD or relative frequency) for the comparison of demographic and disease characteristics between clinical subgroups.

**Conclusions:** For the P-ROs, BASDAI and pain were higher in females diagnosed with nr-axSpA, and the CRP was significantly lower in this group. Peripheral and EAMs were slightly equally prevalent in AS and nr-axSpA in men and women except for uveitis, which is slightly more prevalent in AS. Our data show that AS patients were more frequently male than nr-axSpA patients. These results are in line with previous studies showing that male patients with axial SpA have more structural damage on radiographs than female patients. Among women, this study indicate that pain is more pronounced in non-radiographic axSpA than in AS, potentially revealing that chronic widespread pain (e.g. fibromyalgia) might interfere with the diagnostic accuracy of the non-radiographic axSpA subgroup. However, despite the absence of radiographic changes, patients with nr-axSpA have a burden of illness, with self-reported disease activity and functional impairments comparable with those of patients with structural changes consistent with AS.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2985

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**FRI0461 MUSCLE WASTING IN MALE TNF-α BLOCKER NAÏVE ANKYLOSING SPONDYLITIS PATIENTS: A COMPARISON OF GENDER DIFFERENCES IN BODY COMPOSITION WITH DUAL-ENERGY X-RAY ABSORPTIOMETRY**


Background: Ankylosing Spondylitis (AS) patients have different disease characteristics compared to males. This might be explained by differences in body composition (BC), as women have higher total body fat mass, and adipose tissue can produce adipokines and participate in inflammatory and immunological processes.

**Objectives:** To assess gender differences in BC measured by Dual-Energy X-ray Absorptiometry (DXA) in a cohort of AS patients naïve to TNF-α blockers, and compare the BC with the reference population.

**Methods:** AS patients (Modified New York Criteria), 18 years old or older, who had a whole body DXA analysis before TNF-α blockers were included. Demographic information and disease activity measures (ASDAS and BASDAI) were reported. Fat Mass (FM) was reported as total FM (sum of trunk, arms, legs, and head), BF% (ratio FM/Total body Mass), and Fat Mass Index (FM/M2 kg/m2).

**Fat Free Mass (FFM), calculated as lean mass + bone mineral content, and its index (FFMI kg/m2) were reported. BF%, FMI, and FFMI percentiles, according to the reference population tables, stratified by age and gender, were also reported.

**Results:** Seventy consecutive patients were included, 60% were men. Baseline demographic characteristics were similar in men and women. Women had significantly higher BF% and FMI, and lower FFMI as absolute values (table 1). The FFMI percentile was markedly low in men (31.7%) (Figure 1). After multivariate analysis, an ASDAS-CRP > 3.5 was related with lower FFM in the whole group (β-coefficient -5.1, 95% CI -10.2 to -0.1, P=0.047). ASDAS > 3.5 was related to lower fat content in men and to higher fat content in women. The same relationships were found for BASDAI > 4.

**Conclusions:** Muscle wasting, measured as low FFM compared to the reference population, was found in male TNF-α blocker naïve AS patients, especially in those with active disease. Women had higher volumes of body fat than men, but near the median of the reference population. The relationships between fat content and disease activity support the complex association between adipose tissue and inflammation.

**Acknowledgements:** This study was endorsed by an ASAS (Assessment of SpondyloArthritis international Society) Fellowship.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1180

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**FRI0462 THE PISTOL-GRIP DEFORMITY IS MORE FREquent IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS**

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**Background:** Femoroacetabular impingement (FAI) is characterized by early pathologic contact of the proximal femur with the acetabulum. Finker impingement is the anterior acetabular cause of FAI. Whereas cam deformity seems like a flattening of the anterior contour of the head/neck junction or an osseous hump leading a decreased femoral head/neck offset. Patient with FAI present with a hip or a trochanteric painnously in the sitting position or during or after activity. It might also be an important cause of hip osteoarthritis (OA).

**Objectives:** Therefore in this study we evaluated the frequency of pistol-grip deformity (PGD), described as the most characteristic feature of cam-type FAI, in axial spondyloarthritis (axSpA) patients as a potential alternative cause of hip or trochanteric pain.

**Methods:** A total 180 patients (107 [59%] male, mean age 41.9±12.8 years) with axSpA according to ASAS criteria and 198 patients (120 [61%] male, mean age 40.5±14.8 years) admitted to the emergency department (mostly due to trauma) and who had pelvic X-ray were included in the study. Patients with hip OA, hip prosthesis, acetabular protrusion or who have radiographs taken improper technique were excluded. An experienced radiologist assessed all anteroposterior pelvic radiographs. PGD was determined by demonstration of spherical or non-spherical shape of femur head on AP pelvic radiograph.

**Results:** The axSpA group consists 135 ankylosing spondylitis and 45 non-radiographic axSpA patients. The mean duration of symptoms was 13.8±11.3
years in axSpA patients. Radiographic findings of cam abnormality (figure) were significantly more frequent in axSpA patients in comparison with control subjects (30/150 [20%] vs 17/193 [9%] and P=0.004). Cam-type radiographic abnormality was only present in 2 female control subjects and none of female axSpA patients. FAI was significantly correlated with the presence of HLA-B27 (r=0.213 and P=0.048), smoking (r=0.184 and P=0.018), height (r=0.283 and P=0.001) and gender (r=0.443 and P<0.001).

Conclusions: Our results showed that radiographic findings compatible with PGD were frequent in axSpA patients. In addition to repetitive injury to the proximal femoral physis, new bone formation may be responsible for increased FAI in axSpA. In axSpA patients with hip or trochanteric pain, FAI may be kept in mind as an alternative explanation of the symptoms.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5434

FRIO464 ARTERIAL WALL INFLAMMATION IS NOT AFFECTED BY ANTI-IL17 TREATMENT IN PATIENTS WITH PERIPHERAL SPONDYLOARTHROSIS
L.J.J. Van Mens 1, S.L. Verweij 2, A.W.R. van Kuik 3, E.S.G. Stroes 2, D.L. Baeten 1, 4.
1AMC, Amsterdam Immunology and Rheumatology Center; 2Vascular medicine, Academisch Medisch Centrum; 3Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands; 4UCB, Brussels, Belgium

Background: Patients with spondyloarthritis (SpA), a chronic inflammatory disease, have an increased cardiovascular risk which is partly due to increased inflammatory activity in the arterial wall. IL-17A blockade with secukinumab is an effective treatment for SpA. The role of IL-17A in atherogenesis is controversial, some studies suggest that IL-17A is pro-atherogenic, while others indicate that IL-17A is athero-protective. So, it is not known what the effect is of treatment with IL-17A blockade on inflammatory activity in the arterial wall.

Objectives: To assess the effect of 3 months treatment with secukinumab on arterial wall inflammation in SpA patients with peripheral disease (pSpA).

Methods: We included 20 patients with clinical pSpA in a 12 week open-label trial. Treatment consisted of 300 mg secukinumab once a week during the first 4 weeks and then every 4 weeks thereafter. EULAR DAS response was used to define a responder/non responder state. To measure arterial wall inflammation we performed a 18-fluorodeoxyglucose positron emission tomography with computed tomography (18F-FDG PET/CT) imaging in 18 patients at week 12, which is a validated method to quantify arterial wall inflammation. Arterial wall inflammation is measured in both the ascending aorta and carotids, maximal FDG uptake is shown as the maximal target-to-background ratio (TBRmax).

Results: 18 patients with pSpA (age 44±12, 72% male) and without a previous cardiovascular event underwent imaging. Overall, three months treatment with secukinumab resulted in a significant improvement of disease activity with 17/18 patients achieving a EULAR DAS response (9 good and 8 moderate responders). Correspondingly, CRP levels decreased significantly (baseline: 3.2 [1.2–2.4] mg/dl v.s wk 12: 2.0 [1.0–3.5] mg/dl, p=0.011). Additionally, arterial wall inflammation as measured by PET-CT did not change over the course of the 12 weeks treatment with secukinumab (aorta TBRmax baseline: 3.3±0.9 vs. wk 12: 3.3±0.7, p=0.861; carotid TBRmax baseline: 1.88±0.6 vs. wk 12: 1.76±0.4, p=0.067).

Conclusions: This pilot study in 18 patients with pSpA without any preexisting CV events showed that treatment with secukinumab for 3 months has no effect on arterial wall inflammation as measured by PET-CT. Further research in larger patient groups, over a longer period of treatment, and with different measurements remains warranted to fully elucidate the effect of IL-17A blockade on vascular inflammation.

Acknowledgements: This study was funded by an unrestricted grant from Novartis.

Disclosure of Interest: L. Van Mens: None declared, S. Verweij: None declared, A. van Kuik Grant/research support from: UCB, Pfizer, MSD, Janssen, Consultant for: Novartis, Celgene, E. Stroes Speakers bureau: Amgen, Sanofi, Merck, B. van Houwelingen Grant/research support from: Pfizer, MSD, Janssen, Boehringer Ingelheim, Consultant for: Pfizer, MSD, AbbVie, Novartis, UCB, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, Employee of: UCB.

DOI: 10.1136/annrheumdis-2017-eular.4709

FRIO465 ANGLES OF SACRUM INCLINATION EFFECT ON RADIOLOGIC IMAGING READING IN SPONDYLOARTHROSIS (THE ANTELOPE-DESIR STUDY)
M. Herbette 1, L. Deloix 2, F. Garrigue 1, L. Gossec 3, A. Simon 1, A. Feydi 1, F. de Bruin 1, M. Reijnierse 4, D. van de Heijde 1, D. Loëille 5, P. Claudepierre 6, T. Marhadour 1, A. Saraux 1 on behalf of DESIR cohort. 1Rheumatology; 2Radiology; CHU Brest and Université Bretagne Occidentale, Brest; 3Rheumatology, Pitié -Salpétrière, Paris; 4Neurosurgery, CHU Brest and Université Bretagne Occidentale, Brest; 5Radiology, CHU Cochin, Paris, France; 6Radiology, 7Rheumatology, Leiden, Leiden, Netherlands; 8Rheumatology, CHU, Nancy, France; 9Rheumatology, CHU Creteil, Paris, France

Objectives: To assess the impact of spinal angles on clinical and imaging features of suspicion of axial spondyloarthritids (axSpA).

Methods: The DESIR cohort is a prospective longitudinal cohort study of adults aged ≥18 years with inflammatory back pain (IBP) ≥3 months, <3 years. Baseline lateral lumbar radiography of patients included in DESIR cohort were read by two central blinded fellow readers (and a rheumatologist spine specialist in case of discrepancy) for Sacral Horizontal Angle (SHA), Lumbosacral angle (LSA) and total Lordotic Angle (TLA) measures. On the basis of literature, patients were classified depending on whether they had TLA more or less than 50°, SHA more or less than 40° or LSA more or less than 15°. Associations between angles and baseline clinical variables, presence of X-Rays (New York) and MRI (ASAS and MORPHO proposal definition) sacroiliitis, presence of spinal signs of spondyloarthritids (mSASSS, BASRI-total, SPARCC scores), presence
of spinal degenerative MRI signs on X-rays (yes or no) and MRI (presence of Modic abnormalities, Pfirrmann score, Canal stenosis, Extrusion). High intensity zone Facet osteoarthritis according to central reading (two readers) and axSpA diagnostic confidence (according to local clinician’s confidence on a 0–10 visual analog scale) were assessed by univariate analysis using the chi-square test (or Fisher’s exact test where appropriate) and the Mann-Whitney test. Adjustment for multiple testing was performed according to Bonferroni method.

**Results:** Of 708 patients, data were available for 677, 675 and 672 for SHA, LSA and TLA, measures with a mean value of 39.2°, 14.5° and 51.5° respectively. Clinical features and diagnostic confidence did not differ between the SHA, LSA and TLA groups. More sacrolilits imaging, according to ASAS (41.4% versus 32.0%) and MORPHO definition (48.6% versus 39.3%), were reported in TLA group but the differences did not reach statistical significance. Radiological scores were low with a mean value of 0.49 (±1.83), 0.30 (±0.78) and 4.9 (±9.0) for mSASSS, BASRI-total and SPARCC score, respectively, and no inter-group difference was found. In LSS1, more grade 3 and 4 Pfirrmann class and MDCiscophy (types 1 and 2) were observed for SHA <40°, and TLA <50° (p<0.001) whereas the difference did not reach the significance level for LSA<15° (p<0.05) (table).

**Conclusions:** Lumbar spine morphology is not associated with any clinical variable, presence on X-Rays or MRI of spinal signs of spondyloarthritis or sacroilits. At the LSS1 level, a more horizontal SHA and a reduction of TLA is associated with more degenerative radiological lumbar spine manifestations.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5128

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**FR0467 DEVELOPMENT AND PRELIMINARY VALIDATION OF THE COMPUTED TOMOGRAPHY SACROIACIAL STRUCTURAL SCORE (CT-SSS) FOR ASSESSMENT OF STRUCTURAL LESIONS IN AXIAL SPONDYLOARTHRITIS**

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**Background:** Computed tomography (CT) is considered the imaging benchmark for the assessment of certain structural lesions in the sacroiliac joints (SIJ) of patients with axial spondyloarthritis (axSpA). Availability of low dose radiation techniques may lead to more widespread use, potentially as a structural endpoint in clinical trials research.

**Objectives:** We aimed to validate a new CT-based scoring method, the CT Sacroiliac Structural Score (CT-SSS), for assessing structural lesions in the SIJ.

**Methods:** CT scans of the SIJ from 44 patients (26 females, mean age 49.4 years, mean symptom duration 9.1 years) were reconstructed in the semicoronal plane parallel to the superior border of the sacrum and scoring of lesions was confined to this plane. Structural lesions were scored in consecutive slices in SIJ quadrants (erosion, sclerosis) or SIJ halves (ankylosis) on a dichotomous basis (present/absent) using the same anatomical principles as developed for the SPARCC MRI SIJ inflammation and structural scores. The most anterior slice is defined as visible joint >1cm vertical height and when <3 cm is defined as having only upper iliac and sacral quadrants. A visible joint >3cm vertical height is defined as having 4 quadrants. At the posterior aspect of the SIJ, there is a natural separation of iliac and sacral cortical bone by structures in the ligamentary portion. Scoring is terminated when <1cm of iliac and sacral bone is appositional. Two readers independently scored CT scans without a prior calibration exercise and using direct online data entry onto a schematic of the SIJ. Reliability was assessed by kappa statistics, intra-class correlation coefficient (ICC), and Bland-Altman limits of agreement.

**Results:** Scoring was feasible (5–10 minutes per scan) and both ankylosis (ICC=0.95) and erosion (ICC=0.81) were reliably scored (Table). Scoring was less reliably scored (ICC=0.89). Presence/absence of ankylosis was reliably determined irrespective of whether this was based on a single slice (κ=0.77) or 3 consecutive slices (κ=0.81). Reliable detection was lower for erosion (κ=0.50 for 1 or 3 slices) and sclerosis (κ=0.44 and 0.48 for 1 and 3 slices, respectively). Bland-Altman graph illustrates reliability across the range of scores for ankylosis and erosion.

**Conclusions:** The CT-SSS method is feasible and reliable for scoring ankylosis and erosion with minimal calibration. Scoring requires further standardization and calibration.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2202

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**FR0468 RADIOGRAPHIC HIP INVOLVEMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A STUDY OF ITS PREVALENCE AND DETERMINING FACTORS**

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**Background:** Hip involvement in Ankylosing Spondylitis (AS) is the most frequent extraspinal manifestation and a common cause of disability and limited mobility, often ending with hip replacement. There are few studies analysing the radiographic changes of the hip and their relationship with other disease variables.
Objectives: To determine the factors associated with radiographic hip involvement and its prevalence.

Methods: A cross-sectional study was performed based on patients with AS, excluding the patients with associated psoriasis or inflammatory bowel disease. To assess radiographic hip involvement, we scored the last anteroposterior pelvic radiograph performed using the Bath Ankylosing Spondylitis Radiology Index (BASRI). Demographic, clinical, laboratory, and radiographic data were collected and analysed. We considered the presence of hip disease with a BASRI hip score of at least 2.5. The statistical analyses were done using SPSS 24.0. p < 0.05 was considered statistically significant.

Results: 215 patients were identified, with a mean age of 52±13.6 years and 76.7% of the patients were male. The age at onset was 25.29±8.22 years. 86.4% of the patients were HLA-B27-positive. Regarding their treatment, 27.9% were observed in the age, age at onset and presence of peripheral arthritis. Patients with hip involvement had higher scores in BASRI score, ASDAS CRP and ESR. Axial radiographic involvement assessed with axial BASRI score and total SASSS was associated with hip disease and a significant association was seen between hip involvement and metatropic parameters.

Conclusions: Compared to AS patients without hip involvement, the radiographic hip-involved group are younger at disease onset, more frequently men and complaining of typical inguinal pain, have lower BMI and longer disease duration. AS patients having these concomitant risk factors should undergo further hip assessment in clinical practice.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4159

FR0470 CIGARETTE SMOKING HAS A DOSE-DEPENDENT RELATIONSHIP WITH DISEASE ACTIVITY AND CORRELATES WITH MORE FUNCTIONAL LIMITATION AND WORSE HEALTH ASSESSMENT IN THE PATIENTS WITH ANKYLOSING SPONDYLITIS
Y. Jiang, Z. Liao, Z. Lin, M. Yang, Y. Zhang, Q. Li, J. Gu. Rheumatology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the axial skeleton by causing inflammatory and osteoporiferative changes in the sacroiliac joints and spinal structures [1]. Cigarette smoking is associated with poor outcome in patients with established early AS [2].

Objectives: Our study was to investigate the relationship between cigarette smoking and pain, disease activity, functional limitation, and health assessment in Chinese patients with AS.

Methods: Patients with AS (n=683) from China took part in a cross-sectional survey. Smoking status was obtained by a standardized questionnaire, including smoking status (non-smokers, exsmokers, current smokers), the age when starting smoking, cigarette numbers a day and smoking status of family numbers. The Bath AS Disease Activity Index (BASDAI), the Bath AS Functional Index (BASI), visual Analog scale of pain, Health Assessment Questionnaire for Spondyloarthritis (HAQ-S) were analyzed in terms of smoking status and relationship with pack-year history.

Table 1. Demographic features and clinical and laboratory results of patients with and without different smoking status

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (N=683)</th>
<th>Non-smokers (N=407)</th>
<th>Ex-smokers (N=108)</th>
<th>Current smokers (N=168)</th>
<th>p value</th>
<th>P(1:2)</th>
<th>P(2:3)</th>
<th>P(1:3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.33±6.67</td>
<td>26.04±6.65</td>
<td>27.65±7.84</td>
<td>30.24±7.56</td>
<td>0.000</td>
<td>0.001</td>
<td>0.006</td>
<td>0.069</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>6.47±6.47</td>
<td>5.73±6.08</td>
<td>6.81±6.98</td>
<td>8.05±7.05</td>
<td>0.009</td>
<td>0.094</td>
<td>0.071</td>
<td></td>
</tr>
<tr>
<td>Morning stiffness (VAS)</td>
<td>3.12±2.86</td>
<td>2.84±2.87</td>
<td>2.87±2.53</td>
<td>3.96±2.89</td>
<td>0.000</td>
<td>0.003</td>
<td>0.739</td>
<td></td>
</tr>
<tr>
<td>Overall Pain (VAS)</td>
<td>3.97±2.77</td>
<td>3.78±2.83</td>
<td>3.96±2.70</td>
<td>4.44±2.61</td>
<td>0.005</td>
<td>0.150</td>
<td>0.440</td>
<td></td>
</tr>
<tr>
<td>Nocturnal back pain (VAS)</td>
<td>2.93±2.96</td>
<td>2.63±2.90</td>
<td>2.89±2.73</td>
<td>3.83±3.11</td>
<td>0.000</td>
<td>0.004</td>
<td>0.216</td>
<td></td>
</tr>
</tbody>
</table>

FR0469 DIFFERENCES BETWEEN ANKYLOSING SPONDYLITIS PATIENTS WITH AND WITHOUT RADIOGRAPHIC HIP INVOLVEMENT IN CHINA
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Background: Hip involvement, defined by clinical examination or imaging techniques, is a problem of great concern in Ankylosing Spondylitis (AS) patients as it affects joint functional impairment and poor outcome. It has been shown that early age at disease onset, peripheral manifestation and severe axial disease are risk factors, but other characteristics do not show consistency through studies and data is scarce so far.

Objectives: We aim to describe the phenotype differences between AS patients with and without radiographic hip involvement and to identify potential risk factors for hip involvement.

Methods: AS patients fulfilling the Modified New York Criteria and whose pelvic X-rays have been assessed by at least one radiologist and one rheumatologist were included. Radiographic hip involvement was defined by features of osteophytes around the femoral neck, erosions of the acetabulum, axial migration of the femoral head or hip joint space narrowing. The medical records were retrospectively reviewed and collected. Demographic and disease characteristics were compared by descriptive and bivariate statistics using SPSS v19.0 and stata v12.1 package.

Results: Totally 621 AS patients with hip involvement and 420 patients without hip involvement were analyzed. Statistical significance were found between these 2 groups regarding age at disease onset, gender, BMI, disease duration and presence of peripheral arthritis, with all p value<0.001. Male patients showed strong risk effect on hip involvement with the odds ratio (OR) around 3.27.

Meanwhile, the hip-involved group had lower body mass index (BMI), which may relate to long disease duration or high inflammation level. No significant difference of HLA-B27 positivity, family history and other factors were observed (Table 1). Binary logistic regression results showed that age at disease onset, gender, BMI and disease duration were associated with hip involvement in AS (p<0.001). For the symptoms, among 69 hip-involved and 75 non-hip-involved AS with corresponding records, 83% hip-involved and 35% non-hip-involved patients complained of typical inguinal pain (OR=8.95, 95% CI=3.85–21.37, p<0.001).

Table 1.

<table>
<thead>
<tr>
<th>Hip involvement</th>
<th>AS with hip involvement (n=621)</th>
<th>AS without hip involvement (n=420)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No hip disease</td>
<td>154 (71.6%)</td>
<td>61 (29.4%)</td>
<td></td>
</tr>
<tr>
<td>Age* (years)</td>
<td>49.1±13.63</td>
<td>58.1±11.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at onset* (years)</td>
<td>26.14±8.4</td>
<td>23.16±7.38</td>
<td>0.017</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>113 (73.4%)</td>
<td>240 (91.5%)</td>
<td></td>
</tr>
<tr>
<td>BMI, m (SD)</td>
<td>20.35±3.47</td>
<td>21.31±3.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HLA-B27+, n (%)</td>
<td>132 (85.7%)</td>
<td>370 (88.94)</td>
<td>0.61</td>
</tr>
<tr>
<td>Uveitis, n (%)</td>
<td>40 (26.0%)</td>
<td>13 (21.3%)</td>
<td>0.475</td>
</tr>
<tr>
<td>BASFI score</td>
<td>5.21±9.21</td>
<td>1.47±2.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASRI score</td>
<td>3.79±7.15</td>
<td>7.23±11.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASDAS CRP*</td>
<td>2.07±1.01</td>
<td>2.45±0.95</td>
<td>0.014</td>
</tr>
<tr>
<td>ASDAS ESR*</td>
<td>1.89±0.80</td>
<td>2.52±1.92</td>
<td>0.002</td>
</tr>
<tr>
<td>Schöber's index (cm)</td>
<td>3.61±1.55</td>
<td>2.43±1.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chest expansion* (cm)</td>
<td>4.97±1.84</td>
<td>3.67±2.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cervical rotation* (cm)</td>
<td>72.03±19.73</td>
<td>49.18±28.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral flexion* (cm)</td>
<td>12.96±5.18</td>
<td>7.85±4.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Occiput to wall distance* (cm)</td>
<td>2.49±4.36</td>
<td>8.45±8.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Axial pattern, n (%)</td>
<td>100 (22.2%)</td>
<td>22.21 (14.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BasRI*</td>
<td>5.31±1.30</td>
<td>8.53±3.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total SASSS*</td>
<td>10.24±16.07</td>
<td>30.67±27.31</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Mean ± SD.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4375
Results: Of the all 683 patients, 168 are current smokers, while 108 were significant associated with age, age onset, SDS scores, SRRS scores positively and years of education negatively (P<0.01). SDS scores were associated with age, age onset, SDS scores, SRRS scores positively and years of education negatively (P<0.01). SRRS scores were associated with age, age onset, SDS scores, SRRS scores positively and years of education negatively (P<0.01).

Conclusions: A large number of AS patients were found to have anxiety, depression, sleep disturbance and stressful life events. These problems correlated with each other. Clinicians should pay more attention to psychological disorders and sleep problems in AS patients.

References:

Acknowledgements: None.

Disclosure of Interest: None declared.

DOES AXIAL SPONDYLOARTHRITIS PHENOTYPE CORRELATE WITH IMAGING MORPHOTYPE?

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Background: Traditionally, radiographic imaging was used to describe morphological differences between various types of axial SpA (axSpA). The advent of MRI has improved understanding of disease activity and facilitated the identification of non-radiographic spinal changes, and enabled earlier diagnosis and visualization of structural changes, and facilitated the identification of non-radiographic axial SpA (nr-axSpA). The magnitude of the pathologic changes in the axial skeleton is used to quantify inflammatory and structural outcomes of clinical trials and treatment of patients with axSpA.

Objectives: To examine the MRI morphology of sacroiliitis (SI) and vertebral corner lesions in patients with primary (1°, no psoriasis) and secondary (2°, with psoriasis) axSpA.

Methods: This posthoc analysis was performed on data from patients with axSpA enrolled in the EMBARK trial (NCT01258738). Only patients with baseline MRI were included. Symmetric and asymmetric SI, structural lesions, and corner inflammatory lesions were analyzed in 1° axSpA vs 2° axSpA patients. Data were analyzed using one-way analysis of variance for continuous parameters, and Fisher's exact tests for categorical parameters.

Results: The baseline demographics and disease characteristics between the 122 patients with 1° axSpA and 19 with 2° axSpA were similar. Asymmetric sacroiliitis was seen in significantly fewer 1° (43%) vs 2° (68%) axSpA patients. There were no differences in mean SpondyloArthritis Research Consortium of Canada (SPARCC) scores between 1° and 2° axSpA for any of the 4 SI joint (SJ) quadrants. However, the lower iliac quadrants had the highest SPARCC SJ score and the upper iliac quadrants had the lowest SPARCC SJ scores. When analyzing the 4 spine quadrants (lower/upper anterior and lower/upper posterior), 1° patients had higher total SPARCC spine scores than 2° patients for all 4 quadrants at baseline. Collapsing the 4 quadrants shows that 1° axSpA patients had higher SPARCC MRI of the entire spine (23 discovertebral units [DVU]; mean=5.7) compared with 2° axSpA patients (mean=2.7).

Conclusions: We found 1° axSpA patients had more symmetric sacroiliitis and extensive spinal bone marrow edema compared with 2° axSpA patients. In addition, patients appeared to have more asymmetric sacroiliitis. These data may help physicians accurately diagnose patients and decide best treatment options.


DOI: 10.1136/annrheumdis-2017-eular.4417

FR0474

ANTI-CD74 ANTIBODIES AS DIAGNOSTIC BIOMARKER FOR EARLY AXIAL SPONDYLOARTHRITIS: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE) COHORT STUDY

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Background: Diagnosis of axSpA is often delayed with 5–10 years. A robust biological disease marker had not been detected and could decrease the current diagnostic delay. Two studies showed that serum anti-CD74 IgA antibodies are increased in SpA 1.2.

Objectives: To explore the value of anti-CD74 antibodies as diagnostic biomarker for axSpA patients in early, chronic back pain.

Methods: We tested the prevalence of anti-CD74 IgG and IgA antibodies in patients from the SPONDyOArtRitis Caught Early (SPACE) cohort by enzyme-linked immunosorbent assay (ELISA). Patients from the SPACE cohort have chronic back pain for ≥3 months and ≤2 years with an onset ≥6 months. Results: We included 560 patients of the SPACE cohort, of whom 274 patients were diagnosed with axSpA by a rheumatologist at baseline. Anti-CD74 IgG levels did not differ between patients with and without axSpA (p=0.152, Table 1). Median anti-CD74 IgA levels (tested with either casein or BSA as a blocking buffer) were higher in patients with axSpA (p<0.0001). Despite these differences at the group level, the diagnostic value of the anti-CD74 IgA antibodies was limited as shown by ROC analysis. The optimal cut off according to ROC analysis was an optical density (OD) of 0.875, providing a sensitivity of 38.3% and a specificity of 77.6%. In line with previous reports, further analysis revealed that total IgA levels were elevated in early axSpA patients vs. non-SpA early back pain patients (p=0.008). When correcting the level of anti-CD74 IgA for the total level of IgA, the differentiating capacity of anti-CD74 disappeared for casein but remained intact for BSA (casein: p=0.731, BSA: p=0.038). Additional analyses using the ASAS classification criteria rather than a clinical diagnosis of axSpA, a strict combination of disease diagnosis and radiological criteria (exclusion of patients without 77.6% of 77.6% and 0.875 optical density (OD) of 0.875, providing a sensitivity of 38.3% and a specificity of 77.6%.

Conclusions: Serum anti-CD74 IgA antibody levels, but not serum anti-CD74 IgG levels, are elevated in patients with axSpA versus non-SpA with back pain <2 years duration. However, ROC analyses revealed that these numerical differences of are limited diagnostic value in these patients with early back pain.

Abstract FR0474 – Table 1

| Parameter | Total (n=141) | 1° axSpA with axSpA enrolled in the EMBARK trial (NCT01258738). Only patients with baseline MRI were included. Symmetric and asymmetric SI, structural lesions, and corner inflammatory lesions were analyzed in 1° axSpA vs 2° axSpA patients. Data were analyzed using one-way analysis of variance for continuous parameters, and Fisher's exact tests for categorical parameters.

Results: The baseline demographics and disease characteristics between the 122 patients with 1° axSpA and 19 with 2° axSpA were similar. Asymmetric sacroiliitis was seen in significantly fewer 1° (43%) vs 2° (68%) axSpA patients. There were no differences in mean SpondyloArthritis Research Consortium of Canada (SPARCC) scores between 1° and 2° axSpA for any of the 4 SI joint (SJ) quadrants. However, the lower iliac quadrants had the highest SPARCC SJ score and the upper iliac quadrants had the lowest SPARCC SJ scores. When analyzing the 4 spine quadrants (lower/upper anterior and lower/upper posterior), 1° patients had higher total SPARCC spine scores than 2° patients for all 4 quadrants at baseline. Collapsing the 4 quadrants shows that 1° axSpA patients had higher SPARCC MRI of the entire spine (23 discovertebral units [DVU]; mean=5.7) compared with 2° axSpA patients (mean=2.7).

Conclusions: We found 1° axSpA patients had more symmetric sacroiliitis and extensive spinal bone marrow edema compared with 2° axSpA patients. In addition, patients appeared to have more asymmetric sacroiliitis. These data may help physicians accurately diagnose patients and decide best treatment options.


DOI: 10.1136/annrheumdis-2017-eular.5381
Background: Axial spondyloarthritis (AxSpA) is a severe and potentially debilitating disease, where earlier diagnosis leads to a better prognosis. Although HLA-B27 antigen is strongly associated with AxSpA, this marker may have a low sensitivity in some Middle-Eastern countries. Recent European studies showed a strong association between antibodies against CD74 and AxSpA with a sensitivity of 85.1%, specificity of 92.2%, and positive likelihood ratio (LR) of 10.8. The diagnostic properties of anti-CD74 may have a particular interest in non-European countries with low HLA-B27 prevalence such as Lebanon.

Objectives: In this prospective study, we tested the diagnostic properties of IgG and IgA anti-CD74 as an early diagnostic marker for AxSpA, compared with HLA-B27, in Lebanon, which is known as one of the countries with the lowest HLA-B27 prevalence ever reported.

Methods: Sera of AxSpA patients and healthy blood donors (HBD) were analyzed for HLA-B27 genes (PCP) and for IgG and IgA anti-CD74 (ELISA). The patients were recruited from rheumatology clinics across Lebanon. Clinical assessment and sera sample collection were performed at a center specialized in AxSpA (Hotel-Dieu de France University hospital, Beirut). Inclusion criteria were: age 18–45 years, Lebanese, symptom duration <3 years, AxSpA as per ASAS criteria (imaging arm), no prior biologic therapy. Interpretation of the radiographic images was performed centrally and blindly. Clinical and laboratory assessments of the disease were performed in all AxSpA patients. Comparison between groups was performed with the Fisher exact test and Student’s t-test. For the diagnostic properties of HLA-B27 and anti-CD74, ROC curves were calculated.

Results: 10 AxSpA patients and in 2 HBD (Sensitivity 34.5%, Specificity 97.2%, Positive LR 10.8) and 18–45 years, Lebanese, symptom duration <3 years, AxSpA as per ASAS criteria (imaging arm), no prior biologic therapy. Interpretation of the radiographic images was performed centrally and blindly. Clinical and laboratory assessments of the disease were performed in all AxSpA patients. Comparison between groups was performed with the Fisher exact test and Student’s t-test. For the diagnostic properties of HLA-B27 and anti-CD74, ROC curves were calculated.

Conclusions: In this study in a population with low HLA-B27 prevalence, IgG anti-CD74 antibodies showed higher diagnostic value than HLA-B27 for AxSpA. This is of special interest in populations with low HLA-B27 prevalence, especially on the background of diagnosing AxSpA when using the clinical arm of the ASAS classification criteria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2271

FR0477 PROSPECTIVE OBSERVATIONAL STUDY ON THE EVALUATION OF QUALITY OF LIFE IN PATIENTS AFFECTED BY ENTEROPATHIC SPONDYLOARTHRITIS

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Background: Enteropathtic Spondyloarthropathy (ESpA) belongs to the group of Spondyloarthropathy (SpA) typically associated with inflammatory bowel disease (IBD) as Cohn’s Disease (CD) and Ulcerative Colitis (UC). Joint pain is the most common (22–33%) and significant extra-intestinal manifestation in patients with IBD and its management requires rheumatological and gastroenterological competence in collaboration. No data concerning the Health-related quality of life (HRQoL) have been evaluated in patients affected by ESpA.

Objectives: Prospective study was performed in a combined GastroIntestinal and Rheumatologic “GI-Rhe” clinic, in order to evaluate: 1) prevalence and characteristics of articular manifestations in a group of IBD patients; 2) quality of life, state of health and well-being in ESpA patients.

Methods: Patients affected by IBD who presented musculo-skeletal pain between February 2013 and September 2016 (CD 264 and UC 142) were enrolled. New diagnosis, disease management, adverse events as well as laboratory evaluations were assessed every 3 months during the follow-up. Disease activity, function and quality of life in ESpA patients were assessed by ASDAS-CRP, HAQ-S and EuroQol questionnaire.

Results:

<table>
<thead>
<tr>
<th>IBD-SpA (N=212)</th>
<th>IBD non-SpA (N=215)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47±13.1</td>
</tr>
<tr>
<td>Male (%)</td>
<td>134/63.2</td>
</tr>
<tr>
<td>CD (%)</td>
<td>141/66.5</td>
</tr>
<tr>
<td>UC (%)</td>
<td>71/33.5</td>
</tr>
<tr>
<td>SpA disease duration (months)</td>
<td>37.75</td>
</tr>
<tr>
<td>IBD disease duration (months)</td>
<td>162.2±115.3</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>1.2±1.6</td>
</tr>
<tr>
<td>CDAI &gt;150 (%)</td>
<td>26/18.4</td>
</tr>
<tr>
<td>Mayo score &gt;3 (n)</td>
<td>11/15.7</td>
</tr>
<tr>
<td>HAQ-S</td>
<td>0.5±1.3</td>
</tr>
<tr>
<td>ASDAS</td>
<td>2.1±1.1</td>
</tr>
</tbody>
</table>

A total of 427 patients were evaluated for joint involvement (Table 1). The prevalence of SpA in IBD patients was 49.6% (n=212; UC 71 (43.3%), CD 141 (53.4%)), suggesting that the majority of patients with IBD who complain arthritis may have a concomitant SpA. Other rheumatologic diseases were detected in the study population in 215 patients defined as IBD non-SpA. There was a significantly higher prevalence of active intestinal disease in patients with SpA with respect to IBD-non SpA (CD: CDAI>150 in 18.4% vs 8.2% p=0.004; UC: Mayo score >3 in 15.5% vs 0%, p=0.0004). The evaluation of the EuroQol demonstrated a mean value of 0.59 in IBD-SpA patients and of 0.55 in IBD non-SpA (Figure 1A). In IBD-SpA, the health related status was: decent 69.8%, good 17.9% and bad 9.4%. In IBD-non SpA, the health related status was: decent in 74.8%, good in 17.7% and bad in 7% of patients. In both groups, none of the patients had a neither exceptional nor great perception of QoL. No significant differences were observed between the two groups (Figure 1B).

Conclusions: The joint clinic facilitates diagnosis and management of SpA and IBD. Although IBD-SpA patients showed higher IBD disease activity than IBD-non SpA one, both groups of patients have a good health related QL.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4005
SUBCHONDRAL BONE SCLEROSIS ON COMPUTED TOMOGRAPHY – DOES IT HAVE ANY VALUE IN THE DIAGNOSIS OF INFLAMMATORY SACRILIITIS OR IS IT A NON-SPECIFIC FINDING?

O. Azmat1, R.G. Lambert1, Z. Jibri1, W.P. Maksymowych1, 2

1Radiology; 2Medicine, University of Alberta, Edmonton, Canada

Background: Sclerosis in the sacroiliac joints (SIJ) on radiography and computed tomography (CT) is common but widely considered a non-specific finding. Sclerosis due to degeneration and ostearthrosis is a known cause, however, the extent of sclerosis seen in inflammatory sacroiliitis is unknown.

Objectives: We aimed to determine whether this lesion could be reliably detected and its diagnostic utility.

Methods: 215 CT scans were obtained from patients with a history of low back pain. 107 patients had a clinical diagnosis of spondyloarthritides (SpA) and 108 patients were clinically proven not to have SpA. Groups were age and gender matched (140 males, 75 females, mean age was 45 years). Three musculoskeletal radiologists, blinded to patient demographics and diagnosis, scored the CTs after standardization of lesion definitions and calibration. Erosions, sclerosis, and ankylosis were graded by size and number of articular surfaces/joints involved. Sclerosis was considered definite if located along the cartilaginous compartment, measured >5mm in all 3 planes, and present >5mm from the joint surface. Discrepant scores were arbitrated and inter-reader reliability calculated by intra-class correlation coefficient (ICC). Diagnostic utility of CT lesions was determined by calculating sensitivity and specificity for the clinical diagnosis and by logistic regression.

Results: ICC for sclerosis and erosion for each articular surface ranged from 0.65–0.76 and 0.71–0.78, respectively. ICC for ankylosis was 0.87–0.89. Sclerosis occurred in 87 (81%) cases with SpA and 25 (23%) controls. For a single articular surface the specificity for sacroiliitis between 88–94%, for any two articular surfaces 95–100%, for all 4 articular surfaces 100%. Sensitivity ranged from 14% (4 articular surfaces) to 55% (either ilium). Erosion and ankylosis had a similar specificity range of 91–100% and 92–93%. The odds ratio was 4.9 for presence of definite erosions, and 12.6 for bilateral joint involvement. The odds ratio increased to 84.2 for bilateral erosion and 22.8 for bilateral ankylosis.

Conclusions: When sclerosis measures >5mm in three planes and is located >5mm from a joint perimeter, it has high specificity for sacroiliitis, regardless of how many articular surfaces are involved, with similar specificity to erosion and ankylosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6292

PREDICTORS OF LONG-TERM MODIFIED MINIMAL DISEASE ACTIVITY RESPONSE IN PERIPHERAL SPONDYLOARTHITIS PATIENTS TREATED WITH ADALIMUMAB

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Background: There is a lack of validated outcome measures in non-psoriatic peripheral spondyloarthritis (pSpA). Therefore, a modified version of the minimal disease activity (mMDA)1 was developed and validated. Identification of factors that predict long-term mMDA response in pSpA patients (pts) can facilitate decisions regarding treatment initiation and maintenance.

Objectives: The purpose of this analysis was to determine predictors of long-term mMDA response following adalimumab (ADA) treatment in pSpA pts from the ABILITY-2 study.

Methods: ABILITY-2 was a phase 3 randomized, double-blind trial evaluating the efficacy and safety of 40 mg ADA every other week versus placebo (PBO) over 12 wks followed by open-label (OL) ADA for 64 wks in pSpA pts. This post-hoc analysis included pts who received at least one dose of ADA during the PBO-controlled period or OL extension. The mMDA for pSpA was defined as achieving at least 5 out of the following 6 criteria: 1) TJC78 ≤1; 2) SJC76 ≤1; 3) pain visual analog scale (VAS) ≤15 of 100 mm; 4) pt global activity (PtGA) VAS ≤20 of 100 mm; 5) HAQ-DI ≤0.5; and 6) tender entheseal points <1 (Leeds Enthesitis Index [LEI] or Spondyloarthritis Research Consortium of Canada [SPARCC] Enthesitis Index). In this post hoc analysis, multiple logistic regression with stepwise variable selection was used to determine predictors of long-term (yrs 1–3) and sustained (defined as mMDA for at least 24 consecutive wks) mMDA responses. Variable selection of baseline (BL) pt demographics and disease characteristics were performed with and without mMDA response at wk 16 (mMDA16) as a candidate. In pts achieving mMDA at wk 16, ADA exposure ranged between 4 and 16 wks.

Results: In pSpA pts treated with ADA, mMDA (5/6 LEI or SPARCC) was achieved by almost 41%, 49%, and 50% of pts at yrs 1, 2, and 3, respectively and sustained mMDA response was achieved by 42% of pts. Regardless of mMDA definition, achieving mMDA response at wk 16 (up to 16 wks of ADA) was a robust positive predictor of attaining both long-term mMDA at yrs 1–3 and sustained mMDA (Figure). In the model examining the BL predictors (model without mMDA16), age, BL enthesitis and BL BASDAI scores were most commonly selected as negative predictors for achieving long-term and sustained mMDA. Other selected predictors included BL dactylitis, physician’s global assessment, hsCRP, and male sex; however, these predictors were not consistently selected for all time points or sustained mMDA.

Conclusions: Early mMDA response is a stronger and more consistent predictor of long-term mMDA, whether at 1, 2, or 3 yrs or sustained over time, than BL.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6292

FRI0478

FRI0479
characteristics. The 5/6 versions of mMDA could be an appropriate treatment target in pSpA pts.

References:

Acknowledgments: AbbVie funded the study (NCT01064856), contributed to its design, and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

Disclosure of Interest: L. Coates Grant/research support from: AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, UCB, Consultant for: AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, UCB, S. Abraham Grant/research support from: AbbVie, Celgene, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, Novartis, Pfizer, and UCB, for: AbbVie, Celgene, No-...
pain vs. PaG1: -35.7 and 23.3 [-6.3, 1]. LLAo and ULoa remained constant over the whole range of the VISSCALES.

Conclusions: In patients with SpA, fatigue, pain and PaG1 scores were poorly associated and only poorly explained by other potential explanatory variables.

On the individual level, disagreements between the scores were substantial. The finding of a high degree of interrater emmance, which could indicate understanding patient-reported outcome measures and their diverging interplay across individuals.

References:

Disclose of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4117

FRIDAY, 16 JUNE 2017
Psoriatic arthritis

FR0482 INSULIN RESISTANCE IN PATIENTS WITH PSORIATIC ARTHRITIS
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Background: Inflammation and, levels of inflammatory markers, CRP and other cytokines are important for enhancing insulin resistance in PaS patients. Inflammation and, levels of inflammatory markers, CRP and other inflammatory cytokines are important players for enhancement and development of insulin resistance in psoriatic arthritis patients.

Objectives: To investigate the relation between insulin resistance and psoriatic arthritis presence and disease activity. To investigate the relation between insulin resistance and disease activity in patients with psoriatic arthritis.

Methods: Patients Inclusion criteria: all patients in this study had psoriatic arthritis with disease duration 5 years or more. All under conventional DMARDs treatment in the form of methotrexate 12.5 mg/wk, hydrochloroquine 400mg/day. With no treatment with glucocorticoids, 3 months prior to enrollment in the study and no previous treatment with biologics. All patients were Postmenopausal females with 3 or more years since menopause.

Exclusion Criteria: DM, ischemic heart disease, hypertension, or any other chronic diseases. Smoking, on medications Medications that affect blood lipids, or body composition and metabolic functions. Postmenopausal females who were on hormone replacement therapy.

Grouping: G I: Included 50 postmenopausal females with psoriatic arthritis. G II: Included 25 normal postmenopausal females, as a control group.

Methods: 1. Full medical history and Complete clinical examination 2. Anthropometric measurements: Body mass index (BMI), Waist-hip ratio (WHR). 3. The following laboratory investigations were done: C-reactive protein (CRP), Fibrinogen, Fasting insulin. 4. Measures of insulin resistance: Homeostasis model assessment of insulin resistance (HOMA-IR): (a) HOMA 1-IR: It is calculated according to the following equation: Fasting insulin (µU/ml) X FBS (mg/dl)/405.

(2). Insulin resistance was defined as HOMA-IR > 2.67 as cut-off.

Results: Comparing means of age, BMI, and WHR of both groups’ shows no significant difference. This indicates that both groups were matched and valid for comparison. G I have significantly higher values than the control group in the paired fasting glucose and insulin values, were calculated using the computer it is the updated (or computer) model with nonlinear solutions, which also uses the NHWS was a self-administered, web-based, voluntary, confidential questionnaire. Stratified randomised sampling provided a representative sample of EU adults in France, Germany, Italy, Spain and UK. Respondents completing the arthritis module and reporting PaS diagnosis were stratified on a range of demographic and disease-related parameters and randomised to one of two self-reporting surveys: the National Health and Wellness Survey (NHWS) and determine the impact of treatment, or no treatment, on pt-reported outcomes.

Methods: The NHWS was a self-administered, web-based, voluntary, confidential questionnaire. Stratified randomised sampling provided a representative sample of EU adults in France, Germany, Italy, Spain and UK. Respondents completing the arthritis module and reporting PaS diagnosis were stratified on a range of demographic and disease-related parameters and randomised to one of two self-reporting surveys: the National Health and Wellness Survey (NHWS) and determine the impact of treatment, or no treatment, on pt-reported outcomes.

Methods: The NHWS was a self-administered, web-based, voluntary, confidential questionnaire. Stratified randomised sampling provided a representative sample of EU adults in France, Germany, Italy, Spain and UK. Respondents completing the arthritis module and reporting PaS diagnosis were stratified on a range of demographic and disease-related parameters and randomised to one of two self-reporting surveys: the National Health and Wellness Survey (NHWS) and determine the impact of treatment, or no treatment, on pt-reported outcomes.

Objectives: To investigate the relation between psoriatic arthritis and psoriatic arthritis patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3569

FR0484 IMPACT OF PSORIATIC ARTHRITIS ON PATIENT-REPORTED OUTCOMES IN 5 EUROPEAN UNION COUNTRIES
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Objectives: This non-interventional, cross-sectional, descriptive, exploratory analysis aimed to characterise patients (pts) with psoriatic arthritis (PsA) in the 2016 National Health and Wellness Survey (NHWS) and determine the impact of treatment, or no treatment, on pt-reported outcomes.

Methods: The NHWS was a self-administered, web-based, voluntary, confidential questionnaire. Stratified randomised sampling provided a representative sample of EU adults in France, Germany, Italy, Spain and UK. Respondents completing the arthritis module and reporting PaS diagnosis were stratified on a range of demographic and disease-related parameters and randomised to one of two self-reporting surveys: the National Health and Wellness Survey (SF-36); Work Productivity and Activity Impairment questionnaire and Patient Health Questionnaire-9 (PHQ-9) responses were summarised descriptively.

Results: NHWS was completed by 80,600 adults; 947 completed the arthritis module and self-reported PsA diagnosis. Of these, 65 (7%) reported receiving advanced therapies, 274 (29%) other therapies and 608 (64%) no current treatment. Age and gender were generally balanced between the groups (mean 51–56 years; 51–64% female). More patients on advanced therapies had a body mass index ≥30 (41%) vs other therapies (34%) and no current treatment (28%). Pts on advanced therapies reported more comorbidities (moderate to intense vs other therapies (mean 1.8) and pts with no current treatment (mean 1.7). More pts on advanced therapies were current smokers (49%) vs pts on other therapies (30%) and pts with no current treatment (32%). Prior to treatment with advanced or other therapies, 94% and 74% were self-reported moderate or severe PsA, falling to 58% and 39% respectively, after treatment, compared with 36% and 11% for pts with no current treatment. SF-36 scores and PHQ-9 scores did not widely vary across groups (Table 1). Regardless of treatment groups, pts reported >20% work loss, >45% overall work impairment and >45% activity impairment (Table). More than 60% of pts reporting PaS diagnosis reported no current treatment.

Disclosures: None declared.
In peripheral psoriatic arthritis DKK-1 and PTH are intravenous golimumab in adult patients with PsA.

Methods: This is a multi-center, randomized, double-blind, placebo-controlled trial. Biologic-naive active PsA pts were randomized (1:1) to IV GLM 2mg/kg at weeks (wk) 0, 4, and every 8 wks thereafter or PBO at wk0, 0, 4, 12, and 20 with crossover to GLM at wk24. The primary endpoint was ACR20 response at wk14. Multiplicity-controlled endpoints were ACR50, ACR70, PASI 75, change from baseline in HAQ-DI, enthesitis, dactylitis, SF-36 PCS/MCS scores at wk14; and ACR50 and change from baseline in total modified vdH-S scores at wk14. Efficacy analyses were based on randomized treatment. Adverse events (AE) through wk24 are reported here. Investigators remained blinded through wk60.

Results: the PsA group showed significantly lower Dkk-1 levels when compared to the HC and RA groups. Dkk-1 in the RA group was also significantly higher than in the HC group. A similar trend was documented also for PTH, however a statistically significant difference was observed only when we comparing the PsA vs RA group (table 1, figure 1). No other statistically significant differences in the other markers were found.

Table 1. Values of bone turnover markers (CTX-I, PINP), DKK-1 and sclerostin of PsA, RA patients and control group (mean ± SD).

<table>
<thead>
<tr>
<th>Marker</th>
<th>PsA</th>
<th>RA</th>
<th>HC</th>
<th>P (ANOVA)</th>
</tr>
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<tbody>
<tr>
<td>PINP ng/ml</td>
<td>42.8±16.670</td>
<td>39.1±12.28</td>
<td>34.8±11.25</td>
<td>NS</td>
</tr>
<tr>
<td>CTX-I ng/ml</td>
<td>0.21±1.17</td>
<td>0.32±0.21</td>
<td>0.28±0.01</td>
<td>NS</td>
</tr>
<tr>
<td>Dkk-1 pmol/l</td>
<td>19.45±11.30</td>
<td>44.5±17.81</td>
<td>23.2±1.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sclerostin pmol/l</td>
<td>30.8±24.25</td>
<td>30.75±12.25</td>
<td>32.2±7.28</td>
<td>NS</td>
</tr>
<tr>
<td>PTH pg/ml</td>
<td>21,12±16.63</td>
<td>35.83±13.02</td>
<td>29.69±1.13</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Conclusions: This study demonstrated for the first time that Dkk-1 levels in PsA are lower than in HC, in contrast with RA where they are higher. These results might contribute to explain the different bone involvement of the two different diseases.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2728
Apremilast is associated with long-term (4-year) DAS-28 (CRP) remission and improvements in skin disease: results from a phase III study in DMARD/biologic-experienced patients with active psoriatic arthritis


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Background: Treatment goals for long-term control of skin and joint symptoms in active psoriatic arthritis (PsA) include clinically important changes in DAS-28 (CRP) and improvements in skin disease. PsA can lead to significant physical and associated psoriasis, among patients continuing the study. Apremilast was generally well tolerated with an acceptable safety profile.

Conclusions: Over 208 weeks, Apremilast demonstrated sustained and clinically important improvements in PsA signs and symptoms, including physical function and associated psoriasis, among patients continuing the study. Apremilast was generally well tolerated with an acceptable safety profile.


Background: Psoriatic arthritis (PsA) is a rare disease, with an estimated prevalence of 0.02–0.42% in Europe and US (1). PsA is often regarded as a mild disease, but recent data suggest an increase in comorbidities and mortality, possibly related to systemic inflammation (1).

Objectives: To study all-cause hospitalizations in patients with PsA in the United States (US) from 1993 to 2014.

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary or secondary diagnosis of PsA, and compared them to total all-cause US hospitalizations during the same period. US population estimates and projections for the resident US population were obtained from the US Census Bureau.

Results: There were 789.8 million all-cause hospitalizations in 6.4 billion person-years of observation from 1993 to 2014 (123.4 hospitalizations per 1,000 person-years). During this time period, 332,496 hospitalizations occurred in patients with PsA (5.2 per 100,000 person-years). All-cause US hospitalizations increased from 33.7 million in 1993 to 35.4 million in 2014, an increase of 4.8% over 22 years (Figure, dotted blue line). All-cause hospitalizations in PsA patients increased from 6,866 in 1993 (2.6 per 100,000 person-year) to 33,875 in 2014 (10.6 per 100,000 person-years), a dramatic increase of over 393% (p < 0.0001, Figure solid red line). In 2014, hospitalizations in PsA patients accounted for 163,630 hospital days at a total national cost of over US$1.66 billion.

Conclusions: All-cause hospitalizations in patients with PsA in the US have significantly increased by 393% in the last 22 years, almost 80-fold of the 4.8% increase in US population all-cause hospitalization rate in the same time-period. This calls for an increase need for identification and management of serious and co-morbid conditions in patients with PsA.
CERTOLIZUMAB PEGOL IS ASSOCIATED WITH LONG-TERM IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES IN PSORIATIC ARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-PSA STUDY

D. Gladman1, R. Fleischmann2, K. Harris3, L. Peterson4, P.J. Mease5.
1University of Toronto and Krembil Research Institute, Toronto Western Hospital, Toronto, Canada; 2UT Southwestern Medical Center and Dallas Metropolis Clinical Research Center, Dallas, United States; 3UCB Pharma, Brussels, Belgium; 4UCB Pharma, Raleigh; 5Swedish Medical Center and University of Washington, Seattle, United States

Background: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease that has a substantial impact on patients’ (pts) physical and emotional wellbeing.1 Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-TNF that has been shown to improve patient-reported outcomes (PROs) in pts with PsA over 96 weeks (wk) of treatment in the RAPID-PSA study (NCT01087788).2

Objectives: To investigate whether initial improvements in PROs observed with CZP treatment were maintained over 4 years in the RAPID-PSA study.

Methods: RAPID-PSA was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label to Wk216. Pts were aged ≥ 18 years, with a ≥ 3% body surface area affected by psoriasis of prior anti-TNF exposure (Table). Similar improvements were observed in both CZP dose regimens for all PROs examined, including PtAAP (CFB at Wk216 in ≥ 3% body surface area affected by psoriasis at baseline (BL)]. Data are reported as the mean change from BL (CFB) for pts randomized to CZP at Wk0, with last observation carried forward (LOCF) imputation for Wk24, and LOCF imputation and observed case (OC) values for Wk216.

Results: Of 273 pts randomized to CZP at Wk0, 248 (91%) completed Wk24 and 183 (67%) completed Wk216. Improvements observed to Wk24 of treatment were generally maintained over 4 years (to Wk216) in all PROs assessed, regardless of prior anti-TNF exposure (Table). Similar improvements were observed in both CZP dose regimens for all PROs examined, including PtAAP (CFB at Wk216 in ≥ 3% body surface area affected by psoriasis at baseline (BL)]. Data are reported as the mean change from BL (CFB) for pts randomized to CZP at Wk0, with last observation carried forward (LOCF) imputation for Wk24, and LOCF imputation and observed case (OC) values for Wk216.

References:

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: D. Gladman Grant/research support from: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD, Novartis, Pfizer, UCB Pharma, R. Fleischmann Grant/research support from: Genentech Inc, Roche, Abbott, Amgen, UCB Pharma, Pfizer, Bristol-Myers Squibb, Lilly, Sanofi-Aventis, MSD, Novartis, AstraZeneca, Janssen, Consultant for: Roche, Abbott, Amgen, UCB Pharma, Pfizer, Bristol-Myers Squibb, Lilly.
EFFECT OF THE TIGHT CONTROL TREAT-TO-TARGET STRATEGY ON THE DYNAMICS OF ACTIVE MRI SACROIILITIS IN THE RUSSIAN COHORT OF EARLY PERIPHERAL PSORIATIC ARTHRITIS PATIENTS (PRELIMINARY RESULTS OF AN ONGOING OPEN-LABEL REMARC STUDY)

E.E. Gubarev, E.V. Logina, T.V. Korotaeva, D.E. Karateev, V.A. Nasonova
Research Institute of Rheumatology, Moscow, Russian Federation

Background: Axial involvement in early psoriatic arthritis (pSpA) patients is often poorly diagnosed. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJs) helps to better define spinal involvement and is used as an outcome measure to evaluate treatment of axial disease with TNF blockers. Treat-to-target (T2T) strategy was studied in various manifestations of pSpA except axial involvement.

Objectives: To assess the effect of tight control T2T strategy on the 12-months dynamics of active MRI sacroiliitis (MRI-SI) in peripheral pSpA pts.

Methods: 89 treatment-naive pts (MF=42/47) with active peripheral pSpA, according to CASPAR criteria were included; mean age 36.5±10.9 yrs., disease duration 12.1±10.1 mo., disease activity index (DAS) 5.2±2.8, C-RP 16.1 [6.6; 31.0] mg/l, ESR 22.5±19.2 mm/h. At baseline and every 3 mo. of therapy all pts underwent standard clinical examination of PsA activity. All patients were evaluated for the presence of inflammatory back pain (IBP) by ASAS criteria. In pts having IBP, disease activity was also measured by BASDAI. At baseline MRI of SIJs was performed in 79 pts, both with and without IBP, on Signa Ovation of Gothenburg; 2Department of Medicine; 3Department of Gastroenterology and Hepatology, Sahlgrenska University Hospital, Göteborg, Sweden

Background: Patients with psoriatic arthritis (PsA) are at increased risk of developing cardiovascular disease.

Objectives: To determine the prevalence of cardiovascular risk factors among patients with PsA followed at a Swedish Rheumatology Clinic in comparison with the general population (GP).

Methods: A questionnaire including weight, height, smoking habits, hypertension, diabetes and hyperlipidaemia was sent to all PsA patients registered at the Rheumatology Clinic at Sahlgrenska University Hospital, Gothenburg (N=962). Obesity was defined as body mass index (BMI) ≥30 kg/m² and overweight as BMI 25–29.9 kg/m². Comparison with the Swedish GP was made using data from the national population health survey, “Health on equal terms”, which is sent yearly to 20 000 citizens by the Public Health Agency of Sweden.

Results: 666 (70%) of the PsA patients with mean age 56±11yrs (mean: ∼52) women, responded. Higher prevalence of self-reported obesity and several cardiovascular risk factors was found in the PsA patients compared with the GP: Obesity 28.7% [GP 15% (95% CI 1.45–15.9%)], current smoking 10.5% [GP 9% (8.2–9.3%)], former smoking 43.4% [GP 23% (22.3–24.0%)], never smoking 48.8% [GP 63% (61.9–63.8%)], treatment of hypertension 32.1% [GP 20% (19.6–21.2%)] and diabetes 8.3% [GP 6% (5.4–6.3%)]. Treatment of hyperlipidaemia was reported by 15.0% [GP no data] and overweight by 36.2% [GP 36% (34.5–36.5%)]. Data stratified by age and sex is shown in the table. (Numbers are % and 95% CI.)

Conclusions: Obesity was highly overrepresented among the PsA patients. It is imperative to take action against weight gain in overweight patients and promote weight loss in obese patients with PsA, since obesity may be involved in the pathogenesis of the disease and may fuel disease activity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5049

Disclosure of Interest: E. K. Kristianslund: None declared. K. M. Fagerli: None declared. E. Lie Consultant for: AbbVie, Celgene, Hospira, Pfizer, UCB, A. Wierod: None declared. S. Kalstad: None declared. E. Lie Consultant for: AbbVie, Celgene, Hospira, Pfizer, UCB., A. Bilberg Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Hospira/Pfizer, Roche, Sandoz, UCB, I. C. Olsen: None declared
DOI: 10.1136/annrheumdis-2017-eular.4273

Abstract FRIO492 – Table 1

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<th>Sex</th>
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<th>Former smoking</th>
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<td></td>
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<td>PS ≤ 30</td>
<td>PS &gt; 30</td>
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<td>PS &gt; 30</td>
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<td>♂ 30–44</td>
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<td>♂ 45–64</td>
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<td>20 (18.3–22.3)</td>
<td>7.4</td>
<td>9 (7.6–10.5)</td>
<td>34.7</td>
<td>25 (23.7–27.7)</td>
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p-values for between-year differences.

Estimated DAS28 from mixed-model

Disclosure of Interest: None declared

Abstract FRIO492 – Table 1

<table>
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<td>Age (years), mean (SD)</td>
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<td>40.5 (11.8)</td>
<td>42.5 (12.6)</td>
<td>40.3 (11.1)</td>
<td>42.1 (12.8)</td>
<td>42.9 (11.6)</td>
<td>42.8 (12.4)</td>
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<tr>
<td>Proportion female</td>
<td>33.0%</td>
<td>36.0%</td>
<td>47.8%</td>
<td>38.4%</td>
<td>40.0%</td>
<td>37.0%</td>
<td>38.7%</td>
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<tr>
<td>Years since diagnosis, median (IQR)</td>
<td>4.5 (8.14)</td>
<td>4.6 (7.15)</td>
<td>5.4 (7.16)</td>
<td>3.3 (6.13)</td>
<td>3.3 (6.14)</td>
<td>6.3 (4.8)</td>
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<td>Disease Activity Score 28 joints, mean (SD)</td>
<td>3.04 (1.15)</td>
<td>3.09 (1.20)</td>
<td>2.97 (1.04)</td>
<td>2.76 (1.06)</td>
<td>2.76 (0.91)</td>
<td>2.79 (0.94)</td>
<td>2.60 (0.81)</td>
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<tr>
<td>Clinical Disease Activity Index, mean (SD)</td>
<td>11.02 (6.92)</td>
<td>11.43 (7.92)</td>
<td>10.20 (4.87)</td>
<td>10.08 (4.99)</td>
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<td>9.08 (4.28)</td>
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<td>Simplified Disease Activity Index, mean (SD)</td>
<td>12.52 (6.11)</td>
<td>12.90 (7.21)</td>
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<td>10.45 (3.14)</td>
<td>11.41 (5.97)</td>
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| p-values for between-year differences.

DOI: 10.1136/annrheumdis-2017-eular.4273

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5049

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4273

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3118

Disclosure of Interest: None declared

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3118

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DOI: 10.1136/annrheumdis-2017-eular.3118

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DOI: 10.1136/annrheumdis-2017-eular.3118
DISEASE ACTIVITY TOGETHER WITH DEPRESSION CONTRIBUTES TO WORK DISABILITY IN PSORIATIC ARTHRITIS

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Background: Work disability (WD) is an important functional outcome measure in inflammatory arthritis, which has been studied comprehensively in rheumatoid arthritis and anklyosing spondylitis, however limited data are available in psoriatic arthritis (PsA).

Objectives: The aim of this study was to compare 1) patient-reported outcomes (PROs), including depression/anxiety scores; 2) physician-assessed measures and 2) disease activity using minimal disease activity (MDA) and Composite Psoriatic Arthritis Disease Activity Index (CPDAI) in PsA patients with and without WD.

Methods: Consecutive patients with PsA fulfilling the CASPAR criteria were enrolled. Patients on disability pension, those with early retirement due to arthritis, those unemployed, away from work due to sick leave were considered as having WD. Patients have completed questionnaires on physical function and health-related quality of life and they were assessed for depression/anxiety using the Hospital Anxiety and Depression Scale (HADS-A and HADS-D) and Penn State Worry Questionnaire (PSWQ). Patients underwent musculoskeletal and skin assessments. Disease activity was compared between work-disabled and employed patients using MDA and CPDAI. Mann-Whitney, Chi-square tests and linear regression model were used to perform statistical analysis.

Results: 100 PsA patients were recruited, 18 were retired, leaving 82 patients available for analysis. Thirty-one (17 male, age 50.9±9.7 years) patients had work disability versus fifty-nine (29 male, age 49.1±8.8 years) employed patients. Work-disabled patients had significantly higher HADS-D score (5.07±3.01 vs. 2.57±2.64; P<0.001) and significantly worse PROMs, including HADS-D, EQ-5D, BASDAI, BASFI, ASQoL, BAI, BFR-A, PSWQ and pain levels. The proportion of pts reporting improvements ≥ 20% was assessed. Results are significant relationship was revealed between depression and CPDAI, the relationship between depression and disease activity using CPDAI in PsA patients with and without WD. Significant relationship was revealed between depression and CPDAI, which suggests that disease activity together with depression contributes to work disability in PsA.

References:


Acknowledgements: A.M. Chambers data manager. M.C. Williams statistician. Y. Weindorf, S. Bhaskaran, T. Fox, C. Smardon, S. Pattison, T. Lee. Data Management. Funding: This study was supported by Celltrion, Celltrion Pharmaceuticals, Inc.

CONTRIBUTES TO WORK DISABILITY IN PSORIATIC ARTHRITIS

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SECUKINUMAB PROVIDES RAPID AND SUSTAINED PAIN REDUCTION IN PATIENTS WITH PSORIATIC ARTHRITIS

J.B. McInnes 1, P.J. Mease 2, G. Schett 3, B. Kirkham 4, V. Strand 5, N. Williams 6, T. Fox 7, L. Fricio 8, S. Jügi 9, K.K. Gandhi 10 on behalf of the FUTURE 2 study group. 1University of Glasgow, Glasgow, United Kingdom; 2Swedish Medical Center and University of Washington, Seattle, United States; 3University of Erlangen-Nuremberg, Erlangen, Germany; 4Guy’s & St Thomas’ NHS Foundation Trust, London, United Kingdom; 5Stanford University School of Medicine, Palo Alto; 6RTI Health Solutions, Durham, United States; 7Novartis Pharma AG, Basel, Switzerland; 8Novartis Pharmaceuticals Corp., East Hanover, United States

Background: Pain remains a major clinical challenge in the treatment of psoriatic arthritis (PsA). Secukinumab (SEC) has demonstrated significant efficacy in PsA patients (pts) across a range of quality of life related outcome measures.1,2

Objectives: This post-hoc analysis evaluated change in pain scores from baseline (BL) to Week (Wk) 104 in PsA pts receiving SEC in the FUTURE 2 study.

Methods: FUTURE 2 study design has been reported.2 Mean change from BL to Wk 104 in PsA pts receiving SEC was evaluated using mixed-effects models for repeated measures (MMRM) through Wk 16 and as observed through Wk 104. Proportion of pts reporting improvements ≥ 20% in mean change from BL were assessed. Results are significant relationship was revealed between depression and CPDAI, the relationship between depression and disease activity using CPDAI in PsA patients with and without WD. Significant relationship was revealed between depression and CPDAI, which suggests that disease activity together with depression contributes to work disability in PsA.

References:

1 McInnes IB, et al. Arthritis Care Res 2017;69:1597–605. DOI: 10.1002/acr.23163. Disclosure of Interest: I. McInnes Grant/research support from: AbbVie, Amgen, BMS, Cellgene, Janssen, Lilly, Novartis, Pfizer and UCB. Consultant for: AbbVie, Amgen, BMS, Cellgene, Janssen, Lilly, Novartis, Pfizer and UCB. Speakers bureau: AbbVie, Amgen, BMS, Cellgene, Janssen, Lilly, Novartis, Pfizer and UCB. P. Mease Grant/research support from: AbbVie, Amgen, BMS, Cellgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB. Consultant for: AbbVie, Amgen, BMS, Cellgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB.

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EQUIPMENT OF MELANOTIN IN PATIENTS WITH PSORIATIC ARTHRITIS VIOLATIONS OF EMOTIONAL STATUS

I. Blaginina 1, O. Rebrova 1, N. Bludova 2, O. Volman 2. 1Internal Medicine, St. Lukas State Medical University; 2Lugan's Clinical Regional Hospital, Lugansk, Ukraine

Background: The ability of melatonin to reduce the activity of the sympathetic nervous system tone and of putatory-adrnal system ensures its anti-stress properties. It can be used to reduce psycho-emotional manifestations of chronic pain in patients with psoriatic arthritis (PsA).

Objectives: To evaluate the effect of combined therapy with the use of melatonin in the expression of psycho-emotional disorders as a pain in patients with PsA.

Methods: High levels of anxiety and depressive disorders were established in the survey on Spillerberger Anxiety Scale and on Hamilton Rating Scale for Depression (HRDS) in 43 patients with PsA (≥5 SJC & ≥ 5 TJC; CRP >0.3 mg/dL). The quality of life was studied by questionnaire Medical Outcomes Study Short Form (SF-36). The severity of morning stiffness, pain, patient's health status (EWS) - using the 100-mm visual analog scale (VAS). All patients were receiving a stable dose of MTX for at least 6 months. They were divided into two groups; 1 group (n=22) additionally received 3 mg of melatonin at bedtime for 2 months of observation.

Results: At the end of the observation period the frequency and the level of
severity of depression by HRDS (p=0.0098), and the index of personal anxiety (P=0.009) in group 1 decreased. In the 2nd group above mentioned parameters have not changed. On the 1 group data of SF-36 evaluation: the physical health component has improved - the increase of RP and BP 57.4% and 37.8% from the baseline; vitality and role functioning due to emotional state, have also been increased by 34.3% and 43.5%, respectively. In the 2nd group, investigated parameters have not undergone significant changes in dynamics. In the 1 receiving melatonin group TJC and SJC have decreased by 15% and 22% (p=0.0079, p=0.0022, respectively) and their dynamics in the 2nd group was less significant (p=0.013 and p=0.017, respectively). Also, patients in group 1 have had a more significant reduction in the severity of morning stiffness and joint pain, and in the 2nd group the changes were less significant (respectively, p=0.043, p=0.016). Positive dynamics of CRP in group 1 was more significant (p=0.003), than it was in 2 patients' group (p=0.033).

Conclusions: In the group of patients treated with melatonin was noted improvement in general condition (a significant improvement in the parameters of the physical components of health, reduction of depressive and psycho-vegetative disorders) and also more significant decrease of the intensity of pain and of morning stiffness duration, of TJC and SJC, than in not treated with melatonin patients. Inclusion of Melatonin in the comprehensive PsA therapy promotes not only reduction of depression symptoms and sleep disorders, but also reduces the severity of the chronic pain manifestations and, consequently, improves the quality of life of patients with this disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2378

**FRI0496** COMPARING TOFACITINIB SAFETY PROFILE IN PATIENTS WITH PSORIATIC ARTHRITIS IN CLINICAL STUDIES WITH REAL-WORLD DATA


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**Background:** Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). Two Phase 3 studies have been completed (NCT01877688; NCT01882438) and a long-term extension (LTE) study is ongoing (database not locked; NCT01976364).

**Objectives:** To compare incidence rates (IR) for adverse events (AEs) of special interest in a tofacitinib cohort from the Phase 3 PsA trials with real-world experience in a comparison cohort from the US Truven MarketScan database.

**Methods:** The tofacitinib cohort included adult patients (pts) from 2 Phase 3 studies with ≥6 months PsA diagnosis who met ClASsification of Psoriatic Arthritis (CASPAR) criteria, had active plaque psoriasis, and active arthritis (≥3 swollen joints, ≥3 tender/painful joints) and who were treated with tofacitinib. Pts were grouped by those who received tofacitinib 5 (N=238) or 10 mg (N=236) twice daily (BID) in the 2 Phase 3 studies, and all pts who received ≥1 dose of tofacitinib in the 2 Phase 3 studies or the LTE (tofacitinib all doses, N=783). The comparison cohort (N=774) comprised pts with moderate to severe PsA, defined by ≥3 swollen joints, ≥3 tender joints, ≥2 diagnosis codes on 2 unique calendar days (≥1 by a rheumatologist) between Oct 2010 and Sep 2015, initiating therapy with a systemic agent for PsA. Key Phase 3 study exclusion criteria were applied to the comparison cohort. IRs for serious infection events (SIEs), herpes zoster (HZ), malignancies (excluding non-melanoma skin cancer [NMSC]), NMSC and major adverse cardiovascular events (MACE) were compared.

**Results:** Mean age, gender and diabetes history were generally similar between the tofacitinib and comparison cohorts (48.7–49.5 years, 42.4–49.2% male, 12.2–15.7% with diabetes history). Overall more pts treated with tofacitinib had prior experience with corticosteroids (15.7–28.2%), conventional synthetic disease-modifying antirheumatic drugs (100%) and tumour necrosis factor inhibitors (48.1–55.9%) vs the comparison cohort (11.9%, 46.6% and 36.6%, respectively). IRs for SIEs were lower for the tofacitinib vs the comparison cohort (Table 1). The tofacitinib cohort had a higher rate of HZ vs the comparison cohort (Table 1). IRs for malignancies and MACE were similar between cohorts (Table 1).

**Conclusions:** IRs of AEs of special interest reported in tofacitinib PsA Phase 3 studies were generally comparable to those in a general PsA population comprising pts receiving a range of biologic agents, except HZ, which was higher for pts treated with tofacitinib but similar to the incidence observed with tofacitinib treatment in other indications.

**Acknowledgements:** This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMCC and was funded by Pfizer Inc.


DOI: 10.1136/annrheumdis-2017-eular.2448

**FRI0497** WHAT CHOICES DO RHEUMATOLOGIST MAKE IN ESCALATING DMARD THERAPY IN EARLY PSA?

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**Background:** Psoriatic arthritis (PsA) is a multifaceted disease.

**Objectives:** To newly diagnose PsA patients were included in the Dutch Early south-west Psoriatic Arthritis cohort (DEEPAR) study between August 2013 and March 2016. Initial drug treatment and escalation of therapy were described for all patients. Drivers of treatment changes in the first year were evaluated by mixed

**Table 1. Multivariable mixed effects ordered/ordinal logistic regression of treatment change over time in early PSA**

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Covariates</strong></td>
<td></td>
</tr>
<tr>
<td>Swollen joint count (per joint)</td>
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</tr>
<tr>
<td>Tender joint count (per joint)</td>
<td>0.98</td>
</tr>
<tr>
<td>Tender enthesitis (per joint)</td>
<td>0.94</td>
</tr>
<tr>
<td>BASDAI (per point)</td>
<td>1.05</td>
</tr>
<tr>
<td>Dactylitis index (per point)</td>
<td>1.05</td>
</tr>
<tr>
<td><strong>timpoints (baseline reference)</strong></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>1.55</td>
</tr>
<tr>
<td>6 months</td>
<td>1.35</td>
</tr>
<tr>
<td>9 months</td>
<td>0.45</td>
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<tr>
<td>12 months</td>
<td>1.52</td>
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<tr>
<td><strong>Initial starting values</strong></td>
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<td>[no dmard reference]</td>
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</tr>
<tr>
<td>other adms</td>
<td>0.65</td>
</tr>
<tr>
<td>methotrexate oral</td>
<td>0.49</td>
</tr>
<tr>
<td>methotrexate subcutaneous</td>
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</tr>
<tr>
<td><strong>biologicals</strong></td>
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</tr>
<tr>
<td>biologicals</td>
<td>6.23</td>
</tr>
<tr>
<td><strong>mixed effects parameters</strong></td>
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<tr>
<td>random slope</td>
<td>0.02</td>
</tr>
<tr>
<td>random intercept</td>
<td>-8.30</td>
</tr>
</tbody>
</table>

*In bold p≤0.05*
ordered ordinal regression with outcome treatment change and variables joints (66/68 count), skin (PASI), enthesis (LEI and MASES), dactylitis (LDI) and axial disease (BASDAI).

Results: 323 patients had had baseline assessment in March 2016. Their average age was 50.0 years (SD 13.8) and 49% were male. 80% patients had arthritis disease (MDA >30%) and 76% LDA demonstrated that patients with psoriatic arthritis had higher enthesis subtype, 2% axial disease and 9% dactylitis. Initial treatment consisted of methotrexate (MTX) (52%), in 7% of other synthetic disease modifying antirheumatic drugs (sDMARDS) and due to treatment of psoriasis 3% biologicals. Within the different phenotypes MTX was most frequently started in polyarthritis (93%) followed oligoarthritis (83%), monarticular (53%) and other phenotypes (5%). At 12 months 70% (n=148) stayed on the initial drug. Of those switched, 9 started MTX, within the initial MTX users (n=74) almost equal percentages stopped, switched to metotrex (4%). A smaller percentage (2%) switch to lefunomide in medication were driven by swollen joint count and the presence of dactylitis (Table 1).

Conclusions: MTX was initiated in about half of the early PsA patients. The majority of patients were kept on the initial treatment strategy in first year. Failure on initial drug led to variation in subsequent drugs with additional start of other sdmards, switch subcutaneous MTX, to other sdmards or to biological dmards. Treatment change was driven by Swollen Joint Count and presence of Dactylitis. Skin, Enthesis and Axial disease did not play a role in escalating treatment.

Disclosure of Interest: None declared


FR10498 | OUTCOMES ASSOCIATED WITH ACHIEVEMENT OF VARIOUS REAL-WORLD STUDY ON THE PATTERNS AND COST OF TREATMENT TARGETS IN PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING ADA

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Background: Various instruments are currently used for disease activity and outcome assessment in psoriatic arthritis (PsA). Some measures attempt to incorporate the total spectrum of psoriatic disease manifestations [eg, minimal disease activity index for PsA (DAPSA)]. Whether in patients (pts) with PsA it is sufficient to primarily consider joint disease aspects remains unclear.

Objectives: To compare DAPSA remission and low disease activity (LDA) with MDA and very low disease activity (VLDA) for the presence of residual abnormalities of the respective composing variables.

Methods: This post hoc analysis included pts with PsA receiving adalimumab (ADA) in one of two multicenter studies: ADEPT was a 24-week (wk), randomized, double-blind, placebo-controlled trial; ACCLAIM was a 12-wk, open-label study conducted in Canada in care settings that reflected usual practice. Frequencies of DAPSA remission/LDA and MDA/VLDA were summarized, and the individual PsA manifestations within these states were assessed. ADA was summarized from the following continuous variables: swollen (66) and tender (68) joints, pt pain (PP), cm), and C-reactive protein (CRP, mg/dL). DAPSA remission was defined as ≤ 20mm, HAQ ≤ 0.5, and PASI ≤ 1 swollen joint, ≤ 1 entheseal point, ≤ 4 and DAPSA LDA as > 20mm, HAQ ≤ 0.5, and PASI ≤ 1 swollen joint, ≤ 1 entheseal point, ≤ 4 and 1 joint overlap, and ≤ 14.

MDA was calculated as ≤ 4 for PsA disease activity for joints and ≤ 14 for psoriatic arthritis, with the exception of experiencing numerically higher PP, PtGA, and PASI scores. Whether in patients (pts) with PsA it is sufficient to primarily consider joint disease aspects remains unclear.

Results: Among 151 pts receiving ADA in ADEPT, 33 (22%) each achieved DAPSA remission and LDA at wk 24, and 10 (14%) and 11 (7%) achieved MDA and VLDA, respectively. Pts achieving DAPSA LDA appeared to mirror those in the remaining pts, with 7892 (42.14%) discontinuing, and 1630 (8.75%; overlap ≤ 30 days) and 17,334 (93.03%) prevalent. Almost half (n=8994; 48.27%) of the pts continued treatment change was driven by Swollen Joint Count and presence of Dactylitis. Skin, Enthesis and Axial disease did not play a role in escalating treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3762

FR10499 | REAL-WORLD STUDY ON THE PATTERNS AND COST OF TREATMENT FAILURE IN PATIENTS WITH PSORIATIC ARTHRITIS USING US CLAIMS DATA

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Background: Current treatments for psoriatic arthritis (PsA) are associated with a range of limitations, e.g. side effects, safety concerns and inadequate efficacy. The economic burden of biologic (bDMARD) failure among patients (pts) with PsA is thought to be substantial, but there is a need to quantify this formally.

Objectives: To evaluate PsA treatment failure (i.e. discontinuation and switching rates) in a US managed care setting and its economic consequences.

Methods: Pts aged ≥ 18 years with 2 diagnosis codes for PsA and 1 claim for a bDMARD from 1 Jan 2007 to 31 Mar 2015 in the Truven Health MarketScan® Database (Commercial and Supplemental Medicare) were eligible for the study. Pts were considered incident if they did not have a PsA diagnosis or a bDMARD prescription during 1 year prior to first PsA diagnosis in the study period, and as prevalent otherwise. Pts had a 1-year follow-up from first PsA diagnosis in the study period. The percentages of pts discontinuing a drug, switching to another drug or continuing on the same drug for 1 year from first date of treatment were reported. Healthcare costs for 1 year from initiation of the first bDMARD, (medical and drug costs associated with treatment failures) were reported as cost per-pt-per-month (PPPM), and a generalized linear model was used to analyse the cost after controlling for various demographic variables.

Results: Of the 18,632 pts treated with a bDMARD, 1298 (6.97%) were incident and 17,334 (93.03%) prevalent. Almost half (n=8994; 48.27%) of the pts continued treatment failure was high. Follow-up costs for pts who switched discontinuing, and 1630 (8.75%; overlap ≤ 30 days) switched to another drug. Among incident pts, only 240 (18.49%) continued, 809 (62.33%) discontinued, and 231 (17.80%; overlap ≤ 30 days) and 18 (1.38%; overlap ≥ 30 days) switched to another drug. Pts with an overlap > 30 days were excluded from the analysis. Overall, pts who switched had a higher PPPM total cost ($3217) than those who discontinued ($2650; p < 0.0001) or continued ($2868; p < 0.0001). Similar results were observed in the prevalent and incident groups, respectively, with pts who switched continuing a higher PPPM total cost ($3241 and $3779) compared with those who discontinued ($2583 and $2327; both p < 0.0001) or continued ($2700 and $2600; both p < 0.0001). Increasing age, and increasing ineffectiveness score predicted a higher cost (p = 0.002) and with a 0.49% higher cost in the prevalent group (p = 0.001). Among prevalent pts, females had a 3.08% higher cost than males (p = 0.0068). The Charlson Co-morbidity Index score predicted a higher cost (p = 0.001) and cost of treatment failure as defined by switching or discontinuation were high. Follow-up costs for pts who switched were higher than for pts who continued or discontinued their medication. Baseline age, female sex and comorbidities were associated with higher treatment costs.

References:


AVOIDANCE OF PHYSICAL ACTIVITY LEADS TO REDUCED INFLAMMATORY ENTHESITIS ON ULTRASOUND

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Background: Enthesitis is one of the manifestations of psoriatic arthritis (PsA), but no clear definition for the diagnosis exists. To further evaluate the added value of sonographic evaluation of entheses in diagnosing enthesis, more knowledge on factors associated with sonographic enthesis is needed.

Objectives: We aim to evaluate which clinical characteristics are associated with sonographic enthesis changes in a cross-sectional PsA population.

Methods: established PsA patients were asked to participate, irrespective of enthesitis complaints. Patients were interviewed on history of musculoskeletal complaints (MSC), more specifically if they had complaints during activities and whether they avoided physical activities (during exercise, work, household tasks, hobbies, chores). Tenderness was determined in the MASEI entheses and those in the Leeds Enthesitis Index (LEI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES). Previously we showed that a modified Madrid Sonographic Enthesitis Index (MASEI, i.e. excluding knee enthesis thickness and scoring PD-signal semi-quantitatively) distinguishes entheses of PsA patients from those of healthy volunteers (1). A sonographist unaware of clinical findings scored the modified MASEI. Multivariable linear regressions of structural (erosions, calcifications, structure and inflammatory (thickness, bursitis and PD) modified MASEI scores were performed (transformed for a better distribution). Variables included age, gender, PsA duration, medication use (non/NSAIDs vs. sDMARDs vs. bDMARDs), LEI + MASES and avoidance (no vs. yes).

Results: 84 PsA patients participated (45 males, mean age 55, median disease duration 8 years). Median modified MASEI was 12 (IQR 7.25–17), with a structural component score of 7 (3–10) and inflammatory component score of 6 (3.5–8). 8 patients used no medication of NSAIDs only, 36 used sDMARDs and 40 used bDMARDs. 45 patients reported avoiding activities. In a multivariable analysis, inflammatory modified MASEI was negatively associated with avoidance (i.e. fewer inflammatory changes in patients reporting avoidance) and positively associated with age, BMI and use of biologics. Structural MASEI was positively associated with age only.

Conclusions: Avoiding physical activities is associated with fewer inflammatory changes of the entheses. More inflammatory changes are seen in older or overweight patients and patients on biologicals, in the latter possibly due to more active disease.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3471

REAL-WORLD USE OF SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS IN THE UNITED STATES: PATIENT PROFILE AND DOSING REGIMEN USE

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Background: As of January 15, 2016, secukinumab became the first fully human anti-interleukin-17 monoclonal antibody approved for the treatment of active disease with psoriatic arthritis (PsA) in the United States. Secukinumab may be administered with or without loading of 150 mg or 300 mg (patients with concomitant moderate to severe psoriasis only) at weeks 0, 1, 2, 3 and 4 followed by maintenance dosing every 4 weeks. The use of a loading regimen of secukinumab in a real-world setting of patients with PsA has not been evaluated since its approval in the United States.

Objectives: To better understand the real-world use of secukinumab by describing the demographic, clinical and treatment characteristics (loading vs no loading) of secukinumab-treated patients with PsA.

Methods: Retrospective data from the Symmetry Health Solutions Lx commercial claims database were used to identify patients who had ≥ 1 secukinumab claim between 01/15/2016 and 06/30/2016. Patients who were included in the analysis were aged ≥ 18 years, had ≥ 1 ICD-9 code of 696.0 or ICD-10 code of L40.5 for PsA and had ≥ 1 pharmacy or medical claim in the 12 months prior to their first secukinumab claim (index date). Patient demographics and secukinumab dosages were examined at the index date. Clinical characteristics, comorbidities and treatment history in the 12 months prior to the index date were identified and presented by use vs no use of loading.

Results: A total of 764 patients met the inclusion criteria. The mean (SD) age was 50.7 (11.6) years, 58.5% of patients were female and 39.8% of patients were from the south. The most common specialties prescribing secukinumab to patients with PsA were rheumatologists (52.1%) and dermatologists (30.0%). A total of 608 patients (79.6%) received loading and 156 (20.4%) did not; at the index date, the majority of patients received secukinumab at the 300-mg dose (73.2%) and the loading (70.2%) and no loading (68.6%) groups. Patient demographics, clinical characteristics and treatment history were generally comparable between groups (Table 1). However, more patients with loading had prior oral corticosteroid (OCS; 30.9% vs 20.5%), targeted synthetic disease-modifying antirheumatic drug (tsDMARD; 24.7% vs 17.3%) and biologic (64.3% vs 59.6%) use compared with those without loading. The most prevalent comorbidities were psoriasis (58.6%), hypertension (34.4%) and hyperlipidemia (26.8%). A higher proportion of patients with loading had hypertension (35.2% vs 31.2%), rheumatoid arthritis (RA; 15.3% vs 10.9%), fatigue (13.5% vs 9.0%) and anxiety (13.3% vs 8.3%) and a lower proportion had psoriasis (57.4% vs 64.1%) compared with those without loading.

Conclusions: This US claims-based study found the majority (≈ 73%) of secukinumab-treated patients with PsA were initiated with a loading regimen. Most patients initiated the 300-mg dose regardless of loading. A higher proportion of patients with loading had prior OCS, tsDMARD and biologic use, as well as hypertension, RA, fatigue and anxiety compared with those without loading, suggesting patients who initiated with loading had more refractory disease. These results provide the first insights into real-world use of secukinumab with and without loading in patients with PsA in the United States.

Acknowledgements: This study was supported by Novartis Pharmaceuticals Corporation, East Hanover, NJ.


DOI: 10.1136/annrheumdis-2017-eular.1541
IXEKIZUMAB REDUCES DISEASE ACTIVITY IN ACTIVE PSORIATIC ARTHRITIS PATIENTS WHO HAD PREVIOUS INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR-INHIBITORS

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Background: Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease associated with psoriasis, peripheral arthritis, enthesitis, dactylitis, and spondylitis. Ixekizumab (IXE), a monoclonal high affinity antibody that selectively targets interleukin-17A, has improved disease activity and physical function in bDMARD-naïve patients with active PsA.1 Herein, results are presented from a phase 3 trial (SPIRIT-P2; NCT02349295) with IXE in patients with active PsA and previous inadequate response to tumour necrosis factor-inhibitors (TNF-i).

Objectives: To explore the impact of IXE, as assessed by composite endpoints that incorporate multiple disease domains including peripheral arthritis, skin disease, enthesitis, dactylitis, spinal disease, function, and global disease assessment, up to 24 weeks (wks).

Methods: In this phase 3, multicentre, double-blind study, 363 adult patients with active PsA and a history of inadequate response to TNFi-α were randomly assigned at a 1:1:1 ratio to subcutaneous administration of 80-mg IXE either every 4 wks (Q4W; N=122) or every 2 wks (Q2W; N=123) following a 160-mg starting dose at Wk 0 or placebo (PBO; N=118). TNF-i inadequate response was defined as lack of efficacy to one or two TNFi-α intolerance to TNF-i. Response to treatment and disease activity were measured at Wks 12 and 24 by the following composite endpoints: minimal disease activity with skin component measured with the Psoriasis Area and Severity Index (MDA) or the static Physician Global Assessment of psoriasis (mMDA) and Composite Psoriatic Arthritis Disease Activity Index (cDAPSA), as well as traditional measures by Psoriatic Arthritis Response Criteria (PsARC). Treatment comparisons were made by a logistic regression model for categorical data with missing values imputed by nonresponder imputation (NRI); a mixed model for repeated measures analysis was used for continuous data.

Results: At Wks 12 and 24, significantly more patients receiving IXEQ4W or IXEQ2W achieved MDA, mMDA, and PsARC compared with patients receiving PBO (Table). Results for MDA were similar to mMDA results within each treatment group at each time point. CPDAI total scores for patients receiving IXEQ4W or IXEQ2W were significantly improved compared with results for patients receiving PBO.

Table: Summary of Composite Endpoints at Weeks 12 and 24

<table>
<thead>
<tr>
<th></th>
<th>PBO (N=118)</th>
<th>IXEQ2W (N=122)</th>
<th>IXEQ4W (N=123)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PtGA</td>
<td>6.1 (5.1)</td>
<td>5.8 (3.8)</td>
<td>5.6 (3.4)</td>
</tr>
<tr>
<td>Pt pain</td>
<td>3.1 (2.0)</td>
<td>2.5 (1.6)</td>
<td>2.3 (1.6)</td>
</tr>
<tr>
<td>CRP</td>
<td>20 (17.5)</td>
<td>16 (12.2)</td>
<td>16 (12.2)</td>
</tr>
<tr>
<td>TJC</td>
<td>28 (23.3)</td>
<td>15 (10.6)</td>
<td>11 (7.9)</td>
</tr>
<tr>
<td>SJC</td>
<td>6 (5.4)</td>
<td>4 (2.9)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>DAPSA</td>
<td>12 (9.4)</td>
<td>5.6 (3.4)</td>
<td>5.1 (3.3)</td>
</tr>
<tr>
<td>PsARC</td>
<td>12 (9.4)</td>
<td>5.6 (3.4)</td>
<td>5.1 (3.3)</td>
</tr>
</tbody>
</table>

Conclusions: Treatment with either IXEQ2W or IXEQ4W provides improvement in disease activity across multiple symptom domains, as measured by various composite endpoints, in patients with active PsA and who had a previous inadequate response to TNFi-α.

Disclosure of Interest: [Disclosure information provided]

References:

DOI: 10.1136/annrheumdis-2017-eular.2757

VALIDATION OF NEW POTENTIAL TARGETS FOR REMISSION IN PSORIATIC ARTHRITIS IN PATIENTS TREATED WITH GOLIMUMAB

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Background: Treat to target recommendations in psoriatic arthritis (PsA) stated that the target of treatment should be remission or inactive disease. At that time, no definitions of remission or inactive disease existed and the only validated target available was the minimal disease activity (MDA) criteria. Since then, other potential targets have been developed including very low disease activity (VLDA) and the Disease Activity in PsA (DAPSA) score remission.

Objectives: Using an existing dataset allowing calculation of DAPSA and clinical cDAPSA scores and the Vlda criteria, the objectives were to calculate the proportion of patients achieving these criteria, their prognostic value and the overall patient impact of these disease states.

Methods: BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, golimumab (GLM) or ustekinumab. PsA patients treated with GLM or included. Data collected at baseline, 6 and 12 months (mts) were used. DAPSA remission was defined as: TJC + SJ + Pga + Pt pain + CRP ≤0.4. cDAPSA Remission was defined as: TJG + SJG + PtgA + Pt pain ≤0.4. Low disease activity (VLDA) was achieved when all 7 MDA criteria were satisfied: TJC28≤1, SJ28≤1, PASI<1, Pain (VAS)<15mm, PGA (VAS) <20mm, HAQ ≤0.5 and tender enthesal points ≤1. Correlation between DAPSA, cDAPSA and VLDA were based on bivariate analysis.

Results: A total of 188 patients (53.2% female gender) were included with a mean (SD) disease duration of 5.46 (6.91) years. DAPSA remission was achieved in 5.1%, 24.2% and 30.0% of patients at baseline, 6 mts and 12 mts, respectively. Those patients had a significant reduction in the number of TJC, SJC, enthesitis and dactylitis (<0.043). cDAPSA remission was achieved in 5.2%, 33.1% and 38.3% of patients at baseline, 6 mts and 12 mts, respectively. Those patients had a significant reduction in the number of TJC, SJC and enthesitis only (p<0.002). VLDA was achieved in 2.1%, 17.2% and 15.6% of patients at baseline, 6 mts and 12 mts, respectively and those patients had a significant reduction in the number of TJC, SJC, enthesitis and PASI (p<0.002). The overall correlation for DAPSA or cDAPSA remission vs. VLDA achievement were both at 0.999 (Asymptotic Standard Error <0.027) although this is likely driven by the high number of patients who are not in either state. 75% and 53.3% of patients in DAPSA and cDAPSA remission, respectively, also achieved VLDA (<0.001). In contrast, patients who did not achieve either cDAPSA nor DAPSA never achieved VLDA. Nonetheless, patients in remission had significantly greater HAQ scores (p<0.03) if they had remaining dactylitis or active skin disease (BSA>10%; cDAPSA only).

Conclusions: DAPSA, cDAPSA and VLDA represent new potential target for remission in PsA with VLDA being the most stringent criteria. There was a high level of correlation between these scores although residual activity in dactylitis and skin despite DAPSA remission has some impact on patients’ function.

Disclosure of Interest: [Disclosure information provided]

DOI: 10.1136/annrheumdis-2017-eular.3855
FR0504 APREMILAST EXPANDS IL-10-PRODUCING REGULATORY B CELLS, AND DECREASES TH1 AND TH7 CELLS IN PSORIATIC ARTHRITIS AND PSORIASIS

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Background: IL-10-producing regulatory B cells (Bregs), also known as B10 cells, are decreased and inversely correlated with IFN-γ and IL-17-producing NK and T cells in patients with psoriatic arthritis (PsA) and psoriasis (Ps) (1-3)

Objectives: To assess whether or not apremilast, a PDE4 inhibitor recently approved for the treatment of Ps and PsA, is able to induce IL-10-producing B cells and decrease Th1 cells and Th17 cells in vivo

Methods: PBMCs and magnetically purified B cells were isolated from 21 patients (7 PsA, all responders; 14 Ps, 9 responders) at baseline and post-apremilast treatment (3 months and 6 months in responders; at 3 months in non-responders, as they switched to biologics). Phenotypic analysis of CD3, CD19, CD24, CD27, CD86 and intracellular expression of cytoklastic IL-10, IFN-γ, IL-17 after bacterial CpG (ODN2006) and PMA/ionomycin stimulation was examined by flow cytometry

Results: At 6 months, apremilast significantly increased IL-10-producing Bregs (IL-10+CD19+, B10 cells) compared to baseline and 3 months. B10 cells increase was confined mainly to the transitional Bregs (CD19+CD27+CD24high). IFN-γ+CD3+ (Th1) and IL-17+CD3+ (Th17) cells were significantly decreased at 3 and 6 months (p<0.05, for both). There was an inverse correlation between percentages of B10 cells and IFN-γ+producing CD3+ cells. The percentage of B10 cells were not changed post-treatment in non-responders.

Conclusions: Our data suggest that apremilast may exert its therapeutic effect through the expansion of IL-10-producing Bregs and the decrease of IFN-γ- and IL-17-producing T cells.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4665

FR0506 HLA PROFILES AND THEIR ASSOCIATIONS WITH DISEASE PHENOTYPES IN A CANADIAN PSORIATIC ARTHRITIS (PSA) COHORT

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Background: PSA is a chronic disease with known genetic predisposition that affects 0.3% to 1% of the general population. Certain HLA alleles were reported to be more predominant in PSA and to be associated with certain manifestations

Objectives: To determine HLA alleles prevalence in PSA patients and their association with clinical features and the severity of PSA in these patients

Methods: Two cohorts of early established PSA were followed prospectively.Clinical and laboratory data were collected at 6 months intervals, included PASI scores, nail involvement, joint counts, patient reported outcomes, comorbidities and laboratory parameters. We performed a data-driven consensus on the optimal target to use but also active coaching of the patients and their physicians to adjust treatment according to the optimal targets. Data on patients with HLA typing results that were collected longitudinally during the observation period was used

Results: The cohorts included 265 patients. Of those, one hundred thirty five patients had their HLA analysis done. Fifty one percent of the patients were male, the mean age at onset of PSA 43.07 (19–76) years. Mean age of PSA diagnosis was 33.47 years. Sixty four percent had polyarticular involvement at base line and 17% had documented axial involvement. Forty four haplotypes were reported in our cohort of patients: HLA B27 was present in 33% of the patients (as compared to 6.77% in an Irish control population). HLA A1 was present in 31%, B8 in 21%, B57 in 6%, B44 in 24.5%, B51 in 10%, HLA B62 in 5.6%, HLA B62 in 7%, HLA B4 in 43.6% and Bw6 in 46.5%. The following associations were found to be significant: HLA B49 was negatively associated with age of onset of PSA with a Pearson correlation of -0.10 (P = 0.057), also, HLA A23 had a correlation of -0.23 (P = 0.016). HLA B44 was associated with increased total number of comorbidities, Pearson correlation was 0.33 (P = 0.001).

Conclusion: HLA B22 was associated with more severe PASI score with a correlation of 0.488 (P = 0.008).

Of note: the only case in the cohort with Crohn’s disease had HLA B12 which was previously reported in spondylitis

135 patients were studied,51% were male. The mean age of PSA onset was 43.07 years and 33.4 for PsO. 64% had polyarticular disease while 17% had axial involvement. 42 alleles were studied, of those, HLA B27 was present in 33% of patients (vs.77% controls) HLA A1 in 31%, B8 in 21%, B27 in 6.6%, B44 in 24.5%, B51 in 10%, B58 in 5.6%, HLA B62 in 7%, HLA Bw4 in 43.6% and Bw6 in 46.5%. The following associations were significant: HLA B49 & HLA A23 were associated with age of onset of PSA (correlation of -0.610 (P = 0.007), also, HLA A23 had a correlation of -0.232 (P = 0.016). HLA B44 was associated with increased number of comorbidities (correlation 0.332 (P=0.001)). HLA B22 was associated with severe PASI score (correlation of 0.488 (P = 0.008). Of note: the only case in our cohort with Crohn’s disease had HLA B12 which was previously reported in spondylitis

Conclusions: The majority of patients had polyarticular involvement.HLA B27, HLA Bw4 and HLA B4 were the most frequent alleles. We found high percentage of patients with HLA B27, HLA A1 vs controls.HLA B27 prevalence was higher in patients with axial involvement but it did not reach significance in our cohort. HLA B44 was strongly associated with increased comorbidities (previous reports suggested protective effect of this allele). HLA B22 was associated with more severe PASI scores.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3151
The relationship between 10-year cardiovascular risk scores and disease activity in patients with psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with an increased prevalence of cardiovascular (CV) disease. This increase may in turn be due to a higher prevalence of traditional CV risk factors as well as to persistent inflammatory musculoskeletal and skin disease. Disease activity in PsA is associated with Composites Psoriatic Arthritis (CPSA) across 5 domains of involvement: peripheral joints, skin, entheses, dactylitis and spinal manifestations. Long-term CV risk is evaluated using several methods for general population.

Objectives: (1) To describe CV risk factors and 10-year CV risk scores among patients with PsA; and (2) to correlate with baseline CPDAI in this longitudinal study.

Methods: PsA patients fulfilling the CASPAR criteria were enrolled consecutively from Rheumatology clinics. Fasting bloods were obtained for glucose, insulin, lipids. Patients underwent thorough physical examination, joint and skin assessments and completed questionnaires on health, depression/anxiety and quality of life. Four different CV risk scores were calculated: (1) Framingham Coronary risk score (FCS); (2) American College of Cardiology and American Heart Association (ACC/AHA) 10-year atherosclerotic cardiovascular disease (ASCVD) risk score (FCS); (3) Systematic Coronary Risk Evaluation (SCORE) algorithm; and (4) QRISK2 (2016). CPDAI was calculated with CPDAI cutoff ≤4 representing low/minimal disease activity (LDA) or remission. CPDAI ≥4 represented active disease requiring treatment change.

Results: 100 PsA patients were recruited with mean age 52.4±10.5 (male 55%), Mean disease duration for PsA was 17.9±10 years. 58 patients (age 52.4±9.6, male 60.3%) had CPDAI<4 (LDA Gp) and 41 patients (age 52.4±11.9, male 48.8%) had CPDAI>4 (active Gp) at baseline. There were significantly more patients with BMI ≥35 in active Gp, but mean BMI, waist/hip ratio, blood pressure, fasting glucose, insulin, lipids, and patients taking NSIADs, oral corticosteroids, Metformin and/or biologics treatment were otherwise similar compared to LDA Gp. Skin (Psoriasis Area Severity Index (PASI); Dermatology Life Assessment Questionnaire (DLQI)) assessments together with levels of inflammatory markers such as C-reactive protein (CRP) were also similar in both groups. More active Gp had enthesitis (58.5%) and acute dactylitis (14.6%) (P<0.01 and 0.02, respectively). The mean FCS, ASCVD, SCORE and QRISK2 were similar in both groups (8.5±7.1% vs. 6.2±8.9%, P=0.11, 9.8±9.5% vs. 7.8±7.9%, P=0.54, 2.2±2.6% vs. 2.0±2.7%, P=0.81; 11.2±9.2% vs. 11.3±11.%, P=0.97, LDA Gp and active Gp, respectively). Interestingly, there were more smokers in LDA Gp (60.3% vs. 39.0%; P=0.04) and this likely accounts for the higher number of LDA Gp patients with FCS ≥10%.

Conclusions: We found similar prevalence of traditional CV risk factors and similar 10-year CV risk scores in PsA patients regardless of their CPDAI. Further correlation with measures of disease activity over time will be required.

References:

Disclosure of Interest: N. Ikumi: None declared, F. Farkas: None declared, A. Szentpetery: None declared, B. Kirby Grant/research support from: abbie, O. FitzGerald Grant/research support from: abbie, Pfizer, BMS, Consultant for: abbie, Pfizer, BMS, Celgene, Janssen, Novartis, UCB, Eli Lilly

DOI: 10.1136/annrheumdis-2017-eular.4798

The effect of certolizumab pegol on extra-articular manifestations of psoriatic arthritis over 4 years of treatment in patients with and without prior anti-TNF exposure

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Background: Extra-articular manifestations (EAMs) of psoriatic arthritis (PsA) include nail psoriasis, dactylitis, and enthesitis, which can significantly impact patients’ (pts’) quality of life.1 In the Rapid-Psa trial (NCT01087788), certolizumab pegol (CZP) improved the signs and symptoms of EAMs in pts with PsA over 96 weeks (wk).

Objectives: To report improvements in EAMs of PsA in pts treated with CZP over 4 years, both with and without prior anti-TNF exposure.

Methods: The Rapid-Psa trial was double-blind and placebo-controlled to Wk4, dose-blind to Wk48, and open-label (OL) to Wk216. Pts had active PsA and had failed ≥1 DMRD. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wk0), 4 continued their assigned dose in the OL period. We present EAM data for those pts originally randomized to CZP, with involvement of the particular EAM at baseline (BL), and without prior anti-TNF exposure. EAMs assessed include nail psoriasis (modified Nail Psoriasis Severity Index [mNAPSI]), BL involvement = BL mNAPSI >0), enthesitis (Leeds Enthesitis Index [LEI], BL involvement = BL LEI >0), and dactylitis (Leeds Dactylitis Index [LDI], BL involvement = BL LDI >1). Differences were analyzed with the Wilcoxon non-parametric test and Hedges’ g calculated.

Results: A total of 409 PsA pts were randomized; 273 received CZP from Wk0. Among CZP-randomized pts, 197 had nail psoriasis at BL (199 without, and 38 with, prior anti-TNF exposure), 172 had enthesitis (133 without, and 39 with, prior anti-TNF exposure), and 73 had dactylitis (56 without, and 17 with, prior anti-TNF exposure). Although relatively few pts were anti-TNF experienced, a large proportion of pts both with and without prior anti-TNF exposure with BL involvement went on to achieve total resolution of the respective EAM following 48 wks of CZP treatment (Table). Among pts completing the study, the proportions achieving total resolution were maintained or further increased from Wk48 to Wk216 (Table). Mean scores of all EAMs showed improvements by Wk48 of CZP treatment in pts both with and without prior anti-TNF exposure, which were maintained to Wk216 in pts completing the study (Table).

Table: Improvements in extra-articular manifestations of PsA over 216 weeks of CZP treatment in patients with and without prior anti-TNF exposure (observed values)

<table>
<thead>
<tr>
<th>EAM</th>
<th>Baseline</th>
<th>Week 8</th>
<th>Week 24</th>
<th>Week 48</th>
<th>Week 96</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis Area Severity Index (PASI)</td>
<td>10.8±9.1</td>
<td>3.2±2.8</td>
<td>2.1±2.0</td>
<td>1.9±1.8</td>
<td>1.3±1.5</td>
</tr>
<tr>
<td>Dermatology Life Assessment Questionnaire (DLQI)</td>
<td>11.2±9.1</td>
<td>7.8±7.3</td>
<td>5.8±5.4</td>
<td>4.5±4.0</td>
<td>3.7±3.3</td>
</tr>
<tr>
<td>Leeds Enthesitis Index (LEI)</td>
<td>11.3±10.1</td>
<td>7.8±7.4</td>
<td>6.2±6.3</td>
<td>5.1±4.8</td>
<td>4.3±4.2</td>
</tr>
<tr>
<td>Leeds Dactylitis Index (LDI)</td>
<td>11.3±10.1</td>
<td>7.8±7.4</td>
<td>6.2±6.3</td>
<td>5.1±4.8</td>
<td>4.3±4.2</td>
</tr>
</tbody>
</table>

Conclusions: PsA patients treated with CZP for up to 4 years, both with and without prior anti-TNF exposure, exhibited sustained improvements in the extra-articular manifestations of PsA.

References:

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: O. FitzGerald Grant/research support from: AbbVie, Bristol Myers Squibb, Janssen, Novartis, Pfizer, Consultant for: AbbVie, Celgene, Janssen, Pfizer, Roche, UCB Pharma, R. Fleischmann Grant/research support from: Abbott, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Genentech, Janssen, MSD Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB Pharma, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Genentech, GlaxoSmithKline, Janssen, Eli Lilly, Pfizer, Sanofi-Aventis, UCB Pharma, A. Kavanaugh Grant/research support from: Abbott, Amgen, Bristol-Myers Squibb, Janssen, Pfizer, Roche, UCB Pharma, B. Hoeppken Employee of: UCB Pharma, L. Peterson Employee of: UCB Pharma, D. Gladman Grant/research support from: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD Pharmaceuticals, Novartis, Pfizer, and UCB Pharma, Consultant for: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD Pharmaceuticals, Novartis, Pfizer, and UCB Pharma.

DOI: 10.1136/annrheumdis-2017-eular.1699
SAFETY AND EFFICACY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, UP TO 24 MONTHS IN PATIENTS WITH ACTIVE PsORATIC ARTHRITIS: INTERIM DATA FROM OPAL BALANCE, AN OPEN-LABEL, LONG-TERM EXTENSION STUDY

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Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA). Interim data (database not locked) from <24 months’ participation (3 years’ total treatment duration) for patients (pts) with active PsA in an ongoing, open-label, long-term extension study (LTE; NCT01976364 OPAL Balance) is reported.

Objectives: To evaluate the safety, tolerability and efficacy of tofacitinib in pts with active PsA.

Methods: Pts who were ≥18 years of age, with active PsA (≤35% DAPSA score, ≥12/14 – 14; high disease activity (HighDA): >28; mild disease activity (ModDA): ≤14; low disease activity (LowDA): ≤12). The Kappa statistic was used to describe the agreement between the numbers of pts in respective disease activity categories reported by the 2 independent assessors. A significance level of 0.05 was used.

Results: Amongst the 151 and 162 pts randomized to receive ADA and PBO, respectively, there was 100% agreement between the numbers of pts in respective disease activity categories reported by the 2 independent assessors.

Acknowledgments: This post hoc analysis used data from the ADEPT trial, which included pts with active PsA despite prior DMARD therapy who were randomized to receive ADA or PBO for 24 weeks (wks). Mean RAPID-3 was summarized by visit for each treatment group. Correlations between RAPID-3 and DAPSA over time were assessed through Pearson and Spearman coefficient. Pts were categorized at wk 24 according to DAPSA Remission: ≤12; LowDA: 13-24; ModDA: >24 – ≤; HighDA: >28; low disease activity (MALDA-28) and 54% (PBO) in HighDA. At wk 24, 39% and 34% of pts in ADA and PBO, respectively, exhibited HighDA when assessed by RAPID-3 (13.1 for ADA, 13.3 for PBO) [129]. The Kappa statistic was used to describe the agreement between the numbers of pts in respective disease activity categories reported by ADA, DAPSA, and MDA. Data were as observed.

Conclusions: In a PBO-controlled trial of ADA in pts with PsA, there was good correlation between disease activity captured by pts’ self-assessment, via the RAPID-3, and physician assessment, suggesting the potential utility of pt-derived measures in assessing disease activity.


Acknowledgements: AbbVie: study (NCT00646386) sponsor, contributed to
Scientiﬁc Abstracts

Friday, 16 June 2017

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Table 1. Summary of pooled safety of secukinumab in PSO and PsA
PSO
Any secukinumab
N=3893
Total exposure, patient-years )
7769.0
Min–max exposure (days)
1–1526
Death, n (%)
7 (0.2)
AE’s by EAIR: AE per 100 Pt-years (95% Cl)
Any AE
196.9 (190.3, 203.6)
Any serious AE
7.2 (6.6, 7.8)
Frequent AEs1
Nasopharyngitis
18.2 (17.1, 19.3)
Headache
6.3 (5.7, 6.9)
Upper respiratory tract infections
6.2 (5.6, 6.8)
Arthralgia
5.1 (4.6, 5.6)
AEs of special interest
Candida infections
2.1 (1.8, 2.4)
Serious infections
1.4 (1.2, 1.7)
Inﬂammatory Bowel Disease
0.3 (0.2, 0.4)
Crohn’s disease
0.1 (0.0, 0.1)
Ulcerative colitis
0.2 (0.1, 0.3)
MACE
0.3 (0.2, 0.5)
Neutropenia
0.4 (0.3, 0.5)

PsA
Any secukinumab
N=1128
1907.0
16–1464
4 (0.4)
173.7 (162.5, 185.5)
8.5 (7.2, 10.0)
13.7 (12.0, 15.7)
4.8 (3.9, 5.9)
11.2 (9.6, 12.9)
4.3 (3.4, 5.3)
2.3 (1.6, 3.1)
1.8 (1.3, 2.5)
0.5 (0.2, 0.9)
0
0.1 (0.0, 0.4)
0.3 (0.1, 0.6)
0.7 (0.4, 1.2)

1

Adverse events in the secukinumab group that occurred with an IR >5.0 during the entire safety
period in either of the spooled groups; AE, adverse event; EAIR, exposure adjusted incidence
rate per 100 patient-years; MACE, major adverse cardiac event; N, number of patients in the
analysis.

design, data collection, analysis, interpretation, and abstract writing, review, and
approval. Medical writing: Ben Wolfe of AbbVie.
Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen,
Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pﬁzer, Sun
Pharma, and UCB, Consultant for: AbbVie, Amgen, Bristol Myers, Celgene,
Genentech, Janssen, Lilly, Merck, Novartis, Pﬁzer, Sun Pharma, and UCB,
Speakers bureau: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen,
Lilly, Merck, Novartis, Pﬁzer, Sun Pharma, and UCB, S. Chen Shareholder
of: AbbVie, Inc., Employee of: AbbVie, Inc., F. Ganz Shareholder of: AbbVie,
Inc., Employee of: AbbVie, Inc., W. Tillett Grant/research support from: AbbVie,
Celgene, Novartis, Pﬁzer, and UCB, Consultant for: AbbVie, Celgene, Novartis,
Pﬁzer, and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pﬁzer, and UCB

FRI0511

SECUKINUMAB DEMONSTRATES CONSISTENT SAFETY OVER
LONG-TERM EXPOSURE IN PATIENTS WITH PSORIATIC
ARTHRITIS AND MODERATE-TO-SEVERE PLAQUE
PSORIASIS: UPDATED POOLED SAFETY ANALYSES

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Basel, Switzerland; 6 Novartis Pharmaceuticals Corp., East Hanover, United
States
Background: Pooled safety data from secukinumab psoriasis (PsO) and psoriatic
arthritis (PsA) clinical trial programs after ∼1 year of exposure have been
reported.1,2
Objectives: To report updated longer-term secukinumab exposure safety data
from PsO and PsA studies (data cut-off: 25 June 2016).
Methods: The PsO data pool consisted of 9 Phase III studies in moderate-tosevere plaque PsO and PsA pool consisted of 3 Phase III studies in active PsA.
Secukinumab doses differed in the studies and included intravenous (up to 10
mg/kg) or subcutaneous (s.c.; 75–300 mg) loading, followed by s.c. maintenance
dosing (300, 150 or 75 mg). Placebo patients were re-randomised to secukinumab
at 12–24 weeks depending on study design. Only data for approved secukinumab
300 and 150mg doses were included in analysis. Exposure adjusted incident
rates (EAIR) were used to adjust for differences in exposure.
Results: In both PsO and PsA, the most frequently reported adverse events
(AEs) with secukinumab were non-serious infections of the upper respiratory
tract, headache and arthralgia (Table). The EAIRs of AEs of special interest with
secukinumab including Crohn’s disease, Candida infections, serious infections,
inﬂammatory bowel disease, major adverse cardiac events and neutropenia
(reported in the Table) were similar in both PSO and PsA indications, and
comparable to those reported previously.1,2 No cases of tuberculosis (new onset
or reactivation) were reported.

Conclusions: The safety proﬁle of secukinumab was similar for PsO and PsA
patients supporting its long-term use in these chronic conditions. Secukinumab
long-term exposure safety data is consistent with that previously reported with
shorter-term exposure, including being well tolerated, and without any new safety
signals identiﬁed.
References:
Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen,
Biogen Idec, BMS, Celgene, Crescendo, Janssen, Lilly, Merck, Novartis, Pﬁzer,
and UCB, Consultant for: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Covagen,
Crescendo, Janssen, Lilly, Merck, Novartis, Pﬁzer, UCB, Speakers bureau:
AbbVie, Amgen, Biogen Idec, BMS, Crescendo, Janssen, Lilly, Pﬁzer, and UCB, I.
McInnes Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen,
Lilly, Novartis, Pﬁzer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene,
Janssen, Lilly, Novartis, Pﬁzer, and UCB, Speakers bureau: AbbVie, Amgen,
BMS, Celgene, Janssen, Lilly, Novartis, Pﬁzer, and UCB, K. Reich Grant/research
support from: AbbVie, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene,
Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cliag, Leo,
Lilly, Medac, Merck Sharp and Dohme Corp., Novartis, Ocean Pharma, Pﬁzer,
Regeneron, Takeda, UCB Pharma, Xenoport, Speakers bureau: AbbVie, Amgen,
Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward
Pharma, GlaxoSmithKline, Janssen-Cliag, Leo, Lilly, Medac, Merck Sharp and
Dohme Corp., Novartis, Ocean Pharma, Pﬁzer, Regeneron, Takeda, UCB Pharma,
Xenoport, P. Nash Grant/research support from: AbbVie, Amgen, BMS, Celgene,
Eli Lilly, Hospira, MSD, Pﬁzer, Janssen, UCB, Novartis, Roche; Consultancy fees:
AbbVie, Amgen, BMS, Celgene, Eli Lilly, Hospira, MSD, Pﬁzer, Janssen, UCB,
Novartis, Roche, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lilly,
Hospira, MSD, Pﬁzer, Janssen, UCB, Novartis, Roche, M. Andersson Employee
of: Novartis, K. Abrams Shareholder of: Novartis, Employee of: Novartis, L.
Pricorp Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of:
Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.4991

FRI0512

APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR,
IS ASSOCIATED WITH LONG-TERM (156-WEEK)
IMPROVEMENTS IN BASDAI IN PSORIATIC ARTHRITIS
PATIENTS: POOLED RESULTS FROM 3 PHASE III,
RANDOMIZED, CONTROLLED TRIALS

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Hamburg Eilbek, Hamburg, Germany; 6 University of Orléans, Orléans, France;
7
Celgene Corporation, Summit, United States; 8 Monash University,
CabriniHealth, Melbourne, Australia
Background: In PALACE psoriatic arthritis (PsA) studies, the Bath Ankylosing
Spondylitis Disease Activity Index score (BASDAI) was used as an exploratory
measure in a subset of patients (pts) considered by investigators to have axial
involvement, although PsA spondylitis was not conﬁrmed by imaging.
Objectives: Report the impact of apremilast 30 mg BID (APR) treatment on
BASDAI over 156 wks using pooled PALACE 1–3 data of pts with active PsA
despite prior conventional DMARDs and/or biologics.


Methods: APR treatment outcomes were evaluated in a subset of pts with baseline (BL) BASDAI ≥4 ("subset") over 156 wks.

Results: BL BASDAI ≥4 was reported for 454/1493 (30%) pts. Mean PsA duration was similar between the subset and rest of the PALACE 1–3 population (n=1039); mean BL psoriasis body surface area (BSA) and percentage of pts with ≥3% were slightly higher. The subset had higher mean BL values vs the rest of PALACE 1–3 pts for C-reactive protein (1.12 vs 0.93), pain VAS (83.6 vs 53.8 mm), pt's global assessment of disease activity (62.2 vs 53.5 mm), and physician’s global assessment of disease activity (PhGA; 59.0 vs 53.0 mm) and markedly worse mean HAQ-DI (1.41 vs 0.88), SF-36v2 Physical Functioning (30.6 vs 35.8), and FACIT-F (25.7 vs 31.8) scores. Despite disease activity differences, BL concomitant oral DMARDs were similar in both groups: 1 DMARD in 61.0% (subset) vs 57.8% (rest of PALACE 1–3 pts); methotrexate was the most common DMARD. In the subset, 73.6% had been treated with only oral DMARDs pre-study (44.9% with only 1); 21.5% had prior biologic use. Mean BL BASDAI in the subset was 6.6 with APR and 6.4 with placebo (PBO). Mean BL BASDAI question 2 score, referring directly to spinal and hip pain, was 6.7. APR resulted in greater mean improvement in BASDAI vs PBO at Wk 16 (−1.53 vs −0.91; P=0.0173) and Wk 24 (Table). As early as Wk 16, a 19% mean decrease in the question 2 score was observed vs placebo. Few APR vs placebo pts had BL VAS >50. Other disease measures significantly improved early in treatment, including HAQ-DI, fatigue, PhGA, and mPsARC (Table). Long-term improvement was seen across measures, with mean BASDAI reductions of 2.18 at Wk 52 and 2.19 at Wk 156 (Table) and question 2 reductions of 1.94 and 2.28, respectively; treatment resulted in a shift toward lower BASDAI across the subset, with a significant proportion reaching BASDAI ≤4.

Outcomes at Wk 24, Wk 52, and Wk 156 in Pts With BASDAI ≥4 at BL

<table>
<thead>
<tr>
<th>Wk 24</th>
<th>Wk 52</th>
<th>Wk 156</th>
</tr>
</thead>
<tbody>
<tr>
<td>APR n=158</td>
<td>BD n=160</td>
<td>PAL4 n=127</td>
</tr>
<tr>
<td>BASDAI, mean BL</td>
<td>6.6</td>
<td>6.4</td>
</tr>
<tr>
<td>BASDAI, mean change</td>
<td>−1.86</td>
<td>−0.94</td>
</tr>
<tr>
<td>SF-36v2 PF, mean change</td>
<td>−0.32</td>
<td>−0.17</td>
</tr>
<tr>
<td>Pain VAS, mean change, mm</td>
<td>−1.8</td>
<td>−0.79</td>
</tr>
<tr>
<td>FACIT-F, mean change</td>
<td>−3.80</td>
<td>−1.29</td>
</tr>
<tr>
<td>PGA global assessment of disease activity, mean change</td>
<td>−10.0</td>
<td>5.7</td>
</tr>
<tr>
<td>PhGA, mean change (VAS mm)</td>
<td>−22.1</td>
<td>−7.4</td>
</tr>
<tr>
<td>Proportion meeting mPsARC, %</td>
<td>40.8</td>
<td>20.5</td>
</tr>
</tbody>
</table>

In the may vary slightly for the end points at each time point. For Wk 24, it is the number of pts randomized at BL in the subset, last observation carried forward methodology and non-responder imputation were applied to all pts who did not complete Wk 24 or had missing visits at Wk 24. For Wk 24, only continuous data and binary response, respectively. For Wk 52, it is the number of pts randomized to APR at Wk 16, in the subset with an outcome measured at Wk 52. For Wk 156, it is the number of pts who were randomized to APR (at Wk 16, Wk 156). Wk 156 was calculated as Wk 24 + (Wk 156 − Wk 24). Component level scores were expressed as HR-QL (mPsARC) and PSART (mPsART) scores.

Conclusions: In this post hoc analysis of pooled data, pts reporting BASDAI ≥4 at BL appear to experience greater disease burden, including disability, pain, and fatigue; effective treatment strategies may not have been available. APR treatment resulted in long-term improvements in BASDAI and other measures in pts with clinically suspected axial disease.

Disclosure of Interest: P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB, H. Marzo-Ortega: None declared, A. Poder: None declared, F. Van den Bosch Consultant for: AbbVie, Celgene Corporation, Merck, Pfizer, UCB, Janssen, Eli Lilly, Novartis, Servier, Speakers bureau: AbbVie, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB.}

FR0513 LONG-TERM (156 WEEKS) IMPROVEMENTS IN PHYSICAL FUNCTION OF DMARD-NAÏVE AND DMARD/BIOLOGIC-EXPERIENCED PSORIATIC ARTHRITIS PATIENTS TREATED WITH APREMILAST: DATA FROM A LARGE DATABASE OF 4 PHASE III CLINICAL TRIALS

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Background: Improving and preserving patient (pt) physical function is an important goal for psoriatic arthritis (PsA).

Objectives: To evaluate apremilast’s (APR) effects on physical function/functional status for up to 3 yrs in DMARD/biologic-experienced (PALACE 1–3 [PAL1–3] pooled data) and DMARD-naïve (PALACE 4 [PAL4]) pts with active PsA.

Methods: Pts were randomized (1:1:1) to placebo (PBO), APR 30 mg BD (APR30), or 20 mg BD (APR20) at baseline (BL). The primary endpoint was at Wk16; a long-term extension is ongoing. A detailed study design has been previously presented. Assessed were mean change from BL HAQ-DI scores and proportions of pts reaching HAQ-DI MCID and reaching scores ≤1.0 (below clinical significant disability). APR30 and PAL4 pts had similar BL SJC/TJC and DAS-28 (CRP), indicating active PsA. APR1–3 pts had longer mean duration of PsA and psoriasis, higher PASI scores, and greater corticosteroid use at BL. Despite differences, BL physical disability was clinically significant in both populations (mean HAQ-DI, PAL1–3: 1.0; PAL4: 1.1; PAL4 vs PAL1–3: −0.21 vs −0.30; P=0.0049). At Wk16, physical function significantly improved with APR30 vs PBO (mean HAQ-DI change, PAL1–3: −0.23 vs −0.08; PAL4: −0.21 vs 0.03; both P<0.0001) and more PAL3 vs PAL4 APR30 pts had BL HAQ-DI >1.0 (60% vs 54%), 1.5 (marked difficulty/need for assistive devices, 31% vs 21%), and 1.75 (major disability, 19% vs 10%), highlighting need for early, effective treatment (tx). Few APR30 pts had BL scores ≤0.5 (18–22%) or ≤0.25 (10–14%). As Wk16, overall disability levels also shifted; more APR1–3 vs PAL4 pts had achieved HAQ-DI ≤1.0 (PAL1–3: 56% vs 48%; PAL4: 60% vs 52%). At Wk156, marked achievement of HAQ-DI ≤1.0, ≤0.5, and ≤0.25 was observed in both populations (Table). LOCF analyses confirmed Wk156 results.

Conclusions: With APR30 tx, physical disability improved early; functionality was maintained for up to 3 yrs. Most pts achieved HAQ-DI ≤1.0; many attained minimal/mild physical impairment. Over 40% of pts receiving APR30 earlier in the tx paradigm had functional ability similar to that of population norms after 3 yrs; shorter disease duration and no prior DMARD/biologics use in this population suggests that earlier APR tx may increase the likelihood of maximal functionality for some pts.

Disclosure of Interest: P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB, H. Marzo-Ortega: None declared, A. Poder: None declared, F. Van den Bosch Consultant for: AbbVie, Celgene Corporation, Merck, Pfizer, UCB, Janssen, Eli Lilly, Novartis, Servier, M. McIlraith Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, S. Hall Consultant for: Boehringer Ingelheim, MSD, Roche, Schering-Plough, Servier, Wyeth, Paid instructor for: Amgen, AstraZeneca, Boehringer Ingelheim, Centocor, GSK, MSD, Pfizer, Sanofi Aventis, Sanofi Pasteur, Schering-Plough, Serono, Wyeth, Speakers bureau: Boehringer Ingelheim, GSK, MSD, Pfizer, Roche, Sanofi Aventis, Schering-Plough, Wyeth DOI: 10.1136/annrheumdis-2017-eular.3299
F. Van den Bosch Consultant for: AbbVie, Celgene Corporation, Merck, Pfizer, UCB, Janssen, E. Lespessailles Grant/research support from: Amgen, Eli Lilly, Novartis, Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, Servier. M. McIraith Employee of: Celgene Corporation, D. Nguyen Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, C. Edwards Grant/research support from: Celgene Corporation, Pfizer, Roche, Samsung, Consultant for: Celgene Corporation, Pfizer, Roche, Samsung. Speakers bureau: Abbott, GSK, Pfizer, Roche

DOI: 10.1136/annrheumdis-2017-eular.3019

FR0514

**PSORIATIC ARTHRITIS IS ASSOCIATED WITH DIAGNOSTIC DELAY AND WORSE OUTCOME AT THREE MONTHS WHEN COMPARED TO RHEUMATOID ARTHRITIS: RESULTS FROM THE UK NATIONAL AUDIT FOR INFLAMMATORY ARTHRITIS**

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**Background:** Psoriatic arthritis (PsA) is underdiagnosed in primary care, and can be difficult to distinguish from osteoarthritis. Accumulating evidence suggests that diagnostic delay is associated with poorer functional outcome despite treatment.

**Objectives:** To develop a better understanding of the diagnostic delay and burden of disease in patients with PsA, and to investigate management within the first three months of diagnosis.

**Methods:** Data were analysed on all participants with a final diagnosis of PsA from The National Clinical Audit for Rheumatoid and Early Inflammatory Arthritis, undertaken by the British Society for Rheumatology and commissioned by the Healthcare Quality Improvement Programme, recruited between 1/2/2014 and 30/10/2015. Data were collected from patients and clinicians at baseline and three months. 1016 participants with PsA (mean age 49.4±14.5 years; 54% female) were matched 1:1 by age and sex with participants with Rheumatoid Arthritis (RA).

**Results:** Patients with PsA had a significantly longer delay to presentation and diagnosis than those with RA (p<0.02, Table 1), and this remained significant when adjusted for age, sex, ethnicity and deprivation index; p<0.05). In those with paired results, the mean improvement in IAID score was 1.32 (95% CI 0.99–1.65) in PsA vs 2.37 (95% CI 2.07–2.67) in RA. In patients with high disease activity at baseline (DAS28 >5.1) a good EULAR response was seen in only 21.4% in PsA vs 30.3% in RA. There was a marked difference in the DMARDs initially prescribed, and the differences remained significant when only those with a DAS28 score indicating moderate or high disease activity at presentation were analysed, as shown in Figure 1.

**Conclusions:** This study demonstrates that patients with PsA have a longer delay to diagnosis between both symptom onset and presentation to primary care, and referral to secondary care and diagnosis than those with RA. Despite similar disease impact and physical function at diagnosis, patients with PsA are less likely to receive combination DMARD treatment, and have increased disease burden at three months.

**Disclosure of Interest:** None declared

FR0515

**CLASSIC CARDIOVASCULAR RISK FACTORS AND MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: RESULTS OF A SPANISH MULTICENTER STUDY**

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**Background:** Some cardiovascular risk factors (CVRF) have been related to poorer responses to biological therapy 1. We aimed to evaluate the potential link between the MDA response and the presence of CVRF in patients treated with traditional and/or biological DMARDs.

**Objectives:** The objective has been to evaluate the potential association between classic CVRF and the probability of reaching an MDA response in PsA patients.

**Methods:** Cross-sectional study carried out at 25 rheumatology outpatient clinics in patients who fulfilled the Classification for Psoriatic Arthritis (CASPAR) criteria with at least one year disease duration, and treated with biological or conventional synthetic (cs) DMARDs according to routine clinical practice in Spain. Patients were considered in MDA if they met at least 5/7 of the MDA criteria 2.

**Results:** The relationship between MDA and CVRF was evaluated by uni and multivariate analyses.

**Results:** 227 patients were included, 133 (58.6%) were in MDA state (52% on anti-TNFα monotherapy, 24% on csDMARD monotherapy, 24% on anti-TNFα in combination with csDMARD). Among the classic CVRF, tobacco (crude OR: 1.05), sedentary lifestyle (crude OR: 1.95), hyperuricemia (crude OR: 2.01) and obesity (crude OR: 1.54) were related to the likelihood of MDA in the univariate model (p<0.25). The only CVRF related to the MDA response in the multivariate analysis was a sedentary lifestyle (OR 3.13, 95% CI: 1.50–6.53; p=0.002). We did not find any association between the number of CVRF and the MDA response.

**Conclusions:** Contrary to what has been found in other studies, in this cross-sectional multicenter study we could not find any relationship between traditional CVRF (except for sedentary lifestyle) and MDA. In any case, patients with psoriatic disease should be encouraged to maintain healthy lifestyle habits.

**References:**


**Acknowledgements:** This study was funded by Pfizer.

**Disclosure of Interest:** None declared


FR0516

**ASSESSMENT OF DISEASE REMISSION BY POWER DOPPLER ULTRASONOGRAPHY IN PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Treatment strategies nowadays are targeting clinical remission or low disease activity. In some patients with psoriatic arthritis (PsA) clinical findings defer from the ultrasonographic evidence of inflammation which raise the need for revising the remission criteria in the clinical practice.

**Objectives:** The aim of our study was to estimate the presence of subclinical synovitis by power Doppler ultrasonography (PDUS) in PsA patients, who were considered as being in clinical remission defined by DAS28-ESR (Disease activity score of 28 joints – erythrocyte sedimentation rate) for at least 6 months during the treatment course.

**Methods:** 64 PsA patients in clinical remission based on DAS28 – ESR <2.6 were included in the study. The patients were examined by two independent rheumatologists. The affected joints were assessed by PDUS (MyLab 60, Esaote) for the presence of synovial hypertrophy (SH) and synovitis scored from 0 to 3 based on the presence and intensity of PD signal. Disease activity was determined by the presence of SH ≥2 degree and a positive PD signal.

**Results:** We found a persistent synovitis in 23 (35.9%) of the PsA with clinical remission of the peripheral joint involvement. Active synovitis was also found in 7
Psoriatic arthritis (PsA) is a chronic systemic inflammatory disease. Affecting skin, joints, entheses and dactyly, its impact on health-related quality-of-life (HRQoL) could be substantial. The emergence of tumour necrosis factor inhibitor (TNFi) therapy has dramatically changed the course of disease. Over the past decade new TNFi therapies have emerged (certolizumab pegol and golimumab), changing the synovitis will establish correct criteria for defining and monitoring the disease activity in PsA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6603

FR0518

PRESCRIPTION PATTERNS OF TUMOUR NECROSIS FACTOR INHIBITOR AND USTEKINUMAB IN PSORIATIC ARTHRITIS: A NORDIC POPULATION-BASED COHORT STUDY


Background: Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with skin manifestations, several extra-articular symptoms, various comorbidities, and disability. The emergence of tumour necrosis factor inhibitor (TNFi) therapy has dramatically changed the course of disease. Over the past decade new TNFi therapies have emerged (certolizumab pegol and golimumab), and recently ustekinumab and secukinumab have also become available for PsA.

Objective: The objective of this study was to assess the relative use of biological agents (bDMARDs) in PsA from 2006 through 2014, using data from the Nordic Rheumatology registers.

Methods: Based on data from the observational registers DANBIO, ICEBIO, NOR-DMARD, ROB-FIN, and SRQ registers, PsA patients initiating treatment with bDMARDs as a first or subsequent biological therapy were identified. Adalimumab, etanercept and infliximab were grouped as “first generation TNFi therapies”; certolizumab pegol and golimumab were grouped as “second generation TNFi”. Treatments with ustekinumab during the study period were also identified. Descriptive statistics for prescription patterns of bDMARD therapy were calculated.

Results: A total of 11,458 treatment initiations were identified (DANBIO 3,068, ICEBIO 357, NOR-DMARD 1,113, ROB-FIN 708, SRQ 6,212). 54% of the patients were female. Overall, 5,695 patients initiated a first generation TNFi, 912 a second generation TNFi, and 16 ustekinumab, as their first course of biological therapy. The corresponding numbers for those initiating a second (or more) biological treatment were 3,606, 1,090 and 139 patients, respectively. The figure displays the annual number of treatment initiations stratified by treatment type. The total yearly number of first course biological treatment increased significantly throughout the period (p<0.001), and this was also the case for patients switching therapy (p<0.001), indicating a previously unmet need for biological therapies in the Nordic population. The annual number of patients initiating first generation TNFi both as first and subsequent course of therapy decreased significantly towards the end of the study period (p<0.001). This drop was more than offset by a rapid increase in initiation of second generation TNFi treatments (p<0.001). Ustekinumab was primarily used as second or subsequent course of therapy in PsA. The same pattern was seen when stratified for country (data not shown).

Conclusions: Across the Nordic countries the prescription pattern for biological therapies for PsA has changed significantly over time. After 2012 initiation of the first generation TNFi is decreasing both as first and second course therapy, whereas second generation TNFi are increasing both as first and second course of biologic intervention. Collaboration across registers will allow for robust assessment of the uptake of newer biological therapies.

Acknowledgements: This study was partly funded by a grant from NordForsk and Janssen Pharmaceuticals.


FR0519

EFFECT OF BIOLOGICS ON FATIGUE IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW WITH META-ANALYSIS

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Background: Fatigue is an important aspect of disease both in rheumatoid arthritis (RA) and in psoriatic arthritis (PsA) and is of high priority for patients. In RA, a recent Cochrane meta-analysis found a small effect of biologics on fatigue (standardized mean difference, SMD, 0.43; 95% confidence interval, CI: 0.38–0.49). (1) Little is known about this effect in PsA.

Objectives: To assess the effect of biologics on fatigue in PsA randomised controlled trials (RCTs) and to compare this effect with the effect in the same trials, on pain, through a systematic literature review (SLR) and meta-analysis (MA).

Methods: SLR up to January 2017 in PubMed, Embase and Cochrane trials database and in recent congress abstracts, using key words related to PsA and biologics. All RCTs in PsA of any biologic therapy, assessing fatigue (whatever the...
score used), with data available for fatigue were included. Data were collected by 2 regarding levels of fatigue (6 trials used FACIT, 1 VAS) and pain (if available) at baseline and at the timepoint closest to 24 weeks after the biologic introduction. A MA was performed using RevMan and SMDs were calculated for each trial and each study dose, with fatigue and pain. A SMD >0.5 is usually considered small, between 0.5 and 0.8 moderate and >0.8 as important.

**Results:** After screening 295 publications, 7 RCTs were included in the meta-analysis and assessed TNF blockers (N=3: adalimumab N=2, certolizumab pegol, N=1), secukinumab (N=2), apremilast (N=1) and ustekinumab (N=1) with or without methotrexate, compared to placebo. The studies included 2340 PsA patients: weighted mean age ± standard deviation (SD), 48.7±1.3 years, disease duration 7.7±1.3 years, 53.3% were females. At baseline, joint disease activity was high (weighted mean swollen joint count: 13.0±3.1, HAQ-DI: 1.2±0.1, PASI: 10.4±3.3). Fatigue levels were high at baseline (weighted mean FACIT score: 29.2±1.5). The pooled SMD for fatigue was 0.44 (95% CI 0.35, 0.54) and it ranged 0.04 to 0.71 across drugs and trials with a small to moderate effect (Graph). In 6 of the same studies, the pooled SMD for pain was 0.62 (95% CI 0.52, 0.73) and ranged 0.46 to 0.84.

**Conclusions:** Biologics had a mild to moderate effect on fatigue at 24 weeks in PsA RCTs. No notable differences across drugs were apparent. Effect sizes were higher on pain with a moderate effect. This effect seems similar to effects noted in RA in the Cochrane meta-analysis (1). These results confirm fatigue may be multifactorial in PsA; biologics bring some improvement at the group level but other treatment modalities should be further explored also.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4680

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**Table 1. Change from Baseline in PROs at 16 and 24 Weeks**

<table>
<thead>
<tr>
<th>PRO</th>
<th>Week 16 (total population)</th>
<th>Week 24 (responder analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abatacept</td>
<td>Placebo</td>
</tr>
<tr>
<td>SF-36</td>
<td>n=202</td>
<td>n=186</td>
</tr>
<tr>
<td>PCS</td>
<td>3.76 (0.55)</td>
<td>2.02 (0.57)</td>
</tr>
<tr>
<td>MCS</td>
<td>2.42 (0.70)</td>
<td>1.15 (0.73)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>n=202</td>
<td>n=187</td>
</tr>
<tr>
<td></td>
<td>-0.25 (0.04)</td>
<td>-0.15 (0.04)</td>
</tr>
<tr>
<td>DLOI</td>
<td>n=212</td>
<td>n=189</td>
</tr>
<tr>
<td></td>
<td>-2.28 (0.34)</td>
<td>-1.24 (0.35)</td>
</tr>
<tr>
<td>FACIT-F</td>
<td>n=232</td>
<td>n=189</td>
</tr>
<tr>
<td></td>
<td>-3.67 (0.65)</td>
<td>-2.61 (0.67)</td>
</tr>
</tbody>
</table>

Data are adjusted mean change (SE). *95% CI of difference vs placebo did not cross 0.
Secureukinumab Provides Sustained Improvements in Work Productivity and Health-Related Quality of Life in Patients with Active Psoriatic Arthritis: 2-Year Results from Future 1 and Future 2


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Background: Patients (pts) with PsA experience significant impairment of work productivity (WP) and health-related QoL (HRQoL). Secukinumab (SEC) has previously been shown to rapidly improve symptoms, physical function and HRQoL in pts with active PsA.1,2

Objectives: To assess the impact of SEC on WP and HRQoL through 2 years in TNF inhibitor (TNF)-naive PsA pts and those with an inadequate response or intolerance to TNF inhibitors (TNF-IR) at Week 16/24.

Methods: 606 and 397 pts were randomized to SEC or placebo (PBO) in FUTURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and FUTURE 2 (300, 150 or 75 mg SC), respectively. PBO pts were re-randomized to SEC at Week 16/24. WP was assessed using the WP and Activity Impairment-General Health (WPAI-GH) questionnaire. WPAI-GH included 6 questions to measure absenteeism, presenteeism, work productivity and impairments in unpaid activity because of health problems during the preceding 7 days. HRQoL was assessed using the PsAQoL questionnaire, encompassing 20 statements that pts rate as true or false on the day of completion. Across both trials, approximately 68% of employed pts in both FUTURE 1 and FUTURE 2 were working at baseline (BL); 61 of 100 and 59 of 100 were employed and working at BL in the SEC 300 mg and 150 mg groups of FUTURE 2, respectively. Improvements in all elements of WPAI were also evident with SEC in TNF-naive and TNF-IR pts in both FUTURE 1 and FUTURE 2. Improvements in PsAQoL were reported as early as Week 4 and sustained through Week 104. At Week 104 of FUTURE 2, PsAQoL scores had improved by approximately 46% from BL with SEC 300 mg and 49% with SEC 150 mg in the overall population. Similar improvements were seen in TNF-naive (47% and 51%, respectively) and TNF-IR pts (45% and 45%, respectively). Consistent results were reported in FUTURE 1. The efficacy of SEC was consistent regardless of concomitant MTX use.

Results: SEC provided sustained improvements in WP and PsAQoL in pts with PsA for up to 104 wks, regardless of prior TNF exposure.

Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen, BMS, Celtrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi, and UCB; O. FitzGerald Grant/research support from: AbbVie, BMS, Celtrion, Janssen, MSD, Novartis, Pfizer, Sun Pharma, UCB, L. Coates Grant/research support from: AbbVie, BMS, Celtrion, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB, J. Walsh Consultant for: Novartis, J. Cañete Consultant for: AbbVie, Boehringer Ingeheim, Celgene, Janssen, Lilly, Novartis; V. Bhosekar Employee of: Novartis, L. Pricop Employee of: Novartis, K. Gandhi Consultant of: Novartis, L. Coates Grant/research support from: AbbVie, BMS, Celtrion, Janssen, MSD, Novartis, Pfizer; J. Cañete Consultant for: AbbVie, BMS, Celtrion, Janssen, MSD, Novartis, Pfizer, Sun Pharma, UCB.

References:

The Association between Occupational-Related Mechanical Stress and Radiographic Damage in Psoriatic Arthritis

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Background: Mechanical stress is thought to play a role in the development of psoriatic arthritis (PsA). Mechanical stress is thought to play a role in the development of psoriatic arthritis (PsA). To determine the association between occupational-related mechanical factors and the severity of radiographic peripheral and axial joint damage in patients with PsA.

Methods: A retrospective cohort study was conducted in patients with longstanding PsA (>10 years duration). Patients were asked to report all paid employment since the age of 18. The key predictor variables included various occupational-related mechanical exposures. For each job, the Occupational Information Network (O*NET) was used to rate the level of exposure to 11 workers’ abilities and 16 occupational exposures. The outcomes of interest were the severity of radiographic peripheral and axial joint damage in patients with PsA. Mechanical stress is thought to play a role in the development of psoriatic arthritis (PsA).

Results: 307 eligible patients were analyzed. Univariate analysis identified several occupational factors associated with radiographic damage (Table 1–2). In the multivariable regression analysis prolonged repetitive hand movements were associated with increased Steinbrocker score adjusting for age, sex, PsA duration and lifestyle habits.

Table 1. Linear Regression Analysis – The association between high level of work-related exposure and modified Steinbrocker score

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Univariate analysis</th>
<th>Multivariable Reduced Model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Sitting</td>
<td>-15.7 (-29.2, -2.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hands handle</td>
<td>23.1 (4.4, 42)</td>
<td>0.02</td>
</tr>
<tr>
<td>Repetitive hands motions</td>
<td>33.1 (17.5, 54.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Twisting/Bending</td>
<td>18.8 (4.3, 36.2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Minor burns</td>
<td>21.5 (27.4, 40.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Awkward body position</td>
<td>17.7 (-1.1, 36.5)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Table 2. Linear Regression Analysis – The association between workers’ abilities and modified Steinbrocker score

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Univariate analysis</th>
<th>Multivariable Reduced Model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Manual dexterity</td>
<td>2.5 (0.4, 4.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Arm-hand steadiness</td>
<td>2.7 (0.6, 5.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Finger dexterity</td>
<td>5.3 (1.4, 9.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>Trunk strength</td>
<td>2.0 (0.3, 4.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Wrist-finger speed</td>
<td>3.2 (0.4, 6.8)</td>
<td>0.08</td>
</tr>
<tr>
<td>Extent flexibility</td>
<td>1.9 (0.3, 4.2)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*Each model was adjusted for age, sex, duration of PsA, smoking, BMI, Biologics therapy (ever), DMARDs therapy (ever).
was associated with a higher peripheral joint damage score by mSS, adjusted β=29.5, 95% CI 8.2, 50.8, p=0.007, Table 1), while the association between prolonged time spent sitting and lower mSS was of borderline significance (p=0.085, Table 1). Additionally, occupations that required higher finger dexterity were associated with higher mSS (adjusted β=5.4, 95% CI 1.6, 9.2, p=0.005, Table 2). Regarding axial damage, occupations that involved prolonged walking/running were associated with a higher mSASSS score (adjusted β=4.4, 95% CI 0.1, 8.7, p=0.04). PsA duration was independently associated with both peripheral and axial joint damage (p<0.001).

Conclusions: High level of occupation-related mechanical stress is associated with increased radiographic peripheral joint damage. These findings support the potential role of micro-trauma in the pathogenesis of PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4074

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**FRI0523 SHORT-TERM EFFICACY AND SAFETY OF NEW BIOLOGICAL AGENTS TARGETING THE IL-6, IL-12/23 AND IL-17 PATHWAYS FOR ACTIVE PSORIATIC ARTHRITIS: A NETWORK META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS**

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Background: IL-6, IL-12/23 and IL-17 inhibitors have been found to be highly effective for both skin and joint manifestations of psoriatic arthritis (PsA). Nonetheless, reliable evidence of the comparative benefits and harms for these interventions is absent for treatment selection in daily practice.

Objectives: To investigate the comparative efficacy, safety and tolerability of IL-6, IL-12/23 or IL-17 inhibitors and the proportion attributable to overall treatment for patients with active PsA.

Methods: Randomized controlled trials (RCTs) evaluating the efficacy, safety and tolerability of IL-6, IL-12/23 or IL-17 inhibitors at weeks 24 were identified by a comprehensive systematic literature review (PROSPERO 2016: CRD42016048166). Quality of evidence was assessed following the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. Treatment effects were evaluated based on the intention-to-treat efficacy rates (ACR20, ACR50, safety parameters (any adverse effect [AE], serious adverse effect [SAE]) and tolerability (discontinuation due to AE [DAE]). Pair-wise meta-analyses and Bayesian network meta-analyses using the random-effects model were performed to estimate pooled odds ratios (ORs) and 95% credible interval (CrI). A subgroup analysis was performed to investigate the effects of prior anti-TNF exposure on the efficacy of ustekinumab and secukinumab.

Results: Six trials were identified which included 2411 participants and 11 treatments. All trials were of generally high quality according to Cochrane compliant rules and GRADEpro assessment. Direct comparisons of each biologic showed that secukinumab (300mg monthly) had the highest efficacy in achieving ACR20 and ACR50, safety parameters (any adverse effect [AE], serious adverse effect [SAE]) and tolerability (discontinuation due to AE [DAE]). Pair-wise meta-analyses and Bayesian network meta-analyses using the random-effects model were performed to estimate pooled odds ratios (ORs) and 95% credible interval (CrI). A subgroup analysis was performed to investigate the effects of prior anti-TNF exposure on the efficacy of ustekinumab and secukinumab.

Conclusions: In conclusion, from the available evidence, secukinumab and ustekinumab were found to be the safest and most efficacious short-term treatments for active PsA amongst all the new biologics targeting the IL-6, IL-12/23 and IL-17 pathways.

Acknowledgements: Thank all colleagues working in the Division of Rheumatology, Department of Medicine and Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1469

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**FRI0524 CAROTID ATHEROSCLEROSIS IS ASSOCIATED WITH COMPROMISED VOLUMETRIC BONE MINERAL DENSITY AND MICROSTRUCTURES IN PATIENTS WITH INFLAMMATORY ARTHRITIS**

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Background: Carotid atherosclerosis is associated with compromised volumetric bone mineral density and microstructures in patients with inflammatory arthritis.

Objectives: The aim of this study was to explore the relationship between volumetric bone mineral density (vBMD)/microstructural features and presence of carotid plaque (CP) in patients with inflammatory arthritis.

Methods: 175 inflammatory arthritis patients (81 [46%] PsA, 94 [54%] RA; 70 [40%] males; age: 53±12 years) were recruited into an ongoing prospective study assessing the relationship between inflammation, osteoporosis and carotid atherosclerosis. Carotid plaque and intima-media thickness (IMT) were measured by carotid ultrasound. Areal BMD (aBMD) was measured by dual energy X-ray absorptiometry (DXA). Microstructure features and vBMD of distal radius were measured using high-resolution peripheral quantitative computed tomography (HR-pQCT).

Results: No patients had established cardiovascular disease (CVD). Data from 172 patients at baseline were analyzed for this cross-sectional study. Patients were sub grouped according to the presence or absence of carotid plaque (CP+ group, n=68 [40%] and CP- group, n=132 [60%]). CP+ group were older (59±10 vs 49±11, p<0.001), more likely to be male (54% vs 31%, p=0.002), had higher systolic blood pressure (130±19 vs 124±17 mmHg, p=0.034) and CVD risk (15.7±14.2 vs 7.9±8.6, p<0.001) according to the Framingham Risk Score (FRS) then the CP- group. aBMD, vBMD and microstructure were significantly compromised in the CP+ group. Distal radius aBMD, distal radius total vBMD, trabecular (Tb) vBMD, Tb thickness, cortical (Ct.) vBMD, Ct. thickness and bone volume fraction were 5% (p=0.004), 12% (p=0.001), 8% (p=0.007), 8% (p=0.004), 4% (p=0.007), 10% (p<0.001) and 8% (p=0.007) lower in the CP+ group. The differences remained significant after adjustment for gender, disease type and FRS (Table 1).

Conclusions: Inflammatory arthritis patients with carotid plaque had lower aBMD, vBMD and compromised bone microstructure in the distal radius even after adjustment for gender, disease type and FRS, suggesting that inflammation may be the common link for both conditions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3094
ASSOCIATION OF DYSMOBILITY SYNDROME WITH FRACTURE RISK IN THE MROS COHORT

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Background: Osteoporosis, obesity and sarcopenia are risk factors for fractures and their combination has a negative effect on musculoskeletal health (MSKH). We proposed a score-based approach to define this combination as “dysmobility syndrome (DS)”. DS increases mortality in the NHANES cohort but no data exist on fracture risk. The most widely used fracture risk calculator, the WHO FRAX® tool, does not incorporate several measures of MSKH such as appendicular lean mass, muscle mass or falls. In this analysis of the Osteoporotic Fractures in Men (MOS) cohort, we examine whether individuals with impaired MSKH/DS have a higher incidence of fragility fractures and whether this composite score confers additional risk for fracture, beyond risk estimates provided by FRAX®.

Methods: The MrOS cohort was utilized in this study. The score-based approach to define DS includes six factors with one point assigned to each: appendicular lean mass/height^2 < 7.26 kg/m^2, body fat > 30%, T-score < -2.5, grip strength < 30 kg, gait speed < 1.0 m/s, and falls in last 12 months. A score ≥ 5 indicated DS. We use odds ratios and cox proportional hazard models to analyze risks of major osteoporotic fracture (MOF). Men were censored at the time of fracture or last follow up. We determined the hazards of fracture using presence of dysmobility syndrome, the FRAX® score, and the FRAX® score in quartiles. We used the program R (www.r-project.org) to perform all analyses.

Results: 5827 men ages 74±6 years with a mean BMI of 27.4±3.8 kg/m^2 had complete data necessary for this analysis, 391 males (6.7%) met criteria for DS. 571 (10%) experienced a MOF including 245 (4%) hip fractures. DS increased the hazards of major osteoporotic fracture, beyond risk estimates provided by FRAX®.

Conclusions: In this analysis of the Osteoporotic Fractures in Men (MOS) cohort, we examine whether individuals with impaired MSKH/DS have a higher incidence of fragility fractures and whether this composite score confers additional risk for fracture, beyond risk estimates provided by FRAX®.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3820

LACUNARITY OF TRABECULAR BONE MICROARCHITECTURE, TBLβ, AS A PREDICTOR OF BONE FRIAGILITY FRACTURE AND POTENTIAL INDEX OF ÖSTEOPOROSIS TREATMENT EFFICACY. THE LOTO STUDY

A. Zaia 1, R. Rossi 2, R. Galeazzi 3, P. Sccondi 3, 1Scientific Direction; 2Medical Imaging and Services, INRCA Italian National Research Center on Aging, Ancona, Italy; 3Rheumatology Division, INRCA Italian National Research Center on Aging, Ferrano, Italy

Background: Bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is still the routinely diagnostic approach for osteoporosis. However, BMD alone is not a good predictor of fracture risk while bone microarchitecture emerges as a determinant of bone fragility independent of BMD. High-resolution magnetic resonance imaging (MRI) represents an effective tool for in vivo characterization of trabecular bone microarchitecture (TBA) by noninvasive/nonionizing methods. Nevertheless, texture analysis is not used in clinical practice because of the large number of parameters to be calculated and analyzed. We previously developed a MRI method to provide one parameter (TBLβ) sensitive to TBA changes in aging and osteoporosis 1. Fractal lacunarity was chosen for TBA texture analysis as it is able to describe bone network discontinuity and sizes of bone marrow spaces, whose changes are index of increased fracture risk.

Methods: An observational, cross-sectional and prospective study on over 50s women at risk for bone fragility fractures was designed to validate the method. Sample size was estimated equal to 280 osteopenic/osteoporotic women with/without prior vertebral bone fragility fractures. The main outcome measure is TBLβ as an index of osteoporotic fracture risk. It is calculated by a software prototype of the gray-scale version of our method on L4 axial images acquired by 1.5T MRI spin-echo multislice technique. Results: A complete set of baseline recording, including DXA-BMD, conventional column Rx morphometry, and lumbar spine MRI-spin echo images for TBA characterization, was obtained for 279 out of 309 subjects eligible for the study. Prevalent VF were found in 31.5% subjects, 47.7% of which defined osteoporotic at lumbar spine by DXA-BMD and 67% younger than 65 years. Baseline results from ROC analysis show that the contribution of TBA degeneration (TBLβ=40) to prevalent fractures is statistically higher (p=0.032) than BMD (T-score=-2.5). TBLβ results (Table 1) show that the proposed method is able to discriminate between antosteoporotic therapy developed cancer (p=0.004). After adjusting for potential confounders, patients with antosteoporotic therapy still had a lower cancer risk (p=0.038; HR: 0.428, 95% CI: 0.192–0.955). The cancer risk also increased among smokers (p=0.002; HR: 10.505; 95% CI: 2.375–46.462).

Table 1. Multivariable cox regression analysis of the hazard ratios for cancer

<table>
<thead>
<tr>
<th>Regression coefficient</th>
<th>SE</th>
<th>P value</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-osteoporosis</td>
<td>-0.848</td>
<td>0.409</td>
<td>0.038</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.693</td>
<td>0.584</td>
<td>0.260</td>
</tr>
<tr>
<td>Age</td>
<td>0.029</td>
<td>0.016</td>
<td>0.071</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.352</td>
<td>0.759</td>
<td>0.002</td>
</tr>
<tr>
<td>lver disease</td>
<td>2.012</td>
<td>0.487</td>
<td>0.001</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>-0.338</td>
<td>1.224</td>
<td>0.783</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.856</td>
<td>0.677</td>
<td>0.206</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>0.771</td>
<td>0.597</td>
<td>0.197</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard rate; SE, standard error.

Conclusions: In this study, anti-osteoporotic therapy decrease cancer risk. So we could safely use these drugs in osteoporotic management.
Successful implementation of a pharmacist-led fracture liaison service (FLS) intervention with the goal to prevent additional fragility fractures (FF) in US veterans. We found a high percentage of FF care goals met when pharmacists were involved, whereas it was lower when no pharmacist was involved. Furthermore, 70% of patients had a bisphosphonate ordered, whereas it was 9% when no pharmacist was involved. We included patient education and applied a treatment protocol to be started by Primary Care. The only difference between hospitals was a dedicated nurse from a FLS intervention. The ideal approach to secondary fracture prevention is a pharmacist-led outpatient FLS model. The current results suggest that pharmacists in the FLS model can very effectively implement a FLS intervention.

**Background:** Worldwide, an osteoporosis (OP) care gap exists for individuals with a fragility fracture (FF). Published data shows that US veterans are no exception. To address the OP care gap, fracture liaison services (FLS) are being implemented with the goal to prevent additional FF.

**Objectives:** Here we report the patient outcomes after initiating a FLS at a US Veterans Affairs (VA) hospital.

**Methods:** We identified veterans with a pelvic, hip, and/or femur shaft fracture by querying a central database. Veterans with traumatic fractures, active OP medication, recent dual-energy X-ray absorptiometry (DXA) and/or hospice status were excluded. The remaining veterans were contacted via letter and the responsible primary health care team was sent a template letter with OP management recommendations via the electronic medical record. Recommendations included DXA, laboratory evaluation, and pharmacologic and non-pharmacologic interventions. In most cases, trained clinical pharmacists serving as FLS coordinators performed all tasks with an expert physician available for questions. Presented data are based on a review 4 months after recommendations were sent.

**Results:** The initial query revealed 149 veterans with pelvic, femoral, and/or hip fractures without a recent DXA and/or active OP therapy. Of those, 32 (31 males, 1 female) patients suffered a FF and were included in the FLS intervention. Our study suggests that a pharmacist-led FLS improves post-FF care in US veterans. We found a high percentage of OP care goals met when patients interacted with clinical pharmacists. This observation might be due to the fact that most pharmacists had dedicated training in OP management and their interaction with the patient focused on their FF. In summary, our data suggests that clinical pharmacists trained in OP management can very effectively implement a FLS intervention.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2793
DUAL ENERGY X-RAY ABSORPTIOMETRY TESTING IN DUAL ENERGY X-RAY ABSORPTIOMETRY TESTING INCIDENCE AND RISK FACTORS OF OSTEOPOROTIC FRACTURE

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Background: Estrogen receptor positive breast cancer is commonly treated with aromatase inhibitors (AI). A well-known adverse effect of this therapy is osteoporosis and related bone fractures. National guidelines have promoted the use of dual energy X-ray absorptiometry (DXA) for screening purposes.

Objectives: To evaluate the association between use of DXA among women with breast cancer treated with AI enrolled in Medicare, and subsequent fracture risk.

Methods: Retrospective cohort study using the Texas Cancer Registry (TCR) and the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) data linked with Medicare claims. To help estimate the likelihood of performing a DXA, a multivariable logistic regression model was used. Covariates of age, ethnicity, stage, residence area, and socioeconomic variables were controlled for the analyses. The outcome variable a DXA claim within 12 months after the initiation of the AI therapy. Cox regression model to evaluate time to first fracture after initiation of AI.

Results: The total number of cases within the SEER-Medicare database was 15,350 and in the TCR 4,532. Women aged between 66–74 years and Non-Hispanic white were more likely to get DXA than were Hispanic and Non-Hispanic Black.

In TCR, 2714 patients did not get treatment for osteoporosis in the first 12 months after AI therapy initiation. 2989 patients did not receive treatment for osteoporosis within 12 months of obtaining their first DXA scan. 1330 patients who did not undergo DXA were not treated for osteoporosis; and 1384 patients who underwent DXA got treated for osteoporosis. The duration of AI treatment was negatively associated with the risk of fracture. Women who received DXA scan showed 11% lower risk of fracture than those who were not scanned (HR 0.89 [0.83, 0.94]).

Conclusions: National guidelines suggest to obtain a DXA and start bisphosphonate therapy in female breast cancer patients who are treated with AI therapy. Our data suggests that the majority of women in the TCR and SEER database were not treated for osteoporosis within the first 12 months after initiation of AI therapy. Women who received DXA scan showed a lower risk of fracture than those who were not scanned.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2305
medication use for RA and osteoporosis, and then evaluated the incidence and risk factors for osteoporotic fracture.

**Results:**
The mean age of RA patients was 61.7±11.9 years, and 426 patients were female (88.9%) with 353 postmenopausal women (82.9%). The BMD score of L-spine in RA patients was significantly lower than that in healthy control (2.21±1.41 vs. 2.95±2.11, p<0.001). Osteoporotic fracture was detected in 81 (16.9%) patients with RA. In RA patients, 226 (47.2%) patients met the FRAX criteria for high risk of osteoporotic fracture, and 240 (50.1%) patients satisfied the WHO criteria. The result of the FRAX criteria was affected by the female sex, menopause, smoking, drinking, higher dose of glucocorticoid (<5mg/day), vitamin D use, calcium use and proton pump inhibitor (PPI) use (p<0.05). In multiple linear analysis, the FRAX score to 10-year probability of ≥3% of hip fracture was associated with age (β=0.384, p<0.001), body weight (β=-0.110, p=0.038), erythrocyte sedimentation rate level (β=-0.125, p=0.010), glucocorticoid dose (β=-0.123, p=0.010) and PPI use (β=-0.123, p=0.010). The proportion of patients with high risk of osteoporotic fracture was 47.2% in the FRAX model and 50.1% in the WHO model. Age, female sex, lower BMI, higher risk factors for FRAX criteria were age (OR 1.160, p=0.001), female sex (OR 3.942, p=0.010), body mass index (BMI) (OR 0.889, p=0.001), glucocorticoid dose (OR 1.167, p=0.025) and PPI use (OR 2.552, p=0.019), and those for WHO criteria were age (OR 1.021, p=0.040), glucocorticoid dose (OR 1.109, p=0.046) and smoking (OR 2.924, p=0.031).

**Conclusions:**
Osteoporotic fractures were found in 16.9% of RA patients. The proportion of patients with high risk of osteoporotic fracture was 47.2% in the FRAX model and 50.1% in the WHO model. Age, female sex, lower BMI, higher dose of glucocorticoid, PPI use and smoking were independent risk factors for osteoporotic fracture in RA patients.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4580

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**FR10534**

**REPEATED OSTEOPOROSIS SCREENING IN RHEUMATOID ARTHRITIS: ARE WE COMPLYING WITH GUIDELINES?**

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**Background:**
Osteoporosis rates are higher in patients with rheumatoid arthritis (RA). Patients with RA diagnosed with osteoporosis have a 30% increased risk of major fracture [1]. Monitoring response to osteoporosis treatment is recommended however there is no consensus on how frequently this should be performed. The International Society for Clinical Densitometry (ISCD), National Osteoporosis Foundation (NOF) and the American Association of Clinical Endocrinologists (AACE) all recommend repeat Bone Mineral Density (BMD) assessment within two years after initiating osteoporosis treatment to assess response to treatment [2-4]. Furthermore, the NOF and AACE recommend repeat screening every two years after diagnosis [3,4].

**Objectives:**
To identify patients with RA and osteoporosis
To identify if international guidelines are being achieved for reassessment of BMD within two years of treatment commencement in keeping with international guidelines.

**Methods:**
A database of patients with a diagnosis of RA and osteoporosis who attend the Rheumatology department of the Midlands Regional Hospital, Tullamore since January 2013 was reviewed. Outpatient summaries, date of treatment are not being identified in a timely manner and therefore are at an increased risk of fractures. The results of this audit will make us more vigilant to identify those patients who are treated for osteoporosis that need repeat DEXA screening to ensure that treatment is efficacious.

**Results:**
Ninety-one female patients aged 13–45 years old were evaluated, baseline weight 39.4±5.6 kg and BMI 15.1±1.6 kg/m². Weight and BMI were significantly increased in all patients after treatment. The mean BMD values were significantly increased only at the spine (1.0±3.6%, p<0.009). A positive trend was demonstrated between post-treatment 25-OH-D and BMD changes at the spine (p=0.032). However, only the patients with post-treatment 25-OH-D ≥30 ng/ml showed significantly higher increases in BMD at the spine (2.5% vs 0.5% respectively for 25-OH-D ≥30 ng/ml and 25-OH-D <30 ng/ml, p<0.03; Figure 1). Both P1NP and PTH increased, whereas a significant decrease was found in 25-OH-D and CTX (p<0.05). Post-treatment CTX levels were inversely correlated with spine BMD. A positive relationship was found between changes in weight and P1NP (R²=0.27).

**Conclusions:**
In anorexia nervosa, a hypovitaminosis D status counteracts the efficacy of the weight restoration treatment because of an increase in bone resorption mediated by a secondary hyperparathyroidism. Our study strongly support the use of vitamin D supplements for bone health in anorexia nervosa.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4580

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**FR10536**

**THE METHOD OF CALCULATING THE PROBABLE VALUE OF T-SCORE IN PATIENTS WITH MULTIFOCAL ATEROCALCIFICATION**

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**Objectives:**
To determine probable value of T-score for early detection of osteoporotic syndrome in patients with multifocal atherosclerosis based on the multislice computed tomography (MSCT) evaluation of vascular calcification.

**Methods:**
186 male (60±6.7 years) with multifocal atherosclerosis. All the patients underwent the measurement of BMD with X-ray absorptiometry. Moreover, bone density (BMD) and bone turnover markers of osteoporosis (CS) of coronary and brachiocephalic arteries were obtained using Agatston method.

**Results:**
T-score values of lumbar vertebrae -1.07 [-1.54; 0.40], T-score of the proximal femur -2.01 [2.71; -1.49]. Calcification of the coronary arteries: CS=471.8 [118.2; 916.8], and carotid arteries: CS=113.9 [44.5; 309.8]. Factors that affect the
probable value of T-score in patients with known rates of calcification of the coronary and carotid arteries were obtained by regression analysis. These factors were equivalent density of coronary calcinosis (p=0.0046), the volume of the carotid calcifications (p=0.0039), the mass of calcifications of the carotid arteries (p=0.0054) and the presence of a stenosis of the carotid arteries (p=0.0001). The predictive models for estimating the probability value of T-score has been developed using regression coefficients of each of the factors. The value is equal to the Fisher statistic F=9.52, p-value <0.000001, multiple correlation model’s coefficient is 0.753.

Conclusions: The results of this study indicate that rates of calcification of the carotid and coronary arteries, resulting in the plotted survey on MSCT patients with multifocal atherosclerosis have a high predictive capacity for assessing the probable value of the T-score and early detection of osteopenic syndrome in these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5654

FRIO537 PREVENTION STRATEGY OF OSTEOPOROTIC FRACTURES IN PORTUGAL: AN ANALYSES ON A COHORT OF HIP FRACTURED PATIENTS

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Background: Despite the fact that Portugal has one of the lowest rates of hip fractures in Western Europe, more than 10,000 patients are admitted every year to the Portuguese Health Service due to hip fragility fractures. The burden of the problem will tend to increase in coming years, unless effective preventive measures are put in place.1

Objectives: The aim of our work was to evaluate the percentage of patients under osteoporotic treatment (OT) before and after a hip fracture (HF) and compare this result with the percentage of patients who should be under treatment according to FRAX model and Portuguese cost-effectiveness guidelines (PG) for OT.1

Methods: Patients diagnosed with a HF, between May 1st and October 31st 2013, from a single tertiary hospital, were included in this transversal study. Patients or their primary caregiver were contacted by phone to gather data regarding demographic and clinical features, including risk factors for Osteoporosis (OP) defined by FRAX®. Clinical data was obtained from medical files. FRAX® without mineral bone density was used to calculate the 10 year fracture risk. For each patient the FRAX® was scored according to data available the day before the present HF (ie the current fracture was not considered as a previous fracture for the purpose of risk prediction). Thresholds for therapeutic intervention were defined according to PG: a 10-year probability of a major osteoporotic fracture (OF) ≥11% and/or a 10 year probability of HF <3%.1

Results: The mean age of the population (n=130) was 81.6±8.6 years, and 69.2% were female. Before the current HF, only 23 (17.7%) of the patients had been prescribed some form of medication for OP: bisphosphonates (n=2), strontium ranelate (n=3) and calcium + vitamin D supplementation (n=13); the other patients were not taking any medication. After hospitalization, all 30 patients had a previous fracture, of which 8 patients had ≥1 fragility fracture of the hip; 6 had ≥1 symptomatic vertebral fragility fracture and 16 had ≥2 fragility fractures, independently of the site of the fracture. According to PG, all the 30 (26%) patients should be under OT without the need for FRAX® risk calculation. The mean 10-year major OF probability was 21.2±14% and the mean 10-year HF probability was 13.7±12.9%. According to FRAX®, 104 (80%) of the patients had indication to start OT based on the 10-year risk of major OF and 117 (90%) based on the 10-year risk of HF.

After hospitalization, although all the patients had formal indication for treatment, only 11 (8.5%) patients had received a prescription for OT up to one year after the fracture event.

Conclusions: Similar to other countries, the percentage of patients under OT (before and after HF) in Portugal is extremely low. Risk estimation by FRAX® and application of current PG would allow physicians to identify these patients and introduce appropriate preventive measures. Continued efforts are needed to promote timely prevention, most especially after the first fragility fracture.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3277

FRIO538 EVALUATION OF FACTORS THAT INCREASE FRACTURE RISK IN BREAST CANCER

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Background: Women with breast cancer are at an increased risk of fractures. This is in patients with both active and treated disease. In addition to established risk factors of fractures, patients with breast cancer are exposed to additional factors that further compromise bone strength. These factors primarily include: the malignancy interfering with bone metabolism and breast cancer treatments inducing bone loss.

Objectives: To evaluate fracture risk in active and treated breast cancer patients, and to understand the role bone mineral density (BMD) plays in predicting fracture risk.

Methods: The study population included breast cancer patients with active and treated disease referred to dual-energy X-ray absorptiometry (DEXA) scanning at the Royal Lancaster Infirmary between 2004–2015. Patients on aromatase inhibitors were excluded because of its negative effect on osteostrogen. From this population, we collected BMD measurements of the femur and lumbar vertebra. Alongside information on physical characteristics such as age, height, weight, body mass index (BMI), average tissue thickness, lean and fat mass were measured.

To evaluate other precipitating factors known to increase fracture risk we included: smoking status, steroids use, alcohol, family history of fractures, diagnosis of rheumatoid arthritis and secondary osteoporosis.

Data analysis was done on R 3.3.2 software. Odds ratios were calculated using logistic regression and age adjusted models were compared using the likelihood ratio test. Categorical data was analysed using Chi squared and Fischer’s exact test, while continuous data was analyzed using t-test.

Results: The study population was a total of 306 patients with a mean age of 63.6 years. 146 of the study group had active disease, while 160 patient were breast cancer survivors. Of the total population 87 (28%) had sustained at least one fracture.

Active breast cancer insignificantly increased fracture risk in comparison to the cancer survivor population (OR=1.330, 95% CI=0.801–2.218, p=0.271).

Physical characteristics that significantly increased fracture risk included increased age and decreased average fat percentage (Table 1). BMD reduction in the femoral neck and all vertebrae significantly increased odds of having a fracture (Table 2).

External factors such as smoking status, alcohol consumption, family history and steroid use had no significant effect.

Table 1. Physical Characteristics and Fracture Risk

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.407</td>
<td>1.196–1.803</td>
<td>0.047</td>
</tr>
<tr>
<td>BMI</td>
<td>0.832</td>
<td>0.693–1.074</td>
<td>0.159</td>
</tr>
<tr>
<td>Average Tissue Thickness</td>
<td>0.929</td>
<td>0.847–1.016</td>
<td>0.108</td>
</tr>
<tr>
<td>Average Fat Percentage</td>
<td>0.069</td>
<td>0.005–0.883</td>
<td>0.040</td>
</tr>
<tr>
<td>Fat Mass</td>
<td>0.997</td>
<td>0.994–0.999</td>
<td></td>
</tr>
<tr>
<td>Lean Mass</td>
<td>1.003</td>
<td>1.000–1.006</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Table 2. BMD Results from DEXA Scan

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Neck of Femur</td>
<td>0.035</td>
<td>0.035–0.309</td>
<td>0.002</td>
</tr>
<tr>
<td>Right Neck of Femur</td>
<td>0.063</td>
<td>0.060–0.755</td>
<td>0.013</td>
</tr>
<tr>
<td>Lumber Vertebra Total (L1–4)</td>
<td>0.063</td>
<td>0.013–0.285</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Conclusions: In conclusion, this study emphasizes DEXA measurements are the best predictive tool for fractures in breast cancer patients. Thus further supporting the need for increased BMD surveillance for those diagnosed with breast cancer who are not on aromatase inhibitors.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3829

FRIO539 IMPACT OF THE IMPLEMENTATION OF A FRACTURE LIASON SERVICE IN PHARMACEUTICAL EXPENSES FOR OSTEOPOROSIS

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Background: In 2012 a Fracture Liaison Service (FLS) was implemented in Hospital Dr Negrin

Objectives: To analyze the economic impact of the FLS on pharmaceutical expenditure for osteoporosis.

Methods: Expenditure on osteoporosis medication (government input) was collected from January 1th, 2011 to October 1th, 2016. The data distinguish group I (calcium and vitamin D), group II (Bisphosphonates, denosumab, SERM, SeIF), strontium and teriparatide) and total expenditure (sum of groups I and II). Intravenous bisphosphonates were not included. Gran Canaria island is organized in two health areas; the North and the South areas. The population aged ≥ 65 years in the North and South areas in 2016 were
EVALUATION OF BONE QUALITY USING THE NEW PREVALENCE OF VERTEBRAL BODY DEFORMITIES RELATED TO TREATMENT IN POSTMENOPAUSAL PATIENTS

A. Casabella 1, A. Sulli 1, C. Seriolo 2, G. Botticella 2, L. Molfetta 2, M. Cutolo 1, AOU San Martino; 2Osteoporosis, Bone and Joint Disease Research Center

681 patients (17%) of the 3,917 who receive a drug from group II in the North area were under treatment at 12 and 24 months (1). The estimate is that approximately 75% have indication of bisphosphonate or equivalents. The average adherence for drugs in the January-September 2016 period was similar in both areas (2% in the North area and 2.873 units in the South area. That is, the prescription of group II drugs in the January-September 2016 period was similar in both areas (2% higher in the South area), while for group II it was 36% higher in the North area, being this difference stable between 2011 and 2016.

Between 2012 and 2016, 1,297 patients have been evaluated in the FLS, of which 75% have indication of bisphosphonate or equivalents. The average adherence to treatment at 12 and 24 months is 70% (1). The estimate is that approximately 681 patients (17%) of the 3,917 who receive a drug from group II in the North area in October 2016 derive from the FLS.

Conclusions: The implantation of a FLS, despite surrounding around 16% of the percentage of patients treated with bisphosphonates and equivalents in the health area, Gran Canaria North, does not seem to lead to an increase in pharmaceutical expenditure for osteoporosis. We believe that one of the reasons for the non-increase in spending is the rational use of drugs for osteoporosis.

Disclosure of Interest: None declared


FR0540 EVALUATION OF BONE QUALITY USING THE NEW TRABECULAR BONE SCORE (TBS) TOOL IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Patients affected by Rheumatoid Arthritis (RA) show an increased risk of low bone mass, as a result of multi-systemic disorders including toxic drug, low vitamin D levels and physical inactivity. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) images, that provides an indirect measurement (Score) of bone axial microarchitecture and allows to get information about bone quality (1,2).

Objectives: The aim of this investigation was to evaluate bone quality in RA patients (high risk population) receiving vitamin D supplementation from at least 6 months. The patients were divided into two groups; patients treated with bisphosphonates and equivalents (group I) and non treated (group II).

Methods: 108 female patients (mean age 61±8 years helped by RA and 60 age-matched controls (CNT) (mean age 64±11 years) were enrolled. Bone Mineral Density (BMD, g/cm2) of the lumbar spine (L1-L4) was analyzed using a DXA scan (GE, Lunar Prodigy). Lumbar spine TBS (Nlsight Medimaps) was derived for each spine DXA examination. All patients were evaluated for serum 25 hydroxyvitamin D (25(OH)D) concentrations.

Results: 78 RA patients (80%) presented a bone loss that was significantly lower when compared with control group (p<0.001). Likewise, lumbar spine TBS score was found significantly lower in RA patients compared with CNT (p<0.001).

Finally, RA patients showed lower 25(OH)D concentrations (18.4±1.3 ng/ml) than CNT (26.2±0.9 ng/ml; p<0.04).

Conclusions: This study shows in RA patients a reduction of TBS values that seem placed side by side with reduced BMD values and 25(OH)D serum concentrations. Therefore, TBS could become a new and safe diagnostic tool for the quantification of the bone quality and related osteoporosis, in chronic systemic inflammatory rheumatic diseases, such as RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6126

FR0541 RELATIONSHIP BETWEEN CHRONIC PERIODONTITIS AND BONE MINERAL DENSITY IN A CASE-CONTROL STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS AND NON-INFLAMMATORY JOINT DISEASE

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1Odontology/Periodontology, Dental Clinic Dr Garnier, Santa Cruz de Tenerife; 2Periodontology, UCM, Madrid; 3Nuclear Medicine Department; 4Rheumatology, Hospital Universitario Canarias, Tenerife, Spain

Background: The association between two chronic inflammatory diseases such as rheumatoid arthritis (RA) and periodontitis (PD) may be explained by causal and noncausal pathways. A possible mechanism in the increased PD observed in patients with RA is systemic bone loss due to the inflammatory process itself among others factors. Several studies have reported associations between OP and PD not confirmed in other studies.

Objectives: 1.To determine whether OP is associated with PD and with PD severity.

Methods: Observational cross-sectional, case-control study of RA patients ≥18 yo. meeting ACR/EULAR 2010 criteria for RA in a Rheumatology Dept. and a group with a non-inflamatory joint disease, with at least 4 teeth, without dental prophylaxis or antibiotic intake 6 months before. Socio-demographic and anthropometric variables with smoking status, Graffar scale, stress level, annual dental prophylaxis, and co-morbidities such as diabetes mellitus (DM), dyslipidemia (DS), ischemic cardiovascular disease (ICD) and history of low impact fractures. Dual-energy x-ray absorptiometry (DXA) (g/cm2) was performed with a DXA LUNAR (GE HealthCare) in lumbar spine and femoral neck. Periodontal Variables included plaque index, bleeding on probing, probing pocket depth, recession, clinical attachment level (CAL). Full mouth CAL and periapical x-rays were taken. CAL was classified according to the European Workshop in 2005 (Tonetti), into level 0 (absence), TL1 (mild), TL2 (severe). Statistical Analysis: t-student test, Kruskal Wallis, Chi-square with Stata 13.1.

Results: We studied 344 patients: 187 RA (147 F/40 M) and 157control (101F/56M). Both groups were comparable in age 54.9 (17.9) yo., body mass index 27.8 (4.6), stress level, DM and ICD. Differences in gender (n=0.018) of males in controls, socioeconomic status (lower level in RA), n=0. of current and former smokers RA (19.2%vs 8.9%24.6%vs 11.5%), OP (23.4% RA vs 7.8%), DS (hperglycemia 11.2% RA vs 4.4%). PD was found in 97.3% of RA patients vs 66.2% of controls. DXA was performed in 303 patients: 163 RA/140 controls that showed OP in 38 (23.3%) and 13 (9.3%) of RA and control groups as well as osteopenia in 47 (32.4%) and 16 (11.3%) respectively (p<0.001); 81% of these patients presented PD. There was association between PD and OP/osteopenia, so patients with PD had greater abnormal BMD 88% vs 76.3% with normal BMD; patients without PD showed greater normal BMD with statistically significant difference (23.7% vs 11.1%) (p=0.008).

Conclusions: 1. PD was observed in 81% of the patients evaluated with BMD, of these, 89% and OP/osteopenia, and among the patients without PD a significant normal BMD predominated. 2. PD was found in 97% of RA patients versus 66% of controls; similarly OP was present in 23.3% of RA patients versus 9.3% of controls, with the difference being significant. 3. There was no association between BMD and PD severity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5485

FR0542 PREVALENCE OF VERTEBRAL BODY DEFORMITIES RELATED TO OSTEOPEOROSIS IN PATIENTS WITH NON-TRAUMATIC LUMBAR OR DORSAL ACUTE PAIN

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Background: Presence of vertebral body deformities is considered a relevant issue in order to choose a particular treatment in patients with osteoporosis. However, only remarkable deformities are properly identified and registered while the remainder, usually, striking can just be unnoticed in radiological studies not related to osteoporosis studies. One of the most usual radiographic study of the axial skeleton is the lumbar and dorsal acute pain. This group of patients is, indeed, suitable to establish proportions of any grade of vertebral body deformities as a result of multi-systemic disorders including toxic drug, low vitamin D levels and physical inactivity. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) images, that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality (1,2).

Objectives: The goal of present study is to determine prevalence of vertebral body deformities in postmenopausal patients radiologically assessed due to lumbar or dorsal non traumatic related pain.

Methods: We performed a simple randomization of the registers of female patients with 65 years old or more who consulted due to dorsal or lumbar pain under treatment in septiembre 2016 was calculated.

References:
non-traumatic acute pain. Between 2014 and 2015, all included registries must have had a radiological assessment. The gathering of registries concluded after reach 120% of the estimated sample size for a non finite theoretical population, a precision of 3% and a hypothetical estimated prevalence of 7% based on local previous studies of prevalence of vertebral osteoporotic fractures. Vertebral body measurement criteria were performed according to González et al recommendations from D7 to L5 as far as possible according to the field of study of the radiological chart plate.

**Results:** 275 randomized registries of dorsal and lumbar pain were included (total=550). Among patients with dorsal pain we identified 62 (22.5%), 30 (10.9%) and 16 (6.5%) vertebral deformities grade I, II and III respectively. Among patients with lumbar pain we identified 31 (11.2%), 49 (17.8%) and 33 (12%) vertebral deformities grade I, II and III respectively. Prevalence of any grade of dorsal vertebral deformity was 40.00% (CI 34.39 – 45.89) and lumbar was 41.09% (CI 35.44 – 46.99). The vertebral body deformity grade I and II summed 70.7% while dorsal grade I and II summed 83.6%. From the 93 vertebral body deformities grade I, 6.4% were recognized in their clinical histories, 20.2% of the grade II deformities and 92.1% of the grade III deformities. (P<0.001).

**Conclusions:** Although our population sample is circumscribed to symptomatic patients, our results contribute with prevalence of vertebral body deformities in postmenopausal patients grade I and II and who were mostly unnoticed. Proper identification of vertebral body deformities in patients with osteoporosis is crucial to decide treatment strategies in patients with known osteoporosis. Due to that, prevalence studies of this kind are relevant and useful to avoid diagnostic mistakes.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5605

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### FR0543 WHICH FACTORS CAN HELP PREDICT FRACTURE RATES IN PATIENTS DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE? A CASE-CONTROL STUDY

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**Background:** Inflammatory Bowel Disease (IBD) is a known risk factor for developing low bone mineral density (BMD) osteoporosis, due to malabsorption and treatment with steroids. These patients are more susceptible to fragility fractures. Though the percentage of such fractures is low, they can be associated with impaired mortality and morbidity. The difficulty lies in early detection of patients at an increased risk of fractures. Currently the diagnosis of osteoporosis and prediction of fracture risk are calculated assessing patient BMD on dual energy X-ray absorptiometry (DEXA). However, previous studies suggest that despite a decreasing BMD being significantly associated with an increased risk of fracture, its measurement alone is fairly restricted in predicting them; other patient factors must also be brought into consideration (1).

**Objectives:** To identify specific factors which may assist in the prediction of fracture rates in a cohort of patients diagnosed with IBD.

**Methods:** Patients referred to a DEXA scan in the North West of England were identified and those with a referral reason of IBD were studied. Factors measured at BMD scanning include patient age, height, weight and femoral head bmd, BMD, smoking history, alcohol use, family history of fractures, steroid exposure, rheumatoid arthritis and secondary osteoporosis. Patients were then grouped into cases and controls after adjusting for age and gender. They were then analysed using T tests for continuous variables and Chi squared tests for categorical variables. Univariate and multivariate logistic regression models were then used to identify factors predicting fractures.

**Results:** 938 patients were identified of which 721 (76.9%) were female with an average age of 58 as compared to an average age of 53 in men. 274 patients (29%) had fractures of which 238 were females (87%), at an average age of 63 compared to 60 in men. Men were shown to have a greater risk of fractures. Results of the univariate analysis are shown below.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>All Pts Pts with Fracture Pts without Fracture P-value</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at scan</td>
<td>56.8 vs 62.5</td>
<td>0.01</td>
<td>1.01–1.03</td>
</tr>
<tr>
<td>Height</td>
<td>163.7 vs 161.2</td>
<td>0.21</td>
<td>0.96–1.01</td>
</tr>
<tr>
<td>Weight</td>
<td>71.6 vs 70.0</td>
<td>0.63</td>
<td>0.99–0.99</td>
</tr>
<tr>
<td>Alcohol</td>
<td>52 vs 36</td>
<td>0.24</td>
<td>0.48–0.77</td>
</tr>
<tr>
<td>Smoking</td>
<td>137 vs 109</td>
<td>0.69</td>
<td>1.06–1.79</td>
</tr>
<tr>
<td>Family History</td>
<td>169 vs 53</td>
<td>0.34</td>
<td>1.19–3.75</td>
</tr>
<tr>
<td>RA</td>
<td>49 vs 20</td>
<td>0.20</td>
<td>0.49–0.81</td>
</tr>
<tr>
<td>Secondary op</td>
<td>108 vs 40</td>
<td>0.93</td>
<td>1.02–1.56</td>
</tr>
<tr>
<td>Left Femoral Neck BMD</td>
<td>0.87 vs 0.82</td>
<td>0.00</td>
<td>0.11–0.31</td>
</tr>
<tr>
<td>Right Femoral Neck BMD</td>
<td>0.92 vs 0.86</td>
<td>0.00</td>
<td>0.19–0.62</td>
</tr>
<tr>
<td>Lumbar Spine BMD</td>
<td>1.22 vs 1.01</td>
<td>0.10</td>
<td>0.10–0.54</td>
</tr>
<tr>
<td>BMI</td>
<td>28.7 vs 26.8</td>
<td>0.99</td>
<td>0.97–1.03</td>
</tr>
<tr>
<td>Steroid</td>
<td>617 vs 134</td>
<td>0.49</td>
<td>0.36–0.67</td>
</tr>
</tbody>
</table>

In the multivariate analysis, statistically significant variables were BMI (OR 1.05, 95% CI 1.01–1.09), 1.09 (range: 14.7–40.6), median time of HIV infection was 162.6 months (interquartile range [IQR]: 77.7–283.3), median CD4+ cells nadir was 224 (IQR: 100–332) and steroids being protective.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5625

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### FR0545 COMPARISON OF MINERAL BONE DENSITY IN HIV-INFECTED PATIENTS FOLLOWED IN A SPANISH TERTIARY HOSPITAL WITH THAT OF NON HIV-INFECTED SPANISH POPULATION

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**Background:** Patients with human immunodeficiency virus (HIV) have a higher prevalence of low bone mineral density (BMD) and fractures than the general population, but there are no comparative studies in Spanish population.

**Objectives:** To assess the BMD in HIV-infected patients followed in a tertiary hospital of Madrid and compare it with the ESOSVAL cohort, which included 11035 patients and is representative of non-HIV population seen in Spanish tertiary centers.

**Methods:** We performed a cross-sectional study in which BMD values were determined in a prospective cohort that included HIV-infected patients seen in our center during the period 2010–2015. Collected data included demography, comorbidities, treatment and densitometric variables.

**Results:** 93 patients from a total of 924 with BMD data were eligible for the study after discarding those younger than 55 years, because that group is not included in the ESOSVAL cohort. Mean age of patients of our whole cohort was 53 years (range: 17–83), 117 (74.4%) were women older than 55 years, of whom 83 were men (83%). Most of them were Caucasians, with a mean body mass index 24.1 (range: 14.7–40.6). Median time of HIV infection was 162.6 months (interquartile range [IQR]: 77.7–283.3), median CD4+ cells nadir was 224 (IQR: 100–332) and median maximum viral load was 4.9 log (IQR: 4.3–5.4); concomitant hepatitis C
virology infection was present in 29%. 25% were treated with tenofovir plus protease inhibitors, and 47% with tenofovir plus a non-nucleoside reverse transcriptase inhibitor. The mean value of BMD in lumbar spine (LS) was 0.93 g/cm² (range: 0.84–1.02) and in femoral neck (FN) 0.78 g/cm² (range: 0.69–0.86). For the comparison with the ESOSVAL cohort the worst value of T-score in either LS or FN was chosen and the WHO definitions (osteoporosis ≤ -2.5, osteopenia -1.0 to -2.5); the results are presented in the table. Only the data for the 50-64 and 65-74 years groups were compared because the number of older HIV patients in our center was small. Significant differences were found between the categories of osteoporosis in men in the 65–74 years old group, and that of osteopenia in women in the 55–64 years old group.

**Conclusions:** We observed a statistically significant increase in prevalence of osteoporosis in women in the 65–74 years group, and in osteopenia HIV-infected men in the 55–64 years group, in accordance with the presumed greater risk derived from a variety of causes (treatment, chronic inflammatory status, comorbidities, etc.). A non significant trend towards an increased prevalence of osteoporosis in the 55–64 years group, and in osteopenia in the 65–74 years group was seen. As for women, there was a statistically significant increase in osteopenia prevalence in the 55–64 years group with HIV and a non significant trend towards increased prevalence of osteoporosis in that age group, whereas no significant increase was observed in the 65–74 years HIV group, presumably due to the small number of patients included in it.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6877

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### FR0547

**OSTEOPOROSIS AND BONE METABOLISM IN SYSTEMIC SCLEROSIS**

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**Background:** Systemic sclerosis (SSc) has been associated with bone loss and increased risk for bone fractures. Disease-related factors, age, corticosteroid therapy may be associated with bone loss. More recently, it has been shown to be associated with disease duration, anti-Scl70, and anti-centromere antibodies.

**Objectives:** Here we performed a detailed study on osteoporosis in SSc. We performed bone density assessment by DXA, as well as percutaneous peripheral quantitative CT (pQCT). In addition, we assessed bone biomarkers and correlated bone density and disease-associated measures.

**Methods:** Altogether 44 SSc patients (36 women, 8 men; age: 64.1 years; disease duration: 17.6 years) were randomly recruited for the study. Bone density was assessed by DXA at the lumbar spine and femoral neck. pQCT (Stratec) was able to assess total, trabecular and cortical density. We also determined FRAX, levels of vitamin D, as well as bone markers (Ca, PTH, osteoclast, P1NP, beta-CTX), markers of autoimmunity (ANA, ACA and anti-Scl70) and clinical manifestations of the disease. Statistical analysis was performed by SPSS v2.0.

**Results:** Vitamin D levels were lower (53.9 +/- 36.8 nm) than the normal range (75–100 nm). 34 out of 44 patients (77%) had D-hypovitaminosis. Abnormally increased PTH, P1NP, OC, CTX levels were observed in 10, 7, 2 and 6 patients, respectively. Previous fractures occurred in 19 patients (43%). The vertebral and hip FRAX values were 13.5% and 4%, respectively. By DXA, osteoporosis of the lumbar spine and hip was detected in 10 and 10 patients, while osteopenia was found in 16 and 20 patients, respectively. With respect to pQCT, total and trabecular bone density in SSc patients (248.4 ± 150.9 mg/cm³) was significantly lower than in healthy controls (354 ± 193 mg/cm³, respectively). Higher OC levels were associated with the diffuse form of SSc (R=0.330, p=0.035). Longer disease duration correlated with lower pQCT total (R=–0.341, p=0.023) and trabecular density (R=–0.336, p=0.026). Interestingly, most bone markers (P1NP, OC, CTX) positively correlated with gastrointestinal manifestations. Furthermore, pQCT total bone density was significantly lower in patients with pulmonary hypertension, digital ulcers and DM.

**Conclusions:** A high proportion of SSc patients have osteoporosis or osteopenia, as well as low vitamin D levels. As determined by pQCT, trabecular loss is more common. Both total and trabecular bone loss, as well as bone markers may be associated with disease duration, anti-Scl70 and some organ manifestations. SSc patients should be screened and treated for osteoporosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3645

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### FR0548

**INFLUENCE OF HOMOCYSTINE AND VERTEbral FRACTURES ON PREVALENT ABDOMINAL AORTIC CALCIFICATION IN POSTMENOPAUSAL WOMEN: A MULTICENTRIC CROSS-SECTIONAL STUDY**

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**Background:** Osteoporosis and cardiovascular diseases are two major public health problems. Both are associated with high morbidity, long-term hospitalization, mortality and loss of independence leading to institutionalization. Vertebroplasty using dual-energy X-ray absorptiometry (DXA) also known as vertebral fracture assessment (VFA) is a fast, minimally invasive technique which produces images that are of sufficient quality to be used to diagnose the presence of vertebral deformity consistent with fracture. VFA has demonstrated utility for vertebral visualization and thus is an important tool for fracture detection in women and men. It has been shown also in many populations that this technique can simultaneously identify abdominal aortic calcification (AAC). Hyperhomocysteinemia, a condition that recent epidemiological studies have shown to be associated with increased risk of vascular disease. A potential role of homocysteine in bone fragility has been considered from the observation of a high prevalence of osteoporosis in subjects with homocystinuria.

**Objectives:** The present study aims to investigate the influences of homocystine and vertebral fractures on prevalent abdominal aortic calcification in postmenopausal women.

**Materials and Methods:** A total of 3645 postmenopausal women (50–64 years) were randomly recruited for this study.

**Results:** The prevalence of vertebral fractures was 13.5%. The prevalence of homocystine was 7.5%. The prevalence of AAA was 10.7%. The prevalence of homocystine and vertebral fractures was 10.4%. The prevalence of AAA and vertebral fractures was 9.3%. The prevalence of AAA and homocystine was 7.5%. The prevalence of AAA, homocystine and vertebral fractures was 7.2%.

**Conclusions:** Homocystine and vertebral fractures are associated with prevalent abdominal aortic calcification in postmenopausal women. This study highlights the importance of screening for homocystine and vertebral fractures in postmenopausal women to prevent abdominal aortic calcification.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3645
Objectives: The main of this study was to examine the relationship between plasma homocysteine (HCy), asymptomatic osteoporotic vertebral fractures (VF), using vertebral fracture assessment (VFA) and prevalent abdominal aortic calcification (AAC) in Moroccan postmenopausal women.

Methods: The study cohort consisted of 188 consecutive postmenopausal women with no prior known diagnosis of osteoporosis or taking medication interfering with bone metabolism. Mean age, weight, height, body mass index and plasma homocysteine were determined. Lateral VFA images and scans of the lumbar spine and proximal femur were obtained using a Lunar Prodigy Vision densitometer (GE Healthcare Inc., Waukesha, WI). VFs were defined using a combination of Genant's semiquantitative approach and morphometry. VFA images were also scored for prevalent AAC using a validated 24 point scale.

Results: Fifty-eight (30.9%) patients had densitometric osteoporosis. VFs were identified using VFA in 76 (40.4%) patients: 61 women had grade 1 VFs and 15 had grade 2 VFs. The prevalence of VF on the lumbar spine was 8% (65/812) in the 282 patients seen by the VFA. In the 282 patients seen by the VFA, the prevalence of VF in LS was 3.8% (10/262). In the 282 patients seen by the VFA, the prevalence of VF in FN was 0.9% (2/210).

Conclusions: This study did not confirm that homocysteine is important determinant of extended AAC in postmenopausal women. However, this significant atherosclerotic marker is independently associated with VFs regardless of age.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1447

FR0550 MALE PATIENTS WITH RHEUMATOID ARTHRITIS HAVE AN INCREASED RISK OF OSTEOPOROSIS: FREQUENCY AND RISK FACTORS

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Background: Osteoporosis is a well-known extra-articular manifestation of rheumatoid arthritis (RA) and almost 2 times higher prevalence of osteoporosis was reported in female patients with RA than in healthy subjects. Accordingly, patients with RA are at increased risk of fragility fractures that lead to significant morbidity and mortality and higher healthcare cost. However, most previous epidemiologic studies regarding osteoporosis in RA have focused on female subjects, and little attention has been given to male patients with RA.

Objectives: To compare the prevalence of osteoporosis between male patients with RA and healthy subjects and to identify the risk factors of osteoporosis in male patients with RA.

Methods: By using a cross-sectional design, we recruited 76 male patients with RA aged 50 years and over and 76 sex-matched and age-matched healthy subjects at a university-affiliated rheumatology centre in South Korea from August 2014 to August 2016. We measured bone mineral density (BMD) at L1—4 levels of the lumbar spine and the hip. The prevalence of osteoporosis was evaluated by using dual-energy X-ray absorptiometry (DEXA). We assessed the prevalence of osteoporosis defined as a T-score of ≤−2.5 according to the WHO criteria. We also investigated potential risk factors of decreased BMD and the presence of osteoporosis in male patients with RA using linear and logistic regression analyses.

Results: The mean age and body mass index (BMI) of the male patients with RA were 64.5 years and 22 kg/m², respectively, which were comparable with those of the healthy controls. The overall prevalence of osteoporosis at either the spine or the hip in the male patients with RA was significantly higher than that of the healthy controls (22.4% vs 10.5%, respectively; p=0.049). However, no significant differences in the prevalence of osteoporosis at the spine (19.7% vs 10.5%, respectively; p=0.13) and the hip (3.9% vs 0%, respectively; p=0.245) were found between the patients with RA and the controls. For the male patients with RA, the median disease duration was 37 months, the mean 28-joint Disease Activity Score (DAS28-ESR) was 3.28 and the median modified total Sharp score was 6. An increased titre of anti-cyclic citrullinated antibody showed a trend toward lower L1—4 BMD (p=0.007, p=0.057) in the multivariable linear regression analysis. In addition, DAS28-ESR of ≥3.2 was independently associated with the presence of osteoporosis (OR=3.85, 95% CI=1.13—13.17, p=0.032) after adjusting for confounding factors. The patients with RA whose BMIs were <22 kg/m² had a higher risk of osteoporosis (OR=3.43, 95% CI=1.04—11.33, p=0.043).

Conclusions: Similar to their female counterparts, the frequency of osteoporosis in male patients with RA had an osteoporosis prevalence of about 2.1 times higher than that of the healthy subjects. Increased DAS28-ESR was an independent risk factor of osteoporosis. Our data suggest that appropriate management for osteoporosis in patients with RA is crucial not only for postmenopausal women, but also for men aged 50 years and over.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3061

FR0549 IMPACT OF CHEMOTHERAPY ON BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN WITH BREAST CANCER IN TREATMENT WITH AROMATASE INHIBITORS

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Background: Aromatase inhibitors (AI) have been related to an increased risk of bone loss and fractures in women receiving these drugs as adjuvant treatment, but few studies have assessed the impact of prior chemotherapy (CT) on bone mineral density (BMD) levels associated to AI.

Objectives: To assess the impact of CT prior to the initiation of AI on BMD in postmenopausal patients with breast cancer (BC) seen at a Spanish tertiary care hospital.

Methods: We perform a longitudinal study in patients who received AI after initial CT (CT group) or as adjuvant therapy without prior CT (non-CT group) followed up for 12 months. BMD was assessed by DXA in lumbar spine (LS) and femoral neck (FN) at baseline and after 12 months of AI treatment following the usual protocol of our center, with in vitro coefficient of variation of 1% in both locations and estimated minimal significant change (MSC) of 0.0223 g/cm² in LS and 0.0288 g/cm² in FN. Demographics, neoplastic disease data, and osteoporosis risk factors were collected.

Results: 69 patients (CT group, non-CT group) attended at our center between August 2011 and December 2014 were included. Mean age at diagnosis was 59±7.7 years, most of them have BC stage I-II (84%). Most frequent AI in both groups were letrozole (95%). Baseline characteristics were similar, except for age at diagnosis that was significantly higher in the non-CT group; these data are presented in the table. Mean BMD at the start of AI was significantly lower in LS in the CT group (0.7793 g/cm²) than in the non-CT group (0.8483 g/cm², p=0.018), but no difference in FN (0.6764 g/cm² and non-CT 0.7077 g/cm², p=0.123). A significant difference in LS (CT 0.7685 g/cm², non-CT 0.8397 g/cm², p=0.003) was found in the comparison of BMD means between the two groups at 12 months but not in FN (CT 0.6598 g/cm² and non-CT 0.6689 g/cm², p=0.369).

After 12 months of treatment with AI, mean BMD change in the CT group in LS was -0.0085 g/cm² (95% CI -0.0349, +0.0279, p=0.7077 g/cm², p=0.123) and in FN -0.0107 g/cm² (95% CI -0.0269, +0.0055, p=0.0369) and in FN -0.0165 g/cm² (95% CI -0.0339, +0.0099, p=0.063), while in the non-CT group the mean changes were in LS -0.0085 g/cm² (95% CI -0.0146, +0.0244, p=0.599) and FN -0.0388 g/cm² (95% CI -0.0707, -0.0088, p=0.019). During the study period there was a fracture in each group (CT 2.6%, non-CT 3.3%).

Conclusions: Our results do not demonstrate that CT prior to AI treatment significantly decreased BMD during the first year. Mean change in both LS and FN in CT group was not superior to MSC nor to the change in non-CT group, although they had a significantly lower mean BMD in LS than the latter group and this difference was maintained at the end of the study period.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6391
practice, and it is very important to know risk factors that attenuate its effect in the treatment of osteoporosis.

Objectives: The aim of this study was to identify risk factors for inadequate response to the treatment of osteoporosis by DMAB.

Methods: Sixty-six patients treated with DMAB were observed retrospectively for one year. The mean age was 74.4 years, and 24 women and 42 men were included. We measured BMDs at lumbar and hip by dual-energy X-ray absorptiometry (Hologic Discovery) at baseline and one year later. We evaluated the effects of age, body mass index (BMI), use of glucocorticoid (GC), previous treatment for osteoporosis, BMD at baseline, bone metabolic markers (BAP; bone alkaline phosphatase, NTX; urinary N-telopeptide), serum Ca and P levels and the previous vertebral fractures for inadequate response to DMAB. We defined the cases who could not gain the increase of BMD over 2% at the lumbar vertebrae and 4% at the hip as inadequate responders by taking the measurement error into account.

Results: Dose of PSL was significantly high in non-responder at non-RA trochanter and RA lumbar BMD (p=0.028, 0.006). BAP was higher in non-responder at RA lumbar BMD (p=0.007). Urinary NTX was significantly high in non-responder at non-RA lumbar and RA trochanter BMD (p=0.026, 0.048). Previous treatment for osteoporosis was significantly high in non-responder at non-RA lumbar, total hip and trochanter BMD (p=0.026, 0.022, 0.003). Multivariate logistic analysis including age, BMI, dose of PSL, BMD at baseline, BAP, NTX, Ca and P level as confounders revealed that dose of PSL was the significant risk factors for non-responder at lumbar BMD (OR=6.64, 95% CI 0.433–9.93, p=0.02).

Conclusions: Patients receiving GC might gain an adequate response to the treatment by DMAB for osteoporosis. Reducing dose of GC or alternative treatment regimens might be necessary.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3684
associated with osteoporosis. Adiponectin levels of 43.9 μg/ml and lower were associated with normal bone density.

**Conclusions:** Thus, we revealed that Adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be a useful laboratory marker for OP diagnosis.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4434

**FR0055**

**LEFT VENTRICULAR EJECTION FRACTION AND BONE MINERAL DENSITY AFTER CARDIAC TRANSPLANTATION**


**Rheumatology, Reina Sofia University Hospital/IMIBIC University of Cordoba, Cordoba, Spain**

**Background:** Left ventricular ejection fraction (LVEF) has been directly associated with BMD in patients with heart failure. Nevertheless, no study has linked yet the left ventricular ejection fraction to bone mineral density and fragility fractures in cardiac transplantation.

**Objectives:** The main aim of this study was to evaluate the possible relationship between LVEF and BMD in heart transplantation and the association of LVEF with other factors related to bone metabolism (vitamin D, parathormone (PTH) and markers of bone remodeling in patients with heart transplantation (osteocalcin, telopeptide C terminal (CTX)).

**Methods:** Seventy nine patients (66 male) were included in this cross-sectional study with a mean age of 55.75±14.81 years, body mass index (BMI) values of 26.89±5.35 kg/m² and an average post-transplantation period of 8.46±8.71 years. The LVEF of each patient was evaluated in the beginning of the study using Doppler echocardiography, and the BMD was measured using dual energy X-ray absorptiometry (DXA) at the femoral neck, lumbar spine and hip level. The patients were divided into two groups based on LVEF values: Group A, LVEF ≥ 54% and Group B, LVEF < 54%.

**Results:** A total of 79 patients were included in this present study. BMD in osteoporotic range was found in 31.2% of patients (17.7% in spine,16.52% in femoral neck and 13% in hip). Vitamin D deficiency (<20ng/dl) was detected in 68.4% of patients. Vertebral fracture was found in 30.4% and a 2.6% hip fracture. Bivariate analysis showed that the group of patients with FEV ≤ 65% had a higher proportion of femoral neck osteoporosis (p=0.04), higher proportion of osteoporosis in total hip (p=0.03) and a higher percentage of vertebral fractures (p=0.04) compared with group with LVEF > 65%.

The multiple linear regression analysis indicated that LVEF was independently associated with osteoporosis in spine (B = -5.225, p=0.011), femoral neck osteoporosis (B = -5.411, p=0.015) and vertebral fractures (B = -5.433, p=0.002). In addition, LVEF was associated with osteocalcin levels (B = -0.105, p=0.002).

**Conclusions:** These results suggest that post-transplantation LVEF may have an influence on bone remodeling. However, further studies are needed in order to confirm this in other institutions.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2360

**FR0057**

**DOES WEIGHTED KYPHO-ORTHOSIS (WKO) REDUCE RISK OF FALL IN WOMEN WITH OSTEOPOROSIS? A PRELIMINARY STUDY**


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**Background:** Osteoporosis is a major health problem, particularly in the elderly, because of fragility fractures and their consequences. Hip fractures (HF) are the most ominous outcomes in terms of morbi-mortality.

**Objectives:** The aim of our work was to establish the current mortality and re-fracture rate at 1 and 3 years after HF, as well as their predictors.

**Methods:** The study included all patients aged >40 years, admitted to Coimbra University Hospital between May and October 2013 with the diagnosis of HF. Demographic and clinical data related to the fracture episode was collected from medical files. Patients or the caregivers were contacted to assess potential risk factors at baseline and major post-fracture events at 1 and 3 years after the index HF. The mortality and re-fracture rate 1 and 3 years after fracture were calculated. Possible predictor variables were tested by cox regression analysis: age, gender, Charlson index.

**Table 1. Mortality and re-fracture predictors**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>p-value</th>
<th>Exp (b)</th>
<th>p-value</th>
<th>Exp (b)</th>
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<tbody>
<tr>
<td>Gender</td>
<td>0.106</td>
<td>2.052</td>
<td>0.265</td>
<td>3.089</td>
</tr>
<tr>
<td>Age</td>
<td>0.002</td>
<td>1.075</td>
<td>0.276</td>
<td>0.953</td>
</tr>
<tr>
<td>Katz index</td>
<td>0.116</td>
<td>1.154</td>
<td>0.752</td>
<td>0.918</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>0.020</td>
<td>2.167</td>
<td>0.499</td>
<td>0.638</td>
</tr>
<tr>
<td>BMI</td>
<td>0.812</td>
<td>0.991</td>
<td>0.142</td>
<td>0.891</td>
</tr>
<tr>
<td>Parent hip fracture</td>
<td>0.015</td>
<td>0.355</td>
<td>0.196</td>
<td>0.322</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.453</td>
<td>0.615</td>
<td>0.394</td>
<td>0.473</td>
</tr>
<tr>
<td>Corticotherapy</td>
<td>0.013</td>
<td>0.404</td>
<td>0.639</td>
<td>0.637</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>0.071</td>
<td>0.824</td>
<td>0.140</td>
<td>1.140</td>
</tr>
<tr>
<td>Secular osteoporosis</td>
<td>0.172</td>
<td>0.566</td>
<td>0.154</td>
<td>0.321</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>0.037</td>
<td>0.370</td>
<td>0.980</td>
<td>348544.658</td>
</tr>
<tr>
<td>Charlson index</td>
<td>0.000</td>
<td>1.384</td>
<td>0.835</td>
<td>0.941</td>
</tr>
<tr>
<td>Number of re-fractures</td>
<td>0.860</td>
<td>0.781</td>
<td>0.430</td>
<td>0.474</td>
</tr>
</tbody>
</table>

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular-1780

**FR0058**

**PREDICTORS OF MORTALITY AND RE-FRACTURE AT 1 AND 3 YEARS AFTER HIP FRACTURE**


**Rheumatology, Centro Hospitalar e Universitario de Coimbra, Coimbra, Portugal**

**Background:** Osteoporosis is a major health problem, particularly in the elderly, because of fragility fractures and their consequences. Hip fractures (HF) are the most ominous outcomes in terms of morbi-mortality.

**Objectives:** The aim of our work was to establish the current mortality and re-fracture rate at 1 and 3 years after HF, as well as their predictors.

**Methods:** The study included all patients aged >40 years, admitted to Coimbra University Hospital between May and October 2013 with the diagnosis of HF. Demographic and clinical data related to the fracture episode was collected from medical files. Patients or the caregivers were contacted to assess potential risk factors at baseline and major post-fracture events at 1 and 3 years after the index HF. The mortality and re-fracture rate 1 and 3 years after fracture were calculated. Possible predictor variables were tested by cox regression analysis: age, gender, Charlson index.

**Table 1. Mortality and re-fracture predictors**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>p-value</th>
<th>Exp (b)</th>
<th>p-value</th>
<th>Exp (b)</th>
</tr>
</thead>
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<tr>
<td>Gender</td>
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</tr>
</tbody>
</table>

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1780
CORRELATION OF THE FRACTURE RISK ASSESSMENT TOOL (FRAX) AND ASYMMETRIC MORPHOMETRIC VERTEBRAL DEFORMITIES IN HIV-INFECTED PATIENTS

M. Liop Vitale 1, C. Medina Quiñones 1, C. Macía Villa 1, W.A. Sifuentes Giraldo 1, M. Vázquez Díaz 1, J.L. Caicedo Osorio 1. 1. Rheumatology, Infectious diseases, Hospital Universitario Ramón y Cajal, Madrid, Spain.

Background: Patients infected with the human immunodeficiency virus (HIV) have a high rate of low bone mineral density (BMD) and is thought to be multicausal. Some instruments have been developed to estimate the risk of osteoporotic fracture in the general population such as the WHO Fracture Risk Assessment Tool (FRAX), which allows calculating the 10-year probability of fractures in men and women from clinical risk factors with or without the measurement of femoral neck BMD. The cut-off values for high risk of hip fracture >3% and for major osteoporotic fracture >20%. Although FRAX has been validated in multiple large studies there are no clear recommendations of its use in HIV-infected patients older than 50 years.

Objectives: To evaluate the utility of FRAX tool in the prediction of risk of vertebral morphometric deformity (MVD) in HIV-infected patients over 50 years old seen in a Spanish tertiary care center.

Methods: We performed a cross-sectional study in HIV-infected patients with age 50 years treated in our centre during the period 2014–2016. Demographics and risk factors were collected through a specific survey. FRAX was calculated and risk factors were collected through a specific survey. FRAX was calculated with increasing mortality in patients who suffered a fragility HF.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4473

PREDICTORS OF FRACTURES IN FEMALE PATIENTS WITH ANOREXIA

M. Rahm, M. Bukhari. Rheumatology, Royal Lancaster Hospital, Lancaster, United Kingdom.

Background: Anorexia Nervosa (AN) is an eating disorder characterised by extremely low body weight and body image distortion. It is more common in females and is expected to become increasingly more prevalent. Numerous studies have found AN to have a detrimental effect on bone health. The evidence shows that anorexia is associated with reduced bone mass and strength which increases fracture risk. Few studies have looked at other predictors of fracture in these patients.

Objectives: The aim of this study was to determine whether further predictors of fracture could be found in female patients suffering from anorexia nervosa (AN).

Methods: Female patients with anorexia referred for a bone mineral density (BMD) DEXA scan from June 2006 to October 2014 were identified. This cohort of patients was split into two subgroups depending on their fracture status. Demographics collected on scanning and factors such as age at DEXA scan, height, weight, body fat percentage, BMI, lumbar spine L1-L4 BMD and femoral neck BMD were used to compare the fracture group against the controls. Categorical variables such as smoking, comorbidities (Rheumatoid arthritis), alcohol, family history and steroid use were compared using chi squared test and the T test was used to compare continuous variables. Logistic regression models were used to model fractures unadjusted and adjusting for age at scan.

Results: A total of 193 female patients with anorexia were included: 45 (23.3%) had sustained a fracture. The results of statistical analysis are shown in Table 1. The data showed there is a significant association between having a low femoral neck BMD and increased fracture risk OR 0.036 (95%, CI 0.003, 0.497). The case group was also significantly taller OR 1.061 (95%, CI 1.009, 1.117) and older P 0.0027 (95% combined CI 39.193, 42.682). There was no correlation with any of the categorical variables and fracture risk, see Table 2 for results.

Table 1. Results of statistical analysis of continuous variables

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Significance (P value)</th>
<th>Cases with fractures</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at scan (years)</td>
<td>0.027</td>
<td>45.7 ± SD10.36</td>
<td>39.49 ± SD12.46</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.021</td>
<td>165.08 ± SD74.45</td>
<td>162.66 ± SD68.82</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.129</td>
<td>58.16 ± SD13.68</td>
<td>53.73 ± SD11.83</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>0.536</td>
<td>21.24 ± SD4.31</td>
<td>20.31 ± SD4.43</td>
</tr>
<tr>
<td>Lumbar spine (L1-L4) (g/cm²)</td>
<td>0.053</td>
<td>0.98 ± SD1.18</td>
<td>1.03 ± SD1.44</td>
</tr>
<tr>
<td>Femoral neck BMD (g/cm²)</td>
<td>0.013</td>
<td>0.81±SD0.15</td>
<td>0.86±SD0.14</td>
</tr>
</tbody>
</table>

Table 2. Results of statistical analysis of categorical variables

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases with fracture (45)</th>
<th>Control group (148)</th>
<th>Significance (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker</td>
<td>28.9% (13)</td>
<td>34.46% (51)</td>
<td>0.445</td>
</tr>
<tr>
<td>RA</td>
<td>2.22% (1)</td>
<td>0.68% (1)</td>
<td>0.349</td>
</tr>
<tr>
<td>Alcohol</td>
<td>8.99% (4)</td>
<td>8.78% (13)</td>
<td>0.714</td>
</tr>
<tr>
<td>Family history</td>
<td>31.11% (14)</td>
<td>22.97% (34)</td>
<td>0.403</td>
</tr>
<tr>
<td>Steroid</td>
<td>15.56% (7)</td>
<td>8.78% (13)</td>
<td>0.197</td>
</tr>
</tbody>
</table>

Conclusions: This study demonstrates that fractures in female patients with anorexia are more likely to occur in those who are taller, older at DEXA scan and in those who have a lower femoral neck BMD. This would indicate that cortical bone loss and taller stature are indepent risks in this cohort. Further work using vitamin D levels as a risk should be performed.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3778

SAFETY OF DENOSUMAB IN POST-MENOPAUSAL OSTEOPOROSIS AND IN CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Aubailly 1, T. Barretche 2, B. Combe 3, C. Gauloux-viala 3, C. Lukas 1, J. Morel 1, H. Ohe 1, 1. CHU lapérouse, Montpellier; 2. CHU bordeaux, Bordeaux; 3. CHU Nîmes, Nîmes, France.

Background: Denosumab is a RANK ligand antibody (1) used for the treatment of post-menopausal osteoporosis (OP) and prevention of bone metastases complications (2,3).

Objectives: The aim of this meta-analysis was to assess the safety of Denosumab.

Methods: Data sources included MEDLINE, EMBASE, Cochrane Library, and recent abstracts from ACR and EULAR congresses were searched until March 2016. Randomized controlled trials comparing the safety of Denosumab to placebo or bisphosphonates (BP) in postmenopausal OP and in cancer (either cancer with bone metastases or with hormone therapy) were selected. Data were

Conclusions: The FRAX tool does not identify properly the HIV-infected patients older than 50 years with MVD as well as the patients who need DXA. An alternative could be to perform X-rays of thoracic and lumbar spine as a screening method in HIV-infected patients with risk factors.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5205
extracted by one investigator, confirmed by another, and pooled in meta-analysis using Review Manager software (Cochrane collaboration).

**Results:** 6136 articles were of potential interest, and 19 met the inclusion criteria. 7 articles compared the safety of Denosumab to BP in post-menopausal OP. There was no significant difference when comparing Denosumab with bisphosphonates in 3 articles (RR=0.98, 95% CI=0.98–1.01) or in osteonecrosis of the jaw (ONJ) (RR=1.04, 95% CI=0.81–1.33). Regarding Denosumab versus placebo in post-menopausal OP, 7 studies were included and there was no significant difference in AAE (RR=0.99, 95% CI=0.94–1.01), SAE (RR=1.03, 95% CI=0.96–1.11), however cellullitis was more frequently found with Denosumab (RR=8.03, 95% CI=1.37–48.30). No cases of SAE were recorded. 5 articles were pooled to compare Denosumab with BP in patients with bone metastases and no significant difference was found in AEE (RR=0.99, 95% CI=0.98–1.00), SAE (RR=0.99, 95% CI=0.95–1.03), and ONJ (RR=1.40, 95% CI=0.92–2.13). 4 articles were selected concerning patients treated with placebo and Denosumab in men with prostate cancer without bone metastases. Although no significant difference was found in AEE (RR 1.01, 95% CI=0.99–1.03), use of Denosumab was associated with a significantly increased risk of hip haemorrhage (RR 5.20, 95% CI=1.34–20.13) and of cholecystitis (RR 3.43, 95% CI=1.01–11.69).

**Conclusions:** In post-menopausal OP, Denosumab had a relatively safe profile although significantly more cellullitis occurred when compared with placebo. For patients who were less than 50 years of age, Denosumab was associated with more hip haemorrhage and cholecystitis than placebo.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3900

**Table 1. Proportion, costs and EQ-5D per type of fracture in Portugal and Sweden**

<table>
<thead>
<tr>
<th>Type of fracture</th>
<th>Portugal</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>122 (11)</td>
<td>100 (39)</td>
</tr>
<tr>
<td>Costs (€)</td>
<td>13,434 (12,290–14,576)*</td>
<td>2220 (1626–2575)</td>
</tr>
<tr>
<td>Weighed mean cost (€)</td>
<td>13,434</td>
<td>2867</td>
</tr>
<tr>
<td>Average loss of HRQoL mean (95% CI)</td>
<td>0.29 (0.22; 0.36)*</td>
<td>0.11 (0.06; 0.15)</td>
</tr>
<tr>
<td>Average loss of HRQoL mean (95% CI)</td>
<td>0.38 (0.24; 0.52)</td>
<td>0.10 (0.08; 0.12)</td>
</tr>
</tbody>
</table>

*Based on data published elsewhere.*

Conclusions: The proportion HF/NHF observed in Portugal is similar to the Swedish reference values (0.44/0.56). The highest cost were attributed to hip fractures in both countries, followed by vertebral fractures and lastly by wrist fractures. The HRQoL mean loss was higher for vertebral fractures in both countries. The reported costs of vertebral fractures are much higher than in Portugal which may significantly affect the calculation of cost-effectiveness thresholds for intervention.

References:

Disclosure of Interest: None declared


**FR0562 USE OF TERIPARATIDE AS A CALLUS ACCELERATOR IN NONUNION OF LOWER LIMB**

M. Muratore 1, O.E. Casilli 2, V. Russi 3, P. Piccinni 2, L. Meccarriello 2, L. Quarta 1, E. Quarta 1, G. Rolo 2, M. Filipponi 2, 1U.O. Reumatologia- P.O. “V. Fazzi” Lecce, LECCe, Italy

**Background:** The use of teriparadise in fracture management by high-energy trauma with loss of bone substance and muscle and skin with possible nerve/vascular lesions is poorly documented. The aim of our study is to evaluate how the intermittent administration of teriparadise may affect the bone consolidation newly generated and compression in patients with bone loss and my-skin during treatment reconstruction with the technique of resection Ilizarov-lengthening.

**Objectives:** In large or in the outcomes of these, in which there is loss of bone substance and muscle and skin the technique of reconstruction of Ilizarov (1 mm/day) is used; the main problem is the long time required to reach complete healing with optimal bone consolidation newly generated and the compression of the fixator to ensure the mechanical strength necessary to be able to remove the external fixator (1). The rationale of this study, therefore, was to evaluate the influence of treatment with teriparadise, administered subcutaneously 1 dose 1 day/time/day from a pre-filled syringe of 20mcg and for a period of three months, the evolution radiographic, on the healing time and the external fixator removal and on the functional recovery quality in multiple trauma patient.

**Methods:** In our prospective study, we evaluated two groups of patients: Group 1: 9 patients treated with PTH during bone transport; Control Group 2: 10 patients treated with bone transport.

**Results:** The group compared to the 2 (control group) showed a bone radiographic progression slower newly-generated in the first month of administration of teriparadise; subsequently it was observed an acceleration of bone maturation but not uniform; after about 3 months, the bone maturation accelerates further also at the level of the compression outbreak if already in compression, allowing the removal of the fixator about 1.5 months earlier than the estimated time. This is due to the reduction of the time allowed for “elongation stage” bone that physiologically is around 1mm/day, thus ensuring an optimal functional recovery.

**Conclusions:** The action of teriparadise (2) on bone healing is derived from increased differentiation of cells responsible for bone callus formation, chondrocytes and osteoblasts, mediated in part by increased activation of genes that produce the Wnt, Osterix and Runx2, all fundamental elements in the osteoblastogenesis. Although the sample examined is small for the specificity of the described treatment, the data reported showed that the intermittent administration of teriparadise is able to accelerate the timing for the “elongation stage” bone and therefore the bone healing and reconstructive treatment times in serious loss of substance.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4796
128 PATIENTS WITH SUBACUTE SYMPTOMATIC FRAGILITY VERTEBRAL COMPRESSION FRACTURES: HIGH INCIDENCE OF MORTALITY, FALLING, MONOCONAL GAMMAPATHY OF UNCERTAIN SIGNIFICANCE AND MYELOMA, PERNICTIONS ANEMIA AND VITAMIN B-12 DEFICIENCY: IS THIS A PROFILE OF AN OSTEOPOOROTIC OR AN AGED POPULATION?

M. Dey 1, N. Ben-Shlomo 2, J. Udoff 3, Desert Oasis Healthcare, Palm Springs, California, United States; 2Ben-Gurion Medical School, Beer Sheva, Israel; 3University of California, San Diego Medical School, San Diego, California, United States

Background: Epidemiological studies have identified risk factors for falling and fractures. However there is a paucity of observational studies of patients with symptomatic fragility vertebral compression fractures (VCF). These studies were not done in community based populations and did not evaluate the contribution of factors.

Objectives: To study factors contributing to both osteoporosis and falling in a cohort of community based patients with symptomatic subacute fragility VCF.

Methods: We saw 128 patients with symptomatic subacute fragility VCF in our community based outpatient fracture clinic over a two year period. We performed a complete history and physical, review of past medical records and radiographs, complete blood count, sedimentation rate, chemistry profile, TSH, urinalysis, vitamin B-12, PTH, 25-OH vitamin D, and serum protein electrophoresis (SPE). We performed testosterone level, methylnolonic acid, antiplatelet cell antibody and parathyroid hormone in select cases. We recorded diseases including diabetes, COPD, cardiac, neurological for each patient.

Results: There were 92 females aged 45–98 years (mean 77.7), 36 males aged 39–94 years (mean 77.6). Factors contributing to falling included peripheral neuropathy-61, use of sedatives-43, blindness-12, foot drop-6, dementia-5, Parkinson’s-3, hyponatraemia-2. VCF were precipitated by falls in 94 patients, of which 87 occurred at home. VCF occurred with falling in 8 patients, bending in 3, and were spontaneous in 23. Use of steroids was reported in 18 patients and associated with multiple (-3) fractures (p < 0.0008). Blindness (p = 0.022) and multiple multiple fractures (p = 0.008) were found to be significantly more likely to have peripheral neuropathy (p = 0.056) and 3 or more medical conditions (p = 0.008), Age correlated with the number of diseases (p = 0.0001). Diagnosis based on laboratory studies included vitamin D insufficiency-29, vitamin D deficiency-12, pernicious anaemia-6, vitamin B-12 deficiency-3, monoclonal gammapathy of uncertain significance (MGUS)-10, myeloma-2, hypogonadism-2, and iatrogenic hyperthyroidism-2. Ankylosing spondylitis and lymphoma were diagnosed in one patient each. The average age of those that died was 83.9 years compared to 76.8 of the remaining group (p = 0.0033).

Conclusions: Conditions that increase with age and are associated with an increased risk of falling and fracture include neurological diseases, visual loss, use of steroids and sedatives, MGUS, myeloma, pernicious anaemia and vitamin B-12 and vitamin D deficiencies. These were all in common with our cohort with subacute symptomatic fragility VCF. Accordingly we recommend vitamin B-12 levels and SPE in the evaluation of all patients with VCF. These findings support the emphasis on interventions to reduce the risk of falling in the elderly and to recognize and treat these age-related conditions in an attempt to mitigate the risk of VCF.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2171

FR01565 FRAGILITY FRACTURES IN PATIENTS ON DEPO-PROVERA ARE ASSOCIATED WITH USUAL RISK FACTORS FOR FRACTURE

M. Dey, M. Bukhari. University Hospitals of Morecambe Bay NHS Foundation Trust, Lancaster, United Kingdom

Background: Depo-Provera is one of the most widely-used contraceptives. The side-effects includes loss in bone mineral density (BMD), increased fracture risk (1.2), It is not known if conventional fracture risk factors impact fracture risk in these patients.

Objectives: We set out to determine if the usual risk factors for fracture are associated with increased risk of fragility fractures in patients exposed to Depo-Provera.

Methods: Patients referred for bone densitometry at a scanner in North West of England were analysed. Femoral and vertebral BMD, height, weight and body mass index (BMI) were recorded, in addition to age, diagnosis of rheumatoid arthritis, smoking status, alcohol consumption, family history of fractures, history of secondary osteoporosis, corticosteroid use, total average proportion fat, average tissue thickness, fat mass, and lean mass. Patients with exposure to Depo-Provera were selected for analysis. Initially patients with and without a fracture were compared using Chi-squared test and T-Test. Logistic models were fitted univariately and adjusted for age to analyse association between traditional risk factors and fracture.

Results: 304 females (103 currently and 201 previously on Depo-Provera) were included. 62 (20.4%) had sustained at least one fragility fracture. There was no significant difference in fracture risk between those currently and previously on Depo-Provera (p = 0.176 95% CI). Decreased left femoral BMD significantly impacted fracture risk (p = 0.035 95% CI). All other factors investigated did not significantly increase fracture risk in this cohort (see table below).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>All (n=304)</th>
<th>Patients with fracture (n=62)</th>
<th>Patients without fracture (n=242)</th>
<th>p-value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at scan (years)</td>
<td>36.7 ± 14.0</td>
<td>41.5 ± 10.9</td>
<td>35.2 ± 13.1</td>
<td>0.003</td>
<td>1.02 [1.01, 1.03]</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.2 ± 6.0</td>
<td>163.3 ± 6.0</td>
<td>163.2 ± 6.0</td>
<td>0.99</td>
<td>1.00 [0.95, 1.05]</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.0 ± 12.0</td>
<td>76.9 ± 12.0</td>
<td>70.7 ± 11.0</td>
<td>0.020</td>
<td>1.02 [1.00, 1.03]</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.0 ± 4.0</td>
<td>27.9 ± 3.0</td>
<td>26.5 ± 4.0</td>
<td>0.003</td>
<td>1.03 [1.00, 1.06]</td>
</tr>
<tr>
<td>Smoking (yes)</td>
<td>64 (21.1%)</td>
<td>37 (59.7%)</td>
<td>27 (11.2%)</td>
<td>&lt;0.001</td>
<td>2.50 [1.46, 4.22]</td>
</tr>
<tr>
<td>Secondary operation (yes)</td>
<td>48 (15.8%)</td>
<td>10 (16.1%)</td>
<td>38 (15.7%)</td>
<td>0.82</td>
<td>1.05 [0.50, 2.18]</td>
</tr>
<tr>
<td>Alcohol (yes)</td>
<td>23 (7.6%)</td>
<td>8 (12.9%)</td>
<td>15 (6.2%)</td>
<td>0.020</td>
<td>2.07 [1.02, 4.19]</td>
</tr>
<tr>
<td>Family history of fracture (yes)</td>
<td>77 (25.3%)</td>
<td>17 (27.4%)</td>
<td>60 (24.8%)</td>
<td>0.63</td>
<td>1.06 [0.52, 2.15]</td>
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</table>

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1539

FR01665 TERIPARADIP AND ALENDRONATE IMPROVED BONE LOSS AND HYPERALGESIA IN A MOUSE MODEL OF OSTEOPOOROSIS

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Background: Osteoporosis may cause not only fractures but also chronic back pain in elderly women. Teriparatide (TPTD) and alendronate (ALN) are widely used in clinical for treatment of osteoporosis. Several studies have demonstrated that TPTD and ALN treatments improved skeletal pain in osteoporosis patients.

Objectives: We investigated the effect of TPTD and ALN on pain-related behavior in ovariectomized (OVX) mice. We investigated expression of inflammatory cytokines treated OVX mice.

Methods: 8-week-old female ddY mice were OVX and assigned to 4 groups; SHAM-operated mice treated with vehicle (SHAM), OVX mice treated with vehicle (OVX), OVX mice treated with TPTD (TPTD) and OVX mice treated with ALN (ALN). Mice were started treatment immediately after surgery. For 4 weeks, mice were injected subcutaneously with vehicle or 40 μg/kg ALN twice a week or 40 μg/kg TPTD 5 times a week.

The spinal cord was harvested after 4week, the bilateral distal intercostal metaphys were analyzed three-dimensionally by μCT 4 weeks after surgery (each group; n=8).

Mice mechanical sensitivity was tested using von Frey filaments 4 weeks after surgery. To evaluate the 50% withdrawal threshold, seven von Frey filaments with forces of 0.07, 0.4, 0.6, 1.0, 1.4 and 2.0 g were arranged on the middle of the plantar surface. Data was collected using the up-down method.

To evaluate expression of interleukin-1β (IL-1β), IL-6 and tumor necrosis factor-α (TNF-α), mice were anesthetized and the bilateral hindlimb bone excised. We performed quantitative polymerase chain reaction (q-PCR) from hindlimb bone.

Results: μCT analysis of the distal femur metaphysis showed that bone volume/tissue volume (BV/TV) and trabecular number (Tb.N) were significantly less in the OVX group than in the SHAM group, whereas trabecular separation (Tb.Sp) was significantly greater in the OVX group than in the SHAM group. In the TPTD and ALN group, BV/TV and Tb.N were significantly greater than the OVX group, whereas Tb.Sp was significantly less than in the OVX group. In the ALN group, BV/TV and Tb.N were significantly greater than in the TPTD group, but Tb.Sp was no significance.

The 50% withdrawal threshold was significantly lower in the OVX group than in the SHAM group, and it was significantly higher in the TPTD and ALN group than in the OVX group. And the 50% withdrawal threshold was no significance between the TPTD and ALN group.

The expression levels of TNF-α was increased in the OVX group compared with those in the SHAM group. Other cytokines were not increased significantly in the
Differences in Adherence to Osteoporosis Medications in Patients with Rheumatic Diseases: A 3-Year Retrospective Cohort Study

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Background: Patients with rheumatic diseases (RD) have an increased risk of fracture compared with the general population. To maintain bone health, anti-osteoporotic medications are usually prescribed, but patient adherence to these is often low, leading to limited beneficial effects. The study aims to evaluate adherence to anti-osteoporotic medications in a cohort of patients with RD, and to determine the reasons for non-adherence.

Methods: We conducted a retrospective study of 204 patients (82% women, mean age 54±11 years) with RD (93% = rheumatoid arthritis, 48%= systemic sclerosis, 39%= systemic lupus erythematosus and 24%= ankylosing spondylitis), who were prescribed at least one anti-osteoporotic medication. Patients were followed for 3 years. Visits to rheumatologist and BMD measurements increased subject’s contact for patient’s self-reporting.

Results: 196 (96%) patients started the OP treatment. Among them 26%= alendronate, 24%= received alfacalcidol or supplements of calcium and vitamin D, 16%= strontium ranelate, 12%= ibandronate, 9%= zoledronic acid, 8%= risedronate, 24% received alfacalcidol or supplements of calcium and vitamin D only, 16%= strontium ranelate, 12%= ibandronate, 9%= zoledronic acid, 8%= alendronate, 24% received alfacalcidol or supplements of calcium and vitamin D only, 16%= strontium ranelate, 12%= ibandronate, 9%= zoledronic acid, 8%= alendronate. 105 patients received only the AIs treatment (Group A), whereas the remaining 49 patients (Group B) received also an additional Denosumab treatment, in order to contrast the BMD reduction induced by AIs administration. Follow-up measurements were conducted at two different time points: 12 (T1) and 18 (T2) months from AIs treatment starting. At time T1, patients underwent both DXA and EchoSound scans, while at time T2 only the echographic scans were performed, since DXA cannot be used for short-term follow-ups.

Results: At time T1, the following results were obtained on lumbar spine: Group A showed a BMD decrement, which was equal to -2.07±1.66% (p<0.01) according to DXA and to -2.22±0.89% (p<0.01) according to EchoSound; Group B showed a BMD increase of 4.06%±1.49% (p<0.01) and 4.31±0.62% (p<0.01) as measured by DXA and EchoSound scans, respectively. At time T2, Group A showed a further BMD decrement, resulting in a total decrease of -3.56%±1.07% (p<0.01) according to EchoSound. In the TPTD treatment, a total decrease of 4.88%±0.65% (p<0.01) was observed. Similar results were obtained for femoral neck BMD: a total BMD decrease of -2.37±0.97% (p<0.01) during the whole treatment period was observed in Group A, whereas a total BMD increment of 3.53±0.43% (p<0.01) was measured in the same period in Group B.

Conclusions: By using the EchoSound technology the short-term follow-up of the positive Denosumab effects on BMD reduction in patients treated with adjuvant AIs was feasible and accurate. This approach can be also useful to monitor the therapy effectiveness in patients undergoing specific anti-osteoporotic treatments.

References:

Disclosure of Interest: P. Pisani: None declared, M. Muratore: None declared, F. Conversano: Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study, E. Casciaro: Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study, M. Di Paola: None declared, R. Forcignanò: None declared, M. Ciccarese: None declared, G. Surico: None declared, L. Quarta: None declared, E. Quarta: None declared, D. Costanza: None declared, R. Franchini: None declared, R. Tarparelli: Employee of: Echolight Spa, S. Casciaro: Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study.

DOI: 10.1136/annrheumdis-2017-eular.4060

Evaluation of Bone Microarchitecture in Systemic Sclerosis Patients: Relationships between Trabecular Bone Score (TBS) and Disease Severity

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Background: Systemic sclerosis (SSc) is a rare connective tissue disorder characterized by an increased synthesis and deposition of extracellular matrix in the skin and internal organs (1). Several studies described SSc as potential risk factor for osteoporosis, however, to date the bone quality in SSc is unclear (2). Trabecular bone score (TBS) has been recently proposed as an indirect measure of bone microarchitecture (3).

Objectives: The aim of this study was to assess bone microarchitecture in SSc patients and possible association with disease severity and microangiopathy.

Methods: Twenty-three female SSc patients (mean age 63±12.8 SD years, mean disease duration 92±66 SD months, mean Raynaud’s Phenomenon duration 15±15 SD months) were enrolled after written informed consent. The assessment of disease severity was performed using the Medsger’s severity scale (4). Bone Mineral Density (BMD) measurements at L1-L4, femoral neck and total hip, were performed using DXA Prodigy Densitometer (GE Lunar). TBS was derived for each spine DXA examination using the TBS index (TBS iNsight Medimaps). Nailfold videocapillaroscopy (NVC) was used to assess the microangiopathy based on nailfold video capillaroscopic pattern (NVC) analysis and the microangiopathy evolution score (MES) (5-6). Using the FRAX (Fracture Risk Assessment Tool) we also evaluate the 10-year risk of hip and major joints fractures.

Results: A positive correlation was observed between TBS and Medsger’s general organ score (r=0.5; p=0.01); no other correlations were found between TBS and Medsger’s score. Interestingly, TBS was positively and significantly correlated with modified Rodnan skin score (mRSS) (r=0.01). When the patients were divided in two groups according to presence of linear joint involvement by mRSS, TBS was found significantly higher in the group with mRSS >15 compared to the group with mRSS <15 (1.25±0.08 vs 1.16±0.03; p<0.01) No correlations were found between NVC patterns/MES and bone quality assessment (TBS) or bone density assessment (BMD), only a significant correlation, as expected, was observed...
between MES and skin involvement (mRSS) (p=0.05). On the other hands, FRAX, the major osteoporotic fracture risk, positively correlates with Medsger's kidney disease severity (p=0.04) and Medsger’s lung disease severity (p=0.04); in addition, FRAX, for hip fracture risk, seems to correlate significantly with Medsger's lung involvement severity (p<0.04).

Conclusions: This study demonstrates in SSC patients a relationship between clinical disease severity (organ fibrosis/failure) and altered bone microarchitecture (TBS). In addition, skin involvement was found significantly correlated with altered quality of the trabecular bone architecture (TBS) and a significant increase of osteoporotic fracture risk (FRAX) was found correlated with kidney and lung involvement.

References:
OSTEOCYTES ARE INVOLVED IN THE PATHOGENESIS OF OSTEOPOROSIS IN CHRONIC CHELOSTASIS. EFFECTS OF BILIRUBIN AND BILE ACIDS ON OSTEOCYTIC CELL LINES

Liver and Metabolic Bone Diseases Units, CIBERReh-Hospital Clinic, University of Barcelona, Barcelona, Spain

Background: Mechanisms underlying osteoporosis in chronic cholestasis are complex and not well understood. In this study, we evaluated the effects of unconjugated bilirubin and lithocholic acid on osteocytes, to elucidate the role played by the liver in bone loss.

Objectives: The aim of this study was to analyze the direct effects of increased molecules of cholestasis, such as bilirubin (Bil) and lithocholic acid (LCA), and the potential protective effect of ursodeoxycholic acid (UDCA) on the osteocytes.

Methods: MLO-Y4 in SFM and MLO-A5 osteocyte cell lines were exposed to different times and concentrations with Bil, LCA and UDCA were used to determine: 1) Viability: WST-1 colorimetric method; 2) Differentiation: quantification of alkaline phosphatase (AP) activity; 3) Mineralization: Alizarin red staining quantification; and 4) Apoptosis: quantification of DNA fragmentation and caspase-3 activity.

Results: For LCA (100 μM) and Bil (50 μM) significantly decreased viability in MLO-Y4 from 72 hours (10%) and 48 hours (11%), respectively (p<0.01), and Bil decreased viability (49%) in MLO-A5 from 96 hours (p<0.01). Bil decreased AP activity by 47% after 96 hours, under conditions of differentiation in MLO-Y4 (p<0.01). There were no effects on AP activity in MLO-A5. After 14 days, Bil was associated with a significant mineralization decrease, as high as 87%, in MLO-A5 (p<0.02). Moreover, Bil and LCA increased apoptosis in MLO-Y4, determined by DNA fragmentation (242% and 119%, respectively) and caspase-3 activity (190% and 251%, respectively) after 24 hours. In contrast, UDCA (100 μM) increased viability after 72 hours (11%) and decreased the deleterious effects of LCA or Bil (p<0.02). UDCA increased AP activity in MLO-Y4 after 72 hours under growth conditions (p=0.018), and after 24 hours under differentiation conditions (p<0.01).

Conclusions: Bilirubin and lithocholic acid have damaging effects on osteocyte cells, decreasing viability, differentiation and mineralization, and increasing apoptosis, effects that are neutralized by the UDCA. These results indicate that substances retained in cholestasis impair osteocytic functions, and therefore may be involved in the pathogenesis of osteoporosis in cholestatic diseases.

Disclosure of Interest: None declared


SAFETY OF DENOSUMAB IN A MONOCENTRIC COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: The safety of Denosumab, a fully human monoclonal antibody against RANKL, which was developed for treatment of osteoporosis and prevention of fractures, remains unclear in kidney transplant recipients.

Objectives: Our aim was to assess its clinical and biological tolerance in this specific population.

Methods: Design: Prospective observational monocentric cohort. Inclusion criteria: kidney transplant recipient who received at least one subcutaneous injection of denosumab in his medical history. Analysis: Denosumab was given at a dose of 60 mg every 6 months.

Results: Safety assessment: the following variables were collected every 6 months: infection, reaction at the injection site, plasmatic parameters of renal function and mineral metabolism (estimated glomerular filtration rate, serum creatinine, calcium, 1–25 [OH] vitamin D, PTH).

Patients: Results: Patients were recruited from April 2014 to September 2015. All patients received immunosuppression therapy including prednisolone ≥ 5 mg/d. The main baseline characteristics of the 37 kidney transplant recipients were the following [mean]: male: 41%, age: 60.5 years, BMI: 24.1, transplantation duration: 7.1 years, osteoporotic patients: 36%, osteoporotic patients: 64%, total lumbar spine T-score: -2.04 SD, total hip T-score: -4.22 SD, femoral neck T-score: -2.7 SD, T-score femoral neck: 0.67 g/cm², serum creatinine: 132.8 mmol/L, calcium: 2.33 mmol/L, 1–25 [OH] vitamin D: 93.5 mmol/L, PTH 95: ng/l. All patients were prescribed vitamin D and calcium supplementation.

Conclusions: Bilirubin and lithocholic acid have damaging effects on osteocyte cells, decreasing viability, differentiation and mineralization, and increasing apoptosis, effects that are neutralized by the UDCA. These results indicate that substances retained in cholestasis impair osteocytic functions, and therefore may be involved in the pathogenesis of osteoporosis in cholestatic diseases.

Disclosure of Interest: None declared


QUALITY OF LIFE ASSESSMENT IN POSTMENOPAUSAL OSTEOPOROSIS

S. Novokovic 1, G. Stanoevic 2. 1Institute of rheumatology; 2Health Center "Zvezdara", Belgrade, Serbia

Objectives: To compare two questionnaires a specific one-Osteoporosis Quality of Life Questionnaire (OQLQ) and a general one-Short Form-36 (SF-36), in women with decreased mineral bone density (BMD) and vertebral fractures, and to estimate which one is more useful for everyday work.

Methods: Cross-section study included 50 postmenopausal women with osteoporosis (OP), who were divided in the general questionnaire, and all known risk factors for osteoporosis were confirmed. Osteodensitometry scan (DXA) was performed on lumbar spine, and based on T index value and BMD the subjects were divided in two groups: first group (women with OP), n=25; second group (women with fractures due to OP regardless of BMD), n=25, and with at least 4 months since the last fracture. The quality of life was assessed by two questionnaires: a specific one OQLQ consists of 30 questions divided into 5 areas, which are evaluated from 1 to 7 (the lower the score the more severe function damage and worse quality of life) and the general questionnaire SF-36 containing 36 questions divided into 8 areas (scores from 0 to 100, where the lower value is also a poorer quality of life). Questionnaires were converted into two summarized scales, so as to obtain the total score for: physical (PCS) and mental functions (MCS). The two questionnaires were compared using appropriate statistical methods in SPSS.

Results: There was no significant difference between groups regarding: mean age: first=63.3±6.0, second=64.9±7.8, mean age at the start of the menopause (first=46.8±5.3, second=48.2±4.2 years), mean duration of menopause (first=16.4±6.9, second=17.1±5.9 year), but there was statistically significant difference in the number of risk factors for OP (first=1.81±1.2, second=2.8±0.9, p<0.01). Statistically significant difference between group population (p<0.01) in mean BMD and T score (first-BMD 0.807±0.057 g/cm², T score -3.1±0.249SD, second- BMD 0.931±0.172 g/cm², T score -2.09±1.45SD). The following DXA values were measured in the second group:8 patients normal,6 osteopenia,11-
Objectives: To compare the ability of FRAX and BMD alone in discriminating patients with and without fracture, and their effectiveness in identifying anti-osteoporotic treatment needs

Methods: 1300 rheumatic disease patients on long-term glucocorticoid were screened for vertebral fracture by radiograph from 7 rheumatology clinics. 220 osteoporotic treatment needs were screened for vertebral fracture by radiograph from 7 rheumatology clinics. 220 osteoporotic treatment needs were screened for vertebral fracture by radiograph from 7 rheumatology clinics. 220 osteoporotic treatment needs were screened for vertebral fracture by radiograph from 7 rheumatology clinics.

Results: Both groups of patients were matched in gender, disease type and cumulative glucocorticoid dose (p < 0.1). Patients in the fracture group were older (63±14 vs 59±12 years, p < 0.01), of lower body mass index (22.7±3.5 vs 24.3±7.3kg/m², p < 0.05), with a higher prevalence of previous fracture [38 (34.5%) vs 10 (9.0%), p < 0.01]. Daily intake of vitamin D [77 (70%) vs 54 (49.1%), p < 0.01], and bisphosphonates [23 (20.9%) vs 7 (6.4%), p < 0.01]. A receiver operating characteristic (ROC) curve analysis was performed to determine the ability of FRAX score with or without BMD and MOF alone to discriminate fracture status (Table 1). FRAX at the femoral neck and FRAX score with BMD were able to provide adequate discrimination with their area under curve (AUC) = 0.70. With regards to treatment indication, only 53/110 (48.2%) of the patients with vertebral fracture were identified as having osteoporosis (T-score < -2.5 at hip/spine) by DXA. In contrast, FRAX with BMD were able to identify 71/110 (64.5%) of the fracture patients whom treatment criteria were met, with a power of 0.97 and effect size of 0.38 (a medium effect) at the 0.05 level.

Table 1. Area under ROC curve on discriminating Fracture

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>95% Confidence Interval</th>
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</thead>
<tbody>
<tr>
<td>BMD at Femoral Neck</td>
<td>0.709</td>
<td>0.649-0.778*</td>
</tr>
<tr>
<td>BMD of Total Hip</td>
<td>0.693</td>
<td>0.563-0.763*</td>
</tr>
<tr>
<td>BMD of Lumbar Spine</td>
<td>0.654</td>
<td>0.581-0.727*</td>
</tr>
<tr>
<td>FRAX with BMD MOF</td>
<td>0.705</td>
<td>0.635-0.777*</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>0.720</td>
<td>0.651-0.789*</td>
</tr>
<tr>
<td>FRAX without MOF</td>
<td>0.681</td>
<td>0.610-0.752*</td>
</tr>
<tr>
<td>BMD</td>
<td>Hip fracture</td>
<td>0.687</td>
</tr>
</tbody>
</table>

Conclusions: In rheumatic patients on long-term glucocorticoid, FRAX score was more effective in identifying patients with intervention needs than BMD alone. It is suggested that FRAX should be used as a routine assessment to identify patients, even asymptomatic, for anti-osteoporotic treatment.

Acknowledgements: We would like to acknowledge the Research Grant Council of Hong Kong for funding support (RGC Ref No.1413714).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4531

FR10578 ODONTOID FRACURES IN THE ELDERLY: AN UNKNOWN OSTEoporotic FRACtURE?

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Background: Current WHO definition of osteoporosis excludes cervical fractures. However, in atrumatic odontoid fractures, mainly reported by orthopedic surgeons, bone status has not been described yet [1].

Objectives: To investigate bone status in elderly patients suffering a low energy odontoid fracture.

Methods: We conducted a prospective study from January 2016 to January 2017 in patients ≥65 years old, hospitalized in Nice University hospital for low energy odontoid fracture. An evaluation of bone status was proposed within 3 months after fracture event. Evaluation included demographic data, clinical risk factors of osteoporosis, bone mineral density (BMD) at spine and hip and vertebral fracture assessment (VFA) by dual x-Ray absorptiometry and serum and urine analysis to detect secondary osteoporosis.

Results: 38 patients were hospitalized for odontoid fracture: 8 patients <65 years always after a major trauma (mean age 37±14.5 y) and 30 patients ≥65 years including 3 after a high energy impact. 27 odontoid fractures followed a low energy impact: 18 women and 9 men, mean age 83.8 y. (±10.7). 8 patients died before bone status assessment (5 men and 3 women), 6 died during hospitalization with a mean delay of 3.5 days (±1.87) and 2 after discharge (1 month and 5 month). 3 patients refused bone status evaluation, 5 were lost to follow-up and 1 is awaiting evaluation. Finally 10 patients had bone status evaluation, all women, mean age 84.2 y. (±8.9). None had parental history of hip fracture, 1 had an early menopause, 1 received aromatase inhibitors for breast cancer and 2 had a history of steroid therapy (≥3 months). 3 patients had previously received hormone replacement therapy, 1 received bisphosphonate for 5 years and 4 had calcium + vitamin D supplements. Lumbar spine mean T-score was -1.45 (±1.08), femoral neck mean T-score was -0.99 (±1.6). VFA analysis revealed 4 unknown vertebral fractures. The table summarizes population bone status: 8 patients out of 10 fulfilled diagnostic criteria of osteoporosis, including 6 with previous fractures. 2 patients with T-score > -1 DS didn’t have bMD assessment because of bilateral hip replacement but had previous major osteoporotic fractures.
secondary osteoporosis was detected. Serum vitamin D concentration was \(<30\) ng/mL in 5 patients, including 2 with concentration \(<10\) ng/mL.

**Conclusions:** Our study reveals that odontoid fractures mainly occur in elderly osteoporotic patients after a low energy impact. Although WHO osteoporosis definition excludes cervical fractures, odontoid fracture may be considered as an osteoporotic fracture. Further studies are required to confirm these results.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3503

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**FR0579** **INFLUENCE OF ORAL PREDNISOLONE ON EFFECT OF DENOSUMAB ON OSTEOPOROSIS IN PATIENTS WITH JAPANESE NEUMATOID ARTHRITIS; 24 MONTHS OF FOLLOW-UP - A MULTICENTER REGISTRY STUDY-**

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**Background:** Denosumab (DMB) is a fully human monoclonal antibody to the RANKL that blocks its binding RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, increasing bone density and reducing fracture risk. Osteoporosis (OP) is more frequent in patients with rheumatoid arthritis (RA) than in the general population due to active systemic inflammation as well as the use of glucocorticoid and immobility. However efficacy of DMB is not clear in patients with glucocorticoid-induced OP in RA. Therefore we investigated the influence of oral prednisolone on effect of DMB in patients with Japanese RA from initiation to 24 months at this time.

**Objectives:** This prospective study investigated the efficacy of DMB for 24 months on glucocorticoid-induced OP in RA patients.

**Methods:** Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed DMB from Tsumari Biosciences Communication Registry (TBCR)-BONE between October 2013 and October 2015 were enrolled. The final study cohort of 63 patients received continuous DMB therapy more than 24 months. The DMB dose was 60 mg at once every 6 months. In all cases native or activated vitamin D has been used. We reviewed the results for 24 months about the increase and decrease of bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DXA and bone turnover markers, intact n-terminal propeptide type I procollagen (PINP) and tartrate-resistant acid phosphatase 5b (TRACP-5b).

**Results:** In the patients receiving oral prednisolone group (n=23, GC+) and not receiving group (n=40, GC-) the number of female was each 21 (91%) and 39 (98%) cases (p=0.548). The mean age was 69.8±7.0 and 71.0±7.3 years old (p=0.622); disease duration was 16.0±8.9 and 15.7±12.6 years (p=0.592); the body mass index was 20.7±3.5 and 19.7±3.0 (p=0.335) and the FRAX was 34.2±19.1 and 24.6±13.9 (p=0.040). Clinical findings related to RA and OP at baseline were as follows: CRP 1.2±1.4 and 0.5±1.0 mg/dl (p=0.030); DAS-CRP 3.16±1.7 and 2.50±1.27 (p=0.025); m-HAQ 1.24±0.90 and 0.82±0.82 (p=0.065); P1NP 60.1±38.6 and 56.9±33.5 μg/l (p=0.711); TRACP-5b 513±257 and 505±220 μg/dl (p=0.689); LS-BMD 0.87±0.18 and 0.80±0.14 g/cm² (p=0.074) and TH-BMD 0.60±0.11 and 0.59±0.08 g/cm² (p=0.457). The rate of decreased P1NP from baseline to 6, 12, 18 and 24 months were each -25.6% vs -41.6% (p=0.129) at 6 month, -8.0% vs -42.6% (p=0.031) at 12 month, -19.5% vs -27.5% (p=0.235) at 18 month and -13.8% vs -33.8% (p=0.134) at 24 month and TRACP-5b were each -26.5% vs -38.7% (p=0.710) at 6 month, -22.0% vs -35.1% (p=0.229) at 12 month, -25.2% vs -38.1% (p=0.792) at 18 month and -20.6% vs -27.3% (p=0.063) at 24 month in the GS+ vs GS- group. The rate of increased LS-BMD from baseline to 6, 12, 18 and 24 months were each 4.1% vs 4.6% (p=0.671) at 6 month, 5.3% vs 7.0% (p=0.361) at 12 month, 8.1% vs 8.1% (p=0.438) at 18 month and 10.0% vs 7.7% (p=0.104) at 24 month and TH-BMD were each 3.3% vs 2.7% (p=0.690) at 6 month, 6.4% vs 4.3% (p=0.269) at 18 month and 5.7% vs 4.3% (p=0.945) at 24 month in the GS+ vs GS- group (Fig.1,2).

**Conclusions:** DMB was effective in OP of RA patients. Oral prednisolone use did not influence the efficacy of DMB for 24 months.


**DOI:** 10.1136/annrheumdis-2017-eular.4877

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**FR0580** **PREDICT SARCOPENIA BY SONOELASTOGRAPHY OF QUADRICEPS MUSCLE IN OSTEOPOROTIC PATIENTS**

Y.-C. Chen, C.-H. Ko. Rheumatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, Province of China

**Background:** Reduced muscle mass had associated with high mortality. So it is urgent for simple techniques to early detection sarcopenia. Our objective was to examine the validity of sonoelastography to predict sarcopenia in osteoporotic patients.

**Objectives:** To evaluate the association of sonoelastography and dual-energy X-ray absorptiometry in patients with sarcopenia and osteoporosis.

**Methods:** We conducted an observational study in Kaohsiung Chang Gang Memorial Hospital. Sarcopenia was determined using a dual-energy X-ray absorptiometry. Osteoporosis was defined through estimated bone mass (BM). Sonoelastography was performed over mid thigh over quadriceps muscle. We measure hardness and elastography ratio of quadriceps over subcutaneous fat tissue. ROC analysis was used to find best cut-off point.

**Results:** A total 47 (23 sarcopenia, 24 non-sarcopenia) osteoporotic patients were enrolled. The mean age was 71.04±9.64 years, and most patients (88.9%) were women. Sonoelastography showed sarcopenia patients had more soft than non-sarcopenia patients, furthermore the elastography ratio of quadriceps over subcutaneous tissue was lower than non-sarcopenia patients. When the cut points determined by receiver operating characteristic (ROC) curve analysis were applied, The best cut-point of hardness was 42.5 (sensitivity, 0.969; specificity, 0.066), while the best cut-point of quadriceps over subcutaneous tissue was 70.5% (sensitivity, 1.000; specificity, 0.079).

**Characteristics of study patients**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sarcopenia (n=23)</th>
<th>Non-sarcopenia (n=24)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71.04±9.64</td>
<td>70.82±8.62</td>
<td>0.316</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.80±3.45</td>
<td>23.82±4.56</td>
<td>0.977</td>
</tr>
<tr>
<td>Gender (Female %)</td>
<td>22 (75.9%)</td>
<td>78 (84.8%)</td>
<td>0.624</td>
</tr>
<tr>
<td>EX2/1</td>
<td>0.37±0.15</td>
<td>1.36±0.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hard%</td>
<td>15.44±13.15</td>
<td>76.70±20.12</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** Sonoelastography was easily applicable in patients with sarcopenia and osteoporosis. Using hardness content and elastography ratio of quadriceps over subcutaneous ratio render more information of muscle character. Early detection of sarcopenia with sonoelastography in patients with osteoporosis afford future trend of preventive medicine in geriatric patients.

**References:**

**Acknowledgements:** This study was supported by Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung (grant CMRPGBF1731).
HEPATITIS B INCREASE MORTALITY IN PATIENTS WITH OSTEOPOROTIC VERTEBRAL FRACTURES

Y.-C. Chen, C.-H. Ko. Rheumatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, Province of China

Background: Hepatitis B virus (HBV) is a major cause of chronic liver diseases worldwide, particularly cirrhosis and hepatocellular carcinoma, and the most important liver disease in Taiwan. However, little is known the impact of hepatitis B on osteoporotic patients.

Objectives: This study aimed to determine if hepatitis B can increase the risk of mortality in patients with osteoporotic vertebral fracture.

Methods: This retrospective study reviewed of cases of osteoporosis patients with acute vertebral fractures between 2001 and 2008. All associated co-morbidities were recorded. Kaplan-Meier and cox regression analysis were performed.

Results: There were 432 patients with acute vertebral fractures. The mean age of 72.85±9.28. 31 (7.2%) patients had chronic hepatitis B. Using the Kaplan-Meier curve, hepatitis B had a significant effect on mortality (p<0.001, by log rank test). After adjusting for potential confounders, patients with hepatitis B still had a high mortality rate (p=0.019; HR: 2.436–5.136) 2.137, 95% CI: 1.156–5.136. The mortality rate also increased among smokers (p=0.026; HR: 3.6043.891; 95% CI: 1.056–12.301).

Table 1. Multivariant Cox regression analysis of the hazard ratios for adjacent fracture

<table>
<thead>
<tr>
<th>Variables</th>
<th>Regression coefficient</th>
<th>P value</th>
<th>HR (95CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.127</td>
<td>0.784</td>
<td>0.88 (0.383–0.202)</td>
</tr>
<tr>
<td>Age</td>
<td>0.004</td>
<td>0.785</td>
<td>1.004 (0.976–1.032)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.282</td>
<td>0.041</td>
<td>3.604 (1.056–12.301)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>-0.701</td>
<td>0.396</td>
<td>0.496 (0.098–2.508)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.024</td>
<td>0.446</td>
<td>1.024 (0.964–1.088)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>0.891</td>
<td>0.019</td>
<td>2.436 (1.156–5.136)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.185</td>
<td>0.538</td>
<td>0.831 (0.461–1.498)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-0.271</td>
<td>0.31</td>
<td>0.762 (0.451–1.288)</td>
</tr>
<tr>
<td>Stroke</td>
<td>-0.696</td>
<td>0.248</td>
<td>0.499 (0.153–1.625)</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>0.809</td>
<td>0.145</td>
<td>2.246 (0.758–6.656)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.037</td>
<td>0.946</td>
<td>1.038 (0.351–3.065)</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>-0.971</td>
<td>0.349</td>
<td>0.379 (0.050–2.383)</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard ratio; SE, standard error.

Conclusions: In this study, hepatitis B increase mortality in osteoporotic vertebral fracture patients. We should pay attention to this group in osteoporotic management.

References:

Acknowledgements: We thank Kaohsiung Chang Gang Memorial Hospital for data support.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3614
FR010583 | IGG4-RELATED DISEASE AMONG PATIENTS PREVIOUSLY DIAGNOSED WITH IDIOPATHIC RETROPERITONEAL FIBROSIS. A NATIONWIDE DANISH STUDY

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Background: IgG4-related disease (IgG4-RD) is a recently recognized systemic disease of unknown etiology and prevalence [1]. Retrospective single center series have provided evidence that 13–63% of patients with idiopathic retroperitoneal fibrosis (IRPF) could be reclassified as IgG4-RD. Since immunosuppressants or B-cell targeted therapies may halt or reverse progression, early diagnosis and treatment is important to prevent terminal fibrosis.

Objectives: To confirm the occurrence of IgG4 related retroperitoneal fibrosis (RPF) in Danish patients diagnosed with IRPF.

Methods: The National Danish Pathology Register was searched for biopsy codes relating to retroperitoneal tissue and inflammation from 01.01.2004 through 31.12.2013. Patients below 18 years of age, secondary causes, malignancies, infections, and specimens with multinucleated giant cells or granulomas were excluded. Among 724 candidate cases 68 were identified with IRPF. Among these 25 were left out due to small tissue samples, unavailable patient files or lack of consent. Clinical, laboratory data and imaging were reviewed. Paraffin-embedded tissue blocks were retrieved from 18 pathology departments. Four sections were processed and stained with hematoxylin-eosin, Weigerts elastin and IgG4 immunostaining. Histopathologic features suggesting an IgG4-RD background were recorded (table). Cut-off levels for IgG4 positive cells at ≥ 10 HPF and IgG4: total IgG ratio > 40% were applied. Patients were categorized as definite, possible, or non-inflammatory IRPF according to international consensus [2].

Results: Forty three patients (29 males), median age 56 years were included among which 19(44%) met the criteria for IRPF-RD comprising 7 with definite, 12 with possible IRPF-RD and 24 with 40% or greater IgG4+ cell counts. Twenty-three patients (53%) had ≥ 10 HPF and 4 patients ≥ 10% of IgG4+ cells or IgG4 in IgG4 RPF.

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Results: Forty three patients (29 males), median age 56 years were included among which 19(44%) met the criteria for IRPF-RD comprising 7 with definite, 12 with possible IRPF-RD and 24 with 40% or greater IgG4+ cell counts. Twenty-three patients (53%) had ≥ 10 HPF and 4 patients ≥ 10% of IgG4+ cells or IgG4 in IgG4 RPF.
Methods: We retrospectively investigated factors related to REOI and NDOI in 86 IgG4-RD patients whose follow-up period was more than 12 months. For assessment of factors related to REOI and NDOI, we performed uni- and multivariate Cox regression analysis. On stepwise multivariate analysis, we applied the variables with $P<0.1$ in univariate analysis and the predictors of relapse defined in previous literature, i.e., sex, serum IgG4, IgG, and Ig levels, eosinophil counts, and RF positivity [2, 3], and used the forward selection method (including factors presenting with $P<0.05$).

Results: The patients comprised 57 men and 29 women (mean age 65.9 years). Mean follow-up period was 63.1 months (range 14–150). At diagnosis, their mean serum IgG4 level was 718 mg/dL (range 10.7–5,150). Seventy-one patients were treated with glucocorticoid (GC). REOI was detected at 52.3 months (range 1.0–120) after the diagnosis in 20 patients, including 4 not receiving GC at that time. On the other hand, NDOI was detected at 37.6 months (range 5.0–120) after their diagnosis in 15 patients, including 11 not receiving GC. In univariate Cox regression analysis, blood eosinophil counts [per 100×/L], hazard ratio (HR) 1.072, 95% confidence interval (CI) 1.018–1.129, $P=0.008$ and continuation of GC (vs discontinuation or observation without GC, HR 0.245, 95% CI 0.076–0.793, $P=0.019$) had a significant impact on the time to NDOI, whereas age (per year, HR 0.942, 95% CI 0.899–0.986, $P=0.011$) and ANA positivity (vs negativity, HR 6.632, 95% CI 1.892–23.255, $P=0.003$) had a significant impact on the time to REOI.

Conclusions: The present study suggests that the risk factors of REOI and NDOI in IgG4-RD are different.

References:

Disclose of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2425
CANCER IS FREQUENT IN PATIENTS WITH ANTICENTROMERE PATTERN

M. Akiyama

Methods:
The aim of this study was to examine the association of sIL-2R activity of lymphoproliferative disorders and autoimmune diseases.

Soluble interleukin-2 receptor (sIL-2R) is known as an indicator for T cell activation status of lymphocytes and could be a potential biomarker for disease exacerbation. In some diseases such as lupus, the increase of sIL-2R is observed in some patients with active disease [5,6]. In Sjögren’s syndrome, the levels of sIL-2R are closely correlated with the extent of organ involvements and extra-dacryosialadenitis lesions in patients with IgG4-RD, compared with serum IgG and IgG4, with a cut-off value of 424 U/mL (AUC=0.917, p=0.0001), and in patients with pSS with 513 U/mL (AUC=0.894, p=0.0001). The sIL-2R levels in patients with IgG4-RD decreased significantly after glucocorticoid treatment. Notably, the cases which could be followed up at disease relapse or during glucocorticoid therapy showed the re-emergence of sIL-2R levels.

Cancer preceded the diagnosis of ACA in 19 patients (48.7%), with a mean time to diagnosis of 9.1 years (range 1–18). In the cohort of 350 patients with ACA the prevalence of cancer at some time (10.6%), 3 of them with 2 types of cancer. The most frequent were: Sjögren’s syndrome, 4.6% autoimmune hepatitis and 11 other SAD (polyarthritis, SLE, Raynaud phenomenon, sarcoidosis, mixed connective tissue disease, etc). 45 of these patients (15.9%) had any overlap syndrome. 39 patients had cancer at some time (10.6%), 3 of them with 2 types of cancer. The most frequent were: breast in 9 (23.1%), lung in 5 (11%), NHL in 5 (11%) and colorectal in 4 (10.3%). Cancer preceded the diagnosis of ACA in 19 patients (48.7%), with a mean time to diagnosis of 9.1 years (range 1–18). In the cohort of 350 patients with ACA the incidence was 1.14 per 100 patients per year (20). The mean time to diagnosis of cancer was 7.3 years (range 1–27). The oldest age was the only risk marker of cancer identified (70.8±13.29 years vs 63.9±14.32, p=0.005). There were no differences in the other variables analysed including sex, tobacco, diagnosis of SAD, capillaroscopy pattern, ANA titrations and mortality.

Conclusions: Cancer was frequent in patients with ACA, with a prevalence of 10.6% and incidence of 1.14 per 100 patients per year. The only risk marker of cancer identified in this population was the oldest age

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4455

FRI0589 | CANCER IS FREQUENT IN PATIENTS WITH ANTICENTROMERE PATTERN

C. Vázquez-Tirán[1], V. Alende[2], E. González[3], R. Lorenzo[3], T. Cainzos[3], L. González[3], S. Rodríguez[3], B. Sopeña[2] on behalf of Círculo de estudio de las enfermedades autoinmunes de Galicia (CEAG).


Background: Anti-centromere pattern (ACA) is infrequently seen among antinuclear antibodies (ANA) detected by indirect immunofluorescence (IFI). ACA is associated with systemic autoimmune diseases (SAD), especially systemic sclerosis (SSc). Some studies had recently related ACA with cancer, mostly with breast and lung cancer [1]. However, most published series of patients with ACA lack information about cancer occurrence. A prevalence of cancer of 11.1% was the only reported data, on a series of 45 unselected patients with ACA [2].

Objectives: Our aim was to study the prevalence of cancer in the largest series of patients with ACA, with a long follow-up. Our second objective was to make a cohort to calculate the incidence of cancer and to try to identify risk markers of cancer in these patients.

Methods: We included consecutive patients with at least 2 positive determinations of ANA with ACA by IFI on Hep2 cells between January 1st of 2011 and June 30th of 2015 in 6 Galician hospitals. The authors reviewed each patient’s chart to determine the presence of cancer, its occurrence, and a prevalence of cancer of 11.1% was the only reported data, on a series of 45 unselected patients with ACA [2].

Results: 369 patients with ACA were studied, of which 333 were women (90.2%), with a mean age of 64.7 years (range: 22–92). The mean follow-up from the first positive determination of ACA was 67.6 months (76.7% had a follow-up of patients with ACA at some time (10.6%), 3 of them with 2 types of cancer. The most frequent were: breast in 9 (23.1%), lung in 5 (11%), NHL in 5 (11%) and colorectal in 4 (10.3%). Cancer preceded the diagnosis of ACA in 19 patients (48.7%), with a mean time to diagnosis of 9.1 years (range 1–18). The cohort of 350 patients with ACA the incidence was 1.14 per 100 patients per year (20). The mean time to diagnosis of cancer was 7.3 years (range 1–27). The oldest age was the only risk marker of cancer identified (70.8±13.29 years vs 63.9±14.32, p=0.005). There were no differences in the other variables analysed including sex, tobacco, diagnosis of SAD, capillaroscopy pattern, ANA titrations and mortality.

Conclusions: Cancer was frequent in patients with ACA, with a prevalence of 10.6% and incidence of 1.14 per 100 patients per year. The only risk marker of cancer identified in this population was the oldest age.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4220

FRI0590 | SOLUBLE INTERLEUKIN-2 RECEPTOR LEVELS REFLECT DISEASE ACTIVITY IN IgG4-RELATED DISEASE AND PRIMARY SJÖGREN’S SYNDROME

M. Akiyama, T. Sasaki, Y. Kaneko, H. Yasuoka, K. Suzuki, K. Yamaoka, T. Takeuchi, Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan.

Background: IgG4-related disease (IgG4-RD) is a fibroinflammatory disease characterized by elevated serum IgG4 and infiltration of IgG4* plasma cells at affected organs. The patients with IgG4-RD respond to glucocorticoids (GCs), but one-third of the patients experience disease relapse during tapering of GCs [1]. The risk factors for disease relapse following treatment are unclear.

Objective: The aim of this study was to identify the risk factors of disease relapse following reducing dose of glucocorticoid.

Methods: Consecutive, newly diagnosed patients with IgG4-RD who were followed over 6 months after treatment with GCs in our department were enrolled. The patients were divided into two groups according to the presence or absence of disease relapse. Disease relapse was defined as the appearance of new lesions or the re-enlargement of involved organs that required dose-increase of GCs alone as initial treatment. Ten patients (29.4%) experienced relapses during GCs alone as initial treatment. Ten patients (29.4%) experienced relapses during GCs alone as initial treatment. The patients with ACA were excluded. We checked the presence of any tumour in patients of this cohort at the end of follow-up to calculate the incidence of cancer. Finally, we compared patients with and without cancer by multivariate analysis, with the patients enrolled in this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3301

FRI0591 | RISK FACTORS FOR DISEASE RELAPSE IN IgG4-RELATED DISEASE FOLLOWING GLUCOCORTICOIDS TREATMENT

T. Sasaki, M. Akiyama, Y. Kaneko, H. Yasuoka, K. Suzuki, K. Yamaoka, T. Takeuchi, Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan.

Background: IgG4-related disease (IgG4-RD) is a fibroinflammatory disease characterized by elevated serum IgG4 and infiltration of IgG4* plasma cells at affected organs. The patients with IgG4-RD respond to glucocorticoids (GCs), but one-third of the patients experience disease relapse during tapering of GCs [1]. The risk factors for disease relapse following treatment are unclear.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4455
by 3 (20%), 0 and 1 (14%) and 4 (8%). Histological confirmation was obtained by transthoracic biopsy (66%), cutaneous (12%) or lymph node biopsy (12%) in 90% of the patients. 90% of patients have been treated with oral glucocorticoids and 42% associate immunosuppressive therapy. The ACE levels showed no statistical association with any of the variables studied, although a very clear association (p=0.04754) was observed between the course of the disease and the presence of extrapulmonary symptoms: from the 25 patients without extrapulmonary symptoms, only in 35% of cases the process became chronic.

Conclusions: Our results, in general, coincide with what is published in the literature. In our cohort, initial diagnosis of S was relatively high (29/50 =58%), while misdiagnosis was relatively low (6/50 =12%). The level of ACE does not seem to be clearly associated with the presence of extrapulmonary symptoms, nor with the course of S. However, the presence of extra-pulmonary symptoms seems to lead to a chronic evolution.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5480

FRIO593 ASSOCIATION OF THYMOMA WITH AUTOIMMUNE DISEASES IN A SERIES OF 83 CASES
A. Gonzalez García 1, W.A. Sifuentes Giraldo 2, J.L. Morell Hita 2, J.L. Patier de la Peña 1, 1Rheumatology, 2Rheumatology and Immunology; Ramon y Cajal University Hospital, Madrid, Spain

Background: Thymoma is the most common neoplasm originated from the thymus gland and accounting for 50% of anterior mediastinal tumors. Within its clinical manifestations are included the loss of self-tolerance and the development of autoimmunity.

Objectives: To study the frequency of autoimmune diseases (AD) in patients with thymoma and to describe their clinical characteristics and outcome.

Methods: We performed a retrospective observational study of a cohort of patients diagnosed with thymoma and followed-up in our center between January 1985 and September 2016. The variables evaluated included demographics, thymoma characteristics, clinical and analytical manifestations of autoimmunity, treatment and outcome.

Results: A total of 83 patients were included, 56.6% of them women, with a mean age at diagnosis of the thymoma of 58.4±15.8 years (range: 16–94), 31.3% of which corresponded to type I The classification of Masaoka, 39.1% to II, 17.2% to III and 10.9% to IV. There were one or more AD associated in 41 cases (49.4%). The most frequent diagnoses were myasthenia gravis (19), systemic lupus erythematosus (SLE) (4), subacute cutaneous lupus erythematosus (1), Sjögren’s syndrome (1), rheumatoid arthritis (1), spondyloarthritis (1), sarcoidosis (1), hemolytic anemia (2), pernicious anemia (1), aplastic anemia (1), cutaneous limited systemic sclerosis (1), urticaria-vasculitis, erythroblastopenia (1), recurrent pericarditis (1), thyroid disease (2) and lichen planus (1). The diagnosis of AD preceded to thymoma in 38.2% of cases and was later in the remaining cases. In 4 cases there was also a concomitant primary immunodeficiency (variable common immunodeficiency 3, CD4 immunodeficiency 1). The most frequently identified autoantibodies were anti-acetylcholine receptor (14/41, 34.1%), anti-synthetase muscle (3/41, 7.3%), ANA (11/41, 26.8%), anti-SSA (3/41, 7.3%), antiphospholipids (2/41, 4.9%), and antineutrophil cytoplasmic (1/14, 2.4%). In the comparison of patients with and without associated AD, no significant differences were found regarding age, sex or Masaoka classification. There were 6 deaths, 4 in group with associated AD and 2 in the group without AD, but without significant difference (p=0.3797).

Conclusions: In the analyzed population of patients with thymoma of our center, almost half of them developed AD, which in a major group preceded the diagnosis of neoplasia. The spectrum of autoimmunity associated with thymoma was quite broad, including organ-specific AD such as myasthenia gravis (which is most frequently described in the literature) and autoimmune cytopenias, but also to systemic AD, the most common being SLE. The autoimmunity study should be included in the assessment of the patient with thymoma as it could contribute to the early diagnosis of associated AD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6992

FRIO594 A CASE OF MOSAICISM IN TNF ASSOCIATED PERIODIC SYNDROME (TRAPS)
A. Kontzias 1, C. Calabrese 1, Y.-W. Cheng 2, 1Rheumatology and Immunology; 2Laboratory Medicine, Cleveland Clinic, Cleveland, United States

Background: Tumor necrosis factor receptor (TNFR)–associated periodic syndrome (TRAPS) is an autosomal-dominant disease caused by gain-of-function mutations in the TNFRSF1A gene, which encodes the 55-kd TNFR type I (TNFRI) protein. Mosaicism has been recently identified in a single patient. A 60 year old male presented with a 6 year history of intermittent fever as high as 103.5, lasting 3–4 days with associated peripheral symptoms, arthralgias, myalgias, lymphadenopathy, bilateral episceritis, erythromelalgia rash in his torso. Prednisone up to 60 mg daily only partially alleviated his symptoms and colchicine was ineffective.

Objectives: To explore the role of mosaicism in a patient with adult onset TRAPS phenotype.

Disclosure of Interest: None declared


FRIO592 CLINICAL, ANALYTICAL AND RADIOLOGICAL CHARACTERISTICS IN A COHORT OF PATIENTS WITH SARCOIDOSIS
A. Ruiz Román 1, C. Aguilera Cros 1, M. Arcila Durán 1, M. León Luque 1, M. Lisbona Muñoz 1, J.P. Sanchez Serrano2, J.A. Rodriguez Portal 3, A. Kontzias 1, C. Calabrese 1, Y.-W. Cheng 2, 1Rheumatology, 2Laboratory Medicine, Cleveland Clinic, Cleveland, United States

Background: sarcoidosis is a systemic granulomatous disease, frequently affecting lungs, eyes and skin, although it may damage other organs, among them the musculoskeletal system.

Objectives: To describe the clinical characteristics and radiological pattern in a cohort with predominantly pulmonary sarcoidosis, and to determine the relationship between the levels of angiotensin converting enzyme (ACE), pulmonary radiological stage and sarcoidosis course (chronification or remission)

Methods: Data from 2328 patients in an Interstitial Lung Diseases consultation during the first half of 2016 were analyzed. Out of these, 50 had sarcoidosis.

The delay in the diagnosis of sarcoidosis was defined as the difference in years between the diagnostic suspicion and diagnosis of sarcoidosis.

Chi square tests were used, assuming an error of the first species not higher than 0.05, in order to: 1. Study the association between angiotensin converting enzyme (ACE) levels and binary variables (extrapulmonary symptoms, radiological stage and evolution of S) 2. Determine the association between evolution, the radiological stage and the presence of extrapulmonary symptoms.

Results: We included 29 (58%) women and 21 (42%) men, (mean age of 44±11.7 years). Initial diagnosis: 88% S, 8% lymphoma and 4% tuberculosis. Of the 44 diagnosed cases of S, 24 were on the first visit, 11 the following year and 1 seven years later. Of the 4 lymphomas, 2 were diagnosed of S that same year and the other 2 were diagnosed the following year. Of the 2 tuberculosis, one was diagnosed of S in one year and the other at 4 years. The most frequent extrapulmonary manifestations were cutaneous 24%, followed by the articular, cardiac and ocular in 10%, neurological 8% and renal 4%. In 6% of patients, the first clinical manifestation of the disease was bilateral arthritis of the ankles. The ACE title is increased in 62% of patients, normal in 34%. The mean and standard deviation of the title of patients with an increased ACE value was 150.5 and 35.4 IU/L, respectively. In all patients, x-ray and high resolution tomography were performed, with stage 2 being the most frequent (44%), followed

the higher likelihood of disease relapse following GCs therapy in patients with IgG4-RD.

References:

Acknowledgements: We sincerely thank all the physicians and others caring for the patients enrolled in this study.

Disclosure of Interest: None declared
Methods: DNA was extracted from the patient’s whole blood, saliva and hair root. The TNFRSF1A gene was analyzed by Sanger sequencing in all tissues, and next-generation sequencing in whole blood. In silico molecular modeling was performed to predict the structural and functional consequences of the tumor necrosis factor receptor (TNFR) type I protein mutation.

Results: Sanger sequencing and next-generation sequencing methods revealed differential tissue presence of a missense mutation at c.265 T→C p.Phe89Leu (F89L) Chr12(GRCh37):g.6442960A→G ex3 rs104895245. The mutant allele was present in whole blood and buccal mucosa and absent in hair root, supporting the presence of somatic TNFRSF1A mosaicism. In silico prediction modeling with SIFT and PolyPhen2 suggested that this mutation led to numerous structural rearrangements which resulted in changes in the protein surface profile. The patient had a complete response to treatment with canakinumab an interleukin-1 beta blocker, with resolution of symptoms and normalization of acute-phase protein levels.

Conclusions: This is the second reported case of TNFRSF1A mosaicism in a patient with TRAPS, which was attributable to a de novo mosaic missense mutation in the TNFRSF1A gene, (c.265 T→C) p.Phe89Leu (F89L). The clinical picture in this patient, including the complete response to IL-1 blockade, was typical of that found in TRAPS. This case suggests that adult onset TRAPS phenocopies may be attributed to somatic (or postzygotic) mutations.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3485

FRIO595 | EPIDEMIOLOGY AND COMPLICATIONS OF HOSPITALIZED PATIENTS WITH ADULT ONSET STILL’S DISEASE IN UNITED STATES: A NATIONWIDE ESTIMATE
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Background: There is a dearth of epidemiological studies in the US and worldwide on Adult Onset Still’s Disease (AOSD). Currently, there is no consensus on its incidence and prevalence in different populations. Most studies report a majority of patients below the age of 35.[1]

Objectives: To describe the demographics, complications and mortality of hospitalized patients with AOSD in United States.

Methods: All adult (>18 years) hospitalized patients in 2013 from a nationwide inpatient sample (NIS) database were captured. AOSD patients were identified using the ICD-9 code 714.2 that was in use in 2013. Patients also coded for Rheumatoid Arthritis, Lupus, Myositis, Polymyalgia Rheumatica, Ankylosing Spondylitis and Psoriatic Arthritis were excluded. This was done in order to truly capture patients with strictly AOSD. NIS is the largest all-payer inpatient care database in the United States with approximately 8 million hospitalizations each year. Discharge weights were used to enable nationwide estimates. Descriptive statistics were represented as means/medians for continuous and as frequencies and percentages for categorical variables.

Results: In 2013, 1,410 US patients were coded with the ICD-9 code 714.2 and, after excluding concomitant rheumatic disease diagnoses as per protocol, 1,265 AOSD patients were analyzed. AOSD patients had a mean age of 53.8 (SD - 18.1) years and a median age of 54 years. 70.4% were females. The racial/ethnic distribution showed that 61.6% white, 13.9% African American and 11% Hispanic patients were affected. 56.9% were hospitalized in urban teaching hospitals. The Mid-Atlantic census division had the highest number of patients – 240 (Figure). 35 (2.8%) of patients developed Macrophage Activating Syndrome (MAS). 30 (2.4%) patients had other severe complications of AOSD like disseminated intravascular coagulation (DIC) and thrombotic thrombocytopenic purpura (TTP). Median length of stay was 4 days and median hospital charges were $31,400 (Table). There were 35 inpatient deaths (mortality 2.8%): 71.4% of deaths were in females, 50% in Asians, and 71.4% were in patients in the 54-67 age group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N=1265</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean age in years (standard deviation))</td>
<td>53.9 (18)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Female Sex</td>
<td>890</td>
<td>70.4%</td>
</tr>
<tr>
<td>White</td>
<td>730</td>
<td>61.6%</td>
</tr>
<tr>
<td>Black</td>
<td>165</td>
<td>13.9%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>205</td>
<td>17.3%</td>
</tr>
<tr>
<td>Asian</td>
<td>50</td>
<td>4.2%</td>
</tr>
<tr>
<td>Bed Size of the Hospital</td>
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<td></td>
</tr>
<tr>
<td>Small</td>
<td>140</td>
<td>13.7%</td>
</tr>
<tr>
<td>Medium</td>
<td>270</td>
<td>26.5%</td>
</tr>
<tr>
<td>Large</td>
<td>610</td>
<td>59.8%</td>
</tr>
<tr>
<td>Location/teaching status of hospital</td>
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<td></td>
</tr>
<tr>
<td>Rural</td>
<td>100</td>
<td>9.8%</td>
</tr>
<tr>
<td>Urban non-teaching</td>
<td>340</td>
<td>33.3%</td>
</tr>
<tr>
<td>Urban teaching</td>
<td>580</td>
<td>56.9%</td>
</tr>
<tr>
<td>Macrophage Activating Syndrome</td>
<td>35</td>
<td>2.8%</td>
</tr>
<tr>
<td>Other complications - (DIC and TTP)</td>
<td>30</td>
<td>2.4%</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>35</td>
<td>2.8%</td>
</tr>
<tr>
<td>Length of stay (Median no of days)</td>
<td>4 days</td>
<td>2.8%</td>
</tr>
<tr>
<td>Total Hospital Charges (Median in dollars)</td>
<td>$ 31,400</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

Conclusions: In hospitalized American AOSD patients, the average age was higher than previously thought. This may indicate an aging population with a higher number of comorbidities that justify hospitalization. Mortality increased with age and was higher among women and Asians. To our knowledge, this is the largest epidemiological study of AOSD today in the USA.

References:

Disclosure of Interest: None declared

FRIO596 | ANAKINRA TREATMENT IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A SINGLE-CENTER EXPERIENCE (CASE SERIES)
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Background: Approximately in 5 to 10% of FMF patients there is insufficient response and/or intolerance to colchicine treatment. Several reports have pointed out the efficacy of IL-1 blockade in colchicine resistant FMF subgroup.

Objectives: To review the patients followed in our center with FMF who received Anakinra, an anti-IL-1 receptor antagonist, in terms of outcome and side effects.

Methods: 43 FMF patients who were treated with Anakinra were retrospectively
reviewed with regard to indication, effect on disease activity and acute phase response, adverse events and patient global assessment.

Results: There were 43 patients with FMF (20 M/23 F) who were treated with Anakinra for various indications (colchicine resistant recurrent febrile attacks in 39, colchicine related side effects in 3, both in 1). The mean age of the patients was 39.4±12.6 years. The mean duration of the disease was 19.90±10.52 years. There were various co-existing pathologies among this study group like Ankylosing Spondylitis (4), Psoriasis (1), Behçet’s disease (1), Gout (1), Vasculitis (1), Adult-onset Still’s disease (1), Polymyalgia Nodosa (1) and Celiac disease (1). The mean colchicine dose was 1.84±0.31 mg/dl. As for the dosage, 35 patients were on 100 mg/day, 6 were on 100 mg on alternate days, 2 were on 200 mg/day. The mean duration of anakinra treatment was 10.76±13.64 months. After the initiation of anakinra 29 patients became attack-free, 9 patients reported more than 50% decrease, 3 patients less than 50% decrease, and 2 patients no change in the frequency of the attacks. Mean global pain intensity decreased from 7.55±2.34 to 2.82±2.63 under Anakinra treatment (<0.001).

For the adverse events, eight patients (18%) had allergic reactions under Anakinra treatment (severe disseminated rash in 1 patient and severe joint injection site reaction in 4 patients and tolerable injection side reaction in 3) which necessitated termination of treatment in 5 patients. Anakinra was stopped because of genital rashes and urinary tract infection in one other patient. Worsening of psoriatic lesions was observed in another patient. There were no adverse events in the remaining 41 patients during the course of treatment. On the other hand, treatment was terminated in case of inadequate response in 11 (25%), remission in 2 and patient preference in 3 patients. Nineteen patients are still on Anakinra treatment for 10.09±14.51 months.

Conclusions: Anakinra is an effective and relatively safe alternative treatment in FMF patients with inadequate response or intolerance to colchicine, however, approximately one fourth of the patients stop anakinra for insufficient response. Disclosure of Interest: None declared doi: 10.1136/annrheumdis-2017-eular.5436

FRIO597 | FATIGUE IN FAMILIAL MEDITERRANEAN FEVER (FMF) AND ITS RELATIONS WITH OTHER CLINICAL PARAMETERS
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Background: Fatigue is a common problem in patients with rheumatic disease. It may cause disability and poor quality of life (1). Although fatigue and its determinants are studied in several rheumatic diseases, there is no study in Familial Mediterranean Fever (FMF).

Objectives: The aim of this study is to investigate fatigue in FMF patients as a disabling symptom and its associations with clinical and demographic variables.

Methods: FMF patients were recruited into the study according to FMF Tel Hashomer criteria (2). Control group composed of healthy individuals. Patients with myopathies, erosive arthritis, myopathies, erosive arthritis, systemic sclerosis and certain auto-antibody profiles were excluded. Age, gender, disease duration, education, marital status were noted as demographic features. Number of attacks in the last year, type of attacks (arthritis, myalgia, rash), duration of attacks, dosage of colchicine, genotype and severity of FMF was assessed with PRAS score, visual analogue score of pain (VAS-pain) and VAS-fatigue were used as clinical parameters. Pittsburgh Sleep Quality Index (PSQI), Multidimensional Assessment of Fatigue (MAF), Nottingham Health Profile (NHP), Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS) and Hospital Anxiety and Depression Scale (HADS) were filled out by both control and study group. Assessment of normality was analyzed with Shapiro-Wilk test. Differences in the mean scores of control and study group were compared with independent samples Mann-Whitney U and Kruskal-Wallis test. Relationships between continuous variables was assessed with Spearman’s correlation coefficient (rho).

Results: 61 FMF patients and 61 age, gender (44 female, 17 male in each group) matched controls were enrolled into the study. Mean age of FMF and control group were 43.5±11.8 and 35.8±11.7 years, respectively. The mean disease duration was 82.5±81.7 months. Differences between mean of VAS-pain, VAS-fatigue, PSQI total score, MAF, all subsets of NHP, FSS, FIS, HADS scores of FMF patients were statistically higher than control group (<p=0.001). The correlations between scales assessing fatigue and other outcome measures in FMF patients were significant (rho).

Conclusions: This study has shown that fatigue in FMF is associated with a number of psychological, sleep, quality of life and disease related factors. FMF group had increased pain, fatigue, sleep disturbance and decreased quality of life compared to control group. FMF patients with fatigue may benefit from pharmacological and psychological interventions which target these factors. References:


FRIO598 | CHARACTERIZATION OF PATIENTS WITH AN INITIAL DIAGNOSIS OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE. OBSERVATIONS FROM A LONGSTANDING MONOCENTRIC COHORT
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Background: Evolution from Undifferentiated Connective Tissue Disease (UCTD) to a defined Autoimmune Disease (AID) remains unexplained and usually occurs in the first 3 to 5 years.

Objectives: To determine the frequency and predictors of differentiation from UCTD to AID in a selected cohort of patients originally labelled as UCTD within the first 3 years of follow-up.

Methods: Demographic and clinical features were retrieved: (i) retrospectively, from the AID’s Unit current database in December 2016 (n=195), including Systemic Lupus Erythematosus (SLE), incomplete SLE, Sjögren’s Syndrome (SS), Systemic Sclerosis (SSc), Vasculitis and Mixed Connective Tissue Disease (MCTD); and (ii) from a prospectively UCTD database created in January 2012 (n=48). Inclusion criteria for the latter pertain to ANA positive patients, not fulfilling any of the existing classification criteria for AID and without severe organ involvement [1]. Patients with cutaneous lesions suggestive of lupus, inflammatory myopathies, erosive arthritis, systemic sclerosis and certain auto-antibody profiles were excluded a priori from the definition of UCTD as these are thought to herald defined conditions, as previously defined [2]. Definition of stable UCTD includes patients with at least one clinical manifestation of AID, positive ANA results and disease duration of at least 3 years [3]. Comparisons between stable UCTD and progressing patients were made using Wilcoxon Rank Sum and Chi square tests, p values of <0.05 were considered statistically significant.

Results: Each individual patient was analysed for differentiation into AID at yearly intervals. Overall, the main features of the prospective UCTD cohort were arthralgia (79%), rash (31%), arthritis (19%), sicca symptoms (19%), photosensitivity (17%) and Raynaud (13%). Prospective analysis in the UCTD cohort revealed differentiation in 4/48 patients (8.3%): into rheumatoid arthritis (n=2), psoriatic arthritis (n=1) and SLE (n=1). The main difference between stable UCTD and those that progressed to AID was the presence of arthritis (p=0.003). Median age of onset and symptom duration was similar between both groups. Retrospective analysis yielded very few patients presenting as UCTD (n=5/195); 2/106 SLE; 1/13 incomplete SLE; 1/43 SS; 1/19 SSc; 0/7 VEDOSS and 0/7 MCTD with no distinguishing feature.

Conclusions: Very few patients differentiated in the UCTD cohort after 3 years of follow-up and in our retrospectively studied cohort, in accordance to a previous study [4]. Apart from arthritis, there were no other predicting factors for differentiation to AID. UCTD at disease onset seems to be a rare event.

References:


FRIO599 | A RETROSPECTIVE OVERVIEW OF CLINICAL FEATURES, SEROLOGY AND HISTOLOGY OF IGG4 RELATED DISEASE IN HONG KONG: A DATASET OF 108 PATIENTS FROM FOUR REGIONAL HOSPITALS
C.P. Tang1, K.L. Lee1, K.W. Lee2, W.L. Ng3, M.C. Wan4, K.Y. Yuen5. 1Medicine, PUNHHC, Medicine, HKSH; 2Medicine, UCH; 3Medicine, RH; 4Medicine, QMH. HK, Hong Kong.

Background: IgG4 related disease (IgG4RD) is a spectrum of immune mediated disease with multiple organ involvement characterized by organ enlargement, function loss or obstructive symptoms (1, 2).

Objectives: In this retrospective study, clinical, serological and histological features of IgG4RD patients over the past ten years from four regional hospitals were reviewed.

References:
Methods: Four regional hospitals participated with study period from 1/1/2006 to 30/6/2016. IgG4RD patients were classified into definite, probable and possible IgG4RD according to Japanese Comprehensive Diagnostic Criteria for IgG4RD (3).

Statistical analysis: Association between the individual categorical covariates and the different organ involvement were analyzed by Fisher’s exact test.

Results: 108 patients were included. There were 81 male patients and 27 female patients and the male to female ratio was 3:1. The mean age of diagnosis was 62.8 year old. 57 patients were diagnosed as definite IgG4RD (53%), 14 patients as probable IgG4RD (13%) and 37 patients as possible IgG4RD (34%). Salivary glands involvement was the commonest (M=46.7% vs F=33.3%), followed by pancreas (M=28.4% vs F=18.5%) and biliary system in male (M=24.7% vs F=11.1%) and orbital in female (M=23.5% vs F=18.5%). 53% patients also had multi organ involvement.

Conclusions: Most patients were male with the peak diagnosis at age 50 to 70. Salivary gland and pancreas were the most common organ involved. Most patients had a raised IgG4 level and most histological specimens showed a raised IgG4/IgG ratio greater than 40% per high power field which accounted for 86.9% of the specimens.

FR0601 | HYPERFERRITINEMIC SYNDROME IN A GENERAL UNIVERSITY HOSPITAL

F. Pieringer, I.J. Gandino, J.M. Martinez Perez, S. Ruta, M. Scolini, E.R. Soriano. Rheumatology Section, Medical Services, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Background: Hyperferritinemia is associated with severe inflammatory conditions, such as rheumatic diseases with systemic inflammatory responses, and multiorgan dysfunction syndromes.

Objectives: To determine which diseases are associated with hyperferritinemia in a tertiary hospital; to compare ferritin levels between these different entities and to evaluate relationship between levels of ferritin and mortality in these patients.

Methods: A retrospective study was carried out in which all patients over 18 years of age with at least one determination of serum ferritin equal to or greater than 1000 ng/ml were identified in the laboratory database of our hospital between 1/1/2006 and 6/30/2016. Corresponding electronic medical records were reviewed and demographic and clinical data were collected. Mortality was assessed at the end of follow-up. Descriptive statistical analysis and logistic regression analysis were performed in order to identify variables associated with mortality.

Results: A total of 1979 patients were included, 1235 men (62.4%) with a mean age of 63.2 years (SD 17.2). Only 36 patients (1.8%) presented a diagnostic approach for the diagnosis of IgG4-RD, 2011. Modern Rheumatology. 2012;22(1):21–30.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2145

FR0602 | NATIONAL RECOMMENDATIONS ON THE USE OF IMMUNOMODULATORY DRUGS IN PATIENTS WITH NON-INFECTIONOUS NON-MALIGNANT ANTERIOR UVEITIS


Conclusions: Disease control in FMF is important to prevent amyloidosis and improve the quality of life. Recent studies contribute to the determination of treatment goals. Reducing the colchicine dose may increase drug compliance in this lifelong treatment. In our study, there was no difference between the treatment groups in amyloidosis, MEVF gene mutation or subclinical inflammation. These findings suggest that the dose of colchicine maybe reduced in inactive patients who determined by the number of annual episodes and the ISSF score.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6885
Clinical implications of ultrasonography in monitoring disease activity of relapsing polychondritis in cases

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Background: Anterior uveitis (AU) is the most common pattern of uveitis, that might lead to important ocular complications including blindness. Immunomodulatory drugs have been used in order to prevent recurrences of uveitis. Nevertheless, it is not clear which drug could be preferred in each patient.

Objectives: To access the clinical implications of ultrasonography (US) in monitoring disease activity of relapsing polychondritis (RP).

Results: The 33 recommendations were accepted. They include specific recommendations on patients with non-infectious, non-neoplastic AU, as well as different treatment lines. Methotrexate (MTX) or Sulfasalazine were recommended as a first line drugs in refractory cases to topic treatments in patients with AU and spondyloarthritids, inflammatory bowel disease, psoriasis, idiopathic HLA-B27 positive or negative AU. Etanercept was recommended for patients with TRAPS syndrome, and for those with other autoinflammatory syndromes canakinumab or anakinra. In case of bilateral sarcoidosis, relapsing polychondritis or TINU syndrome, MTX was recommended along with systemic steroids. For patients with a flare of AU and Behçet disease, systemic steroids along with azathioprine or a calcineurin inhibitor were recommended. The indication of an immunomodulatory drug in patitines with multiple sclerosis was considered to be decided with a neurologist. For patients refractory to all above exposed and or intolerant, depending on AU type, a change to another immunomodulatory drug or to an anti-TNF was recommended (adalimumab, infliximab, certolizumab or). Except for patients with TINU, etanercept was not recommended because current evidence does not support the use of it to prevent AU flares.

Conclusions: In patients with non-infectious, non-neoplastic AU, these recommendations on the use of immunomodulators might be a guide in order to help in the treatment decision making, due to the lack of robust evidence in other globally accepted algorithms.


Methods: Three cases of a 78-year-old man with RP, a 74-year-old woman with RP associated with optic perineuritis and a 42-year-old woman with RP associated with uveitis were assessed by US before and after treatments.

Results: Ultrasonography (US) of the auricle before treatment showed low-echoic swollen auricular cartilage with increased power Doppler signals (PDS) in all cases. US findings corresponded to the above-mentioned biopsy findings. After treatment with prednisolone combined with methotrexate, the auricular swelling completely resolved in all cases. Then, US findings also showed dramatic reductions in swelling of cartilage with the decrease in PDS.

Conclusions: US imaging can be used to differentiate between inflammation, vascular lesions, and tumors in the ear pinna. RP could be differentiated from the damage of repeated trauma (i.e. rugby) with producing subperichondrial serous effusion. As in the present cases, US imaging of the external ear and auricular cartilage in RP also facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1769

SUCCESSFUL TREATMENT OF ARTHRITIS INDUCED BY CHECKPOINT INHIBITORS WITH ANTI–INTERLEUKIN-6 RECEPTOR ANTIBODY: A CASE SERIES

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Background: Immune checkpoint inhibitors (CPIs) have significantly improved outcomes for patients with various cancers. However, CPIs are associated with immune-related adverse events (irAEs). Two to three percent of patients receiving a CPI develop arthritis. In general, severe irAEs are treated with a high-dose steroid and a tumor necrosis factor inhibitor (TNFi), usually infliximab; however, TNFi treatment is sometimes contraindicated and, furthermore, entails a theoretical concern of impairing antitumor immunity. Therefore, evidence showing the clinical benefits of non-TNFi biologics in the treatment of irAEs is of immediate interest.

Objectives: We described the effects of anti–IL-6R antibody for the treatment of arthritis-irAE.

Methods: Three patients receiving CPI developed arthritis and were treated with anti–IL-6R antibody. Patients were followed up to 15 months.

Results: All patients had metastatic melanoma (Table 1). No patient had a
history of autoimmune disease at the time of initiation of CPI treatment. One patient developed arthritis 8 weeks after the completion of anti-CTLA-4 antibody treatment. Two patients were receiving anti-PD-1 antibody when they developed arthritis. Patient 2 continued to receive anti-PD-1 antibody despite of arthritis-irAE while patient 3 discontinued anti-PD-1 antibody due to arthritis-irAE. The pattern of arthritis symptoms consisted of small and large joints. Patient 1 had a positive rheumatoid factor (unknown baseline) and patient 3 had a positive ANA (known positive prior to CPI treatment). All patients were treated with anti-IL-6R antibody, which was well tolerated. All patients experienced a 40–100% reduction in global assessment, swollen joint count, and tender joint count, and these effects were maintained for up to 15 months of treatment (Figure 1). As of December 2016, all patients were alive; one patient was in complete remission and two patients had experienced progression of their melanoma.

Conclusions: These three cases suggest that anti-IL-6R antibody is an effective alternative to NFi for the treatment of arthritis-irAE.

Acknowledgements: None

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6532
Results: We studied 100 patients/180 affected eyes (54M/46W), mean age 40.7±10.1. The ocular pattern was panuveitis (n=62), posterior (27) and anterior uveitis (11). Before IFX they received iv MP (28), cyclosporine (75), azathioprine (56), metotrexate (43) and others (33). IFX dose ranged between 3–5mg/kg/4 or 8 weeks. In patients in remission IFX was optimized (n=28) or stopped (n=20).

Conclusions: IFX is an effective long-term treatment in refractory Uveitis of BD. Optimization and even discontinuation of IFX after remission is possible.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6226

FR0608 | STUDY OF ARTICULAR SARCOIDOSIS IN A TERTIARY CARE HOSPITAL

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1Rheumatology Department of the University Health Care Complex of León; 2University of León, León, Spain

Background: Sarcoidosis is a systemic granulomatous disease, being the joint involvement a poorly studied manifestation.

Objectives: To describe the clinical and demographic characteristics of patients with sarcoidosis, paying particular attention to the joint involvement and its possible relationship with other extra-articular manifestations, as well as the treatment received.

Methods: A retrospective, observational study that included 104 patients who were admitted to the Hospital of León between January 2011 and December 2015 with main or secondary diagnosis of sarcoidosis; according to clinical onset, imaging tests and/or anatomopathological study. The variables studied were: age at onset, sex, type of joint involvement, forms of extra-articular involvement, serologic parameters and drugs received. Statistical analysis was performed using SPSS v22.0, p<0.005.

Results: 57.7% of the patients included in the study were women with a mean age of 53.4±18.4 years. At the systemic level, 35% of them presented fever, 66.3% lymphadenopathy and 4.8% splenomegaly. 97.1% of the patients presented pulmonary involvement, with stage II being the most common (46.2%). Only 8 patients had cardiac abnormalities. Ocular involvement was observed in 10.6%.

Conclusions: To the factors to predict relapse. Recent research has shown the usefulness of FDG-PET/CT for IgG4-RD because it is more sensitive than conventional imaging to detect organ involvement of the disease. It has been suggested that FDG-PET/CT is also useful for monitoring therapeutic response of IgG4-RD.

Objectives: We investigate the usefulness of FDG-PET/CT imaging and serological biomarkers to predict relapse in IgG4-related disease.

Methods: We analyzed 24 patients with IgG4-RD treated for more than 1 year between 2008 and 2016 in our facility. The diagnosis for IgG4-RD was based on comprehensive diagnostic criteria for IgG4-RD. All cases underwent FDG-PET/CT at least once, and laboratory data were collected from the medical records retrospectively. Levels of serum C-reactive protein (CRP), eosinophil/leukocyte ratio, serum IgG, IgG4, IgA, IgM, sIL-2R and serum complement were investigated.

Results: The patients had a mean age of 67.9 years (range: 50–87 years). In the cases with high FDG uptake on FDG-PET/CT, they had a greater number of organ involvements, higher serum IgG and sIL-2R levels. Eight patients experienced relapses following treatment. Higher serum IgG predicted relapses of IgG4-RD. FDG-PET/CT findings at baseline were not associated with relapse. FDG-PET/CT was performed in 13 patients after initiation of treatment and 4 patients had a relapse. There were no significant reduction of abnormal FDG uptake in 6 patients, and 4 of 6 patients relapsed.

Conclusions: In this study, we examined the factors to predict relapse in IgG4-RD. Patients with higher serum IgG were regarded as a risk of relapse, but FDG-PET/CT findings at baseline were not associated with relapse. FDG-PET/CT reexamined after initiation of treatment is useful to predict relapse of IgG4-RD.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5648

FR0610 | PROBLEMS IN THE DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER IN TURKEY

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Background: The diagnosis of FMF (Familial Mediterranean Fever) can be missed or delayed even in a country like Turkey, one of the most prevalent places for FMF (1).

Objectives: We compared the duration of delay in diagnosis before and after the publication of MEF1, and assessed the patients related with the diagnosis of FMF.

Methods: We studied 143 (102 F, 41 M) consecutive patients with FMF seen 2000-2016 in the Rheumatology Outpatient Clinic of Istanbul Cerrahpaşa Medical Faculty. The median age of the patients was 34 years [IQR:27–45]. The F/M ratio was 2.4. The initial symptom was abdominal pain in the majority (n=134, 89%), followed by fever (n=114, 75%), arthritis (n=66, 44%), pleuritic pain (n=21, 14%), arthralgia (n=11, 7%) and other complaints (n=14, 9%). The median age at initial symptom was 10 years (IQR:6–23). The median delay in diagnosis was 8 years [IQR:2–15]. This was significantly shorter in Group 2 (median: 4 years [IQR:0–11]) than that observed in Group 1 (median: 10 years [IQR:6–17]), as shown in Table 1.

A total of 110 patients (73%) were diagnosed with one or more diseases or syndromes other than FMF. These were appendicitis (n=50, 45%), gastrointestinal diseases (n=44, 40%), acute rheumatic fever (n=36, 33%), inflammatory
arthritis (n=18, 16%), gynecological diseases (n=11, 10%) kidney stones (n=9, 8%) and others (n=34, 31%). As shown in Table, the frequency of patients with misdiagnosis, was significantly lower in Group 2 (66%) compared to Group 1 (84%). A total of 59 patients (39%) received other long-term treatments, mainly monthly penicillin (n=20, 13%). There were 41 surgical interventions in 36 patients (24%), before the diagnosis of FMF, the most common being appendectomy in 31, gynecological operations in 5, cholecystectomy in 3 and others in 2 occasions. It was noted, that the frequency of surgical operations was significantly decreased in Group 2 (12%) compared to Group 1 (27%) (Table). The absence or presence of MEVF mutations was assessed in 69 patients (46%) before the diagnosis or after to reinforce the diagnosis. As expected, this was significantly more frequent in Group 2 (59%) compared to Group 1 (33%) (Table). Seventy patients (46%) were diagnosed as FMF only after someone else in the family (n=44) or a friend (n=26) had a similar diagnosis. The frequency of these patients was similar when Group 1 and 2 were compared.

Table: Demographic and clinical characteristics of Group 1 (patients seen before 2000) and Group 2 (patients seen after 2000) .

<table>
<thead>
<tr>
<th>Male/Female, n</th>
<th>Group 1 (n=70)</th>
<th>Group 2 (n=73)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current age, med (IQR) years</td>
<td>42 [31-55]</td>
<td>19 [14-54]</td>
<td>&gt;0.001</td>
</tr>
<tr>
<td>Delay in diagnosis, med (IQR) years</td>
<td>10 [6-18]</td>
<td>4 [3-11]</td>
<td>&gt;0.001</td>
</tr>
<tr>
<td>Misdiagnosed patients, n (%)</td>
<td>59 [84]</td>
<td>46 [66]</td>
<td>0.011</td>
</tr>
<tr>
<td>Diagnosis after diagnosis, n (%)</td>
<td>39 [57]</td>
<td>9 [12]</td>
<td>0.026</td>
</tr>
<tr>
<td>Assessment of MEVF mutations, n (%)</td>
<td>23 [33]</td>
<td>43 [59]</td>
<td>0.005</td>
</tr>
<tr>
<td>Diagnosed as FMF after someone else, n (%)</td>
<td>27 [39]</td>
<td>38 [52]</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Conclusions: Although there is considerable decrease in delayed diagnosis of FMF, there is still significant amount of misdiagnoses after the year 2000, even in a geography where FMF is highly prevalent.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4970

ASSESSMENT OF PANNICULITIS CLINICAL OUTCOMES: RISK FACTORS FOR RECURRENCE AND PREDICTORS OF SLOW REGRESSION OF INDURATIONS

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Background: Currently there’s no clear understanding of the clinical course and outcomes of panniculitis with predominant involvement of subcutaneous adipose tissue (SAT), which is often associated with the involvement of locomotor system and viscera. Consistent elaboration of both is of paramount importance, as it may give a deeper insight into clinical and curative factors which may have impact on the disease prognosis.

Objectives: To assess clinical outcomes of panniculitis (risk factors for recurrence and predictors of slow regression of inductions).

Methods: 186 pts (172 females, 14 males) aged 43.5±14.5 years with different types of Pn, who were at the record of V. A. Nasonova Research Institute of Rheumatology during 2009–2015 yy. Disease duration varied from 1 week to 20 years.

Constitutional symptoms, n (%) | 31 (59.6) |
| Fatigue | 16 (30.7) |
| Night sweats | 15 (28.8) |
| Weight loss | 14 (26.9) |
| Fever | 13 (25) |
| Retropertioneal fibrosis, n (%) | 23 (44.2) |
| Lymphadenopathy, n (%) | 20 (39.2) |
| Any cardiovascular involvement, n (%) | 15 (28.8) |
| Periarthritis | 12 (23.1) |
| Pericardium | 5 (9.6) |
| Coronary periarteritis | 4 (7.7) |
| Abdominal aort aneurysm | 1 (1.9) |
| Ocular pseudotumor, n (%) | 12 (23.1) |
| Orbitalism/proptosis | 6 (11.5) |
| Extrabiliary muscles | 6 (11.5) |
| Pancreas, n (%) | 12 (23.1) |
| Major salivary glands, n (%) | 11 (21.2) |
| Lacrimal glands, n (%) | 9 (17.3) |
| Medistrial fibrosis, n (%) | 6 (11.5) |
| Ear, nose, sinuses, n (%) | 5 (9.6) |
| Lung fibrosis, n (%) | 5 (9.6) |
| Skin, n (%) | 4 (7.7) |
| Pleruma, n (%) | 4 (7.7) |
| Gall bladder and Biliary ducts, n (%) | 4 (7.7) |
| Thyroid, n (%) | 3 (5.8) |
| Liver, n (%) | 3 (5.8) |
| Kidney (mass), n (%) | 3 (5.8) |
| Pachymeningitis, n (%) | 2 (3.8) |

Breast involvement: (n=1), tubulointerstitial nephritis (n=1).
H-FERRITIN AND PRO-INFLAMMATORY CYTOKINES ARE INCREASED IN THE BONE MARROW OF ADULT PATIENTS AFFECTED BY MACROPHAGE ACTIVATION SYNDROME

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Background: During macrophage activation syndrome (MAS), an inflammatory life-threatening syndrome, extremely high levels of serum ferritin may be observed. Ferritin is an intracellular iron storage protein comprising 24 subunits that may be divided in heavy (H) and light (L) subunits, based on their molecular weight. The H/L-subunits ratio may change, depending on the specific tissue and the physiologic status of the cell. In the normal condition, ferritin enriched in H subunits (H-ferritin) may be mainly observed in the heart and kidneys [2].

Objectives: We investigated the tissue expression of both H- and L-ferritin as well as pro-inflammatory cytokines expressing these molecules, in the inflammatory BM infiltrate of MAS patients. In addition, the co-expression of IL-1β, TNF-α, IFN-γ and H- or L-ferritin, within the inflammatory cells, was assessed. Finally, we explored if the imbalance between H-ferritin and L-ferritin as well as the number of ferritin positive cells may be considered helpful bio-markers to assess the severity of these patients.

Methods: We analyzed the bone marrow (BM) biopsies, by immunofluorescence of 10 adult MAS patients affected by rheumatic disease to assess the presence of: i. both H- and L-ferritin; ii. the number of CD68+/H-ferritin+ and CD68+/L-ferritin+; iii. the tissue pro-inflammatory cytokines, IL-1β, TNF, IFN-γ, and we correlated these data with clinical and laboratory data. Furthermore, the presence of ferritin cells was assessed in the sera of the same patients by western blot analysis.

Results: We observed an increased tissue expression of H-ferritin and of pro-inflammatory cytokines (IL-1β, TNF, IFN-γ). Western blot analysis, in the sera, of H-ferritin microscopic cells of the tissue. Furthermore, an increased number of CD68+/H-ferritin+ cells and an infiltrate of cells co-expressing H-ferritin and IL-12, suggesting an infiltrate of M1 macrophages, were observed. Tissue H-ferritin levels correlated with the decreased counts of WBC (p=0.01) and PLT (p=0.002) and the increased values of serum ferritin (p=0.012) and C-reactive protein (CRP) (p=0.0058); and with the tissue expression of IL-1β (p=0.006). The number of CD68+/H-ferritin+ cells correlated with the decreased counts of WBC (p=0.03) and PLT (p=0.007), and with the increased serum ferritin levels (p=0.0086) and CRP (p=0.049). The analyses concerning tissues L-ferritin as well as the number of CD68+/L-ferritin+ cells and the same parameters failed to show any significant result.

Conclusions: We observed an increased tissue expression of H-ferritin associated with an increased expression of IL-1β. Interestingly, in the BM inflammatory infiltrate an increased number of CD68+/H-ferritin+ cells was shown. Of note, tissue expression of H-ferritin as well as the number of CD68+/H-ferritin+ significantly associated with the hematological involvement of the disease, suggesting possible bio-markers to assess the severity of these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5415

SARCOIDOSIS AND CANCER: DIFFERENT PATTERNS OF ASSOCIATION IN A MULTICENTER COHORT FROM SOUTHERN EUROPE


Background: Sarcoidosis was diagnosed with the criteria proposed by the ATS/ERS/WASOG SEMI) created a national registry (SARCOGEAS) of patients with sarcoidosis. The cohort included 1082 patients (82% biopsy-proven, 618 women, mean age 47yrs). Association with neoplasia was detected in 135 (13%) patients in whom cancer preceded the diagnosis of sarcoidosis had a higher frequency of sarcoidosis diagnosed incidental (20% vs 4%, p=0.011) and a lower frequency of ocular sarcoidosis (3% vs 16%, p=0.001, OR 4.06), and laboratory findings. The certainty of OM was classified as grade 0 (not investigated), grade 1 (no sign of OM), grade 2 (clinical sign of OM), grade 3 (signs of OM in laboratory findings or imaging) and grade 4 (histological proven OM), respectively.

Results: We included 151 patients with biopsy-proven chronic sarcoidosis. Mean age was 50±15 years with a male predominance (87 [57.2%] vs 65 [42.8%] patients).

Discussion of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6716

FRI0613

H-FERRITIN AND PRO-INFLAMMATORY CYTOKINES ARE INCREASED IN THE BONE MARROW OF ADULT PATIENTS AFFECTED BY MACROPHAGE ACTIVATION SYNDROME

A complete response was achieved in 52.5% of patients and partial response (-50% of regression) in 40%. Two patients deceased due to l GV4-RD associated problems and no malignancy was observed (median follow up: 18 months).

Conclusions: We observed similar features with previous European cohorts although no male predominance was seen. Even though conventional immunosuppressive treatments were in use in more than half of patients, treatment had switched to rituximab ~50% patients owing to resistance or relapses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4315

FRI0614 FREQUENCY OF ORGAN MANIFESTATIONS IN CHRONIC SARCOIDOSIS


Background: Chronic sarcoidosis is a systemic disease of unknown etiology, characterized by the histological finding of granulomas in involved organ systems. The most often affected organ is the lung with approximately 90–95%. Systemic data of organ manifestations other than the lung are scarce and show a wide range from 1–2% to 50% depending on the series.

Methods: We analyzed data of newly diagnosed chronic sarcoidosis in 3 tertiary hospitals. We analyzed data on organ manifestations (OM), type of OM and laboratory findings. The certainty of OM was classified as grade 0 (not investigated), grade 1 (no sign of OM), grade 2 (clinical sign of OM), grade 3 (signs of OM in laboratory findings or imaging) and grade 4 (histological proven OM), respectively.

Results: We included 151 patients with biopsy-proven chronic sarcoidosis. Mean age was 50.8±9 years with a male predominance (87 [57.2%] vs 65 [42.8%] patients).

Discussion of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5420

FRI0615 SARCOIDOSIS AND CANCER: DIFFERENT PATTERNS OF ASSOCIATION IN A MULTICENTER COHORT FROM SOUTHERN EUROPE

A complete response was achieved in 52.5% of patients and partial response (-50% of regression) in 40%. Two patients deceased due to l GV4-RD associated problems and no malignancy was observed (median follow up: 18 months).

Conclusions: We observed similar features with previous European cohorts although no male predominance was seen. Even though conventional immunosuppressive treatments were in use in more than half of patients, treatment had switched to rituximab ~50% patients owing to resistance or relapses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4315
sarcoïdosis was more frequently observed in those patients with a previous history of neoplasia, while the association with hematological neoplasms was linked to a higher frequency of sarcoidosis involving ENT and bone marrow.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3700

FR0616 EYE MANIFESTATIONS OF PATIENTS WITH MUCKLE-WELLS SYNDROME

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Background: CAPS is a rare autoinflammatory disease associated with mutations in the CIAS1 gene, encoding for NLRP3 that result in overactivation of the inflammasome. Muckle-Wells syndrome (MWS) is a rare autosomal dominant disease which causes episodic fever attacks, sensorineural deafness, recurrent hives, arthritis and eye involvement.

Objectives: Here we present the findings of eye involvement in a family whose 11 members have MWS.

Methods: Clinical data was collected during the course of ongoing patient care.

Results: We evaluated the clinical features of 11 patients who were referred to a tertiary care center. The median age of the patients was 25 years (range: 9–65). The ratio of females/males was 1.2 (6/5). All patients had arthritis with exacerbation on exposure to cold and recurrent episodes of pink eye. The median age of onset of ocular involvement was 8 years (2–45). We observed severe eye involvement in 36% of our cases, including band keratopathy, severe damage of corneal stroma and neo-vascularization. Corneal involvement and clounding was detected in four patient. Two of those had the diagnosis of keratoconus as well. Patients with keratoconus had corneal scarring due to corneal hydrops verified with corneal topography. The other two patients with corneal clounding had band keratopathy. One of those patient was a 17 year old girl who had recurrent uveitis with hypopyon which necessitated the use of intravitreal dexamethasone implant. She also had posterior synchia of the iris to the lens. The other eye of that patient had signs of phthisis bulbi. The other patient with band keratophathy was a 46 years old male who had optic atrophy and tractional fibrovascular membranes at the posterior pole of the eye. Anakirna was used for treatment of 5 cases, and canakinumab of 3 cases. It was observed that the frequency of conjunctivitis decreased after anti IL-1 therapy. There was no mutation detected in the study of MEFV (all exons), TNFRSF1A (exons 2 to 7), MVK (all exons), NLRP3 (all exons). One of those patient was a 17 year old girl who had recurrent uveitis with hypopyon which necessitated the use of intravitreal dexamethasone implant.

Conclusion: Here we presented our clinical experience with MWS in a family of 11 members. The clinical manifestations of this disease varied from mild (e.g. arthritis) to severe (e.g. phthisis bulbi). The combination of anti IL-1 therapy and the use of intravitreal dexamethasone implants was useful in some patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3352

FR0617 DIAGNOSTIC SENSITIVITY OF CUTOFF VALUES OF IGG4-POSITIVE PLASMA CELL NUMBER AND IGG4-POSITIVE/CD138-POSITIVE CELL RATIO IN TYPICAL MULTIPLE LESIONS OF PATIENTS WITH IGG4-RELATED DISEASE

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Background: Immunoglobulin G4-related disease (IgG4-RD) is a recently recognized systemic inflammatory disease with multi-organ involvement [1]. Diagnostically, two of the most important hallmarks of IgG4-RD are high IgG4-positive plasma cell (PC) counts and high IgG4/IgG ratios in affected organs. Although the International consensus statement (ICS) on the pathology of IgG4-RD adopted different IgG4-positive PC counts among affected organs for the diagnosis to differentiate IgG4-RD mimickers from IgG4-RD [2], histological and immunohistochemical findings of the specimens from not only one but multiple organs in the same patient has not been evaluated.

Objectives: This study aimed to investigate the diagnostic sensitivity of the cutoff values of IgG4-positive PC number and IgG4-positive/CD138-positive cell ratio proposed by the International consensus statement (ICS) on the pathology of IgG4-RD in typical multiple lesions of patients with IgG4-RD.

Methods: We evaluated IgG4-positive PC number and IgG4-positive/CD138-positive cell ratio in 35 samples from 16 IgG4-RD patients having more than two typical lesions of IgG4-RD.

Results: We evaluated twelve submandibular, eleven ophthalic, four skin, four kidney, two pancreatic, and one bronchus and prostate lesion each in 16 patients with typical clinical, serological, and radiographic features. Concerning IgG4+ PC number per high power field, most ophthalic (8/11), kidney (4/4), pancreatic (2/2) and bronchus (1/1) fulfilled the cutoff value of ICS, whereas many in the submandibular (5/12) and skin lesions (0/4) did not. In contrast to the absolute number, almost all lesions fulfilled the cutoff value of IgG4+CD138+ cell ratio. In five cases, only one or two lesions in the same patient fulfilled the cutoff value of ICS, while the others did not.

Conclusions: These results suggest that ICS criteria have different sensitivities among the affected organs in diagnosing IgG4-RD.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4170

FR0618 ADALUMUMAB IN NON-INFECTIONOUS UVEITIS – EFFICACY ACROSS DIFFERENT ETIOLOGIES IN THE VISUAL I AND VISUAL II TRIALS

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Background: There is increasing interest in understanding the efficacy of adalimumab across different etiologies of uveitis. No prospective analysis has been conducted to date to determine the efficacy of adalimumab among non-infectious uveitis patients with different etiologies.

Objectives: To assess adalimumab (ADA) efficacy in active and inactive, non-infectious uveitis across different etiologies in patients who were recruited as part of the VISUAL program.

Methods: Exploratory data analyses from two global phase 3, double-masked trials: VISUAL I (patients with active uveitis despite ≥ 2 weeks of prednisone 10–60 mg/day) and VISUAL II (patients with inactive disease dependent on 10–35 mg/day of prednisone to maintain inactivity) were performed. Patients received placebo (PBO) or ADA subcutaneously (80 mg week 0, followed by 40 mg every other week from week 1 up to 80 weeks). In VISUAL I, all patients received a prednisone burst followed by taper to 0 mg by week 15. In VISUAL II, prednisone taper to 0 mg was mandatory by week 19. The primary endpoint was time to treatment failure (TF) at or after week 6 for VISUAL I, and at or after week 2 for VISUAL II. For this analysis, patients were categorized into different uveitis etiologies which they presented at study entry. Hazard ratios (HR) for time to TF were obtained for each uveitis etiology.

Results: The efficacy of ADA was significantly greater than PBO in the largest subgroup of patients with idiopathic uveitis (VISUAL I: 103 and VISUAL II: 90) etiology in both VISUAL I and VISUAL II trials. All other subgroups showed similar results.

Figure: Hazard ratios of time to treatment failure by uveitis etiologies.

VISUAL I (A) and VISUAL II (B) clinical trials.
a trend in favor of ADA, except for Sarcoidosis subgroup in the VISUAL II trial (Figure). Overall safety for both trials has been previously reported.2,3

Conclusions: These exploratory analyses from the VISUAL I and VISUAL II trials show significantly higher efficacy in ADA-treated patients over PBO in “idiopathic/other” diagnoses of patients with both active and non-infectious uveitis. Though beyond the aim of the study, these analyses suggest that ADA-treated patients had a prolonged time to treatment failure compared to PBO.


Accomplishments: AbbVie funded the VISUAL I and VISUAL II studies and provided writing support. All authors contributed to the development of the content. The authors reviewed the manuscript and approved the abstract. The authors maintained control over the final content. Medical writing assistance was provided by Gaurav Patki, PhD of AbbVie Inc.


DOI: 10.1136/annrheumdis-2017-eular.2389

FRI0619 COMPARING CANAKIMUNAB AND ANAKINRA IN YOUNG GREEK WOMEN WITH RESISTANT RECURRENT PERICARDITIS

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Objectives: We studied 18 patients with RRR (all women, from 14 to 36 years old) determining the existence of mutation from the inference database (25 genes, from MEVF and TNFRSF1A to MVK and SLC29A3, all related with autoimmune diseases). All the patients were proven positive to one of the above mutations (all heterozygous) and then treatment with anakinra (n=9, 100mg sc once daily) and canakinumab (n=9, 150mg sc q4w) was practiced.

Results: During the study (3 years), all anakinra patients stopped receiving per os glucocorticoids and were free of any new pericarditis episodes. 3 of them (33%) stopped any treatment after a year of anakinra therapy and none was presented with any side reactions.

On the contrary, all canakinumab patients were not able to free themselves of the glucocorticoid treatment, since at least one new episode of pericarditis to each patient was recorded. Two of them were free of pericarditis the last year of the study (though being treated with 2.5mg prednisolone per os daily).

Statistically speaking, the use of IL-1R antagonist in recurrent – resistant pericarditis associated with autoimmune mutations was proven much more successful (p<0.01) than the use of the IL-1b Mab.

Conclusions: Though the sample of patients (n=18) was too small in order to set us able to reach any safe conclusions, it is quite possible that anakinra may be one effective solution that can prevent the long term administration of corticoids to patients with recurrent pericarditis Canakinumab was not recorded with similar positive results.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6289

FRI0620 MIR-204-3P INHIBITS THE PRODUCTION OF TLR-RELATED CYTOKINES IN FAMILIAL MEDITERRANEAN FEVER BY TARGETING THE PIK3 SIGNALING PATHWAY

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Background: MicroRNAs (miRNAs) are endogenous small RNAs and post-transcriptionally regulate gene expression by pairing with target. There has been emerging evidence showing the association of aberrantly expressed circulating miRNAs in the serum with the pathogenesis or progression of diseases including cancer and autoimmune disease. Although a number of circulating miRNAs associated with inflammation have been identified, the roles of them in patients with FMF and the underlying mechanism remain to be elucidated.

Objectives: The aim of this study was to identify a serum miRNAs profile and potential biomarkers in FMF and clarify their gene targets for understanding the pathogenesis of autoinflammatory diseases.

Methods: We performed miRNA microarray in the serum from FMF in attack and in remission. We subsequently examined the expression of miRNAs that varied before and after the attack in macrophages derived from THP-1 cells stimulated with toll-like receptor (TLR) ligands. Macrophages derived from THP-1 cells transfected with pre-miRNA and anti-miRNA were stimulated with TLR ligands for 24 hours. We collected the supernatants for the quantification of inflammatory cytokine production. To identify the target genes, we overexpressed its miRNA and performed Agilent expression microarray. Transfection with reporter construct and pre-miRNA and anti-miRNA was performed to confirm suppression of target mRNA.

Results: We found that mir-204–3p was greatly decreased in the serum from FMF patients in attack. In vitro study, the expression of mir-204–3p was suppressed by LPS stimulation in macrophages derived from THP-1 cells. Inhibition of mir-204–3p significantly induced the production of TLR4-related cytokines whereas overexpression of mir-204–3p inhibited their production. Bioinformatic analysis showed that mir-204–3p is predicted to target genes implicated in TLR pathway through regulation of PIK3 signaling. Reporter assay revealed that mir-204–3p directly suppressed the luciferase activity of 3’UTR of PIK3CG reporter construct.

Conclusions: These data suggest that serum mir-204–3p has a potential as a useful biomarker among patients with FMF and that mir-204–3p plays a critical role as a suppressor to regulate the production of TLR4 related cytokines by targeting the PIK3 signaling pathway.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2813

FRIO621 PREDILETANCE OF DIFFERENT ORBITAL ANATOMIC STRUCTURES AFFECTATION IN IG44-RELATED OPHTHALMIC DISEASE: SINGLE CENTER EXPERIENCE

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Background: According to 2009 Japanese nationwide survey of IgG4-related Tissue Necrotizing Disease (IgG4-RD), orbit is the leading site of affection [1]. However diagnostic criteria and nomenclature of IgG4-RD were developed a few years later [2,3].

Objectives: To evaluate the peculiarities of clinical, laboratory, histological and immunohistochemical presentation of IgG4-related orbital disease (IgG4-ROD).

Methods: During 2004 – 2016, 82 patients were diagnosed with IgG4-RD GS of whom had IgG4-RD (men – 17, women - 66). The diagnoses of IgG4-RD and IgG4-ROD were established using comprehensive diagnostic criteria [2,3]. In all patients full clinical, ophthalmological, dental and serological (rheumatoid factor, C-reactive protein, IgG, IgD, IgM, IgA, ANA, anti-Ro/La, O3/O4 complement) examination was carried. In all cases diagnosis was verified pathomorphologically with immunohistochemical staining (anti-CD 138, CD 68, IgG, IgG4, k-chain, l-chain), but only in 43 patients the diagnosis of IgG4-RD was established on orbital tissues biopsy. Some patients at baseline were tested on B-cell clonality
A RETROSPECTIVE COHORT STUDY ABOUT THE CLINICAL CHARACTERISTICS OF IGG4-RELATED DISEASES

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Background: Immune globulin (Ig) G4-related disease (IgG4-RD) is an increasingly recognized systemic autoimmune disease in the past decade, and encompasses a wide spectrum of disorders previously considered to be unrelated, but with common pathologic, serologic, and clinical features. There have been several hundred literatures on IgG4-RD published in the past few years, however, we still cannot well characterize this complicated disease, including clinical features, treatments as well as mechanisms, which promotues us to further describe this disease.

Objectives: To describe the clinical presentations, laboratory features, imaging manifestations, treatments and evolutions in a cohort of 34 Chinese patients with immune globulin G-related diseases (IgG4-RD).

Methods: A retrospective study was performed in Wuhan Tongji Hospital. Electronically stored records of clinical, laboratory, imaging, and histological features were reviewed. The diagnoses were made according to comprehensive features were reviewed. The diagnoses were made according to comprehensive

Conclusions: In our cohort of IgG4-RD patients orbit is the leading site of the disease (64.5% of patients) and the disease onset (75% of patients). The majority of patients have concomitant orbital lesions (89%) and systemic course of the disease with other organ involvement (72%). Most often affected orbital anatomic structures are lacrimal glands, extraocular muscles, retrobulbar infiltration with optic nerve thickening and fibroinflammatory lesions of eyelids. MALT-lymphoma of lacrimal gland and local AL-amyloidosis can complicate the long history of IgG4-ROD. Monoclonal serum secretion and B-cell clonality in the tissue in 23% of patients can potentially act as a background for lymphoma formation.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4283
Methods: Twelve TNFi naïve AS patients (female 7/12; age 39±11 years) with high disease activity (BASDAI 5.5±1.1) were included. [18F]fluoride PET-CT scans were performed before initiation of TNFi therapy. In 2 patients, biopsies were obtained from PET identified spine lesions for histologic analysis. Of the remaining 10 patients, a second [18F]fluoride PET-CT scan was performed after 12 weeks of TNFi treatment. PET scans were scored visually for positivity by two blinded expert readers. Subsequently, [18F]fluoride uptake was quantified in PET positive (PET+) lesions using the standardized uptake value corrected for individual integrated whole blood activity concentrations (SUVAUC). Clinical response to TNFi was defined according to ASAS20 at 24 weeks.

Results: At baseline, in all patients at least one axial PET− lesion was found. In spine, 6/10 patients showed 84 lesions (range 2.30-63% thoracic spine, primarily costovertebral joints) and in the SI joints in 9/10 patients were PET+ (Fig A). Histological analysis of PET+ lesions in the spine confirmed local osteolysis and sometimes synovitis was present in PET− degenerative lesions. Quantitative PET analysis revealed significantly lower [18F]fluoride uptake in spine lesions at baseline in responders than in non-responders. This difference remained after 12 weeks of treatment (mean difference in SUVAUC: -0.5, 95% CI [-0.7,-0.2], p<0.001). After 12 weeks of TNFi treatment, [18F]fluoride uptake in clinical responders decreased significantly in the costovertebral (mean difference SUVAUC: -1.0, 95% CI [-1.3,-0.7]) and SI joints (mean difference in SUVAUC: -1.2, 95% CI: [-2.3,-0.2]) (fig B) in contrast to non-responders (mean difference in SUVAUC: -0.4, 95% CI: [-2.3,1.6]) and +0.4, 95% CI: [0.6, 1.4], respectively).

[18F]fluoride uptake in other spinal lesions such as bridging syndesmophytes showed heterogeneous response without a significant decrease in [18F]fluoride accumulation over time at a group level.

Conclusions: [18F]fluoride PET-CT enables non-invasive visualization of (changes in) lesions with bone formation of the whole spine and SI joints in clinically active AS patients, which is confirmed by histological signs of osteolysis formation. Part of these lesions, in particular costovertebral lesions in spine and SI joints, decreased in clinical responders to TNFi (and not in non-responders), whereas other spinal lesions remained unchanged at a group level.

Disclosure of Interest: None declared

FRIO0625 IMPROVEMENT OF JOINT INFLAMMATION AS ASSESSED BY MRI AND POWER DOPPLER ULTRASOUND (PDUS) IN AN OPEN LABEL STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB (PSARTROS)

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Background: Secukinumab, an anti-interleukin 17A monoclonal antibody, showed significant improvement of signs and symptoms of psoriatic arthritis (PsA) in FUTURE 1 study. Available studies used conventional radiography, not allowing a deeper imaging analysis of the inflammatory changes during application.

Objectives: To assess short term efficacy of secukinumab on inflammation and structural damage according to change in OMERACT-EULAR ultrasound score and the MRI PsAMRIS score in PsA patients.

Methods: PsA patients with active disease (TJC and SJC ≥ 6), were included in the 24 week open label prospective PSARTROS study and treated with subcutaneous secukinumab 300 mg once weekly over 4 weeks, then once every 4 weeks. Baseline 1.5T MRI hand scans and ultrasound imaging of 28 joints were performed at baseline and after 24 weeks of treatment. MRI was scored according to PsAMRIS, ultrasound for synovial hypertrophy and Doppler activity according to OMERACT scores. Statistical significance was set at p<0.05.

Results: 20 patients, mean age 52±9.9 years, 60% female, mean disease duration 6.7±5.9 years, 50% naïve for biological therapy, were included in the study. Three patients were early discontinued (recurrent pharyngitis, lack of efficacy, withdrawal of consent), and were not included into the longitudinal analysis. Baseline DAS28 was 5.0±2.96, baseline DAPSA was 32±12.1. On baseline MRI, all patients had at least one inflammatory sign (synovitis: 90%, osteitis: 20%, periaricular inflammation: 25%, flexor tenosynovitis: 35%, bone proliferation: 30%, erosions: 60%). Baseline composite PsAMRIS score showed a more severe phenotype when compared to antiDNA-negative patients (p from 0.026 to 0.041) and did not differ significantly from patients with MS. When regional hubs were analysed, patients with SLE and MS showed a reduced strength compared to HC (p from <0.0001 to 0.001 at multiple comparison). Hub strength impairment was more pronounced in MS when compared to SLE and preferentially involved hubs located in fronto-temporo-parieto-occipital cortices, subcortical nuclei (including the thalamus, caudate nucleus and putamen) and cerebellum (p from 0.001 to 0.05 at multiple comparison). No significant associations were found between global structural parameters, clinical diagnosis of neuropsychiatric SLE, other SLE sub-phenotypes, presence of antiphospholipid antibodies, antiphospholipid syndrome and SLE-related damage burden.

Conclusions: Structural alterations of global and regional brain connectivity occur in patients with SLE, irrespectively of the clinical phenotype. AntiDNA-positive patients are characterized by a more severe phenotype, which is similar to that of patients with relapsing-remitting MS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4264

FRIO0624 STRUCTURAL MRI-BASED CONNECTOMICS IN SLE: A PILOT STUDY

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Background: Neuropsychiatric manifestations are common in patients with systemic lupus erythematosus (SLE). Furthermore, subclinical brain damage occurs in a even higher fraction of patients. However, little is known about the effect of these phenomena on brain connectivity. MRI-based connectomics relies on graph analysis of structural and functional images to detect alterations of the topographic organization of the brain and has been successfully employed to dissect network disassembly in neuroinflammatory diseases such as multiple sclerosis (MS) and Devic’s syndrome.

Objectives: To investigate the topographic organization of the brain of patients with SLE with and without neuropsychiatric manifestations.

Methods: Thirty-two patients with SLE (12 with overt neuropsychiatric involvement as per ACR criteria) were enrolled and compared with 32 healthy controls (HC) and 32 patients with relapsing-remitting MS, all matched for sex, age and disease duration (where applicable). Diffusion tensor (DT) and dual-echo MRI scans were obtained. Structural connectivity matrices between 116 cortical and subcortical brain regions were estimated and global and nodal network metrics were calculated.

Results: Conventional MRI revealed that patients with SLE had significantly higher T2-lesional volumes when compared to controls (p<0.0001). Patients with definite NPSLE had a higher lesion burden (p<0.0006). Network strength, transitivity and global efficiency were all significantly impaired in patients with MS and SLE when compared to HC (p<0.0001). MS and SLE were also characterized by higher average path length when compared to HC (p<0.0001). Global structural alterations were more significant in MS patients than in patients with SLE (p from 0.005 to 0.01 at multiple comparison). However, antiDNA-positive patients (n=24)
was 11.6±12.8 and baseline PsAMRIS synovitis score was 3.7±3.3. Baseline ultrasound synovial hypertrophy and Doppler activity were 6.2±4.5 and 3.5±4.0, respectively. Specific MRI and ultrasound scores were significantly correlated with DAS28 and DAPSA at baseline. Clinical disease activity parameters significantly improved at follow up (DAS28: 2.9±4.05, p<0.001; DAPSA: 8.8±5.8, p<0.001). PsAMRIS synovitis score (r=0.24) as well as composite PsAMRIS score (r=0.810.0) decreased longitudinally with secukinumab treatment (p=0.034 and p=0.039, respectively). There was no progression in erosion or proliferation scores between baseline and follow-up. Synovial hypertrophy and Doppler activity in ultrasound also significantly improved with secukinumab treatment (2.3±3.5; p<0.009 and 1.8±2.7; p=0.003, respectively). A significant percentage of patients reaching minimal disease activity showed residual signs of synovitis in the MRI and US (66% and 50%, respectively).

Conclusions: Secukinumab significantly improves MRI and ultrasound signs of joint inflammation in patients with PsA.

Acknowledgements: This study was supported by an unrestricted grant from Novartis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5094

FRIO627 | ULTRASOUND HAND EXAMINATION IS MORE SENSITIVE IN DIAGNOSING HAND OSTEOARTHRITIS THAN CONVENTIONAL RADIOGRAPHY: COMPARISON BETWEEN DIFFERENT ULTRASONOGRAPHIC SCORES

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Background: Hand osteoarthritis (OA) diagnosis is based on a combination of clinical, imaging features and assessment of risk factors, together with clinical associations and outcomes (1). In a real-life context, clinicians face difficulty in differentiating between OA and other hand arthropathies, particularly when the clinical examination is equivocal (e.g. no obvious bony enlargement with the characteristic distribution for hand OA).

Objectives: This is the first study to investigate the usefulness of a standardised ultrasound (US) examination protocol for hand joints in diagnosing hand osteoarthritis (OA) and the correlations between several US scores and clinical, inflammatory and radiographic parameters, aiming to explore which type of investigations are the most useful for diagnosing hand OA.

Methods: We conducted a cross-sectional study including 62 patients, ultimately diagnosed with hand OA based on the ACR diagnosis criteria (2). We compared the 34 joint score of the hand, with smaller, pre-defined joint scores including two scores of 22 and 12 joint each, and another 10 and 6 joint scores for OA. We correlated the US findings with radiographic scores (2108 joints).

Results: Radiographic osteophyte scores correlated very well with the predefined US scores detailed above (R=0.381 to 0.645, P<0.05), despite having a low sensitivity for detection of osteophytes (58.6%), and an even lower sensitivity for detection of erosions (38.4%) when compared with the 34 joint US score. There was a good correlation between different US scores (R=0.53 to 0.97, P<0.05), apart from the 6 joint score excluding the proximal interphalangeal joints (R= -0.01 to 0.207, P<0.05).

Conclusions: US examination of the hands can facilitate the diagnosis of hand OA in patients who do not fulfil the ACR criteria, by identifying the presence of osteophytes with the particular distribution and number required for diagnosis in a proportion of patients that was three times higher than that of patients diagnosed based on clinical examination and hand radiography alone.

References:

Acknowledgements: S. Hussain and P. Sikavukamaran contributed equally to this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2713

FRIO626 | ANALYSIS OF CORRELATION AND CAUSES FOR DISCREPANCY BETWEEN QUANTITATIVE AND SEMI-QUANTITATIVE DOPPLER SCORES IN SYNOVITIS IN RHEUMATOID ARTHRITIS


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Background: Doppler US is used for the evaluation of synovitis in RA. The amount of Doppler signals are measured in the synovial tissue according to either semi-quantitative (SQS) or quantitative scoring (QS) methods. None of the SQS amount of Doppler signals are measured in the synovial tissue according to either SQS method. Association between QS and SQS was studied using correlations and multilevel models taking into account the clustering of ratings at the rater, patient and joint levels.

Methods: Adult patients with RA and inadequate clinical response to anti-rheumatic therapy were examined with US. Dorsal US of the wrists, MCP and MTP 2–5 were performed. US images with sign of synovitis were collected and US scores detailed above (R=0.381 to 0.645, P<0.05), despite having a low sensitivity for detection of osteophytes (58.6%), and an even lower sensitivity for detection of erosions (38.4%) when compared with the 34 joint US score. There was a good correlation between different US scores (R=0.53 to 0.97, P<0.05), apart from the 6 joint score excluding the proximal interphalangeal joints (R= -0.01 to 0.207, P<0.05).

Results: Radiographic osteophyte scores correlated very well with the predefined US scores detailed above (R=0.381 to 0.645, P<0.05), despite having a low sensitivity for detection of osteophytes (58.6%), and an even lower sensitivity for detection of erosions (38.4%) when compared with the 34 joint US score. There was a good correlation between different US scores (R=0.53 to 0.97, P<0.05), apart from the 6 joint score excluding the proximal interphalangeal joints (R= -0.01 to 0.207, P<0.05).

Conclusions: US examination of the hands can facilitate the diagnosis of hand OA in patients who do not fulfil the ACR criteria, by identifying the presence of osteophytes with the particular distribution and number required for diagnosis in a proportion of patients that was three times higher than that of patients diagnosed based on clinical examination and hand radiography alone.

References:

Acknowledgements: S. Hussain and P. Sikavukamaran contributed equally to this study.

Disclosure of Interest: None declared


FRIO628 | ULTRASOUND SHOWS SIGNS OF INFLAMMATION IN MOST PATIENTS WITH RHEUMATOID ARTHRITIS IN LONGSTANDING CLINICAL REMISSION, IRRESPECTIVE OF CONVENTIONAL SYNTHETIC OR BIOLOGIC DMARD THERAPY

U. Møller Døhn, C.H. Brahe, M.L. Hetland, V. Fana, S. Krabbe, M. Ammitzbøll-Danielsen, M. Østergaard, L. Terslev, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark

Background: None of the currently accepted remission criteria in rheumatoid arthritis (RA) incorporate inflammation on imaging. Signs of inflammation on ultrasound (US) and magnetic resonance imaging are frequently seen in RA patients in clinical remission (1–3). It is not known whether patients in longstanding clinical and radiographic remission obtained through a DAS28 driven treat to target (T2T) strategy by conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) or by biologic (bDMARD) therapy differ with respect to US detected synovitis.

Abstract FRIO628 – Table 1

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<tr>
<td>Grade 1–2</td>
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<td>0.72</td>
<td>1.0</td>
<td>0.85</td>
<td>0.99</td>
<td>0.82</td>
<td>0.96</td>
<td>0.77</td>
<td>0.98</td>
<td>0.92</td>
<td>0.98</td>
<td>0.92</td>
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</table>

*Cut-off between grade 0 (G0) and G1: 0%; between G1 and G2: 10%; between G2 and G3: 50%.
**OBJECTIVES:** In RA patients in longstanding clinical and radiographic remission, achieved by a DAS28-driven T2 strategy, to investigate if US signs of inflammation differ between RA patients, treated with csDMARD or bDMARD (+/- csDMARD).

**METHODS:** Eighty-seven patients with RA in longstanding clinical (continuous DAS28 >2.6 for the preceding year) and radiographic (no progression for at least 1 year) remission, were included in the study. US of elbows, wrists, MCP joints, knees, ankles and MP joints were performed. Inter-reader agreement was assessed in a random subset of 42 cases using the intra-class correlation coefficient (ICC). Proportion of patients with any sign of MRI inflammation was noted. Mann-Whitney U test was used to compare intra-class correlation coefficients (ICC) of psA and PsO patients. Clinical variables were compared with inflammation scores for any association.

**RESULTS:** Of the 87 patients fulfilling DAS28 remission criteria at entry and CDAI remission was fulfilled in 76% and 79% in the csDMARD and bDMARD group, respectively. Complete absence of any sign of US inflammation (GSS=0 and CDAI=0) was seen in 0% and 14% in the csDMARD and bDMARD groups, respectively (p<0.01), while minimal US inflammation (GSS≤1 and CDAI=0) was seen in 33% and 40% (NS). CDAI in at least one joint was seen in the majority of patients in both groups, 58% and 57% respectively.

**CONCLUSIONS:** This study corroborates a high proportion of psoriasis patients with subclinical disease of the small joints of foot. Patients with nail involvement had a higher risk of subclinical disease. The cohort is being assessed longitudinally to determine the clinical utility of MRI feet in predicting subsequent development of PsA in patients with psoriasis.

**REFERENCES:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5705

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**FR00630 CAN WHOLE BODY MRI AT BASELINE IDENTIFY DEFINITE INFLAMMATORY ARTHRITIS PATTERNS IN UNDIFFERENTIATED ARTHRITIS?**

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**Background:** When diagnosing inflammatory arthritis (IA) early, focal joint imaging may not reflect the overall inflammatory burden/distribution. Whole body MRI (WBMRI) offers the potential to feasibly scan most joints in a single session.

**OBJECTIVES:** The aims were (i) to describe the WBMRI pattern of disease in early IA (ii) to identify patterns associated with subsequent definite IA.

**METHODS:** Patients were recruited with early inflammatory joint symptoms and/or signs of IA. Clinical data included age, gender, symptom duration, CRP HLA-B27, RF, CCP Ab and tender/swollen joint counts. Using 3T WBMRI, T2-weighted fat suppressed spine/SIJ images pre contrast and 3D VIBE Dixon images of peripheral joints and entheses post IV contrast were acquired. Images were consensus scored for inflammation/erosion at the spine, SIJ, GHJ, SCJ, wrist, MCP,PIP, hip, knee, ankle, mid/ hind foot, MTP and IP joints plus shoulder, ASIS, greater trochanter, knee, Achilles and plantar fascia entheses. Subjects were clinically classified as IA baseline and 1 year as undifferentiated arthritis (UA), CCP+RA, CCP-RA or Spondyloarthritis (SpA). Clinicians were unaware of the MRI findings.

**RESULTS:** 39 patients (23 female) were recruited; mean age 43 years, median symptom duration 18 months (7, 24), TJC 5 (2.1), SJC 1 (0.3) and CRP 2 (2.2). At baseline, 14 were classified as definite disease (RA or SpA) and 25 (14 female) as UA with mean age 40 years, median symptom duration 16.5 months (9.8, 24.3), TJC 3 (1.8), SJC 0 (0.1), CRP 2 (2.2) and 3 (12%) were HLA-B27 positive. The distribution of WBMRI findings in the classified (i.e. definite IA) group was predominately small joint and tendon-based in the CCP+ RA group, large joint based with 50% having SIJ disease in the CCP- group and similar findings in the SpA group. In the non-classified group (i.e. pUA and rUA), the distribution of pUA was both axial and peripheral, involving joints and entheses, with 25% having SIJ disease, compared to 12% in the rUA group were similarly distributed but less frequent with no cases of SIJ disease. After 1 year of clinical/laboratory follow-up, 8 were identified as pUA, 6 rUA, 7 CCP-RA, 6 CCP-RA and 12 as SpA. Table 1 shows WBMRI disease distribution by 1 year diagnostic category. All the affected WBMRI sites in the diagnostic work-up would have appropriately classified 6 further cases of definite SpA, from the pUA and 3 from the CCP-RA groups.

**DISCLOSURE OF INTEREST:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5763

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**FR00629 MAGNETIC RESONANCE IMAGING (MRI) INFLAMMATION OF THE FEET DEMONSTRATES SUBCLINICAL INFLAMMATORY DISEASE IN CUTANEOUS PSORIASIS PATIENTS WITHOUT CLINICAL ARTHRITIS**

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**Background:** Up to 40% of patients with cutaneous psoriasis may develop psoriatic arthritis (PsA). Early detection of PsA by advanced imaging techniques results in better response to therapy. There are very few studies evaluating the MRI findings in feet of patients with psoriasis and PsA. The study was divided into those without arthritis (PsO) and PsA groups. All consenting patients underwent non-contrast MRI of the right foot. Demographic and physical examination details were recorded. PsO patients completed the early arthritis in psoriasis (EARP) questionnaire. Two trained readers scored the MRI inflammation (synovitis, tenosynovitis, enthesitis) using a modification of the PsAMRIS scores (PsAMRIS).

**Objectives:** This study sought to evaluate inflammation at the smallest joints of feet in a subset of psoriasis patients without clinical arthritis, using an office-based extremity MRI (eMRI) as compared to the findings in overt PsA patients. The inclusion of affected WBMRI sites in the diagnostic work-up would have appropriately classified 6 further cases of definite SpA, from the pUA and 3 from the CCP-RA groups.

**Results:** A total of 83 patients (30 PsO and 53 PsA) with 75% males and mean age of 42.2±11.6 years were included. ICC for all three variables between the readers was very good (>0.8). There was no statistical difference between the median eMRI inflammatory scores in PsA and PsO patients (p=0.493). Evidence of inflammation was present in 64% and 67% patients in the PsO and PsA groups, respectively (Table 1). Higher NAPSI scores were associated with presence of MRI inflammation (p=0.022).

**Table 1. PsAMRIS variables for MRI inflammation of foot in PsO and PsA subgroups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>PsO (n=53)</th>
<th>PsA (n=30)</th>
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<tbody>
<tr>
<td>Synovitis</td>
<td>34 (64%)</td>
<td>19 (63%)</td>
</tr>
<tr>
<td>Osteitis</td>
<td>2 (4%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Flexor tenosynovitis</td>
<td>5 (17%)</td>
<td>8 (27%)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>34 (64%)</td>
<td>20 (67%)</td>
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</table>

**Conclusions:** This study corroborates a high proportion of psoriasis patients with subclinical disease of the small joints of foot. Patients with nail involvement had a higher risk of subclinical disease. The cohort is being assessed longitudinally to determine the clinical utility of MRI feet in predicting subsequent development of PsA in patients with psoriasis.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5763
Conclusions: In the persistent UA group and CCP-RA group, WBMRI findings at baseline already showed a definite pattern of spinal disease. Therefore the use of WBMRI findings at presentation in addition to clinical assessment would allow clinicians to classify a proportion of patients earlier.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5051

**FR00631**

**PREDICTIVE VALUE OF POWER DOPPLER ULTRASONOGRAPHY (PDUS) IN THE DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS**

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Background: There is a short window of opportunity for early diagnosis and treatment of rheumatoid arthritis, that may be crucial for reaching remission and a low rate of radiographic progression. High resolution power doppler ultrasonography (PDUS) is helpful in early detection of synovitis and allows an accurate classification of patients with joint inflammation.

Objectives: To establish whether the presence of basal power doppler signal in patients with very early arthritis may be helpful in order to establish the risk of final diagnosis of rheumatoid arthritis according ACR criteria 1987 at a year of follow up.

Methods: We studied the presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, PIPs, knees) and 44 joints (28 joints and in addition hips, ankles, tarsus, and MTPs), with a mid-range equipment GE L5, in 70 patients with suspected early arthritis. The patients were included with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with < 12 months of duration of the symptoms. Presence or not basal erosions (score ≥ 5 in at least one joint by modified Sharp method) for each patient were registered (65 patients with basal hands and feet radiology available). Presence of RF and ACPA positive were recorded as well. At one year follow-up was established whether patients met criteria for RA according 1987 ACR or not. Statistical study: Chi-square, Fisher exact test, p univariant and Odds Ratio calculation.

Results: The presence of basal power doppler signal in ≥ 1 joints of 44 (PD44) in baseline view shows statistically significant association to RA diagnosis at 12 months by ACR 1987 classification criteria, p<0.003, OR=5.43 (1.71–17.24) but the presence of at least one joint with power doppler signal of 28 joints (PD28) did not (p=0.051). Presence hypertrophic synovium with PD44 or not, in at least one joint (HSORPD44) was associated to RA diagnosis as well p=0.024; OR=24.20 (2.98–196.34) and p=0.003 OR 12.93 (1.59–104.94). There was a correlation between DAS28 and the MRI synovitis score (r=0.59, p=0.04), REE (r=0.60, p=0.04) and RE (r=0.58, p=0.05), US Doppler in the long axis (r=0.60, p=0.04), but not with RAMRIS synovitis, erosions or BME nor with REE. The MRI wrist synovitis score did not correlate with the Doppler score on the sagittal and axial views, nor with US B mode score. This was true also for the three individual MRI joints slices of the wrist, the REE and the RE. The figure shows from the left the pre-contrast axial MRI image, the post-contrast and the fusion images.

Conclusions: Although both MRI and Doppler are good indicators of disease activity in RA, they seem not to be interchangeable. This may be due to the fact that MRI and US show different features of synovitis or, alternatively, that MRI comprised the whole wrist whereas US visualized only its dorsal area. Although our preliminary data do not support the use of fusion images, these should be investigated on larger number of patients with a more extended PD approach.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5433

**FR00632**

**MRI-US FUSION IMAGES FOR RHEUMATOID ARTHRITIS: CAN Doppler SUBSTITUTE FOR GADOLINIUM?**

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Background: MRI is increasingly used to objectively assess disease activity and damage in patients with rheumatoid arthritis (RA), especially in clinical trials. The preferred scoring method is the RAMRIS, which implies the use of gadolinium, an intravenous contrast agent, to assess synovitis.

Objectives: We evaluated in a small preliminary study if the fusion of MRI and US Power Doppler (PD) images could avoid gadolinium.

Methods: In 12 patients (10 women) affected by at least one involved wrist, were studied. Mean age was 58.8±9.1 years and mean disease duration was 54.5±56.1 months. Disease activity (DAS28-CRP) was evaluated on the day of the examinations.

MRI was performed on a 3.0 T extremity-dedicated machine (Osc an 0.3 T, Esaote, Genova Italy) and US by MyLab Twice ultrasound scanner with a virtual navigator software (Esaote, Genova, Italy). T3D sequences were used in the fusion images (parameters: TR/TE/NEX 38/16/1 matrix, 192*192*39, FOV 160°/160°). Magnetic field strength was 12.7 GHz and magnetic field gradient was 0.4 MHz. Gadolinium contrast agent was not used to acquire fusion images. MRI synovitis was scored by the RAMRIS and with the contrast-enhanced dynamic method resulting in rate of early enhancement (REE) and relative enhancement, (RE) The US score was the Global OMERACT-EULAR Synovitis Score (GLOESS) and its individual parts.

Results: Inter-reader agreement for PD by weighted kappa was 0.75 (75%CI 0.53–0.96) for the sagittal and 1 (75%CI 1–1) for the axial view. It was 0.85 (75%CI 0.69–0.98) for MRI synovitis.

There was a correlation between DAS28 and the MRI synovitis score (r=0.59, p<0.04), REE (r=0.60, p<0.04), and RE (r=0.58, p<0.05). US Doppler in the long axis (r=0.6, p<0.05) and in the axial axes (r=0.86, p<0.01), but not with B-mode synovial effusion (r=0.56, p=0.056). The GLOESS correlated with DAS28 (r=0.66, p<0.019), but not with RAMRIS synovitis, erosions or BME nor with RE.

The MRI wrist synovitis score did not correlate with the Doppler score on the sagittal and axial views, nor with US B mode score. This was true also for the three individual MRI joint slices of the wrist, the REE and the RE. The figure shows from the left the pre-contrast axial MRI image, the post-contrast and the fusion images.

Conclusions: Although both MRI and Doppler are good indicators of disease activity in RA, they seem not to be interchangeable. This may be due to the fact that MRI and US show different features of synovitis or, alternatively, that MRI comprised the whole wrist whereas US visualized only its dorsal area. Although our preliminary data do not support the use of fusion images, these should be investigated on larger number of patients with a more extended PD approach.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5433

**FR00633**

**WHICH ARE THE ULTRASOUND LESIONS UNDERLYING DACTYLITIS?**

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Background: Dactylitis, defined as a diffuse swelling of a digit is a hallmark feature of peripheral spondyloarthritis (SpA), particularly in psoriatic arthritis, with a prevalence between 16% and 18%.

Objectives: This study aims to assess the frequency of the pathological lesions in dactylitis using ultrasonography (US) and to evaluate their association with patient-reported tenderness.

Methods: Thirty-four dactylitis from 20 consecutive patients suffering from peripheral spondyloarthropathy were examined by ultrasound. At US examination, the entire digit was scanned both on dorsal and palmar/plantar sides. The following US pathological lesions were scored: soft tissue thickness, soft tissue edema, soft tissue vascularity, synovitis of metatarsophalangeal (MCP)/metatarsophalangeal (MTP), of proximal interphalangeal (PIP) and of...
DO ANTHROPOMETRIC FACTORS INFLUENCE MEDIAN NERVE SIZE IN HEALTHY INDIVIDUALS? AN ULTRASOUND VOLUMETRY STUDY


Background: Some (but not all) ultrasound studies of median nerve dimensions at the wrist have suggested that anthropometric factors such as height and weight are among the possible sources of variability in the normal population but this has not been systematically studied.

Objectives: The purpose of our study was to establish if hand and wrist volume or other standard anthropomorphic factors influenced median nerve size in normal subjects using standard ultrasonographic techniques. If median nerve size is predictably related to anthropomorphic factors, adjusted normal reference ranges would improve the diagnostic precision of the test for carpal tunnel syndrome.

Methods: We studied 30 healthy subjects: 14 females and 16 males. We measured their height, weight, arm span, finger span and wrist circumference.

Ultrasoundography of the median nerve was carried out at the entrance to the carpal tunnel and at a second level 2 cm proximal to the wrist using an Esaote MyLab Class C ultrasound with a 12–18MHz linear probe. The wrist was marked at the distal wrist crease and 2cm proximally. Hand and wrist volume were measured using water displacement volumetry.

Results: The intra-rater reliability of volumetry measurements was excellent for both hand and wrist volumetry with a Cronbach alpha of 0.99 and 0.88 respectively. The intra-rater reliability for median nerve measurements was excellent with a Cronbach alpha of 0.96. The median nerve dimensions were not significantly different between male and female subjects, nor between the dominant and non-dominant hands. The mean median nerve cross sectional area (CSA) at the distal wrist crease was 10.68 mm² and at a point 2cm proximal to this it was 10.18 mm². The mean difference in CSA between these two points was 0.5 mm². The median nerve CSA was not significantly related to height, weight or hand size. It was not correlated with hand or wrist volume. No significant differences were found in relation to hand dominance or gender.

Spearman’s correlation between median nerve CSA (distal, right wrist) and anthropometric factors were assessed according to OMERACT scores (0–3). Nail bed vascularization architecture, dilatation of capillaries, presence of megacapillaries and avascular areas were found to be closely related to median nerve size in normal individuals.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3834
endothelial dysfunction in systemic lupus erythematosus – a case-control study and an updated meta-analysis and meta-regression

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Background: Endothelium-dependent flow-mediated dilation (ED-FMD), a biological marker of endothelial dysfunction, is apparently impaired in patients with systemic lupus erythematosus (SLE). However, such observation is inconsistent because of the lack of standardization of the methodology of ED-FMD measurement and inclusion of patients with different comorbidities amongst different studies.

Objective: Firstly, we evaluated if ED-FMD is indeed impaired in SLE patients naïve of cardiovascular disease and its traditional risk factors. Secondly, we aimed to determine if the putative contribution of SLE to endothelial dysfunction is in fact confounded by demographic-, disease- and treatment-related factors.

Methods: We assessed and compared the brachial artery ED-FMD (baED-FMD) using the Prosound Alpha-10 ultrasound system® between SLE patients without cardiovascular disease and cardiovascular risk factors and healthy controls (HC) matched for age, gender and body mass index (BMI). Exclusions were pregnancy, a history hypertension, diabetes mellitus, chronic kidney disease, cardiovascular and cerebrovascular diseases, and statin therapy. SLE-related disease activity and organ damage are not apparently related to endothelial dysfunction, the presence of diabetes mellitus, renal disease and diastolic hypertension are potential contributors to endothelial dysfunction in SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4329

FRM0636

ENDOTHELIAL DYSFUNCTION IN SYSTEMIC LUPUS ERYSITEMATOSUS – A CASE-CONTROL STUDY AND AN UPDATED META-ANALYSIS AND META-REGRESSION

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Background: Ultrasoundography (US) has demonstrated to be an accurate tool for the diagnosis of calcium pyrophosphate deposition disease (CPPD) (1). Recently, the OMERACT “US in CPPD” task force, has created new definitions for CPPD identification by US, that demonstrated to be reliable at the knee joint, bridging a gap affecting the old definitions (2). The aim of this study was to evaluate the association between US, for the first time the new OMERACT US criteria for CPPD, and SFA findings for identifying patients affected by CPPD.

Objective: The aim of this study was to evaluate the association between US, for the first time the new OMERACT US criteria for CPPD, and SFA findings for identifying patients affected by CPPD.

Methods: We enrolled all the consecutive patients, aged more than 60 years referred to our outpatient clinic from September 2016 to December 2018, for knee pain and that presented knee effusion of any grade. Patients with suspected chronic inflammatory conditions were excluded.

Results: Seventy-one SLE patients and 71 HC were studied, and there were 6 men in each group. The mean±SD age and BMI of SLE patients and HC were 70.29±10.93. Subsequently, a US-guided arthrocentesis was performed, and the synovial fluid was collected and analyzed by a compensated polarized light microscopy (AxioLab A.1 [Zeiss]) by an expert observer in order to assess the presence of CPP crystals. Both observers were blinded to clinical and to each other findings. The Chi-squared test was used to correlate the US and SFA findings.

Results: Forty-nine patients (28 men and 21 women) were enrolled in the study, with a mean age of 70.29±10.93. Twenty-eight subjects were affected by CPPD at SFA and 26 patients were affected by CPPD at SFA and 26 patients...
were identified as affected by CPPD at US. In 4 patients, the SFA was positive and the US was negative, while in 2 patients the SFA was negative and the US positive. Using the chi-squared test, a very strong association was found between the exams, with a p-value <0.0001.

**Conclusions:** The new OMERACT US criteria for CPPD identification have already demonstrated to be reliable, considering the good to high kappa values yielded in previous multi-observer studies (2). This preliminary study, indicates that the new criteria seem to be also accurate for diagnostic purposes as they strongly correlate with the SFA for the presence of CPPD in knee joints. Further validation studies that will be able to assess the diagnostic accuracy of US are already in the research agenda of the OMERACT group “US in CPPD”.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5164

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**FR00639 COMPARISON OF ULTRASOUND AND MRI IN THE DIAGNOSIS OF PROXIMAL AND DISTAL BICEPS TENDON PATHOLOGY**

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**Background:** Disorders of the long head of the biceps brachii tendon (LHBt) are commonly recognized as a source of shoulder pain. Ultrasound (US) is thought to be of limited value in the diagnosis of partial-thickness tear and non-tear abnormalities of the LHBt because of the difficulty to assess its intra-articular proximal portion. Braesseur recently described that placing the arm in extension/external rotation increased LHBt intra-articular portion visibility.

**Objectives:** The goal of this study was to determine if the systematic assessment of the intra-articular portion of the tendon, from the rotator interval to its glenoid insertion, with the arm placed in extension/external rotation could increase US sensitivity.

**Methods:** This was a cross-sectional study. All patients referred for the treatment of a rotator cuff disease (rupture, tendinopathy, calcific deposit) with an available US and MRI were included. US was performed blinded from the results of the clinical examination. LHBt was studied at the proximal, intra-articular part of the tendon remains challenging. MRI sensitivity to transdermal NSAID and a RR of 2.26 compared with oral NSAD treatment (P=0.001 and P=0.01, respectively). The only independent factor that demonstrated a 100% success treatment rate was the presence of power Doppler signal treated using steroid injection.

**Conclusions:** US findings are useful predictors of therapeutic response in patients with trochanteric pain. In general terms, we found that patients with US acute findings have an increased probability of treatment success when treated with steroid injection while those with US chronic findings have an increased probability of success when treated with NSAIDs (transdermal or systemic).

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6556

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**FR00640 STRUCTURAL DAMAGE PROGRESSION IN LUPUS ARTHRITIS: A PROSPECTIVE OBSERVATIONAL STUDY**

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**Background:** Joint involvement is one of the main causes of chronic pain and disability in SLE patients (pts); despite arthritis in SLE is usually considered mild, joint erosions and deformities can be observed with significant impact on patient’s quality of life. Imaging techniques are more sensitive than joint count in detecting synovitis and early joint damage.

**Objectives:** This study was aimed at evaluating the progression of joint damage in SLE and at evaluating predictive factors for damage accrual.

**Methods:** Consecutive SLE pts with active hand-wrists synovitis (detected by joint

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**Table 1**

<table>
<thead>
<tr>
<th>LHB</th>
<th>MRI</th>
<th>US distal</th>
<th>US proximal</th>
<th>Arthroscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>99</td>
<td>90</td>
<td>111</td>
<td>78</td>
</tr>
<tr>
<td>Subluxation</td>
<td>15</td>
<td>6</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Effusion</td>
<td>12</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Tear</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Flattened</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Thickening</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Nodular</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

We calculated the sensitivity/specificity of MRI and US (at the proximal and distal level) in the detection of LHBt changes using arthroscopy as gold standard (Table 2).

**Table 2**

<table>
<thead>
<tr>
<th>MRI</th>
<th>US proximal</th>
<th>US distal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>52%</td>
<td>59%</td>
</tr>
<tr>
<td>Specificity</td>
<td>96%</td>
<td>88%</td>
</tr>
<tr>
<td>PPV</td>
<td>90%</td>
<td>77%</td>
</tr>
<tr>
<td>NPV</td>
<td>73%</td>
<td>77%</td>
</tr>
</tbody>
</table>

We calculated the sensitivity/specificity of MRI and US (at the proximal and distal level) in the detection of LHBt changes using arthroscopy as gold standard (Table 2).

**Conclusions:** US has a good specificity but a poor sensitivity in the detection of LHB tendon changes even when a systematic and careful study of the proximal part of the tendon is undertaken. If detection of distal changes of the tendon in the inter-tubercular groove seems feasible with US, the involvement of the more proximal, intra-articular part of the tendon remains challenging. MRI sensitivity remains also poor. Overall, arthroscopy still remains the gold standard to detect LHB tendon intra-articular pathology.

**References:**

**Disclosure of Interest:** None declared

count and/or ultrasounds) were enrolled in this 5-years prospective observational study. Clinical assessments as well as joint ultrasound (US) and MRI were performed at baseline and after 5 years. Each patient underwent a non-dominant hand–wrist US examination using a Logiq 9 with a linear probe operating at 14 MHz. Synovitis was defined as the presence of synovial hypertrophy and/or the presence of PD signal (PD) at baseline or in at least a recent one of the arthritis (≤1 year of duration). 22 pts (26.8%) showed clinical signs of synovitis, 56 (68.2%) presented positive hand-wrists US (synovitis) and in 14 (26.6%) PD signal was also recorded. Six pts (11.7%) already showed erosions at standard X-Ray, while MRI revealed at least one BE in 30 and 54 patients respectively, for a cumulative mean erosive burden of 9.2 erosions (range 1–63). After 5 years of follow-up, 34 pts consented to repeat the assessment; 11 (33%) had JA and 18 (29%) were still presenting clinical signs of synovitis; 28 pts (82.3%) showed synovitis at US with PD in 7 cases (20.9%). The final mean erosive burden resulted 12.3 (range 2–82) with a significant increase from the baseline evaluation (p=0.001). Overall, 16 pts achieved joint damage. Interestingly, erosion progression was observed also in 12 pts with negative joint count but positive US at baseline. The presence of PD at US and BME at baseline was associated with higher erosive burden at follow-up (p=0.03 and p=0.02 respectively).

Conclusions: Arthritis and SLE can be persistent over time and progress to joint damage even in a short term period despite treatment; normal joint count at physical examination but US findings of synovitis can be associated with erosion progression over time. The presence of PD at US and bone marrow edema at MRI was associated with a more severe damage progression. US and MRI can be used for the clinician to identify patients at higher risk of severe damage to be treated with a more aggressive therapeutic strategy targeting arthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6016

FR0641 Wrist Inflammation as Assessed by Magnetic Resonance Imaging is Associated with Patient-Reported Physical, Impairment, Global Disease Activity and Pain in Early Rheumatoid Arthritis: Long-Term Results from Two Randomized Controlled Trials

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Background: Studies in established rheumatoid arthritis (RA) have shown that radiographic progression is associated with increasing health assessment questionnaires (HAQ). However, most studies have failed to demonstrate this association at the early stage of the disease. In addition, little is known about how specific pathologies, e.g. joint inflammation, tenosynovitis and joint damage, contribute to different patient-reported outcomes (PROs).

Objectives: To examine the association between MRI wrist inflammation and damage with PROs in patients with early RA.

Methods: MRI of the wrist and hand were obtained from 210 early RA patients participating in two investigator-initiated, randomized, controlled studies (CIMESTRA/OPERA), which aimed at achieving inflammatory control by use of conventional and/or biologic drugs combined with intra-articular injection of glucocorticoids. The image-sets were assessed according to the RA MRI scoring systems for conventional and/or biologic drugs. Performing the scoring, a trained radiologist unaware of the clinical picture and diagnosis assessed the sections on tendon, bone erosion, synovitis and joint space narrowing. The MRI images were also reassessed for associations between MRI features and HAQ, patient global visual analogue scales (VAS-PtGlobal) and VAS pain for status and change scores, independently of swollen joint count and level of C-reactive protein.

Results: Fifty-seven pts were enrolled (female 91.2%, mean age 44±12.2 years, mean disease duration 15.9±9 years);43 (75.4%) completed the follow-up, 3 died (1.9%) and 14 (22.6%) were lost to follow-up. MRI inflammation, but not damage, showed statistically significant associations with HAQ, VAS-PtGlobal and VAS pain for status and change scores, independently of swollen joint count and level of C-reactive protein. Synovitis and tenosynovitis were the MRI features most consistently associated with PROs, particularly VAS-PtGlobal and VAS pain (Table 1). MRI synovitis and tenosynovitis mean scores increased with the level of difficulty to cut meat and open a milk carton (p<0.01), and similar patterns were seen for other hand-related HAQ items. As an additional analysis, the metacarpophalangeal joints were included in the analyses, but this did not strengthen the associations between MRI pathology and PROs.

Conclusions: MRI-assessed inflammation, but not damage, in the early RA wrist is associated with patient-reported physical impairment, global disease activity and pain, and the amount of wrist inflammation influences physical hand function.


DOI: 10.1136/annrheumdis-2017-eular.1555

FR0642 The Potential Value of Positron Emission Tomography (PET)-Scan in Systemic Sclerosis for the Quantitative Assessment of Interstitial Lung Disease

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Background: Interstitial lung disease (ILD) in systemic sclerosis is treated by immunosuppressive drugs (e.g. cyclophosphamide), aimed at reduction of inflammatory response. Differentiation between inflamed and non-inflamed fibrotic tissue might help to develop treatment stratification, with the aim of improving the prognosis of (subgroups of) SSc-ILD patients. 18F-Fluorodeoxyglucose Positron Emission Tomography (18F-FDG PET) scan might be a promising tool to detect inflamed lung areas, which are not currently shown in a semi-quantitative setting [1, 2].

Objectives: This study aims to investigate the potential role of 18F-FDG PET –scan for the quantitative assessment of metabolically active SSc related ILD.

Methods: 18F-FDG PET -scans of 22 patients with systemic auto-immune disease, including 9 with SSc, 9 with systemic lupus erythematosus (SLE) and 4 with primary Sjögren's syndrome (pSS), were retrospectively analyzed. FDG uptake was quantitatively measured within 2cm² Regions of Interest (ROI’s) at apical, medial and basal lung levels. A total of 22 ROIs were drawn in each patient. SUVmean values of all ROI’s were corrected by the median SUVmean bloodpool value. Subsequently, the average of 6 posterior basal SUVmean values
was divided by the average of 6 posterior apical SUVmean values (basal/apical ratio). High Resolution Computed tomography (HRCT)-scans and Pulmonary Function Tests (PFT) were examined to confirm the diagnosis of ILD and to specify the pattern of fibrosis. Results: Mean age of patients was 69.4 (SSc-ILD), 62.5 (SSc without ILD), 36.9 (SLE) and 49.3 (pSS). In SSc patients, the mean disease duration was 5.0 (SSc-ILD) and 4.4 (SSc without ILD) years. Diffuse cutaneous sclerosis was present in 2 SSc-ILD and 1 SSc without ILD patients, while other SSc patients were diagnosed with limited cutaneous SSc. ILD was present in 5 out of 9 SSc patients as confirmed by HRCT and PFT. ILD was active in 3 out of 5 SSc-ILD patients. Posterior basal/apical SUVmean ratios of SSc-ILD patients were significantly increased compared to SSc patients without ILD (p=0.016), and compared to SLE and pSS patients without ILD (p=0.001 and p=0.016, respectively), which is shown in Figure 1.

Conclusions: Our findings demonstrate that 18F-FDG PET -scan is potentially useful for the quantitative assessment of active ILD lesions in SSc patients. The technique may therefore provide opportunities to select the patients with inflammatory regions in ILD that are most likely to respond to immunosuppression.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3677

FR10644 SUBCLINICAL ULTRASONOGRAPHIC CHANGES OF THE ANTERIOR CHEST WALL JOINTS IN ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS AND THEIR ASSOCIATION WITH CHEST EXPANSION

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Background: Anterior chest wall (ACW) joints can be involved during the course of Rheumatoid arthritis (RA) and ankylosing spondylitis (AS), however, its clinical implications appear to be undetermined by the rheumatoid arthritis community.

Objectives: To determine the prevalence and types of subclinical ultrasonographic changes in the ACW joints in RA and AS patients and their association with the chest expansion.

Methods: The study was conducted on 132 sternocostal joints (SCJ) and 66 manubriosternal joints (MSJ) in 66 subjects (22 AS, 22 RA, and 22 control). Ultrasound (US) assessments were performed to detect synovitis, erosions, ankylosis, osteophytes, or doppler signals. Chest expansion was measured. In each group, Disease Activity Score (DAS28) and Health Assessment Questionnaire Disability Index (HAQDII) were recorded. In AS group, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were recorded.

Results: US detected subclinical changes of ACW joints in (74.2%) of RA, (77.3%) of AS, and (21.2%) of control groups. There was a highly significant difference between total US changes in RA (74.2%) and control (21.2%) (p<0.001) and also between AS (77.3%) and control (21.2%) (p<0.001). Non of our control had neither erosions nor ankylosing in MSJ. MSJ ankylosing was significantly higher in AS (77.3%) than RA (18.2%) (p<0.001). MSJ ankylosing was highly associated with limited chest expansion in both RA and AS (P<0.001). All patients (100%) in both groups (RA and AS) with MSJ ankylosing by US had limited chest expansion. In RA group, ultrasonographic changes were found to be higher with smoking, longer disease duration and high DAS28. In AS group, ultrasonographic changes were found to be higher with older age, male sex, smoking, longer disease duration and high BASDAI and BASFI.

Table 1. Comparison between RA and AS as regard ultrasonographic changes of anterior chest wall joints

<table>
<thead>
<tr>
<th></th>
<th>RA n (%)</th>
<th>AS n (%)</th>
<th>χ²</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCJ synovitis</td>
<td>34 (77.3)</td>
<td>24 (54.5)</td>
<td>5</td>
<td>0.02*</td>
</tr>
<tr>
<td>SCJ PO activity</td>
<td>14 (31.8)</td>
<td>12 (27.3)</td>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>SCJ erosion</td>
<td>32 (72.3)</td>
<td>28 (63.6)</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>SCJ osteophyte</td>
<td>4 (4.5)</td>
<td>6 (13.6)</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>MSJ ankylosing</td>
<td>4 (16.2)</td>
<td>14 (63.6)</td>
<td>9.2</td>
<td>0.002*</td>
</tr>
<tr>
<td>MSJ erosion</td>
<td>9 (40.9)</td>
<td>4 (18.2)</td>
<td>2.7</td>
<td>0.09</td>
</tr>
<tr>
<td>MSJ osteophyte</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

* n: number; χ²: chi-square test; PD: Power Doppler signals.

Conclusions: US detected subclinical changes of ACW joints in a high percentage of RA and AS patients. No erosions or ankylosing in MSJ were found in the healthy individuals. MSJ ankylosing is more in AS than RA. Relatively, ankylosing of MSJ by US is highly associated with limited chest expansion in RA and AS. Up to the best of our knowledge, our study was the first study that detected subclinical changes of ACW joints in RA and AS by US.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2245

FR10643 ENTHESITIS AND FOOT DISABILITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Enthesitis is a primary clinical feature of ankylosing spondylitis (AS). Lower extremity entheseopathy may cause foot pain and functional disability. Detection of entheseal injury by using physical examination may be insufficient. Musculoskeletal ultrasonography is a noninvasive and low-cost method for detecting enthesis readily.

Objectives: The aims of this study were to evaluate enthesis by using musculoskeletal ultrasonography and foot disability in patients with AS, to compare healthy controls, and to determine the correlation of enthesis score and foot function with disease activity and functional status.

Methods: In this study, 101 patients with AS and 42 healthy controls were examined for enthesis site abnormalities by using gray-scale ultrasonography. The findings of enthesis were assessed by using the Glasgow Ultrasound Enthesitis Scoring System (GUESS). The foot function index (FFI), which comprised of pain, disability, and activity limitation subscales, was measured in all the patients with AS and healthy controls for assessment of foot function. Disease activity and functional status were assessed using the Bath AS Disease Activity Index (BASDAI) and Bath AS Functional Index (BASF), respectively, in patients with AS.

Results: The median GUESS score was 8.00 (1.00–23.00), and, the median total FFI and scores in all the pain, disability, and activity limitation subscales were 14.70 (0.00–75.20), 16.60 (0.00–82.80), 16.10 (0.00–84.40), and 4.00 (0.00–60.00), respectively in patients with AS. The GUESS score, total FFI, and all the subscales scores were significantly higher in the patients with AS than in the controls (p<0.000). GUESS score showed no correlation with BASDAI and BASFI. In patients with AS, total FFI and scores for all subscales showed positive correlations between BASDAI and BASFI, respectively (r=0.00, r=0.66, r=0.00, r=0.50, r=0.05; p=0.00, p=0.00, p=0.00, p=0.05, p=0.05). The severities of enthesitis and foot disability were higher in patients with AS. Patients with AS may undergo ultrasonographic examination for enthesal foot involvement. Foot disability is related with disease activity and function. Foot involvement and disability should be evaluated comprehensively and managed properly.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5112
Background: Diabetes mellitus (DM) is characterized by chronic hyperglycemia states and the development of specific microvascular disorders such as retinopathy and nephropathy. Conventional methods are usually used to study the vascular compromise of this entity, however, the use of capillaroscopy for the evaluation of capillary microarchitecture is not frequently used.

Objectives: The objective of this study was to identify vascular alterations in patients with type II diabetes mellitus and to determine the relationship between capillaroscopic findings and clinical manifestations.

Methods: Observational, descriptive and prospective of patients with diabetes mellitus II selected by inclusion and exclusion criteria and after presenting signs/symptoms or history of any collagen disease, trauma presence in the nailfold due to cosmetic treatment or nail polish, were excluded. The capillaroscopy was performed by an experienced dermatologist in a room with an ambient temperature of 20–23°C. The fourth and fifth fingers of the nondominant hand were chosen. Capillaries were observed using a 10× magnification capillaroscope (Dino-Lite) and photographs of the last distal row of capillaries were taken.

The following capillaroscopic parameters were considered: capillary diameter (ectasia and giant capillaries), cross-linked capillaries, capillary tortuosity, ramified capillaries, avascular zones, hemorrhages, dominant morphology, subpapillary venousplexus visibility, cuticularis and SD pattern. The images were analyzed by an experienced dermatologist. Data was analyzed using SPSS. The non-parametric correlations were performed by tau_b Kendall and values were considered statistically significant when p<0.01 and they had two tails.

Results: 65 patients were included in the study, with a mean age of 57 years [39–80], of which 75% [49] were women and 25% [16] men. The capillaroscopic findings were evident in 83% of the study population. The most frequent alterations were tortuous capillaries in 63% [41], cross-linked capillary in 59% [38], avascular areas in 48% [34], ectasias in 31% [25]. In smaller frequency, giant capillaries 14% [9], arborified capillaries 11% [7], no haemorrhages, no SD pattern. The capillaroscopic findings representing vascular damage were greater in patients with Diabetes Mellitus than in the control group (Figure 1). Moreover, the capillary morphology in the control group was open versus tortuous in patients with DM. Those patients with capillaroscopic alterations had a longer time of evolution of the disease with an average of 12.8 years, compared to those who did not present alterations that had a mean evolution of the disease of 8.5 years, which shows that those capillaroscopic alterations represent progressive endothelial damage. In addition, an association between the presence of retinopathy and capillary damage at the nail bed level was demonstrated (p<0.001).

Conclusions: Capillaroscopy has proven to be a non-invasive, reproducible and reliable technique for the evaluation of vascular microarchitecture within a large group of rheumatoid diseases of the scleroderma spectrum. However, it has been shown previously that can be applied in other diseases outside the field of Rheumatology such as diabetes, being a tool that should be known by primary care physicians and healthcare workers.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1422
CONCORDANCE BETWEEN THE TUBERCULIN SKIN TEST STANDARDIZED PROCEDURES FOR ULTRASOUND IMAGING

I. Aktas

Table 1. Results of ocular Doppler ultrasound over right (RT) and left (LT) sided arteries

<table>
<thead>
<tr>
<th>Range</th>
<th>Mean</th>
<th>S.D.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OA-PSV</td>
<td>P</td>
<td>6.7–57</td>
<td>27.5</td>
</tr>
<tr>
<td>OA-EDV</td>
<td>P</td>
<td>0.0–16.3</td>
<td>6.9</td>
</tr>
<tr>
<td>OA-RI</td>
<td>P</td>
<td>0.63–1</td>
<td>0.76</td>
</tr>
<tr>
<td>CRA-PSV</td>
<td>P</td>
<td>6.5–37</td>
<td>13.203</td>
</tr>
<tr>
<td>CRA-EDV</td>
<td>P</td>
<td>1.6–11.8</td>
<td>4.4297</td>
</tr>
<tr>
<td>CRA-RI</td>
<td>P</td>
<td>0.45–0.79</td>
<td>0.70</td>
</tr>
<tr>
<td>PCA-PSV</td>
<td>P</td>
<td>6.4–45.7</td>
<td>13.82</td>
</tr>
<tr>
<td>PCA-EDV</td>
<td>P</td>
<td>2.2–11.4</td>
<td>4.69</td>
</tr>
<tr>
<td>PCA-RI</td>
<td>P</td>
<td>0.49–0.76</td>
<td>0.63</td>
</tr>
<tr>
<td>OA-RI</td>
<td>P</td>
<td>0.60–0.68</td>
<td>0.63</td>
</tr>
</tbody>
</table>

C = Control, LT = Left, P = Patients, RT = Right, S.D = Standard Deviation.

Conclusions: Behçet's disease patients with ocular involvement have lower CRA, PCA and OA blood flow velocities than healthy control. CDU is helpful in early diagnosis of Behçet's disease patients with ocular involvement have lower CRA, PCA-RI P 0.49–0.76 0.63 0.06 0.409 P 0.53 -0.68 0.87 1.16 0.435 PCA-PSV P 6.4–45.7 13.82 8.35 0.352 P 6.1 -21.6 13.4 4.22 0.872 CRA-EDV P 2.2–11.4 4.69 2.46 0.09 P 1.9 -7.3 4.7 1.65 0.386 CRA-RI P 0.45–0.79 0.70 0.07 0.19 P 0.27–0.80 0.66 0.69 0.083 OA-RI P 0.60–0.68 0.63 0.02 0.09 P 0.59–0.69 0.63 0.02 0.029

Methods: Patients who have been receiving biologic therapy due to chronic inflammatory arthritis were included in this study. Demographic and clinical data, TST and IGRA results were recorded. The agreement between IGRA and TST results was evaluated by Kappa coefficient.

Results: A total of 35 patients were included; 15 (42.8%) were male and mean age was 43.74±12.72 years. Of the 22 TST positive patients, 13 (37.1%) were IGRA negative. Of the 13 TST negative patients, 3 (8.6%) were IGRA positive. Nine (25.7%) patients were positive for either of the two tests and 10 (28.6%) patients were negative for both tests. There was statistically significant discordance between two tests (p<0.021; p<0.05) (Table 1). While positive rate of TST was 62.9%, positive rate of IGRA was 34.3% and Kappa consistency coefficient between two tests was 15.4% (p=0.283; p<0.05).

Table 1. Agreement between IGRA and TST results

<table>
<thead>
<tr>
<th>IGRA</th>
<th>TST</th>
<th>Total</th>
<th>p</th>
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<tbody>
<tr>
<td>Negative n (%)</td>
<td>Positive n (%)</td>
<td>Total n (%)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>10 (28.6)</td>
<td>13 (37.1)</td>
<td>23 (65.7)</td>
</tr>
<tr>
<td>Positive</td>
<td>3 (8.6)</td>
<td>9 (25.7)</td>
<td>12 (34.3)</td>
</tr>
<tr>
<td>Total</td>
<td>13 (37.1)</td>
<td>22 (62.9)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: It is very common in rheumatology practice to administer anti-tuberculosis prophylaxis according to the TST. IGRA may reduce the number of patients in whom tuberculostatics are prescribed, especially in BCG recipients in endemic populations, resulting in a benefit of avoiding possible side effects. Furthermore, IGRA is also important for detecting the cases of LTBI that would be missed by TST. Confirmation in larger studies is necessary.

References:

3. FRI0649 STANDARDIZED PROCEDURES FOR ULTRASOUND IMAGING IN PAEDIATRIC RHEUMATOLOGY: PROGRESS OF A EULAR TASK FORCE

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Background: Musculoskeletal ultrasound (MSUS) is a useful imaging technique in paediatric rheumatic diseases (PRD). US has several advantages over other imaging techniques: it is non-invasive, radiation free, rapid, highly accepted by the patient and does not require sedation for scanning in younger children. However, MSUS examination is incriminated to be an operator dependent technique. Moreover, the variability of normal sonoanatomy in children, due to ossification, makes the acquisition and interpretation of MSUS images difficult. The variability in background and experience of ultrasonographers in different countries requires an international multidisciplinary effort for an optimal standardization of MSUS performance in PRD.

Objectives: To perform a systematic literature review on guidelines for MSUS in children published by international societies and articles on how to perform MSUS scanning in children. This represents the first step for an EULAR taskforce, which objective is to develop EULAR Standardized Procedures for Ultrasound Imaging in Pediatric Rheumatology through a consensus process among rheumatologists, paediatric rheumatologists, and radiologists highly experienced in the performance, teaching and research in paediatric MSUS in rheumatologic disease.

Methods: The objective was reformulated according to the PICO-adapted approach, as follows: body parts, ultrason, and scanning procedures. For each component several synonyms were used. Search limits were applied for animal studies and age. The literature search was performed in Medline and Embase from databases inception to 1st June 2016. References identified were imported into a bibliographic manager and duplicates were removed. To identify eligible studies the remaining articles were assessed by title and abstract. Only articles in English were retained. From the selected studies, data about the examined area, patient position, probe placement, scanning method, landmarks and pathologies using a predefined data collection form.

Results: The literature search resulted in 6059 articles, of which 4856 were captured in Medline and 1203 in Embase. Figure 1 shows the the study flow-chart for article selection. After removing duplicates and scanning titles and abstracts, 295 articles remained for detailed review. After full-text review, 107 articles were excluded. The main reason for article exclusion after full-text review was the lack of standardized examination. Of the remaining articles, 2 described shoulder structures, 14 elbow structures, 5 wrist structures, 9 hand structures, 25 hip
The OMERACT Ultrasound scoring system (USSS) of joint in RA

Informatics & IRIBHM, School of Medicine, ULB, Brussels, Belgium

Results: machine reproducibility was assessed by kappa statistics for discrete variables scoring of the OMERACT US expert was quantified by proportions. The inter-US agreement between each participant with the OMERACT US expert as gold standard. To assess the reliability of the USSS by using different US experts, 9 data (3 patients x 3 joints). The reliability was low for detecting JE (ICC ≤ 0.211. The reliability was low for detecting JE (< 0.001). Acceptable reliability among machines was found for SH, BE and PD (table 1).

<table>
<thead>
<tr>
<th>Table 1</th>
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<tr>
<td>Kappa values</td>
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<tr>
<td>H/G</td>
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<tr>
<td>Kappa values</td>
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<tr>
<td>SH</td>
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<td>PD</td>
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<td>BE</td>
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<tr>
<td>Corresponding P-values</td>
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<td>H/G</td>
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</table>
| Correlation Coefficients (ICC) for UCOASMI and classical metrology measurements were calculated.

Conclusions: The reproducibility of the UCOASMI, obtained through the UCOTrack® motion analysis system in the 3 centers, was very high, in contrast to the lower reproducibility of the Schober test and other measures of classical metrology. The reliability of this system opens the door to using this technology to monitor SpA patients and in future research studies.

References:

Acknowledgements: Funded by MSD, Spain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5435
SALIVARY GLAND ULTRASOUND IS RELATED TO ULTRASOUND DETECTED PATHOLOGY IN THE ENTHESIS OF THE LOWER LIMB IN AN AGE STRATIFIED COHORT OF ASYMPTOMATIC SUBJECTS -A PROSPECTIVELY DESIGNED DESCRIPTIVE CROSS-SECTIONAL STUDY

Methods: We conducted a cross-sectional study comparing MN US parameters of SSc patients followed up at our Rheumatology Unit and control subjects. Exclusion criteria included body mass index (BMI) > 30, previous wrist trauma and known diagnosis of carpal tunnel syndrome. Forty-eight out of 62 SSc patients and 45 healthy age and sex matched controls were enrolled. Subjects were consecutively evaluated in our Department. A General Electric LOGIQ S8 US with a 15 MHz linear transducer was used for assessment. MN cross-sectional area (MNA) and perimeter (MNP) of both sides of each person were measured at the level of the carpal tunnel inlet. For comparative analysis, the mean MNA and MNP of combined right and left side were used. Patients’ relevant clinical and demographic data were collected. Modified Rodnan skin score (mRSS), hand mobility (HAMIS) and SSc Severity Scale (SScSS) were also assessed. Statistical analysis included Chi-Square test, Mann-Whitney U-test, Kruskal-Wallis and Spearman correlation coefficient. P value <0.05 was defined as statistically significant.

Results: A total of 186 MN were assessed by US. Both groups had the same proportion of diabetes and history of tunnel carpal surgery (>p=0.803 and p=0.339, respectively). Median of MNA and MNP were significantly higher in SSc patients (7.5 mm² [6.6 to 9.5] and 13.8 mm [12.4 to 15], respectively) (median [interquartile range]) compared with controls (7.0 mm² [6 to 8] and 12.9 mm [11.7 to 14], respectively) (p=0.021 and p=0.018, respectively). Higher mRSS correlated with higher MNA (Spearman’s rho=0.335, p=0.02) and MNP (rho=0.336, p=0.02).

Conclusions: We confirmed an increased MNA and MNP in SSc patients in comparison with healthy age and sex matched controls. Patients in the oedematous phase of skin involvement and patients with higher skin thickness assessed by mRSS showed higher MNA and MNP values. Wider mRSS, mRSS and mRSS were significantly different between the phases of skin involvement (p=0.007 and p=0.009, respectively), being higher in patients in the oedematous phase (median MNA of 9.25 mm² [7.5 to 11.5] and median MNP of 14.5 mm [13.5 to 16]).

References:

SALIVARY GLAND ULTRASOUND IS RELATED TO AUTOIMMUNITY IN PRIMARY SJÖGREN SYNDROME

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Background: Primary Sjögren syndrome (pSS) is a systemic autoimmune disease involving exocrine glands, mainly ocular and salivary glands. Salivary gland ultrasound (SGU), of submandibular and parotid glands, in pSS is characterized by hypo/anechoic rounded areas within gland parenchyma, losing gland texture and homogeneity of the glands (typical SGU). SGU is a reliable imaging technique for assessing gland echostructure in pSS.

Objectives: The aim of our study is to evaluate the relation between typical SGU and clinical laboratory data in pSS

Methods: We performed SGU to 100 patients with pSS from our rheumatology department selected randomly from a database. We used a semiquantitative score from 0 to 3. Grades 0 and 1 were considered as normal and grades 2 and 3 were considered as typical for pSS. We retrospectively collected demographics (age, gender, disease duration), clinical (extra-glandular manifestations, parotid swelling and lymphomas) and laboratory data (ESR, CRP, rheumatoid factor (RF), antinuclear antibodies (AAN), anti-SSA and anti-SSB antibodies). We divided the patients into 3 groups depending on their autoimmunity profile. Complete seropositive group were patients with RF, AAN and antiSSA or antiSSB positives simultaneous or sequentially. Simple seropositive group were patients with any positive autoantibody (RF/AAN/antiSSA or antiSSB) but not all of them together. Finally, patients without positive autoantibodies were included in the seronegative group.

Results: We excluded 7 patients because they were diagnosed with secondary SS. From 93 pSS patients analyzed, 32 (frequency 34.5%) had a typical SGU. Demographics, extra-glandular manifestations and lymphomas were similar between patients with typical SGU and patients with normal SGU. Parotid swelling and longer disease duration were associated with a typical SGU (p<0.05). Parotid swelling positive autoantibodies (AAN, RF, antiSSA and antiSSB) had more frequently a typical SGU. Complete seropositive group had the highest frequency of typical SGU, followed by simple seropositive group. All seronegative patients had a normal SGU. SGU relate with autoimmunity is shown in table 1

Conclusions: Longer disease duration and parotid swelling were associated with typical SGU. Typical SGU was associated with positive autoimmunity, moreover all seronegative patients had a normal SGU

References:
entheses or increased inflammatory markers in the blood. The dominant leg was examined with US using a Logiq 9 (GE Medical, Milwaukee, WI, USA) with a 6–15 MHz transducer and a fixed pre-set with Doppler settings optimised for inflammatory flow. Both GS and Doppler examination were made. The entheses were examined for hypoechoegenicity, increased thickness, enthesophyte/calcifications, erosions, and Doppler activity.

Results: No subjects had clinical signs of tendon or joint disease. Seven displayed various degrees of hypermobility and seven had various degrees of flatfoot; some in combination. None of the blood tests indicated any pathology.

On US erosions were only seen in one Achilles insertion (not shown in table). The Doppler activity was not measured in plantar fascia due to attenuation of the heel pad. All other US pathology present is seen in the table below.

Conclusions: Only minor pathological findings in the entheses of the lower limb were present in an age stratified cohort of healthy persons. The changes most frequently seen were bony changes in the insertion of the quadriceps and Achilles tendons. A weak tendency toward more pathological findings was seen in this cohort among men, compared to women, and additionally, with increasing age. The findings suggest that US can be used to diagnose/examine subjects for pathological changes of the entheses although with caution regarding entheseophytes of the quadriceps and Achilles tendon.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3708

FR0055 ULTRASOUND FINDINGS OF FEEDING VESSELS AND BONE SURFACE IRREGULARITY IN WRIST JOINTS OF HEALTHY CONTROLS

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Background: Musculoskeletal ultrasound (MSKUS) is capable of visualizing synovitis and bone damage such as erosion. In particular, synovial vascularity as measured by power Doppler (PD) is correlated to rheumatoid arthritis disease activity, and PD signal reveals the prevalence of subclinical synovitis overlooked on physical examination. It is frequently difficult to distinguish bone erosion from normal concave surface of the bone. It is necessary for us to know these normal structures well in evaluating disease activity by using MSKUS. Here we examine the normal feeding vessels and bone surface irregularity in wrist joints.

Objectives: To clarify the distribution of feeding vessels in wrist joints and lunate surface irregularity of healthy controls by using MSKUS.

Methods: The dorsal side of the bilateral wrists was scanned in 2 perpendicular planes with 2D-probe in healthy volunteers. The distribution and bilaterality of feeding vessels in healthy controls (n=30) were as follows:

Above-trapezoid (Rt:100.0%, Lt:100.0%, Blt:100.0%), intra-extensor digitorum tendon sheath (Rt:30.0%, Lt:30.0%, Blt:10.0%), above-trapezoid (Rt:23.3%, Lt:30.0%, Blt:10.0%), above-triangular fibrocartilage complex (Rt:16.7%, Lt:30.0%, Blt:6.7%), distal radial side of the radio-carpal joint (Rt:20.0%, Lt:23.3%, Blt:0.0%), distal end of the ulna (Rt:10.0%, Lt:16.7%, Blt:0.0%), dorsal side of the lunate (Rt:6.7%, Lt:0.0%, Blt:0.0%), palmar side of the extensor digitorum tendon sheath (Rt:0.0%, Lt:3.3%, Blt:0.0%). Feeding vessels from vascular channels were depicted at lunate (Rt:53.3%, Lt:46.7%, Blt:43.3%), the distal side of the radius (Rt:20.0%, Lt:16.7%, Blt:3.3%), triquetrum (Rt:10.0%, Lt:16.7%, Blt:0.0%) and capitate (Rt:6.7%, Lt:10.0%, Blt:0.0%). The frequency of the bone surface irregularity at lunate in healthy volunteers (n=47) and the transverse diameter (TD) (Mean±S.D.) of those were Rt longitudinal plane:57.4% (TD:21.6±3.3mm), Rt transverse plane: 51.1% (TD:20.2±3.1mm), Lt longitudinal plane: 68.1% (TD:26.2±2.8mm), and Lt transverse plane: 42.6% (TD:29.5±3.1mm). Bilateral evaluation of those was 53.2%.

Conclusions: MSKUS evaluation in wrist joints revealed various normal vessels and bone surface irregularity of lunate. It is necessary to distinguish a normal pattern from a pathological pattern in MSKUS examination.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3745

FR0056 SEMIAUTOMATIC ANALYSIS OF EROSION VOLUME BY HR-PQCT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: HR-pQCT is a high resolution CT dedicated to human extremities. It has been used mainly for osteoporosis, while in more recent years it has been applied to research in rheumatoid arthritis (RA).

Objectives: The purpose of this study is to develop a method to quantify the volume of erosions in RA patients semiautomatically using second generation HR-pQCT.

Methods: Twenty patients with RA (70±8 years, 15 female, 5 male) participated in this study. The second and third MCP joints were scanned using HR-pQCT (XtremeCT II, Scanco Medical, Switzerland) at the voxel size of 61μm. The erosion volume was measured semiautomatically using the dedicated software (TRI/3D-BON, Ratoc System Engineering, Tokyo).

Results: In a total of 37 joints (3 joints were excluded due to severe deformities), 40 erosions were detected by HR-pQCT (palpable size: 9 erosions, metacarpal side: 31 erosions). The average volume of the erosions was 1.84mm³, minimum 0.08mm³, and maximum 16.3mm³.

Conclusions: The semiautomatic method to quantify the volume of erosions at MCP joints in RA patients by HR-pQCT was developed. The opinion as to whether concave regions are pathological erosion or physiological concave, vascular channel or recess of osteophyte is occasionally difficult and should be performed by an experienced tester.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4144

FR0057 COMPARATIVE STUDY OF PAROTID ULTRASONOGRAPHY AND PAROTID GLAND ECT IN PREDICTING THE PATHOLOGICAL BIOSPY OF THE SALIVARY GLAND IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME

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Objectives: To investigate the value of Parotid Ultrasonography and parotid gland radionuclide imaging in predicting salivary gland biopsy of primary Sjögren’s syndrome (pSS).

Methods: Sixty - five patients with primary Sjögren’s syndrome and 38 patients with non - Sjögren’s syndrome were enrolled in the Department of Rheumatology and Immunology, Xinjiang Uyghur Autonomous Region People’s Hospital from October, 2015 to June, 2016. All patients were accepted the check of Parotid Ultrasonography, Parotid Glan ECT and labial gland biopsy. The data were analyzed statistically.

Results: The sensitivity and specificity of Parotid Ultrasonography in pSS were 65% and 76%, respectively. The area under the ROC curve was 0.935±0.024 for the diagnosis of pSS. The positive predictive rate of parotid gland ultrasonography was 84.0% and the negative predictive rate was 94.4%. Parotid scintigraphy in pSS in the sensitivity of 80.0%, specificity of 69.1%. The positive predictive rate of parotid gland radionuclide imaging for labial gland biopsy was 78.9% and the negative predictive rate was 87.5%. The diagnostic value of Parotid
Ultrasoundography in pSS group is superior to that of parotid gland radionuclide imaging, which can effectively reduce the complication of invasive operation.

Conclusions: The diagnosis of pSS by parotid gland ultrasoundography is superior to that of parotid gland radionuclide examination. For patients with atypical clinical manifestations who are negative for anti-SSA and/or anti-SSB antibodies, there is no need for a labial biopsy of the labial glands to reduce the number of complications associated with unwanted invasive procedures.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6257

**FR00658** LEG ELEVATION DOES NOT SUBSTANTIALLY AFFECT TBS RESULTS

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**Background:** Lumbar spine dual energy X-ray absorptiometry (DXA) scans are typically acquired with the patient’s legs elevated on a positioning block thereby flattening the normal lumbar lordosis. With GE densitometers it is also possible to acquire lumbar spine scans with the legs down. BMI values obtained with legs down vs. legs elevated does minimally differ, however it is unknown if leg elevation affects trabecular bone score (TBS) results.

**Objectives:** The purpose of this study is to assess the effect of leg position on TBS.

**Methods:** Lumbar spine (L1-L4) DXA scans were acquired in legs up and legs down positioning using GE Healthcare Prodigy and IDXA densitometers. The ‘OneScan’ feature mode was not used. These scans were analyzed using enCORE software v 12.3 or 14.1. All scans were re-processed using Medimaps TBS Calculator v2.3 or TBS Insight v3.0.2 to obtain TBS results. Linear regression and Bland-Altman analyses were performed to compare TBS results in the legs up vs. legs down position.

**Results:** Sixty-four women, mean age and BMI 65.1 years (range 28.2–86.6) and 28.4 kg/m² (range 18.1–34.8) were studied on three Prodigy densitometers. Fifty women, mean age and BMI 68.6 years (range 15.2–92.5) and 26.2 kg/m² (range 19.9–35.1) were studied on a IDXA densitometer. With Prodigy and standard legs up positioning, the L1-L4 BMD ranged from 0.738–1.549 g/cm² and was highly correlated with legs down positioning, R² =0.99. TBS results ranged from 1.072–1.632 and were also highly correlated, R² =0.93 with a mean bias of -0.005 TBS units between leg positions (Figure). With IDXA and standard legs up positioning, the L1-L4 BMD ranged from 0.753–1.622 g/cm² and was highly correlated with legs down positioning, R² =0.97. TBS results ranged from 1.040–1.455 and were also highly correlated, R² =0.99 with a mean bias of 0.00 TBS units between legs positions (data not shown).

**Conclusions:** Leg positioning minimally affects TBS results with GE Healthcare Prodigy and IDXA densitometers but the difference from legs up to legs down is likely of no clinical significance.

**Disclosure of Interest:** D. Krueger: None declared. E. Siglinsky: None declared. D. Tran Employee of: Medimaps. L. Del Rio: None declared. N. Binkley: None declared

DOI: 10.1136/annrheumdis-2017-eular.5136

**FR00660** IMPACT OF ULTRASOUND IN TREATMENT DECISION OF RHEUMATOID ARTHRITIS

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**Background:** Ultrasound (US) is an important tool to support the clinician in the diagnosis and treatment monitoring of rheumatoid arthritis (RA). The EULAR recommended it for the follow up of RA patients. In spite of the evidence supporting the value of US, the real impact in treatment decisions is not clearly defined.

**Objectives:** To investigate the impact of US findings in the treatment decisions of rheumatologists in patients with RA in a real-life setting. Additionally, to verify the US findings that play a role in change of treatment, types of changes and their distribution.

**Methods:** RA patients were included. As a first step, the rheumatologist performed a clinical examination (including DAS28) and recorded the treatment approach suggested according his clinical evaluation (i.e. starting, changing or stopping the previous suggested therapy). Additionally, the clinical rheumatologist recommended it for the follow up of RA patients. In spite of the evidence supporting the value of US, the real impact in treatment decisions is not clearly defined.

**Results:** A total of 128 RA patients were included [female 117 (91.4%), male 11 (8.5%)], with mean ± SD disease duration of 9.88±8.22 years. Ninety-four patients (73.5%) had active disease according the DAS 28, whereas 34 (26.5%) were considered in remission. US findings influenced a change in the treatment in 56 cases (43.7%) (47 with clinical active disease and 9 in remission). Among the main reasons that induced a change in the treatment based on the US examinations were: grade of synovitis (25%), higher number of synovitis than clinical examination (16.6%) and presence of power Doppler (PD) (16.7%). The most frequent treatment changes were increasing dose or start a new combination of DMARDs [39 patients (69.5%)]. The multiple logistic regression analysis showed that synovitis of 2nd metacarpophalangeal joint (MCP) was the US finding that reported the reasons which induced to change or not the treatment after the US examination.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6257
FR00661 | CAPILLAROSCOPY IN PATIENTS WITH SILICA EXPOSURE. A CASE CONTROL STUDY

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Background: Exposure to silica dust has been associated with different autoimmune diseases and immunological abnormalities in which microvascular involvement is very common, as systemic sclerosis, systemic lupus erythematosis, inflammatory bowel diseases, antiphospholipid syndrome or dermatomyositis.

Objectives: To show capillaroscopic findings in patients exposed and not exposed to silica and to analyze the differences between both groups.

Methods: A case control design was made. Cases (Si+) were subjects exposed to silica (with and without silicosis). Controls (Si-) were healthy subjects not exposed to silica. Capillaroscopy was made with ZO® Optical stereo microscope with Optikam® camera adapted and with USB Digital Microscope Video epiluminiscence Dino-Lite® in each patient. The capillaroscopic alterations were evaluated according to a semiquantitative method. Background data on CVRF and variables related to capillaroscopy were collected. A comparative study was done.

Results: Capillaroscopy was performed on 61 Si+ and 12 Si- subjects. Mean age was 56.4 years (SD: 8.2) in Si+ and 53.1 years (SD: 9.1) in Si-. There were no significant differences in CVRF: hypertension (13.5% Si+ and 8.3% Si-), diabetes mellitus (3.3% Si+ and 8.3% Si-) and tobacco exposure (18.0% Si+ and 25.0% Si-). It was observed capillary dilation in 24 (33.9%) Si+ and only in 3 (25.0%) Si-. The dilation score was mild in all Si- while in Si+ was mild in 41.7%, moderate in 36.6% and severe in 21.7%. It was observed capillary distortion in 12 (17.0%) Si+ and only in 1 (8.3%) Si-. The capillaroscopic general pattern showed differences between both groups: it was normal in 24 (42.1%) Si+ and 9 (75%) Si-; slightly irregular in 30 (52.6%) Si+ and 3 (25%) Si- and unstructured in 3 Si+ (5.3%) and in none Si-.

Conclusions: The current study shows significant differences between the capillaroscopic of subjects exposed and not exposed to silica, with a trend in more frequency and severity of capillary dilatation, greater frequency of tortuosity in a severe degree and more frequent irregular capillaroscopic pattern in the exposed patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6689

FR00662 | ASSESSMENT OF BONE DENSITY, STRUCTURE, AND CORTICAL INTERRUPTIONS OF FINGER JOINTS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING HIGH-RESOLUTION PERIPHERAL QUANTITATIVE CT

M. Peters 1, A. Scharmaga 1, A. van Tubergen 1, D. Loefen 1, R. Weijers 1, B. van Rietbergen 2, 1Unidad de Enfermedades Autoinmunes Sistémicas y Trombosis, 2Laboratorio de Nutrición y metabolismo, República Dominicana

Background: Rheumatoid arthritis (RA) is characterized by peri-articular bone loss. In patients with RA, lower bone density and structural integrity, and an increased number of erosions compared to healthy controls (HCs) has been demonstrated using High-Resolution peripheral Quantitative CT (HR-pQCT) (1,2). The assessment of such parameters using HR-pQCT is, therefore, a promising tool for the follow-up of bone involvement in MCP joints in patients with RA.

Objectives: To investigate the cortical and trabecular bone density, structure, and cortical interruptions in MCP joints in early and late RA patients compared to HCs using HR-pQCT imaging.

Methods: The 2nd and 3rd MCP joint of 70 subjects (mean age 53.1 (SD 9.2) years) were evaluated by HR-pQCT (82x-m isotropic voxel size); 38 HCs, 10 early RA (diagnosis <2 years ago) and 22 late RA (diagnosis ≥2 years ago). Images were analyzed for cortical interruptions, and for cortical and trabecular bone density and structure. Descriptors were analyzed per joint by one-way ANOVA with Bonferroni post-hoc testing or Kruskal-Wallis with Mann-Whitney post-hoc testing, as appropriate.

Results: Significant differences with respect to all parameters were found across the groups (Table 1). In early and late RA, the percentage of joints with at least 1 interruption was higher, and trabecular core thickness, total density and cortical density were lower than in HC. In addition, in late RA, number of interruptions, interruption volume and trabecular separation were higher, and trabecular density was lower than in HC. Bone loss at the cortical and trabecular bone was primarily observed at the rim of the joint (Figure 1, arrows).

Table 1. Comparison of cortical interruptions, and bone density and structure parameters across early RA patients, late RA patients and HCs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Early RA</th>
<th>Late RA</th>
<th>HC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical interruption parameters</td>
<td>n=39</td>
<td>n=73</td>
<td>n=82</td>
<td>0.025</td>
</tr>
<tr>
<td>Percentage of joints ≥ 1 interruption, %</td>
<td>69.5</td>
<td>89.7</td>
<td>82.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of interruptions</td>
<td>1.50 (1.49)</td>
<td>2.64 (2.95)</td>
<td>5.22 (6.32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interruption volume, mm³</td>
<td>1.49 (5.16)</td>
<td>2.05 (6.76)</td>
<td>39.31 (78.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bone density parameters</td>
<td>n=50</td>
<td>n=31</td>
<td>n=68</td>
<td>0.001</td>
</tr>
<tr>
<td>Total vBMD, mg HA/cm³</td>
<td>327.3 (35.3)</td>
<td>295.8 (38.9)</td>
<td>286.4 (65.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trabecular vBMD, mg HA/cm³</td>
<td>202.1 (20.6)</td>
<td>185.0 (21.6)</td>
<td>177.3 (40.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cortical vBMD, mg HA/cm³</td>
<td>685.8 (42.8)</td>
<td>643.7* (58.2)</td>
<td>694.7* (73.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bone structure parameters</td>
<td>n=50</td>
<td>n=31</td>
<td>n=68</td>
<td>0.001</td>
</tr>
<tr>
<td>Trabecular number, mm¹</td>
<td>1.68 (0.31)</td>
<td>1.45* (0.29)</td>
<td>1.52* (0.37)</td>
<td>0.004</td>
</tr>
<tr>
<td>Trabecular thickness, μμ</td>
<td>102.3 (15.3)</td>
<td>109.1 (17.8)</td>
<td>98.6 (14.7)</td>
<td>0.009</td>
</tr>
<tr>
<td>Trabecular separation, μμ</td>
<td>513.9 (116.9)</td>
<td>608.4 (132.4)</td>
<td>611.4* (204.6)</td>
<td>0.007</td>
</tr>
<tr>
<td>Distribution of trabecular separation, μμ</td>
<td>550.6 (287.0)</td>
<td>729.5 (306.1)</td>
<td>689.8 (368.9)</td>
<td>0.029</td>
</tr>
<tr>
<td>Cortical thickness, μμ</td>
<td>440.0 (99.2)</td>
<td>363.2* (90.2)</td>
<td>357.5 (132.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are displayed as mean (SD) or otherwise described. *Significantly different from HC, p<0.05. v-p-value obtained across the groups. vBMD, volumetric bone mineral density.

Figure 1. Typical examples of MCP joints; (a) HC, (b) early RA patient, and (c) late RA patient. The 3D reconstructions are shown (I) with corresponding 2D slices thick axial slices (ii). The arrows indicate locations of loss of trabecular and/or cortical structure in the early and late RA patients compared to the HC.

Conclusions: Bone density and structural integrity were impaired in early and late RA patients compared to HCs whereas the number of cortical interruptions is increased. The assessment of such parameters using HR-pQCT is, therefore, a promising tool for the follow-up of bone involvement in MCP joints in patients with RA.

References:

Disclosure of Interest: M. Peters: None declared, A. Scharmaga: None declared, A. van Tubergen: None declared, D. Loefen: None declared, R. Weijers: None declared, B. van Rietbergen Consultant for: Scanco Medical AG, P. Geusens: None declared, J. van den Bergh: None declared

DOI: 10.1136/annrheumdis-2017-eular.4132

FR00663 | EVALUATION OF A FLUOREOENZYME IMMUNOASSAY (ELIA-CTD) IN THE SCREENING OF PATIENTS SUSPECTED FOR AUTOIMMUNE CONNECTIVE TISSUE DISEASES

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Background: Detection of auto-antibodies directed against nuclear antigens (nuclear antibodies or ANA) have important diagnostic and prognostic implications in connective tissue diseases (CTD). The conventional indirect immunofluorescence assay on Hep-2 cell line (ANA-IFA) is the most commonly used method to detect ANA. The ANA-IFA can be labor intensive and suffers from lack of specificity.

Conclusions: ANA-IIF can be labor intensive and suffers from lack of specificity. ANA-IIF can be labor intensive and suffers from lack of specificity. ANA-IIF can be labor intensive and suffers from lack of specificity.
Objectives: To evaluate the utility of a new fluoroenzyme Immunoassay “EliA-CTD” as an alternative for screening patients suspected for autoimmune connective tissue diseases.

Methods: Six hundred and fifteen (1600) consecutive patients’ sera submitted for anti-nuclear antibodies were tested using the ANA-IIF (Diasorin S.P.A., Saluglia, Italy) and the new automated EliA-CTD screen (Phadia GmbH, Frieiburg, Germany). ANA testing was ordered by both primary and secondary care physicians. The EliA-CTD screening assay is a fluoroenzyme immunoassay which is performed on the Phadia-250 automated platform. The EliA-CTD assay contains ANA-targeted recombinant antigens including dsDNA, Sm-D, Rb-P, PCNA, U1-RNP (70, A, C), SS-A/Ro, SS-B/La, Centromere B, Scl-70, Fibrillarin, RNA Polymerase III, Jo-1, Mi-2, and PM-scl. The test results are expressed as ratio, with >1.0 considered positive. For ANA-IIF, the cut off for positive results was 1:40 or greater. Additionally, further testing for dsDNA and other extractable nuclear antigens (ENA) was undertaken on a subset of sera that were ANA-IIF+ or EliA-CTD+ whenever there was discrepancy between the two methods.

Results: The overall agreement between the two methods was 84.2%. Three hundred and eight (308) out of 1600 (19.3%) samples tested positive by ANA-IIF positive as compared to 101/1600 (6.6%) for the EliA-CTD assay. Additional testing showed that 105 samples were positive for ENA including dsDNA. Of those, 101 were EliA-CTD positive and 81 were ANA-IIF positive. By incorporating those results, the calculated sensitivity and specificity for the EliA-CTD were 97.1% and 99.7% respectively with positive and negative predictive values for the EliA-CTD assay of 96.1% and 99.8%, respectively. The corresponding sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the ANA-IIF assay at different dilutions is shown below:

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Sensitive (%)</th>
<th>Specific (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:10</td>
<td>77.3</td>
<td>94.9</td>
<td>29.0</td>
<td>98.2</td>
</tr>
<tr>
<td>1:100</td>
<td>60.3</td>
<td>93.5</td>
<td>32.4</td>
<td>98.4</td>
</tr>
<tr>
<td>1:1000</td>
<td>57.4</td>
<td>97.4</td>
<td>41.3</td>
<td>98.4</td>
</tr>
<tr>
<td>1:10000</td>
<td>46.5</td>
<td>98.7</td>
<td>48.8</td>
<td>98.5</td>
</tr>
</tbody>
</table>

Conclusions: The new automated EliA-CTD assay shows superior sensitivity and specificity compared to the conventional labor intensive ANA-IIF. The EliA-CTD can be used as an upfront screening tool for connective tissue diseases. Depending on the clinical details, any EliA-CTD positive results could be confirmed by additional testing including ANA-IIF testing to elucidate the titers and pattern.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2461

FRIO0665 ANTI-HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN ANTIBODIES (ANTI-HRNRP) AND OTHER AUTOANTIBODIES FOR DETECTION OF EROSIve ARthropathy in Systemic Lupus Erythematous with Joint INVOLVEMENT in COMPARISON BY JOINT X-RAY

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¹Physical Medicine, Rheumatology & Rehabilitation, Faculty of Medicine, Assiut University, Egypt; ²Diagnostic Radiology, Assiut University Hospital; ³Clinical Pathology, South Egypt Cancer Institute, Assiut, Egypt

Background: Joint involvement in SLE is very common, affecting 90% of patients at some stage in the course of their disease. 1Arthritis featuring prominent radiological erosion in SLE is less common; however, in a small subset of patients an erosive pattern similar to RA develops. 2 Anti-heterogenous nuclear ribonuclear protein A2 (anti-hnRNP-A2) occur in about one-third of patients with RA but rarely in other arthritides such as OA, PsA or reactive arthritis. Interestingly, in SLE patients anti-hnRNP-A2 autoantibodies were found to be significantly associated with erosive arthritis (3).

Objective: To investigate joint involvement in SLEs and its relationship with autoantibodies to the hnRNP A2/B1 and A2, rheumatoid factor (RF), Antinuclear antibody (ANA) and Anti-double stranded DNA (Anti-DSDNA) and correlation with articular involvement by joint x-ray.

Methods: Case series study comparing diagnosis of arthritis by hand and wrist x-ray with anti-hnRNP A1 and A2 in Fourty SLE patients aged 17–60 years old with disease duration 1–17 years complaining of arthralgia or arthritis. A controlled group of 21 clinically normal persons, age and sex matched and blood

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2461

Table 1. Comparison of erosive features in SLE patients with and without erosive arthritis (EA)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SLE patients with EA</th>
<th>SLE patients without EA</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Factor, N (%)</td>
<td>5 (50)</td>
<td>30 (25)</td>
<td>35</td>
<td>0.079</td>
</tr>
<tr>
<td>Anti-erosion (OR&gt;5.0)</td>
<td>8 (80)</td>
<td>14 (46.7)</td>
<td>22 (55)</td>
<td>0.069</td>
</tr>
<tr>
<td>Anti-doubd-stranded DNA, N (%)</td>
<td>9 (90)</td>
<td>13 (43.3)</td>
<td>22 (55)</td>
<td>0.011*</td>
</tr>
</tbody>
</table>

Table 2. Comparison of radiological findings of hand X-ray in SLE patients with and without erosive arthritis (EA)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SLE patients with EA</th>
<th>SLE patients without EA</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint involvement</td>
<td>21 (70)</td>
<td>30 (75)</td>
<td>51</td>
<td>0.204</td>
</tr>
<tr>
<td>Joint erosion</td>
<td>9 (90)</td>
<td>30 (85)</td>
<td>39</td>
<td>0.001*</td>
</tr>
<tr>
<td>MCP subluxation</td>
<td>7 (70)</td>
<td>10 (25)</td>
<td>17</td>
<td>0.001*</td>
</tr>
<tr>
<td>Interference of cortical surface, N (%)</td>
<td>7 (70)</td>
<td>1 (3.3)</td>
<td>8</td>
<td>0.001*</td>
</tr>
<tr>
<td>Narrowing of joint space, N (%)</td>
<td>1 (10)</td>
<td>0</td>
<td>1</td>
<td>0.250</td>
</tr>
</tbody>
</table>

Note: *p<0.05 compared to group.
samples are drawn and centrifuged. RF and auto-antibodies to nuclear antigens anti-nuclear antibodies (ANA) and anti-double stranded DNA were determined in all the patients. All patients underwent X-rays of the hands and wrists.

Results: Anti-hnRNP A1 showed highly significant difference between study and control. Anti-hnRNP A2 showed significant difference between study and control.

Conclusions: This study showed a high frequency of erosive arthropathy and autoantibody to both hnRNP antigens might become useful marker for joint involvement in SLE patients and identify SLE patients prone to develop joint damage.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4487

FR06667 INCREASED PREVALENCE OF SUBCLINICAL ATHEROSCLEROSIS IN MODERATE-SEVERE PLAQUE PSORIATIC PATIENTS


Background: Recent studies suggest that plaque psoriasis may be a risk factor for major adverse cardiac events. This has important therapeutic implications for cardiovascular (CV) risk stratification and prevention in patients with severe psoriasis. For that reason surrogate markers of subclinical atherosclerosis and CV mortality such as carotid plaques (CP) have been studied by carotid US examination.

In most studies of psoriasis done before, the results have shown an increased prevalence of carotid plaques, but it is not always the rule.

Objectives: To compare the prevalence of CP between patients with moderate-severe psoriasis and the general population.

Methods: A cross-sectional study that included 40 patients with moderate-severe psoriasis (PASI>10, BAS>10%), that fulfilled definitions for initiating treatment with a biological agent and 40 age-, sex- and traditional CV risk factors-matched healthy control subjects. Patients with history of CV events, diabetes mellitus, and chronic kidney disease or body max index (BMI) >35 were excluded. Carotid ultrasonography was performed by a MyLab 70 scanner (Esaote; Genoa, Italy), then carotid plaque was defined according to the Manheim Consensus Conference criteria. Statistical analysis: Qualitative data were expressed as number and percentages and quantitative data as (MD). Student’s t test or Mann-Whitney U were used to compare continuous variables, as appropriate. Chi2 test or Fisher test were used for qualitative variables.

Results: The main data of the patients are summarized in the Table. It is important to highlight that it is based on a young population (mean age=40 years). The two groups did not present significant differences except for high sensitivity C-reactive protein (hsCRP). As expected given the age of the group, CV risk measured by SCORE was low (0%) with a mean of 0.2 ± 0.15. No patient had a very high CV risk as measured by SCORE (>5%).

Patients with psoriasis had a long-standing disease (17.05±11.63 years). The presence of carotid plaques was found in a total of 10 patients with plaque psoriasis (25%), 5 of them had bilateral plaques) and one in the control group (2.5%) without bilateral plaques), p<0.003.

FR06666 THE RECALL SURVEY: CAN ULTRASOUND AFFECT CLINICIANS’ DECISIONS ABOUT CHANGING TREATMENT IN RA?

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Background: In Rheumatoid Arthritis (RA) treatment response is assessed using standard clinical disease activity measure. However ultrasound (US) is able to show subclinical synovitis in patients (pts) with RA who are in clinical remission (CR); further studies are still required to delineate the impact of US findings in the management of RA pts in daily clinical practice.

Objectives: To investigate the influence of US on the clinicians’ treatment choices in pts with RA.

Methods: In 2015 an educational event (RECALL Survey) focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy. In every center, the local rheumatologists provided RA pts to be examined by US. Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). Bilateral US examinations of wrists, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, using a Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe. All US findings were scored using a 4 degree semiquantitative scoring system.

Results: 465 pts were evaluated. Clinicians, after US evaluations, changed therapy in 23.7% of pts, did not change therapy in 35.5% of pts.In general changes of therapy tended to be made by clinicians when joint effusion or power Doppler signal were present (table 1–2). The presence of erosion did not influence the clinicians’ decisions.

Table 1. Changes of therapy and joint effusion

<table>
<thead>
<tr>
<th>Joint Effusion</th>
<th>Score ≤0</th>
<th>Score &gt;0</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in therapy No</td>
<td>79</td>
<td>165</td>
<td>244</td>
</tr>
<tr>
<td>Yes</td>
<td>11</td>
<td>99</td>
<td>110</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>178</td>
<td>268</td>
</tr>
</tbody>
</table>

Table 2. changes of therapy and Power Doppler signal

<table>
<thead>
<tr>
<th>Power Doppler Signal</th>
<th>Score ≤0</th>
<th>Score &gt;0</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in therapy No</td>
<td>129</td>
<td>36</td>
<td>165</td>
</tr>
<tr>
<td>Yes</td>
<td>24</td>
<td>86</td>
<td>110</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>122</td>
<td>275</td>
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</tbody>
</table>

Conclusions: Ultrasound may be a useful tool in daily rheumatologic practice to help clinicians make decisions about how to treat patients with RA. US results, especially joint effusion and Power Doppler signal, may influence the choice of clinicians to modify a patient’s treatment regime.

 Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5320

FR06668 SONOGRAPHIC AND ANATOMICAL DESCRIPTION OF THE SUBTALAR JOINT

P. Mandl1, D. Bong2, P.V. Balint3, H.B. Hammer4, M. Miguel5, E. Naredo6, I. Möller6 on behalf of Anatomy for the Image. 1Rheumatology, Medical University of Vienna, Vienna, Austria; 2Rheumatology, Universitat de Barcelona, Institut Pau de Reumatologia, Barcelona, Spain; 3Rheumatology, National Institute of Rheumatology and Physiotherapy, Bucharest, Hungary; 4Rheumatology, Diakonicheum Hospital, Oslo, Norway; 5Pathology and Experimental Therapeutics, Universitat de Barcelona, Barcelona; 6Rheumatology, Joint and Bone Research Unit. Hospital Universitario Fundación Jiménez Díaz and Autónoma University, Madrid, Spain.

Background: The subtalar joint is commonly affected in many rheumatic and musculoskeletal diseases; however, subtalar joint involvement is often neglected or missed during clinical examination due to the fact that the joint is difficult to examine and most clinicians have a limited understanding of its anatomy.

Objectives: To provide a detailed anatomical and US description of the subtalar joint, a single joint that, anatomically, is divided into two separate compartments: the anterior subtalar joint (ASTJ) and the posterior subtalar joint (PSTJ).

Methods: Cadaveric specimens of the ankle and foot were examined in detail by ultrasound (US) by rheumatologist experts in musculoskeletal US. The ASTJ of all
the specimens were injected with colored latex while the PSTJs were respectively injected with 1ml of latex of a contrasting color under US guidance. Following the injections, the joints were frozen and cut into 2 centimeter sections from medial to lateral in the sagittal plane. Sections were examined independently by three authors for the presence of latex within the ASTJ, PSTJ and, also, to look for the presence of synovial (sub)-articular latex extravasation or the spread of latex to adjacent articulations by means of a communication with the ankle joint or the adjacent portion of the subtalar joint.

**Results:** Six cryopreserved intact ankle-foot specimens from three male and three female cadavers (two right and four left), with a mean age of 74 years (range, 66–80 years) were studied. A recommended list of standardized scanning technique which allows sonographers to evaluate both compartments of the subtalar joint (ASTJ and PSTJ) from the medial, lateral and posterior aspect were developed. All of the specimens (6/6, 100%) contained the appropriate colored latex in the appropriate subtalar joint compartment with minimal leakage into the surrounding soft tissues (Figure 1). Of note, five of the six (5/6, 83%) specimens revealed communication between the PSTJ and the posterior subtalar joint. There was no communication between the ASTJ and the subtalar joint, nor was there evidence of spread of the latex, i.e. communication, from one subtalar joint compartment to the other.

![Figure 1](image.jpg) Anatomical specimen showing the anterior subtalar joint (filled with green latex) and the posterior subtalar joint (filled with red latex); C: calcaneus, N: navicular, T: talus.

**Conclusions:** Lack of communication between the ASTJ and the PSTJ and the communication between the PSTJ and the posterior recess of the tibiotalar joint are compatible with other studies. Our study highlights the importance of employing cadaver specimens in musculoskeletal ultrasound, and presents a number of options for US imaging of both the ASTJ and PSTJ that also provide access to these distinct compartments for the purpose of aspiration and injection.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2675

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**FR10669 VALIDITY OF SEVEN-JOINT VERSUS SIMPLIFIED TWELVE-JOINT ULTRASONOGRAPHY SCORING SYSTEMS IN ASSESSMENT OF RHEUMATOID ARTHRITIS ACTIVITY**

R. El-Gohary, A. Ahmed, A. Khalil, H. El-Gendy, K. Gado, Internal Medicine, Rheumatology & Clinical Immunology Subspeciality, Kasr Al-Ainy, New Kasr El-Aini Teaching Hospital, Cairo, Egypt

**Background:** Musculoskeletal ultrasonography imposes itself as a reliable tool for the disease activity assessment of rheumatoid arthritis (RA) being more sensitive than clinical in detection of synovitis. There is no consensus on the exact joint number should be examined. Naredo et al. developed reduced 12-joint count while Backhaus et al. scored only seven small joints. Although both were found to reflect disease activity it is suitable in a busy clinic to assess the lowest joint counts.

**Objectives:** To investigate the validity of 7-joint ultrasonography (US7) scores in assessment of disease activity in Egyptian RA patients compared with simplified 12-joint ultrasonography (US12) scores and correlate both to composite disease activity indices.

**Methods:** Fifty Egyptian RA adult patients diagnosed according to the ACR1987 criteria were subjected to detailed history, 28 tender & swollen joint counts (TJC, SJC). The disease activity was assessed by calculating DAS28-CRP, SDAI and CDAI. The Ultrasonographic assessment was performed using a LOGIQp6 with 10–13 MHz broadband linear array transducer by one well-trained blinded rheumatologist. The synovial hyperechogenicity on GS & PD images were graded using a semi-quantitative 0–3 scale. The simplified US12 was performed as originally described. However the GS & PD synovitis were computed in two separate scores instead of one. The US7 was performed at the clinically dominant side as described by Backhaus et al. Two Sum-US7 scores were added; Sum (GS)-US12 after grading the GS-tenosynovitis and Sum (PD)-US12 with SDAI and CDAI (V values 0.02, 0.009 and 0.001). Kappa values were 0.80 & 0.96 for GS & PD interobserver reliability and 0.96 & 1.0 for GS & PD intraobserver reliability.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2675

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**FR10750 THE COURSE OF SUBCLINICAL JOINT INFLAMMATION DURING PROGRESSION FROM ARTHRALGIA TO CLINICALLY DETECTABLE ARTHRITIS, A LONGITUDINAL MRI STUDY**

R.M. Ten Brinck, H.W. van Steenberghe, L. Mangus, A.H. van der Helm-van Mil, Rheumatology, Leiden University Medical Centre, Leiden, Netherlands

**Background:** Subclinical joint inflammation in the phase of arthralgia preceding RA can comprise synovitis, bone marrow edema (BME) and/or tenosynovitis. It is unknown in what time order the different tissues in a joint become inflamed or progress with inflammation. It has been postulated that synovitis is an initial process that is succeeded by bone involvement (“outside-in hypothesis” presuming that synovitis precedes BME and erosions). Alternatively, it is suggested that inflammatory cells in the bone marrow migrate via bone pores to the synovium, promoting synovitis (“inside-out”), then BME precedes synovitis. Thirdly, these processes can occur or progress simultaneously. Serial MRI studies can reveal time-relationships. This longitudinal MRI study on patient-level determined the course of joint inflammation during progression from arthralgia to clinical arthritis.

**Objectives:** To increase the comprehension on the course of MRI-detected subclinical joint inflammation during progression from arthralgia to clinical arthritis, both in ACRA-positive and ACRA-negative patients.

**Methods:** We longitudinally followed 29 patients that all progressed from Clinically Suspect Arthralgia to clinical arthritis. 1.5T MRI on hand and foot joints was performed at presentation with arthralgia and subsequently at the development of clinical arthritis. MRIs were evaluated for BME, synovitis and tenosynovitis (summed in the total inflammation score) and erosions by three readers (ICCs 0.98, 0.96 and 0.97) that were blind to clinical data and the order in time. Analyses were repeated in arthritis patients that fulfilled the 2010 criteria for rheumatoid arthritis, and in ACRA-positive and ACRA-negative patients separately.

**Results:** At presentation with arthralgia the mean age was 43 years, 72% was female, and 28% was ACRA-positive. Median duration to clinical arthritis was 17 weeks. At the time of arthritis development 65% fulfilled the 2010-criteria. During progression from arthralgia to clinical arthritis the median total inflammation score increased from 4.5 (IQR 2.8–7.6) to 8.9 (IQR 2.0–13.5), p<0.01. The BME score increased over time (p=0.04), as did the synovitis score (p=0.002). The tenosynovitis and erosion scores increased as well, though not statistically significant (p=0.10 and p=0.07 respectively). Analyses within the patients that developed 2010-RA revealed that BME (p=0.047), synovitis (p=0.005) and tenosynovitis (p=0.004) all increased significantly, in contrast to the erosion score. At presentation with arthralgia, BME and synovitis scores were higher in ACRA-positive than in ACRA-negative patients; during progression to clinical arthritis the different types of inflammation increased similarly in ACRA-positive and ACRA-negative patients.

**Conclusions:** During progression from arthralgia to clinically evident rheumatoid arthritis, BME, synovitis as well as tenosynovitis progress simultaneously.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2908
This study aims to investigate the nail bed changes seen in patients with PsA and OA using US and MRI, and to determine the impact of nail bed score. There was no relationship between clinical or US detected nail scores and grip strength. There was a strong relationship between the presence of clinical nail change and the failure load (in Newton) and constraint (in Mpa) were measured. Bone Volume Fraction (BV/TV), Trabecular Thickness (Tb.Th), and Trabecular Spacing (Tb.Sp) were measured in MRI images using a Digital topological analysis (Bone J). Measurements were performed by two observers in order to characterize the inter-rater reliability. Statistical analyses were performed using SPSS. Correlations between variables were analyzed using Pearson's r, linear regression and Stepwise regression. A p value of 0.05 was considered as significant.

Results: The inter-rater reliability for bone microarchitecture parameters quantification was good. Tb.Th and Tb.Sp measured using high-field MRI were 0.94 and 0.95 respectively while the BV/TV fraction was 0.93. The mean BMD was 0.86±0.20 g/cm^2. The failure load and the constraint measured during the compression tests were 2600±1276N and 1.57±0.81 Mpa respectively. Interestingly, the variables measured during the mechanical tests were significantly correlated with the BMD. Regarding the bone indices quantified using high-field MRI, a significant linear relationship was observed between the trabecular spacing and the BMD (R=−0.23, p<0.01) and the constraint values to failure (R=−0.18, p=0.04). A stepwise regression with backward elimination demonstrated that combining BV/TV and BMD improved the relationship with the constraint measurements with an adjusted R^2=0.384 for BMD alone and an adjusted R^2=0.41 for BMD + BV/TV.

Conclusions: In the present study, we demonstrated for the first time that the variables characterizing the vertebral bone microarchitecture quantified using ultra-high field MRI were significantly correlated with biomechanical parameters. In addition, we illustrated that the vertebral bone strength was better described by a variable combining BMD and trabecular bone spacing.

Disclosure of Interest: None declared

4. In TCZ group, CRP and ESR were significantly lower than the other groups, although other clinical indicators were comparable (Table).

Conclusions: US revealed that CR in TCZ-using can be overestimated by BL-based, SDAI-based, and DAS28-based CR criteria. For TCZ users, CDAI-based CR criteria is more reliable than the other criteria.

Disclosure of Interest: None declared


FR10674 U sing Higher Image Resolution of Magnetic Resonance Imaging of the Cervical Spine Identifies More Inflammatory and Structural Lesions in Patients with Axial Spondyloarthrit is

S. Krabbe1, M. Østergaard1, J. Møller2, I.J. Sørensen1, B. Jensen1, O.R. Madsen1, S.J. Pedersen1. 1Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen; 2Department of Radiology, Herlev Hospital, Herlev, Denmark

Background: The vertebrae of the cervical spine are rather small and it may be difficult to assess if small areas with signal intensity changes represent the bones, joints or entheses, or derive from the surrounding blood vessels.

Methods: Forty-nine patients with axial spondyloarthritis according to the ASAS criteria started anti-TNF treatment and had "standard" resolution (std-res) and "high" resolution (high-res) MRI sequences of the cervical spine performed at baseline and after 48 weeks. 3 patients had follow-up scan already after 6–24 weeks due to study exclusion.

Std-res: STIR sequence: Voxel size 5.0 mm³ (slice thickness 4.0, spatial resolution 1x1.25); T1W sequence: voxel size 4.5 mm³ (slice thickness 4.0, spatial resolution 0.9x1.25).

High-res: STIR sequence: Voxel size 3.1 mm³ (slice thickness 3.5, spatial resolution 0.8x1.11); T1W sequence: voxel size 1.4 mm³ (slice thickness 3.0, spatial resolution 0.6x0.76).

Images were assessed in known chronology by an experienced axSpA MRI reader (SJF) blinded to clinical data. High-res and std-res were read in random order.

MRI lesions of inflammation, fat and new bone formation were defined according to the Canada-Denmark working group [1,2]. Erosions were not assessed.

Results: Inflammatory lesions: In 9 of 43 patients (21%), inflammatory lesions were detected in the cervical spine at baseline at std-res, while this was detected in 14 of 43 patients (33%) at high-res. Using high-res, as compared to std-res, 6 patients were reclassified from negative to positive for inflammation, 1 patient was reclassified from positive to negative, and 6/28 patients remained classified as positive/negative, p=0.13 by Exact McNemar test. The mean inflammation score was significantly higher at high-res compared to std-res (1.7 SD 4.5) vs. 0.8 (SD 2.7), p=0.04 by pair-test).

Fat lesions: 11 of 43 patients (26%) had fat lesions in the cervical spine at baseline using std-res, while 10 of 43 patients (23%) had this using high-res. The mean fat score was significantly higher at high-res compared to std-res (1.6 SD 3.5) vs. 0.8 (SD 1.8), p=0.02 by pair-test).

Bone spurs/ankylosis: 11 of 43 patients (26%) had bone spurs/ankylosis of the cervical spine at baseline at std-res, while 10 of 43 patients (23%) using high-res. The mean new bone formation score was significantly higher at high-res compared with std-res (2.7 (SD 6.1) vs. 1.4 (SD 3.5), p=0.01 by pair-test).

Responsiveness: Standardized response mean for inflammation score at std-res was 0.15, and at high-res 0.14. Structural lesions remained largely unchanged in all patients.

Conclusions: More patients were classified as having inflammatory lesions in the cervical spine when using high-res MRI compared to std-res. Likewise, mean scores of inflammatory lesions, fatty lesions and new bone formation were significantly higher compared with std-res. Further studies are needed to investigate the clinical significance of these findings as well as the frequency of these minor lesions in healthy controls.

ClinicalTrials.gov: NCT01029847.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3200

FR10675 Obtaining Synovial Biopsies from the Wrist in Patients with Newly Diagnosed Untreated and Longstanding Rheumatoid Arthritis Followed by Intramuscular Glucocorticoid and Methotrexate Initiation Is Safe and the Glucocorticoid Treatment Significantly Reduces Disease Activity

S.A. Just1, C. Nielsen2, E.K. Højberg1, H.D. Schroder2, I.M.J. Hansen4, T. Barrington2, H.M. Lindengaard1, 1Rheumatology; 2Clinical Immunology; 3Clinical Pathology, Odense University Hospital, Odense; 4Medicine, Svendborg Hospital, Odense University Hospital, Svendborg, Denmark

Background: The minimal invasive ultrasound-guided synovial biopsy (USG-SB) method has been shown to be safe and tolerable. The method has accelerated the research field of using synovial biopsies focusing on early diagnosis, disease stratification, biomarker studies and in the future optimal treatment selection for the individual patient. Here synovial biopsies obtained from patients with early arthritis before therapy initiation are essential. A major issue in newly diagnosed RA patients but also in RA patients with longstanding active RA, is to combine an effective fast working treatment with safely obtaining synovial tissue without delaying therapy and patient’s initiation. In the EULAR early arthritis recommendations, prompt treatment initiation is recommended by combining glucocorticoid bridge therapy with disease-modifying antirheumatic drugs (DMARD). It is therefore essential that accepting synovial biopsy, does not delay start of fast remission-inducing treatment. Especially if synovial biopsies by the USG-SB method in the future shall be used systematically for detailed disease stratification and personalized treatment decisions.

Objectives: Safety of using intramuscular glucocorticoid injection (IGI) immediately after the USG-SB procedure in patients with newly diagnosed untreated RA and longstanding active RA, and the effect of IGI on disease activity after 4 weeks.

Methods: Wrist synovial biopsies were taken at inclusion and after 6 months from 22 patients with newly diagnosed, untreated RA and 15 with longstanding RA (>5 years). After biopsies patients were offered an IGI of 2 ml of methylprednisolone acetate (Depo Medrol) 40mg/ml. Early RA patients were also started on methotrexate. Disease activity scores in 28 joints (DAS28) were recorded at day of biopsy and again after 4 weeks. Safety data were obtained after 5 days (telephone), 2 weeks (questionnaire) and at first clinical evaluation (4 weeks) after biopsy. Patient-reported outcomes (PRO) with pain, swelling and stiffness of biopsied joint were obtained at day of biopsy and after two weeks.

Results: At present time, all patients have undergone first biopsy and 18/37 second biopsy. At the EULAR congress complete data will be presented. 68% of all patients accepted IGI after first biopsy currently 39% after second procedure. Patients accepting IGI after first biopsy did not have higher DAS-28 (early RA group (p=0.15), longstanding RA (p=0.06)). Time to first follow-up was not significantly different for patients accepting IGI (early RA group (p=0.17), longstanding RA (p=0.05)). Two weeks after biopsy, PRO was not significantly different when comparing IGI vs non-IGI treated. For all patients, DAS-28 was significantly reduced in the group receiving IGI at first clinical evaluation after synovial biopsy (p=0.004, without IGI ΔDAS28: -0.5, with IGI ΔDAS28: -1.7).

Conclusions: Start of treatment with IGI combined with DMARD after obtaining synovial biopsies by the USG-SB procedure from patients with early untreated RA and longstanding RA is safe, and reduces disease activity more than without IGI.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2491

FR10676 A Proposal for a Simple Ultrasound Method for the Diagnosis of Early Rheumatoid Arthritis

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Background: At this point, the classification criteria for rheumatoid arthritis (RA) are well known and generally applied in clinical practice. (1) Ultrasound (US) assessment can help in distinguishing the patients with early RA (ERA) within the patients with early inflammatory arthritides (EIA).

Objectives: The aim of this study was to develop an US method for the diagnosis
Concordance between fingertip and nailbed perfusion as assessed by PDUS is equal to 0.7988. The lower 97.5% confidence interval limit is 0.6433.

Association between capillary density, and fingertip and nailbed perfusion as assessed by PDUS is shown in Table 2.

Table 2

<table>
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<th>Parameters</th>
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<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>p-value</th>
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<tr>
<td>Age</td>
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<td>16.5 (12.0–20.0)</td>
<td>17.0 (13.0–21.0)</td>
<td>18.0 (14.0–22.0)</td>
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<td>Duration of symptoms</td>
<td>2.89 (1.5–4.2)</td>
<td>3.76 (2.5–5.0)</td>
<td>4.5 (3.0–6.0)</td>
<td>5.0 (3.5–6.5)</td>
<td>0.001</td>
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<tr>
<td>CAPS (mm)</td>
<td>1.5 (1.0–2.0)</td>
<td>2.0 (1.5–2.5)</td>
<td>2.5 (2.0–3.0)</td>
<td>3.0 (2.5–3.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: To our knowledge, this is the first study to correlate NVC and PDUS findings in SSc patients. Fingertip and nailbed PDUS grade concordance was found to be satisfactory. The mean capillary density tends to be greater with respect to grade 1. This is particularly evident comparing grade 4 and grade 1. As such, these two imaging techniques provide different and potentially complementary information on SSc-related peripheral microvascular involvement.

There is potential clinical utility in these observations that has yet to be unlocked fully.

References:

DOI: 10.1136/annrheumdis-2017-eular.3859

FR00678 | ULTRASOUND-GUIDED SYNOVIAL NEEDLE BIOPSY: SINGLE CENTER EXPERIENCE OF AN EMERGING, MINIMALLY INVASIVE TECHNIQUE IN CLINICAL PRACTICE AND RESEARCH
V.C. Romao 1, 2, J. Polido-Pereira 1, 2, R. Barros 1, E. Vieira-Sousa 1, 2, R. Luiz 1, E. Vitorino 1, F. Saraiva 1, J.E. Fonseca 1, 2, Rheumatology Department, Hospital de Santa Maria, CHLN, 2Rheumatology Research Unit, Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon; 3Pathology Department, Hospital de Santa Maria, CHLN, Lisbon, Portugal

Background: Synovial biopsy remains an important tool in clinical practice and research for the study of synovitis. Ultrasound-guided needle biopsy (USNB) has recently emerged as a minimally invasive technique, which enables collection of high quality synovial tissue with very good patient tolerance.

Objectives: To report the experience with USNB in our department, since its introduction in late 2013.

Methods: We reviewed the clinical files of all patients who had an USNB in our department. Degree of US joint synovitis was evaluated on a semi-quantitative scale (0–3) in terms of synovial thickness (ST) and power Doppler (PD). Since 2015, we assessed patient tolerance and acceptance of the procedure using a standardized questionnaire, which includes visual analogue scales (VAS) of pain, stiffness and swelling of the biopsied joint. Changes in US and VAS scores were assessed using the Wilcoxon signed-rank test.

Results: Forty-eight patients had 53 USNB, mostly for diagnostic purposes (79%), performed by 4 different operators - Figure 1. All types of joints were biopsied, mostly medium sized (26 wrists, 7 ankles), but also large (3 knees, 4 shoulders, 6 elbows, 3 hips) and small (1 sternoclavicular, 1 naviculocuneiform, 1 metacarpophalangeal and 1 proximal interphalangeal) joints, 2 bursae (subacromial) and 1 tendon sheath. USNB was repeated in the same joint (wrist) twice in 3 patients and three times in one patient. Procedures were well tolerated, with 67% of patients classifying it as easy or very easy, 28% reporting no or only mild discomfort and 77% considering likely/very likely to accept to repeat the biopsy. An increase in analgesic medication in the days following the biopsy was reported by 13 out of 44 questioned patients. After a median of 8 days following the procedure, a significant decrease was observed in VAS scores of pain, stiffness and swelling of the biopsied joint, although 23% and 31% of the patients reported small increases in these scores (median 9.5, 11 and 10mm, respectively). There was no significant change in US scores pre- and post-biopsy, with only 3 and 2 patients having an increase in ST or PD scores, respectively. Biopsies were overall safe, with 6 minor immediate adverse events (11%). There were no cases of haemarthrosis, joint/periarticular

FR00677 | ROLE OF NAILFOLD VIDEOCAPILLAROSCOPY AND 22-MHZ DOPPLER ULTRASOUND IN THE ASSESSMENT OF SYSTEMIC SCLEROSIS-RELATED DIGITAL VASCULOPATHY
T. Schioppo 1, 2, A. Orent 1, 2, P. Boracchi 1, 2, O. De Luca 2, A. Mugro 2, PL. Meroni 1, 2, F. Ingegnoli 1, 2 on behalf of OPERA study group.

Background: Microvascular damage plays a critical role in the initiation and perpetuation of systemic sclerosis (SSc). A comprehensive approach should investigate both superficial and deep layers of peripheral microcirculation. In addition to nailfold videocapillaroscopy (NVC), a well-established technique to evaluate outer skin layer vessels, power Doppler ultrasound (PDUS) has been recently used to study microcirculation in the inner levels [1].

Objectives: To study the severity of microvascular involvement in patients with SSc by using both NVC to measure capillary density (outer layer at the nailfold area) and PDUS to detect perfusion (deeper layers at the nailfold and pulp area).

Methods: 100 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 XVG by means of linear array transducer (10–22 MHz). Doppler Power settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PFR 750 Hz). PDUS measurements included sagittal scan of nailbed and fingertip qualitatively graded from 1 (no signal) to 4 (marked hyperemia) [2], and resistivity index (RI) of ulnar and radial proper digital arteries. Capillary density (number/mm) was calculated by NVC with magnification 200X performed on two images of the same digits examined by PDUS.

Results: 100 SSc patients, 87 (87%) women, 86 (86%) limited cutaneous SSc, median age 62.2 years old, median disease duration 8 years were evaluated. 7 (7%) patients had UAO. Concordance between fingertip and nailbed perfusion assessed by PDUS is reported in Table 1.

In ROC analysis, a cut-off of the US score of 4 had best results for sensitivity and specificity (73.3% and 82.1%, respectively), with an area under the curve of 0.812. The US score correlated with the levels of RF, ACPA, DAS28 and SDI (p < 0.001). The time needed for performing the ultrasound examination was less than 10 minutes.

Conclusions: The proposed US method proves to be reliable in identifying patients with ERA. The binary mode of US evaluation allows even persons with little training in US examination to diagnose patients. As the costs and time needed for US evaluation are low, the method is valuable in clinical practice for a rapid assessment of patients with ERA.

References:
[2] Capillary density

Table 1. Demographic, clinical, laboratory and US data of the study patients – data are either n (%), mean ± SD or median (IQR)

Table 2.
infection or neurovascular damage. Two patients reported transient limitation of the 5th and 1st digit extension following a biopsy of the wrist and 1st extensor compartment tendon sheath, respectively, with no detectable tendon ruptures on US; 1 patient had a muscular hematoma of the extensor muscles of the forearm following an elbow biopsy.

**Conclusions:** In our center, USNB has proved to be an effective technique for collection of synovial membrane that can be used for diagnostic and research purposes. The vast majority of the procedures were well tolerated, without significant worsening of local joint symptoms or synovitis, and safe, without major adverse events. Importantly, patients' concordance to repeat a USNB was mostly high.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4342

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**Table 1. Demographic and clinical data**

| Age (mean, yr) | 50±13 |
| Gender M:F | 50:46 |
| Psoriasis/PsA duration (mean, yr) | 19±13.6/6±8 |
| PASI | 3.9±8.9 |
| ASDAS-PCR | 2.2±1 |
| Back pain (%)/Inflammatory back pain by ASAS (%) | 70%/30% |
| HLA-B27 (%) | 4.4% |
| Current DmARD Tx (%)/Current biologic Tx (%) | 45%/35% |

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**Table 2. Whole spine MRI findings**

<table>
<thead>
<tr>
<th>Active Inflammatory Lesions</th>
<th>N (%) patients</th>
</tr>
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<tbody>
<tr>
<td>≥1 BME corner</td>
<td>22 (23%)</td>
</tr>
<tr>
<td>≥1 posterior elements enthesitis</td>
<td>4 (4%)</td>
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<th>Structural Lesions</th>
<th>N (%) patients</th>
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<tbody>
<tr>
<td>≥1 corner erosion</td>
<td>10 (10.4%)</td>
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<tr>
<td>≥1 fatty corner</td>
<td>30 (31%)</td>
</tr>
<tr>
<td>≥1 syndesmophytes</td>
<td>30 (31%)</td>
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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4444

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**Table 2. Whole spine MRI findings**

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4285

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**Table 2. Whole spine MRI findings**

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4444

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**DOI:** 10.1136/annrheumdis-2017-eular.4285
CLINICAL VALIDATION STUDIES OF THE 2012 CLASSIFICATION CRITERIA FOR EARLY RHEUMATOID ARTHRITIS (ERA) IN A DOMESTIC MULTI-CENTER COHORT

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Background: Recently, a new classification criteria for early rheumatoid arthritis (ERA) have been developed.

Objectives: To evaluate the value of 2012 classification criteria for early rheumatoid arthritis (ERA), 2010 ACR/EULAR classification criteria, and 1987 ACR classification criteria in the diagnosis of early RA.

Methods: Early arthritis patients with age more than 16 years, disease duration no more than 1 year, Cat least one joint swelling and tenderness were enrolled in a multicenter, open, cross-sectional study cohort. The patients were diagnosed as RA or other non RA disease by 2 trained experienced rheumatologists. Detailed recorded the clinical and laboratory parameters include disease duration, morning stiffness duration, RF, anti-CCP, ESR, CRP etc.The sensitivity and specificity of three RA classification criteria were compared by McNemar test. The areas under the ROC curve (AUC) of each RA classification criteria were analyzed using MedCalc software.

Results: A total of 310 patients were randomly enrolled in this study, including 182 ERA and 128 non-RA. The sensitivity (88.5%) of ERA criteria were much higher than that of 1987 ACR criteria (45.6%, χ²=75.013, P<0.0001), and not significantly different with the 2010 ACR/EULAR criteria (91.8%, χ²=1.042, P=0.05). The specificity of ERA criteria (91.4%) were similar to those of 2010 ACR/EULAR criteria (87.5%, χ²=1.0, P=0.05) and 1987 ACR criteria (96.1%, χ²=3.1, P<0.05). The AUC of ERA criteria was 0.962 (95% CI: 0.934, 0.980), which was slightly better than that of the 2010 ACR/EULAR criteria [0.959 (95% CI: 0.931, 0.978), Z=4.0, P=0.0001], and much higher than that of the 1987 ACR criteria [0.885 (95% CI: 0.845, 0.919), Z=4.517, P<0.0001].

Conclusions: Overall evaluation, the diagnostic value of ERA criteria is better than 1987 ACR and 2010 ACR/EULAR criteria in early rheumatoid arthritis. Compared to 2010 ACR/EULAR classification criteria, ERA criteria is obviously more simple and practical.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3112

FRI0681 FOLLOW-UP OF TREATMENT RESPONSE WITH DYNAMIC DOPPLER ULTRASOUND IN RAYNAUD'S PHENOMENON

U. Toprak 1, Z. Ozbaklan 1, M. Edugan 3, S. Parlak 1, S.C. Sandikci 1, T. Kaya 4, S. Sayilsoy 1, 1Department of Radiology, Suleyman demirel University, Isparta; 2Department of Rheumatology, Ankara Numune Education and Research Hospital, Ankara; 3Department of Rheumatology, Istanbul University, Capa School of Medicine, Istanbul; 4Department of Radiology, Ankara Numune Education and Research Hospital, Ankara; 5Department of Radiology, Eskişehir Demagi University, School of Medicine, Eskişehir, Turkey

Background: This study aims to investigate the role of flow parameters obtained by dynamic Doppler ultrasound in the objective follow-up of treatment response in Raynaud’s phenomenon (RP) cases.

Methods: The study included newly diagnosed 33 patients with primary RP (PRP), 31 patients with secondary RP (SRP), and 26 healthy controls. The control group was evaluated with Doppler once, while the patients before treatment and on the third month of the treatment. Baseline and post-cold provocation diameter (BD, CPD, mm) and flow volume (BFV, CPFV, mL/min); post-cold provocation flow starting time (FST, min), and flow volume normalization time (FVNT, min) were recorded. Statistical analysis: for comparison of the ex of the groups: chi-square test, for analysing the pre and post treatment doppler parameters: Wilcoxon test and to comaprison of the PRP and SRP post treatment values to controls using Krusal Wallis test. A p value less than 0.05 was considered statistically significant.

Results: Before-after treatment, there was no significant improvement in the BD in both PRP and SRP groups (0.79±0.17–0.82±0.19 vs. 0.66±0.13–0.68±0.14 PRP vs. SRP, respectively), while FST did not significantly improve in the PRP group (1.5±2.7–0.61±1.41 vs. 3.13±4.81–1.58±2.36 (p<0.05)). A significant improvement was observed in baseline flow volume (3.08±2.96 vs 3.91±3.39 (p: 0.002), flow volume normalization time (7.24±7.60 vs 3.84±3.39 (p: 0.0001), after cold provocation flow volume (1.18±1.26 vs 2.17±2.16) (p: 0.0001), after cold provocation diameter (0.63±0.15 vs 0.70±0.16) (p: 0.005) in PRP group after treatment.

In SRP group, only baseline iometer changes were not influenced by the treatment, all other post treatment parameters were improved in all SRP cases including baseline flow volume (2.14±1.94 vs 2.80±2.19) (p:0.009), after cold provocation diameter (0.56±0.15 vs 0.63±0.13) (p: 0.004), after cold provocation flow volume (1.07±2.40 vs 1.46±2.67) (p: 0.004), flow starting time (3.13±4.81 vs 1.58±2.36) (p: 0.021) and flow volume normalisation time (9.58±18.49 vs 3.32±3.56) (p: 0.0001).

There was an improvement in parameters after the treatment in both RP groups comparing by the control groups (p<0.01).

Conclusions: Doppler ultrasound is an objective, cost-effective, safe (does not include radiation), and easy-to-use method in the follow-up of RP patients on macrovascular level with or without cold provocation before and after treatment.

Acknowledgements: Keywords: Raynaud Phenomenon, treatment, Doppler ultrasound
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3122

FRIDAY, 16 JUNE 2017

Epidemiology, risk factors for disease or disease progression

FRI0682 CAUSES OF DEATH IN 350 PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES (SARD)

J.G. Ovalles-Bonilla 1,2, O. Fernández 3, J. Martínez-Barrio 1, L. Valor 1, D. Hernández 1,2, I. Janta 1, B. Serrano 1, C. Sáenz 1, R. González 1, M. Correoyo 1, L. García 1, A. López 1, A. Silva 1, J.C. Nieto 1, C. González 1, I. Montesagudo 1, F.J. López-Longo 1,2, 1Rheumatology, Hospital General Universitario Gregorio Marañón; 2Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Madrid, Spain

Background: The major SARD have an increased mortality compared to the general population. It is well known that the main causes of death in Systemic Lupus Erythematosus (SLE) are infections (INF), cardiovascular events (CV), neoplasia...
early treatment with methotrexate was associated with lower risk estimates [HR 0.71 (95% CI 0.60,0.83)], which was not clearly seen with other DMARDs [HR 0.94 (95% CI 0.82,1.0)]).

References:

Disclosure of Interest: None declared
Individuals who developed GCA after inclusion in the two health surveys were identified by linking the health survey database to the local patient administrative register and the regional patient administrative register. Four controls for every validated case, matched for sex, year of birth and year of screening, were selected from the database. Fasting blood samples had been obtained and analyzed using standard methods as part of the health survey. Potential predictors of GCA examined in conditional logistic regression models.

Results: There were 76 cases with a confirmed clinical diagnosis of GCA (61% female; 65% biopsy positive; 95% fulfilled the ACR criteria for GCA). The mean age at diagnosis was 70 years, and the median time from screening to diagnosis was 20 years (range 2–32). The cases had significantly lower fasting blood glucose (FB-glucose) at baseline screening compared to controls (mean 4.7 vs 5.1 mmol/l; odds ratio (OR) 0.49 per mmol/l; 95% confidence interval (CI) 0.30–0.79). Current smokers had a reduced risk of GCA (OR 0.35; 95% CI 0.18–0.70). The negative association between baseline FB-glucose and GCA remained significant in analysis adjusted for smoking (OR 0.46 per mmol/l; 95% CI 0.28–0.76). Both cholesterol (mean 5.6 vs 6.0 mmol/l) and triglyceride levels (median 1.0 vs 1.2 mmol/l) were lower among the cases at baseline screening, with significant negative associations with subsequent GCA in crude and smoking-adjusted (ORs with 95% CI 0.66 per mmol/l; 0.46–0.94 for cholesterol, 0.33 per mmol/l; 0.16–0.69 for triglycerides) models. The effect of FB-glucose on the risk of GCA was stronger in men compared to women (smoking-adjusted ORs per mmol/l 0.11; 95% CI 0.03–0.37, and 0.77; 95% CI 0.50–1.88, respectively). Apart from this, results were similar in women and men.

Conclusions: Development of GCA was associated with lower FB-glucose, lower cholesterol and triglyceride levels at baseline, all adjusted for current smoking. These findings are in line with the previous findings of a reduced prevalence of diabetes mellitus at the time of diagnosis of GCA (1). This suggests that metabolic factors influence the development of GCA.

References:
LIPID PEROXIDATION AS RISK FACTOR FOR ENDOTHELIAL RISK OF FRACTURE AMONG PATIENTS WITH GOUT:

1, R. Whittle 1, S. Muller 1, E. Roddy 1,2, C. Mallen1, L. Stojanovich

By now none of the followed individuals had any evidence of

Disclosure of Interest:

Scientific Abstracts

Disclosure of Interest:

practical value of routine AAB screening in healthy individuals without clinical antibody positivity (p<0.001, 95% CI 0.690–0.957, respectively).

DOI: 10.1136/annrheumdis-2017-eular.3761

None declared

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5951

FR00689 LIPID PEROXIDATION AS RISK FACTOR FOR ENDOTHELIAL DYSFUNCTION IN ANTIPHOSPHOLIPID SYNDROME (APS) PATIENTS

L. Stojanovich, N. Stanisavljevic, A. Djokovic, M. Zdravkovic. Internal medicine department, University Hospital Center Bezanjska Kosa, Belgrade, Serbia

Background: APS pathophysiology is not clear enough yet since it has been implicated that aPL can activate cells (endothelial cells, monocytes, platelets), interfere with hemoctatic reactions and activate complement reactions [1,2].

Objectives: The aim of this study was to evaluate oxidative stress markers and it relations to endothelial damage as risk factor for thrombosis in patients with primary (PAPS) and secondary (SAPS) antiphospholipid syndrome (APS) in correlation to traditional risk factors.

Methods: Flow mediated (FMD) and nitroglycerine (NMD) induced dilation of the brachial artery were studied in 140 APS patients (90 PAPS, 50 SAPS) and 40 controls matched by age, sex and conventional risk factors for atherosclerosis. Markers of oxidative stress: lipid hydroperoxides (LOOH), advanced oxidation protein products (AOPP), total sulphhydryl groups (SHG) and paraoxonase 1 activity (PON1) were determined by spectrophotometric method.

Results: Oxidative stress dominate in APS patients. LOOH and AOPP correlate to lipid fractions (p<0.05), unlike PON1, ISHG that correlated to antiphospholipid antibody positivity (p<0.05). FMD was lower in APS patients comparing to controls (p<0.001). Cholesterol is independent variable for FMD impairment in control group (p=0.011); LOOH in PAPS (p=0.004); LOOH, aCL and triglycerides in SAPS patients (p=0.009, p=0.049 and p=0.012, respectively); Combined predictive of aCL and LOOH is better for FMD impairment than LOOH alone in both PAPS and SAPS patients (AUC 0.727, p=0.001, 95% CI 0.616–0.837 and AUC 0.824, p<0.001, 95% CI 0.690–0.957, respectively).

Conclusions: Endothelial dysfunction is doubtlessly present in APS patients with oxidative imbalance as additional risk factor among other risk factors for clinical event. Anticardiopin antibodies affect endothelial dependent vasodilatation in SAPS patients. We demonstrated synergistic effect of aCL and LOOH as risk for endothelial impairment in both PAPS and SAPS patients.

References:


Acknowledgements: This work was supported by research grant number 175041, and TR 32040 for 2011 - 2017, issued by the Ministry of Science of the Republic of Serbia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2872

FR00690 RISK OF FRACTURE AMONG PATIENTS WITH GOUT: A POPULATION-BASED COHORT STUDY

A. Abdul Sultan 1, R. Whittle 1, S. Muller 1, E. Roddy 1,2, C. Mallen 1, M. Blagoevick-Bucknall 1, T. Helliwell 1, S. Hider 1,2, Z. Paskins 1,2, 1Research Institute for Primary Care & Health Sciences, Keele University, Staffordshire;

2Haywood Academic Rheumatology Centre, Staffordshire and Stoke-on-Trent Partnership Trust, Stoke-on-Trent, United Kingdom

Background: Gout is the most common type of inflammatory arthritis, affecting 2.4% of adults in the UK and is associated with a number of co-morbidities. Our understanding of the association between gout and fracture risk is limited with previous studies offering conflicting results.

Objectives: To determine the role of ULT in fracture prevention.

Methods: Utilising primary care records from Clinical Practice Research Datalink we identified patients with gout between 1990 and 2004 who were followed up until 2015. Each gout patient was individually matched to 5 individuals without gout based on age, sex, and registered practice. Absolute rate (AR) of fracture and hazard ratios were calculated using Cox regression models. We further stratified our analysis by age, gender and ULT prescription.

Results: We matched 35,857 patients with incident gout to 148,407 controls. Overall, we found no increased risk of fracture among gout patients compared to controls. However, men with no evidence of ULT had higher absolute risk of fracture compared to controls (AR=39 versus 26 per 10,000 person-years, corresponding to a 23% (HR=1.23; 95% CI 1.12–1.36) increased risk. The risk was particularly high for vertebral (HR=1.50; 95% CI 1.20–1.87) and wrist fracture (HR=1.45; 95% CI 1.21–1.74). Those treated with ULT had a 12% (HR=0.88; 95% CI 0.79–0.98) lower risk of fracture. Similar findings were not observed for women.

Conclusions: We found higher risk of vertebral and wrist fractures among men with gout not prescribed ULT. Those prescribed ULT had lower risk of fracture compared to the general population. Further research is needed to understand the role of ULT in fracture prevention.

Acknowledgements: CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and a NIHR Research Professorship in General Practice. TH is funded by a NIHR Clinical Lectureship in General Practice and AAS is funded by NIHR Postdoctoral Fellowship. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3761

FR00691 ASSOCIATION BETWEEN PERIODONTITIS AND THE RISK OF PALINDROMIC RHEUMATISM: A NATIONAL, POPULATION-BASED, CASE-CONTROL STUDY

H.-H. Chen 1, W.-C. Chao 1, Y.-M. Chen 1, D.-Y. Chen 2, 1Department of Medical Research; 2Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, Province of China

Background: Some patients with palindromic rheumatism (PR) may develop a chronic connective tissue disease, mainly rheumatoid arthritis (RA). About one to two-thirds of PR patients developed RA during a period of follow-up. Periodontitis (PD) has been found to be associated with RA risk. However, the association between PD and PR is unknown.

Objectives: To estimate the association between a history of PD and the risk of incident PR.

Methods: This study used a nationwide, administrative database to identify PR cases and non-PR controls. After exclusion of individuals with rheumatoid arthritis, systemic lupus erythematosus, Sjögren’s syndrome, systemic sclerosis, dermatomyositis or polymyositis before the first PR diagnosis date (index date), we identified 4,421 newly-diagnosed PR cases from 2007 to 2012 and randomly selected 44,210 non-PR controls matched (1:110) for sex, age, and the year of the index date. After adjusting for comorbid diabetes mellitus, we estimated odds ratios (ORs) with 95% confidence intervals (CIs) by conditional logistic regression analysis to quantify the association between a history of PD and the risk of PR. The influences of the lag time and severity of PD were examined by calculating ORs for subgroups of patients based on time intervals of last PD-related visit and the index date and PD-related cumulative cost and visit number.

Results: This study showed an association between a history of PD and newly diagnosed PR (OR, 1.51; 95% CI, 1.41–1.61). The association remained significant after variation of PD definitions. The magnitude of the association was...
greater in those who had shorter lag time between the last date of PD diagnosis and PR index date and those who had a higher number of visits for PD or greater cumulative cost of PD-related visits.

Conclusions: This study demonstrated a time- and dose-dependent association between PD exposure and PR risk.

References:

Acknowledgements: The authors would like to thank the Biostatistics Task Force of the University of Alabama at Birmingham, Birmingham, United States.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4719

J. Singh, J. Cleveland, University of Alabama at Birmingham, Birmingham, United States

Background: Recent studies have shown that hyperuricemia and gout, a condition with hyperuricemia associated with joint inflammation and/or renal manifestations, are associated with a higher risk of coronary artery disease (CAD), acute cardiovascular events including myocardial infarction (MI) and stroke, and cardiovascular mortality. Emerging data suggest that gout and hyperuricemia may also be associated with cardiac arrhythmias such as atrial fibrillation.

Objectives: To assess whether allopurinol use is associated with a reduction in the risk of ventricular arrhythmias (VA).

Methods: We used the 5% random sample of Medicare beneficiaries from 2006–2012 to examine new allopurinol use and the risk of incident VA. Multivariable Cox regression analyses were adjusted for demographics (age, race, gender), comorbidity, cardiac medications and conditions associated with VA. We calculated hazard ratios (HR) and 95% confidence intervals (CI).

Results: Of the 28,755 episodes of new allopurinol use, 2,538 were associated with incident VA (8.8%). Among patients with incident VA, 54% were male, 78% were White, and the mean Charlson-Romano comorbidity score was 4.8. The crude incidence of VA per 1,000,000 person-days declined as the duration of allopurinol use increased: 1–180 days, 151; 181 days-2 years, 105; and >2 years, 85. In multivariable-adjusted analyses, compared to non-use, allopurinol use was associated with lower HR of VA of 0.82 (95% CI, 0.76 to 0.90). Compared to allopurinol non-use, longer allopurinol use durations were significantly associated with lower multivariable-adjusted HR for VA: 1–180 days, 0.96 (95% CI, 0.85 to 1.08); 181 days to 2 years, 0.76 (95% CI, 0.68 to 0.85); and >2 years, 0.72 (95% CI, 0.60 to 0.87). Multiple sensitivity analyses adjusting for cardiac conditions, anti-arrhythmic drugs and alternate definitions confirmed our findings with minimal/no attenuation of estimates.

Conclusions: Allopurinol use and use duration >6 months were independently associated with a lower risk of VA. Future studies need to assess the pathophysiology of this potential benefit.

Disclosure of Interest: J. Singh Grant/research support from: Takeda, Savient, Consultant for: from Savient, Takeda, Regeneron, Merz, Iroko, Bioberca, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, J. Cleveland: None declared
DOI: 10.1136/annrheumdis-2017-eular.5811

FR10693 SYNOVIAL CHANGES DETECTED BY ULTRASONOGRAPHY AND THEIR ASSOCIATION WITH OSTEOARTHRITIS-RELATED KNEE PAIN: A 1-YEAR PROSPECTIVE COHORT STUDY
A. Sarmanova 1,2, M. Hall 1,2, G.S. Fernandes 1,4, A.M. Valdes 1,2, D.A. Walsh 1,2, M. Docherty 1,2, W. Zhang 1,2, Division of Rheumatology, Orthopaedics and Dermatology, The University of Nottingham; Pain Centre, Arthritis Research UK; 3School of Health Sciences, The University of Nottingham; 4Centre for Sports, Exercise and Osteoarthritis, Arthritis Research UK, Nottingham, United Kingdom

Background: Recently an important role for synovial pathology in the initiation and progression of knee osteoarthritis (OA) has been emphasized. Our previous cross-sectional study showed that synovial changes on US associated with knee pain (KP), but the association was confounded by radiographic severity [1].

Objectives: To examine whether these synovial changes associate with KP changes over 1 year.

Methods: 220 participants with early KP (<3yrs duration) identified from the Knee Pain and Related Health in the Community (KPIC, n=5614) survey in Nottingham, UK formed the cohort for this study. All participants had bilateral US and radiographic examination at baseline, and US was repeated after 1 year. KP was defined as pain in or around the knee on most days for at least a month, and KP severity was measured using a numerical rating scale (NRS 0–10). Change in KP severity was defined according to a Patient Global Impression of Change. Synovial changes (effusion, hypertrophy and Power Doppler (PD) signal) were measured by two observers (inter-observer concordance correlation was 0.8 (0.6 to 0.9) for effusion and 0.7 (0.5 to 0.9) for synovial hypertrophy). Standardised radiographs (semi-flexed weight-bearing and flexed skyline views) were scored using the Nottingham Line Drawing Atlas (NLSA). Radiographic OA was defined as definite joint space narrowing (grade 2) plus definite osteophyte (grade 2) in any compartment. An absolute change in effusion/synovial thickness/pain scores was calculated by subtracting the baseline measure from the follow-up measure within individuals. A correlation analysis was used to examine the association between changes in pain and changes in US values. Potential baseline predictors for KP worsening were examined using multivariate logistic regression analysis.

Results: Of 220 participants in this cohort, 165 (75%) had US measurements at baseline and follow-up (mean age 61yrs: 61% women; 24% ROA). The mean NRS score decreased from 4.4 to 3.01 mm. The mean depth of the effusion and synovial hypertrophy changed from 4.01 mm to 5.37 mm, and from 1.82 to 2.45 mm, respectively. There was no correlation between changes in pain in NRS and changes in US-detected synovial change (Figure 1).

At 1 year follow-up, 58% reported that their KP had improved from baseline, 16% reported worsening, and 27% reported no change in KP. After adjustment for age, gender and BMI baseline US features did not predict worsening pain, whereas ROA did (OR=4.06 95% CI 1.55 to 10.61).

Conclusions: This study extended previous work that US-detected knee “synovitis” was not a predictor of change in OA symptoms, whereas baseline radiographic OA severity was. It suggests that synovial changes detected by US might reflect aspects of OA pathology discrete from mechanisms driving OA pain change.


Acknowledgements: Arthritis Research UK (Grant Refs: 20777 and 20194) and National Institute for Health Research (NIHR) studentships.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5764

FR10694 PREVALENCE OF RHEUMATIC DISEASE IN AN ADULT POPULATION FROM COLOMBIA. A COPCORD METHODOLOGY STUDY
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Background: Rheumatic diseases are the leading cause of permanent disability. In our country are the fourth cause of consultation in health institutions. The COPCORD model constitutes an effective tool in the determination of the prevalence of diseases. Globally, this model has been carried out in Asia, Europe and in some countries of Latin America. In Colombia the epidemiology of rheumatic diseases is not known globally; this would be the first national study that uses the data collection questionnaire using the COPCORD instrument.
Objectives: To estimate the prevalence of rheumatic disease and related factors in a Colombian population over 18 years of age in six Colombian cities.

Methods: A cross-sectional analytical study was designed in people older than 18 years. A probabilistic stratified sampling method using three stages. The first stage of sampling was the selection of cartographic sectors in each city. The second stage of sampling was the selection of blocks of each sector. The third stage of sampling was the homes of each block. All household members were surveyed.

The sample size was calculated to be 6,528 people (2336 from Bogotá, 1220 from Medellín and Cali each, 746 from Barranquilla, 503 from Bucaramanga and Cúcuta each). The COPCORD questionnaire adapted for Colombia, was applied in the first stage by standardized interviewers. Positive cases were reviewed at home by a first year rheumatology fellow. To assess whether it is a rheumatic disease; the positive cases for a probable rheumatic disease were reviewed by a second year rheumatology fellow and reviewed again with laboratory and image studies by a certified rheumatologist to establish the definitive diagnosis.

Results: 3,146 men and 3,547 women were included. Pain in the last 7 days not associated with trauma was reported in 3,213 (48%) participants. The most frequent sites were knees (right 31%, left 29%), hands (right 25%, left 24%), lumbar spine (16%) and shoulders (right 16%, left 14%). Table 1 depicts the prevalence of rheumatic diseases in Colombia.

Table 1. Prevalence of Rheumatic Disease in Colombia

<table>
<thead>
<tr>
<th>Prevalence (%)</th>
<th>Variation Coefficient</th>
<th>CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>10.81</td>
<td>6</td>
</tr>
<tr>
<td>Gout</td>
<td>0.56</td>
<td>26</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>0.72</td>
<td>22</td>
</tr>
<tr>
<td>Soft Tissue Rheumatism</td>
<td>25.82</td>
<td>6</td>
</tr>
<tr>
<td>Mechanical Low Back Pain</td>
<td>7.24</td>
<td>7</td>
</tr>
<tr>
<td>Inflammatory Low Back Pain</td>
<td>0.65</td>
<td>26</td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>0.39</td>
<td>51</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>1.49</td>
<td>15</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>0.05</td>
<td>56</td>
</tr>
<tr>
<td>Sjögren Syndrome</td>
<td>0.08</td>
<td>61</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>0.03</td>
<td>100</td>
</tr>
<tr>
<td>Systemic Redderma</td>
<td>0.02</td>
<td>100</td>
</tr>
<tr>
<td>CHIKV Infection</td>
<td>6.68</td>
<td>8</td>
</tr>
</tbody>
</table>

CI: confidence interval; CHIKV: chikungunya virus.

Conclusions: Our study shows a similar prevalence to those worldwide in scleroderma, dermatomyositis, systemic lupus erythematosus, and spondyloarthritis. A lower prevalence was observed in Sjögren Syndrome, fibromyalgia, gout and osteoarthritis. A slightly higher prevalence of rheumatoid arthritis was observed in our population. The high prevalence of rheumatoid arthritis and soft tissue rheumatism should increase awareness in our governmental health entities given their long term disability risk.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5646

FRI0696 IMPACT OF ADALIMUMAB THERAPY ON BRACHIAL ENDOTHELIAL FUNCTION AND LARGE ARTERY STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Anti-TNFα treatment may improve endothelial function and mechanical properties of large artery stiffness in patients with inflammatory rheumatic diseases, however studies remain controversial.

Objectives: To study the effect of TNFα blocker with adalimumab for 24 weeks on brachial endothelial function and sub-clinical markers of atherosclerosis in patients with inflammatory rheumatic diseases.

Methods: A total of 26 patients (14 males, 12 females; mean age, 47±11 years) with inflammatory rheumatic diseases (16, rheumatoid arthritis; 9, anklyosing spondylitis, 1, psoriatic rheumatism), resistant to disease-modifying antirheumatic drugs, were studied before the first infusion of adalimumab and again after 24 weeks of treatment. Endothelial function was assessed by measuring flow mediated dilatation using an ultrasound Doppler technique on the brachial artery. Other markers of sub clinical atherosclerosis were assessed by arterial stiffness via aortic pulse wave velocity, augmentation index and central blood pressure, and carotid intima-media thickness. Data for body mass index, disease activity using DAS-PDR and BASDAI, C-reactive protein, fasting glycaemia, and lipid profile were collected before treatment and after 24 weeks.

Results: 24 weeks of adalimumab therapy resulted in a reduction of disease activity score and serum levels of C-reactive protein. No significant differences were found in body mass index, total cholesterol, triglycerides and fasting glycaemia. Brachial blood pressure and heart rate remained similar, as well as carotid intima-media thickness. After 24 weeks of treatment with adalimumab, flow mediated dilatation improved significantly; central systolic and diastolic blood pressure decreased significantly; however central pulse pressure, augmentation index and arterial pulse wave velocity remained unchanged.

Conclusions: In patients with inflammatory rheumatic diseases, treatment with adalimumab for 24 weeks resulted in a significant improvement of endothelial function and central arterial pressure.

Disclosure of Interest: A. L. Demouy Grant/research support from: Abbvie, K. Aissi: None declared, B. Chauvédier: None declared, S. Carinj: None declared, P. Rossi: None declared

DOI: 10.1136/annrheumdis-2017-eular.6128
FR0697

FRENCH NATIONWIDE SURVEY OF CHRONIC PAIN PERCEPTION IN 1739 PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM

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Background: Pain is a major symptom in chronic inflammatory rheumatism. Pain intensity doesn’t always correlate with disease activity and it can persist even when RA seems in clinical and biological remission. Little is known about the patients’ perception of their treatment efficacy on pain, of pain in their life and their expectations for pain management. A French patients association (AFPRic) conducted a national survey to explore patient’s point of view on pain in their rheumatism.

Objectives: Describe in patients with chronic inflammatory rheumatism, their perception of treatment efficacy on pain, the impact of pain in their life and their expectations on pain care, in a nationwide survey.

Methods: A nationwide survey with a 20-item questionnaire was conducted. The questions were developed by patients and rheumatologists in focus groups. Questionnaires were e-mailed to every member of the association (9065 members). Answers were collected until the 17th July 2016. Answers were anonymous.

Results: One thousand thirty nine patients (response rate 19.2%) answered the questionnaire with 1510 women (86.8%), mean age was 59 years [18–85 years].

For more than half of the patients, their rheumatism had, since the 10 years of evolution. Rheumatoid arthritis was the main rheumatism with 1377 patients (87%). Among the 1194 patients (76%) under conventional DMARDs 46.4% considered the cDMARDs efficacy on pain was between 70 and 100%, on the other hand for 17.7% of the patients, cDMARDs efficacy on pain was less than 30%. Among the 744 patients (47.6%) receiving a biological DMARD, 66.2% considered bDMARDs efficacy on pain was between 70 and 100% and 10% considered it was 30% or less. Among the 658 patients (42.3%) receiving oral corticosteroids, 56.6% considered corticosteroids’ efficacy on pain between 70 and 100% and 12% not considered it was less than 30%. Patients were asked to rate the weight of pain among their symptoms, for 38% of the patients pain represents 70 to 100% of the symptoms of their rheumatism, for 31.7% it represents 40 to 60% and for 30.3% 30% or less. The mean weight is 51.55% Among the patients of the 46.8%, considered that pain is underestimated by health professionals. For 37.2% of the patients, their current treatments are not appropriate for their current pain intensity. Finally 528 (35.7%) patients are not wish to participate to support groups with health professionals. For 37.2% of the patients, their current treatments are not appropriate for their current pain intensity. Finally 528 (35.7%) patients are not wish to participate to support groups with health professionals specialized in pain care.

Conclusions: This nationwide survey on pain among chronic inflammatory rheumatism patients shows that even in the biological DMARDs era, pain is the main concernment symptom for the patients. It is striking in this large cohort that almost half of the patients consider their pain insufficiently taken care of.

Acknowledgements: This study received an institutional grant from UCB Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5781

FR0698

PREVOTELLA AND ALLOPREVOTELLA SPECIES CHARACTERIZE THE ORAL MICROBIOME OF EARLY RHEUMATOID ARTHRITIS

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Background: We previously showed that in this early rheumatoid arthritis (ERA) cohort with a mean disease duration of <6 months, a clinically significant loss of clinical attachment loss as surrogate of alveolar bone loss is detectable compared with a matched healthy control cohort (1). Evidence is accumulating that distinct pathogens residing in reservoirs such as the oral cavity, the lung or the gut may play a role in driving the pathogenesis of RA (2–3).

Objectives: To characterize the oral microbiome associated with ERA.

Methods: 16S amplicon sequencing was used to analyze 88 samples of the supragingival and subgingival microbiome of 22 patients with ERA and 22 matched healthy controls. Oral and periodontal status, clinical activity of ERA and periodontitis, and socio-demographic parameters were used as explanatory variables in the next generation DNA sequencing analysis.

Results: Overall, a total of 4,702,161 16S RNA high-quality sequences were yielded. Using a distance-based similarity of ~97% for species-level operational taxonomic units (OTUs) clustering, a total of 1,048 OTUs were identified (Fig. 1). The oral microbiota was equally rich and diverse in ERA and control group. Subgingivally, Prevotella oris, Prevotella oralis, Prevotella nigrescens, Alloprevotella rava and Alloprevotella tannaeae were associated with early RA independent of severity of periodontitis.

Conclusions: Prevotella and Alloprevotella species were enriched in patients with early RA independent of severity of periodontitis. Further studies are needed to test a causal relationship of these species with onset and/or disease progression of RA.

References:


FRI0699

DETERMINANTS OF 12-MONTHS PERSISTENCE IN ANKYLOSING SPONDYLITIS PATIENTS INITIATING SUBCUTANEOUS TNF-ALPHA INHIBITORS

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Background: Biotherapies such as subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFis) have transformed the management of inflammatory joint diseases such as ankylosing spondylitis (AS). The assessment of SC- TNFis persistence and its determinants is needed.

Objectives: The objective of this study was to describe treatment persistence in real-world settings, and identify the determinants of persistence among AS patients initiating treatment with an SC-TNFi.

Methods: The French national health insurance scheme database lists all outpatient and inpatient healthcare consumption for individuals covered by the general health insurance scheme. Using French claims data, AS was diagnosed using Long Term Disease status and hospital admission, based on ICD-10 codes. Patients were then identified through prescription filled for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 2012/07/01 and 2013/12/31. A patient was considered as non-persistent in the event of a prolonged interruption of the therapy lasting 91 days or more. Persistence was estimated with Kaplan Meier analysis. Determinants of persistence in the 12 months before initiation were identified using Cox models.

Results: A total of 9,098 patients with AS were identified. In the descriptive analyses of the 12 months persistence, differences were observed for AS patients, with rawon-adjusted persistence rates of 93.2% for CZP, 49.3% for ETA, 52.4% for ADA and 54.5% for GLM. Results of the Cox model are presented, including hazard ratio for biotherapy, adjusted on sex, age, socio-economic status, and criteria on disease severity. The variables biotherapy, socio-economic status and hospital admission for IRMD did not meet the proportionality hypothesis of risks.
and were corrected by the addition of a variable integrating the interaction with time.

Table 1. Determinants of 12-month non-persistence (Cox model).

<table>
<thead>
<tr>
<th>SC-TRFis</th>
<th>GLM</th>
<th>C2P</th>
<th>ETA</th>
<th>ADA</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.00</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>2.70</td>
<td>2.13</td>
<td>3.42</td>
<td>&lt;0.0001</td>
<td>1.95</td>
</tr>
</tbody>
</table>

Conclusions: Non-persistent patients were more likely female, with deprived socio-economic status, multiple comorbid conditions, and multiple line of biotherapy. Age, hospital admission for IRMD and treatment with GLM (adjusted on C2P, ETA and ADA) decreased the risk of non-persistence. Further analyses are needed to assess the impact of non-persistence.

Disclosure of Interest: B. Fauret Grant/research support from: AbbVie, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen Employee of: PELYcon, C. Jacquemin

1. **WEARING AN ACTIVITY TRACKER**

2. **MODERATELY DURING WEEKS WHERE PATIENTS REPORTED FLARES**

3. **DOES PARITY INFLUENCE JOINT DAMAGE PROGRESSION IN WOMEN WITH RHEUMATOID ARTHRITIS?**

4. **Abstract**

5. **FR0700**

6. **PHYSICAL ACTIVITY DECREASED SIGNIFICANTLY BUT MODERATELY DURING WEEKS WHERE PATIENTS REPORTED FLARES: A 3-MONTH STUDY OF 170 RHEUMATOID ARTHRITIS (RA) OR AXIAL SPONDYLOARTHRITIS (AXSPA) PATIENTS WEARING AN ACTIVITY TRACKER**

7. **C. Jacquemin,** 1, H. Servy 2, A. Molto 3, J. Sellam4, V. Foltz 1, F. Gandjbakhch 1, C. Hudry 2, S. Mitrovic 2, B. Fauret 1, L. Gossec 2, **Rheumatology, La Pitie-Salpetriere Hospital, Paris; 2**Sano, e-Health services, Gantanne, 3Rheumatology, Cochin Hospital; 4Rheumatology, Saint Antoine hospital; 5Rheumatology, Private practice, Paris, France

8. **Background:** RA and axSpA natural history comprises periods of low disease activity and flares. There is much interest in the concept of flares. Studies have indicated flares may alter patient quality of life, however, there are few data linking flares to quantifiable outcomes.

9. **Objectives:** The objective was to assess longitudinally the association between patient-reported flares and physical activity assessed objectively using an activity tracker.

10. **Methods:** This prospective multi-center observational study (ActConnect) included patients with definite RA (ACR/EULAR criteria) or axSpA (ASAS criteria) owning a smartphone. Physical activity was assessed continuously over 3 months by the number of steps using an activity tracker, and flares were self-assessed weekly using a specific flare question ("has your disease flared up during the last 7 days") with a categorical response according to: no flare, 1 to 3 days flare, or >3 days flare. The relationship between flares and physical activity for each week (time point) was assessed by linear mixed models adjusted on rheumatoid disease, sex, age, obesity, biologics and employment status.

11. **Results:** 170/178 patients (91 RA and 79 axSpA patients; 1553 time points) were analyzed: mean age 45.5±12.4 years, mean disease duration 10±8.7 years; 60 (35.3%) were males and 90 (52.9%) received biologics. Disease was well-controlled (mean DAS28: 2.3±1.2; mean BASDAI: 3.3±2.1). Physical activity was moderate (mean steps/day, 7067±2770). Flares were frequent (25.5% of the questionnaires); most (76.8%) were of short duration. Flares, in particular >3 days flares, were independently associated with less weekly physical activity (p=0.02–0.03), leading to a relative decrease of physical activity of 12–21% and an absolute decrease ranging from 836 to 1462 steps/day (Table 1).

12. **Conclusions:** Flares were frequent in these low-disease patients, though most flares were of short duration. Flares were related to a moderate decrease in physical activity, confirming objectively the impact of patient-reported flares.

13. **References:**


15. **Disclosure of Interest:** None declared

16. **FR0701**

17. **DOES PARITY INFLUENCE JOINT DAMAGE PROGRESSION IN WOMEN WITH RHEUMATOID ARTHRITIS?**

18. **C. Alpigaz-Rodriguez 1,** F. Förger 1, D. Courvoisier 1, C. Gabay 1, A. Finckh 1 on behalf of Physicians of the Swiss Clinical Quality Management Program for Rheumatoid Arthritis. **Rheumatology, Department of Medical Specialties, Geneva University Hospitals (HUG), Geneva; Inselspital, Bern, Switzerland**

19. **Background:** Disease activity and severity of rheumatoid arthritis (RA) appear to be worse in women than in men [1]. The role of parity on disease activity is controversial, since pregnancy is characterized by a lower disease activity, but the postpartum period may in increase in activity [2]. Radiographic joint damage progression represents the cumulative impact of disease activity and allows us to study the long term effect of parity.

20. **Objectives:** To study the impact of parity on radiographic progression in women with RA.

21. **Methods:** This is an observational cohort study of RA patients included in the Swiss Clinical Quality Management in Rheumatoid Arthritis (SCQM-RA). Patients enrolled are followed-up yearly and have x-rays assessments at regular intervals. Information about female hormonal factors, such as pregnancies, breastfeeding, menstrual cycles and hormonal treatment were retrospectively retrieved using a questionnaire. For this analysis we included women with at least two x-rays and full information on reproductive factors. The primary outcome was the rate of radiographic progression (Ratiening erosion score) and the secondary outcome was functional disability progression (Health Assessment Questionnaire-Disability Index (HAQ-DI)). We compared the rate of progression between parous and nulliparous women using a multilevel regression model for longitudinal data.

22. **Table 1. Characteristics of women SCQM**

23. **General and disease characteristics**

<table>
<thead>
<tr>
<th>Parous</th>
<th>Nulliparous</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=458</td>
<td>n=285</td>
</tr>
<tr>
<td>Age, years, median (IQR)</td>
<td>49 (40–57)</td>
</tr>
<tr>
<td>Body mass index, kg/m2, median (IQR)</td>
<td>24 (22–26)</td>
</tr>
<tr>
<td>Ever smoking, % (n)</td>
<td>281 (64)</td>
</tr>
<tr>
<td>Alcohol consumption, g/week (n)</td>
<td>144 (53)</td>
</tr>
<tr>
<td>Disease duration, years, median (IQR)</td>
<td>0.4 (0–1.5)</td>
</tr>
<tr>
<td>DAS28, median (IQR)</td>
<td>3.8 (2.8–5.8)</td>
</tr>
<tr>
<td>HAQ-DL, median (IQR)</td>
<td>0.8 (0.3–3.3)</td>
</tr>
<tr>
<td>Erosion score, %, median (IQR)</td>
<td>2.0 (0.5–4.3)</td>
</tr>
<tr>
<td>DMARD treatment, % (n)</td>
<td>325 (77)</td>
</tr>
<tr>
<td>Biologic treatment, % (n)</td>
<td>40 (11)</td>
</tr>
<tr>
<td>CS-Rheumatoid, % (n)</td>
<td>10 (27)</td>
</tr>
<tr>
<td>Number of pregnancies, median (IQR)</td>
<td>2 (1–2)</td>
</tr>
<tr>
<td>Ever breastfeeding, % (n)</td>
<td>263 (69)</td>
</tr>
</tbody>
</table>

24. **Disclosure of Interest:** None declared

25. **DOI:** 10.1136/annrheumdis-2017-eular.63000
Results: A total of 726 women were analysed, of which 438 (60%) were parous, with a median number of pregnancies of 2 (IQR: 2–3), a mean of 4.8 x-rays per patient and 10.9 years of follow-up. Baseline patients and disease characteristics were balanced, but parous women were older than nulliparous (median of 49 vs 45 years, p=0.001) (Table 1). During follow-up, erosion progression did not differ significantly between parous and nulliparous women (p=0.94). In a subanalysis, the radiographic progression during the active parous period was not different [0.6% (95% CI: 0.5 to 0.8) vs 0.5% (95% CI: 0.4 to 0.7) by year, respectively, p=0.28]. The decrease of the HAQ-DI score overtime was not different between parous and nulliparous women (p=0.21), and it was not different during the active parous period [0.03 (95% CI: -0.03 to -0.01) vs -0.02 (95% CI: -0.03 to -0.01) by year, respectively, p=0.67]. We did not find differences in radiographic progression or HAQ-DI score between women with a singleton pregnancy and multiparous women.

Conclusions: In women with RA, the progression of structural damage and of functional disability did not differ between parous and nulliparous women. Among parous women, the active parous period was not associated with more radiographic damage progression. Although postpartum period is associated with increase in disease activity, our results suggest that parity does not have a negative long term impact on structural damage.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1354

Table 1. Annual incident cases of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and polymyalgia rheumatica (PMR) in the town of Campobasso.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>RA cases</th>
<th>PsA cases</th>
<th>PMR cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–29 yr</td>
<td>18 (4/14)</td>
<td>19/10/9</td>
<td>12 (2/3/7)</td>
</tr>
<tr>
<td>30–49 yr</td>
<td>1 (0/1)</td>
<td>3 (1/1/3)</td>
<td>4 (1/2/1)</td>
</tr>
<tr>
<td>50–65 yr</td>
<td>1 (0/1)</td>
<td>7 (1/6)</td>
<td>12 (3/7/2)</td>
</tr>
</tbody>
</table>

Results: The aim of the CAMPO-RE study was to assess the new incidence cases of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Polymyalgia Rheumatic (PMR) attending a primary rheumatology outpatient’s clinic of new institution, integrated in the community of Campobasso, a small town in the centre of Italy.

Methods: Campobasso has a population of 49,501 inhabitants (1st January 2016) and Public Health is managed from a single health authority in the entire area. In Italy, all citizens are registered with a National Health System of General Practitioner Physicians (GPP). Between 1st June 2014 to 31st May 2016 all consecutive adult patients, sent by GPP of the municipality of Campobasso with a new incident case were included. A final diagnosis was made using the most recent classification criteria.

Results: Of the 1077 patients (96.3%) were included in the current analyses, of these 64.9% had 2-year follow-up data. Duration of joint swelling before inclusion (median [25–75 perc.]) was 34 (13–66) days, mean (SD) age 46.1 (14.8) years, 54.7% were females, 16.9% anti-CCP positive, and 21.9% anti-CCP and/or RF positive. Presence of mono-, oligo- (2–4 swollen joints), and polyarthritis (>5 swollen joints) had approximately the same frequency, 32.5, 35.7 and 31.8%, respectively.

After 2 years 33.0% used DMARDs, and a further 9.3% had joint swelling without DMARD use. The arthritis resolved in the remaining 57.6%. The most common clinical diagnoses and their respective outcomes are shown in Figure 1. The most common final diagnoses were undifferentiated arthritis (UA) (39.9%), rheumatoid arthritis (RA) (22.7%), reactive arthritis (17.1%), psoriatic arthritis (6.0%) and sarcoid arthritis/Löfgren’s syndrome (6.2%). A final diagnosis of sarcoid arthritis, reactive arthritis and UA carried the best prognoses, with resolution of disease without DMARDs in 91.0, 85.9 and 73.7%, respectively. Patients presenting with polyarthritis developed persistent disease more often than patients with oligo- or monarthritides (67.6%, 34.9 and 26.0%, respectively) (p<0.001).

Conclusions: Among 1077 patients with ≥6 weeks duration, UA was the most common diagnosis after 2 years. 22.7% were diagnosed with RA and 6.0% with psoriatic arthritis. The arthritis resolved without DMARDs in the majority of the patients. This, as far as we know, is the first study to describe the whole range of diagnostic outcomes in an unselected cohort of recent-onset arthritis, as well as the persistency of disease according to each diagnosis.

Disclosure of Interest: E. S. Norli: None declared, G. Hetland Brinkmann: None declared. T. K. Kvien Consultant for: Tore K Kvien has received fees for speaking and/or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celtrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktail, Orion...
ANALYSIS OF RISK FACTOR FOR PREGNANCY OUTCOMES IN 142 PREGNANCIES COMPPLICATED WITH CONNECTIVE TISSUE DISEASE

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Background: Recently, many connective tissue disease (CTD) patients wish to become a mother because immunosuppressants and biologics enable to improve the outcome of underlying CTD and quality of life respectively. However, CTD during pregnancy can cause major complications, especially in pregnant patients with underlying disease exacerbation, some complications during pregnancy especially in preterm birth, for light for dates (LFD) and premature rupture of membrane (PROM).

Methods: We investigated the risk factors of preterm birth, LFD (light for dates) and perinatal perinatal morbidity during pregnancy especially in preterm birth, for light for dates (LFD) and premature rupture of membrane (PROM) in 23 CTD patients.

Results: In 23 among all cases underlying disease were exacerbated, and these occurred most often in PM/DM (60%), MCTD (33.3%), RA (15.3%) and SLE (13.3%). In SLE, SS cSSc and PM/DM, preterm birth and LFD were closely related to disease exacerbation and LFD of corticosteroid, pulse therapy, and these were extracted as risk factors for these perinatal complications. Preterm birth was also associated with low complement (CH50) and high titer of anti-dsDNA antibody and LFD was associated with high titer of anti-dsDNA antibody before pregnancy. However, there was no significant association with these factors in threatened premature delivery and PROM. In RA, perinatal complications were more influenced by methotrexate and biologics before pregnancy. However, only LFD was related to doses of corticosteroid during pregnancy.

Conclusions: We extracted disease exacerbation and dose of corticosteroid, pulse therapy during pregnancy and also low complement, high titer of anti-dsDNA antibody before pregnancy. However, there was no significant association with these factors in threatened premature delivery and PROM. In RA, perinatal complications were more influenced by methotrexate and biologics before pregnancy. However, only LFD was related to corticosteroid during pregnancy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5662

FR0704

HLA-DRB1 ALLELES ARE ASSOCIATED WITH MARKERS OF ENDOTHelial INJURY IN FIRST-DEGREE RELATives OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) patients experience higher cardiovascular disease (CVD) risk and CVD-related mortality. MHC class II HLA-DRB1 alleles, or the shared epitope (SE), has also been linked to endothelial dysfunction in RA patients. It is not known whether this association exists in individuals who are RA-free, but who are at higher risk due to being a first-degree relative (FDR) of an RA patient.

Objectives: To determine the association between HLA-DRB1 alleles (*0401, *0404, *0405, *0408) and markers of endothelial injury in FDRs of RA patients, a population free of RA and RA-related medications.

Methods: From the Studies of the Etiology of RA, SERA, (a multicenter prospective study of preclinical RA, started in 2002), 113 FDRs who had been positive for any of 5 RA-related autoantibodies (Abs): rheumatoid factor (RF), RF isotypes – IgM, IgG, IgA, or anti-cyclic citrullinated peptide (anti-CCP2) on at least one of their visits, and 100 FDRs who had never been Ab positive were selected, frequency matched on age, sex, and field center site. No FDR met the 1987 ACR Criteria or 2010 EULAR/ACR Criteria for RA. In cross-sectional testing of single samples from baseline, the following were measured: inflammatory markers: soluble intracellular adhesion molecule-1 (sICAM), soluble vascular cell adhesion molecule-1 (sVCAM) and E-selectin; and high resolution HLA-DRB1 typing for the*0401, *0404, *0405, *0408 alleles using real-time polymerase chain reaction. ANCOVA was used to evaluate associations between HLA-DRB1 alleles, sVCAM, sICAM, and E-selectin, adjusting for age, sex, race, body mass index (BMI), Ab status, ever smoking, and current statin use.

Results: Among 213 FDRs, age was 50±18 yr, BMI was 27±6, 75% were women, 83% were Caucasian, 35% ever smoked, 11% were currently taking statins, and 38% were SE positive. sVCAM was significantly higher by 1.53ng/mL in FDRs with the HLA-DRB1*0404 allele (p=0.009) compared to FDRs without the *0404 allele (Table 1). E-selectin was higher by 23ng/mL in FDRs with the HLA-DRB1*0405

Table 1. Differences in levels of endothelial injury markers by HLA-DRB1 alleles in FDRs of RA patients

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
<th>ICAM (ng/mL)</th>
<th>p-value</th>
<th>VCAM (ng/mL)</th>
<th>p-value</th>
<th>E-selectin (ng/mL)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE Positive</td>
<td>81 (38)</td>
<td>11.6 (8.8)</td>
<td>0.15</td>
<td>55.7 (32.5)</td>
<td>0.09</td>
<td>3.7 (2.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>SE Negative</td>
<td>404</td>
<td>5.26</td>
<td>2.6 (1.0)</td>
<td>0.85</td>
<td>14.1 (5.7)</td>
<td>0.06</td>
<td>1.0 (1.5)</td>
</tr>
<tr>
<td>SE Positive</td>
<td>403 (21)</td>
<td>11.9 (3.9)</td>
<td>0.13</td>
<td>13.5 (54.9)</td>
<td>0.009</td>
<td>6.4 (3.4)</td>
<td>0.06</td>
</tr>
<tr>
<td>SE Negative</td>
<td>408</td>
<td>2 (1)</td>
<td>55.1 (44.0)</td>
<td>0.21</td>
<td>186.0 (163.1)</td>
<td>0.26</td>
<td>22.9 (10.8)</td>
</tr>
<tr>
<td>SE Positive</td>
<td>408</td>
<td>6 (3)</td>
<td>6.6 (25.4)</td>
<td>0.79</td>
<td>7.1 (94.1)</td>
<td>0.94</td>
<td>0.4 (2.5)</td>
</tr>
<tr>
<td>SE Negative</td>
<td>404</td>
<td>55 (26)</td>
<td>2.6 (10.0)</td>
<td>0.80</td>
<td>-14.1 (37.0)</td>
<td>0.70</td>
<td>0.4 (2.5)</td>
</tr>
</tbody>
</table>

[n=213 (92 Ab+, 121 Ab−).]
FR0707 DRUG LEVELS AND ANTIDRUG ANTIBODIES IN THE DEVELOPMENT OF PARADOXICAL PSORIASIS AND PALMOPLANTAR PUSTULOSIS

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Background: The pathogenesis of psoriasis and palmpoplantar pustulosis induced by Tumor Necrosis Factor inhibitors (TNFi) is largely unknown. Only one study, in rheumatoid arthritis patients, investigated the relation with infliximab drug levels in the development of psoriasis or palmpoplantar pustulosis and demonstrated no relation with of trough concentrations in these events (1). However, psoriasis and palmpoplantar pustulosis were not studied separately.

Objectives: To study the differences in drug levels and antidrug antibodies (ADA) of TNFi in rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients who developed de novo psoriasis, palmpoplantar pustulosis and those who did not develop skin adverse events.

Methods: In this retrospective study data was collected from the observational cohorts of consecutive RA and AS patients in whom TNFi was started. At every visit, serum samples were collected. We quantified the samples before/one time of the event the patients who developed psoriasis or palmpoplantar pustulosis, for the patients with no skin adverse events (control group) at 24 or 28 weeks. Drug levels and ADA were measured with an Enzyme-linked immunosorbent assay and antibody binding test respectively.

Results: A total of 830 TNFi naïve patients with RA and AS were included, of whom 21 developed psoriasis (n=11) or palmpoplantar pustulosis (n=10). These patients were only observed in the adalimumab and etanercept cohorts. Sixteen patients with an event and 585 patients in the control group had serum samples available to quantify drug levels and ADA. No statistical significant differences were found in drug levels of adalimumab and etanercept for both RA and AS patients (table 1). Moreover, no statistical significant differences were observed in the detection of ADA between the three groups. However, no ADA were detected in patients who developed psoriasis or palmpoplantar pustulosis compared to the overall 13.9% of the RA patients and 25.5% in AS patients.

Table 1. Differences in drug levels and detection of anti-drug antibodies between palmpoplantar pustulosis, psoriasis and control group

<table>
<thead>
<tr>
<th>Drug levels</th>
<th>Adalimumab (μg/ml; median (IQR))</th>
<th>Drug levels</th>
<th>Etanercept (μg/ml; median (IQR))</th>
<th>Anti-drug antibodies</th>
<th>Adalimumab</th>
<th>Etanercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Palmpoplantar pustulosis n=3</td>
<td>7.6 (0.1–12.0)</td>
<td>n=1</td>
<td>4.4</td>
<td>n=3</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Psoiriasis n=3</td>
<td>8.5 (6.5–10.0)</td>
<td>n=2</td>
<td>2.3 (1.5–3.1)</td>
<td>n=2</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Control group</td>
<td>n=153</td>
<td>7.4 (4.0–10.0)</td>
<td>n=89</td>
<td>2.7 (1.9–3.9)</td>
<td>n=151</td>
<td>21 (13,9)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.992</td>
<td>0.380</td>
<td>0.674</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>Palmpoplantar pustulosis n=3</td>
<td>9.0 (6.5–10.0)</td>
<td>n=1</td>
<td>1.7</td>
<td>n=3</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Psoiriasis n=1</td>
<td>10.0</td>
<td>n=2</td>
<td>1.3 (0.8–1.7)</td>
<td>n=1</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Control group</td>
<td>n=46</td>
<td>8.5 (1.7–11.3)</td>
<td>n=2</td>
<td>2.9 (1.4–4.0)</td>
<td>n=47</td>
<td>12 (25.5)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.754</td>
<td>0.406</td>
<td>0.754</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RA: rheumatoid arthritis; AS: ankylosing spondylitis; Control group: patients who did not develop skin adverse events; IQR: interquartile range; no: number of patients. p-value < 0.05 was considered statistically significant.

Conclusions: Patients who develop paradoxical psoriasis and palmpoplantar pustulosis have adequate drug levels and no ADA were detected.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4570

FR0708 NEUROPATHIC PAIN IS A WEAK PREDICTOR OF NEW ONSET CHRONIC WIDESPREAD PAIN

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Background: Regional pain (e.g. back pain) predicts incident chronic widespread pain (CWP), the clinical hallmark of fibromyalgia. Up to 20% of patients with CWP have neuropathic pain (NP). People with CWP and NP report similar pain characteristics including allodynia (pain in response to normal touch), have common risk factors (age, sex, body mass index, smoking and socioeconomic status) and a shared genetic predisposition. Whether NP is a risk factor for CWP is not known.

Objectives: To test the hypothesis that among persons free of CWP, NP would increase the risk of developing CWP.

Methods: In a population based study participant’s pain reports were coded and those free of CWP (ACR criteria: pain lasting >3 months in the axial skeleton and contralateral body quadrant) were identified. Participants also completed the Pain Quality Questionnaire, a simple index for NP origin which has a significant impact on population levels of CWP. Therefore, the genetic predisposition to RA could contribute to parallel development of atherosclerosis during the preclinical period of RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.15642

FR0709 PREVALENCE OF RHEUMATIC DISEASES BASED ON COPCORD STUDIES: A SYSTEMATIC REVIEW

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Background: Despite many efforts, to date there has been no focused attempt to derive a robust estimate of the prevalence of rheumatic diseases (RDs) to quantify how this is influenced by other factors than they examined in every local study, however, the problems magnitude is rising and due the demographic transition and the increase in the life expectancy.

Objectives: To determine, through a systematic review and meta-analysis, the prevalence of RDs in the adult general population and explore its heterogeneity.

Methods: MEDLINE, EMBASE, BIREME, LILACS and Web of Science were searched using a search strategy combining key words and related database-specific subject terms to identify relevant cross-sectional based on COPCORD methodology studies. Also was developed a manual search. Included articles were assessed for risk of bias and quality based on the STROBE statement. Prevalence figures for RDs were analyzed according to female percentage of sampled individuals, mean age and sample size. A mixed effect model was used to obtain the combined prevalence and a meta-regression to estimate the effects of other variables.

Results: 44 out from 127 papers were included in English, Spanish or Portuguese. Estimates for any RDs prevalence ranged from 7.2% to 62.3% (26.9%; 95% CI 18.3%–25.6%). For rheumatoid arthritis (RA), the prevalence varied between 0.2% and 16.4%. SLE (systematic lupus erythematosus) was the less frequent (1.1%–6.2% [1.04%; 95% CI 0.4%–1.6%]). fibromyalgia (FM) had a mean prevalence of 2.1% (95% CI 1.0%–3.2%) and osteoarthritis: 13.5% (95% CI: 10.6%–16.4%). SLE (systemic lupus erythematosus) was the less frequent condition with average prevalence of 0.14% (95% CI: 0.05%–0.28%). The random-effects pooled prevalence for any RDs was 25% (95% CI: 18.0%, 31.1%). Prevalence was higher in studies with bigger sample size (Hedges’ g effect size coefficient: 0.0014, p<0.002). There was evidence of relevant heterogeneity in the analysis (p<0.001) and for RDs, RA and FM the sample size was positively associated to the perceived heterogeneity. No effects were found for SLE

Conclusions: This was found significant variation among the prevalence across this
review, in particular, related to the sample size used in each study. Two facts must be accounted for, first the statistical difficulties associated to the estimation of small prevalence and the consequent heterogeneity of the estimates, and, second the limited number of studies including in the meta-analysis. Nonetheless, there is evidence about big heterogeneity what can correspond to non-observed variables, in particular, life-styles, and environmental or genetic traits.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3919

**FR0710**

**MONOSODIUM URATE CRYSTAL DEPOSITION ASSOCIATED WITH THE CHANGE OF RADIOGRAPHIC GRADE AT THE SACROILIAC JOINT IN AXIAL SPA: A DUAL-ENERGY CT STUDY**

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**Background:** Previous studies have revealed that ankylosing spondylitis (AS), as the progenitor of axial spondyloarthropathy (AxSpA), has been characterized by the insidiously progressive nature of sacroilitis and spondylitis. Dual-energy computed tomography (DECT) has recently been used to analyse the deposition of monosodium urate (MSU) crystals with higher sensitivity and specificity. However, it remains unclear whether the existence of the MSU crystal deposits detected by DECT at the sacroiliac joint in patients with AxSpA also contributed to the existing structural damage.

**Objectives:** We performed this study to show the DECT MSU crystal deposits in AxSpA patients without coexisting gout were recruited. The plain radiographs of the sacroiliac joint were obtained, along with the DECT scans at the pelvis and the clinical variables. All statistics based on the left or right sacroiliac joint damage grading (0–4) were calculated independently. Bivariate analysis and ordinal logistic regression was performed between the clinical features and radiographic grades at the sacroiliac joint.

**Results:** At painful joints or skeleton regions, large quantities of MSU crystal deposits were found in 186 patients with AxSpA, as depicted in green with DECT. The average MSU crystal volume at the left sacroiliac joint, the right sacroiliac joint, and the pelvis were 0.902±1.345, 1.074±1.878, and 5.272±29.44 cm³, values which were correlated with serum uric acid concentrations (r=0.727, 0.740, 0.896; p<0.001). At the left and right sacroiliac joint, the presence of MSU crystal deposits (+1.451, 43.684; p<0.01) and the volumes of MSU crystals (Z=9.198, Z=34.607; p<0.05) were statistically different among groups divided by the ASDAS scores. In bivariate analysis, wide clinical variables were associated with the changes in sacroiliac joint damage. When others factors were adjusted in the ordinal logistic models, the AxSpA duration, total back pain, BASFI score, and volume of MSU crystallization were the risk factors for the radiographic grade at the left sacroiliac joint (AOR=1.187, 1.428, 3.837, 2.018; p<0.05). The same risk factors were obtained for the right sacroiliac joint, except for total back pain. Additionally, the simplified models excluded the repeated variables; the AxSpA duration, BASFI score, and the volume of MSU crystallization at both sides of sacroiliac joint served as risk factors for the radiographic grade (left-AOR=1.180, 3.800, 1.925; right-AOR=1.190, 3.034, 1.418; p<0.01).

**Conclusions:** Large quantities of MSU crystal deposits detected by DECT were found in AxSpA patients without coexisting gout. In addition to AxSpA duration and BASFI score, the MSU crystal deposits at the sacroiliac joint in those patients independently increased the risk of structural joint damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1417

**FR0711**

**DISCORDANCE OF THE FRAMINGHAM CARDIOVASCULAR RISK SCORE AND THE 2013 AMERICAN COLLEGE OF CARDIOLOGY/AARHEUMATOLOGY CARDIOVASCULAR RISK ASSOCIATION RISK SCORE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS**

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**Background:** Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are associated with an increased risk of cardiovascular (CV) disease, and multipliers to traditional 10-year CV risk scores, such as a EULAR-recommended 1.5 multiplier in RA, have been proposed to capture this increased CV risk. The discordance between CV risk assessment by the Framingham risk score, a modified Framingham risk score (with a 1.5 multiplier), and the more recent 2013 American College of Cardiology/American Heart Association (ACC/AHA) risk score has not been well-studied in patients with rheumatic diseases.

**Objectives:** To determine the proportion of discordant 10-year Framingham risk scores and 2013 ACC/AHA risk scores in subjects with SLE and RA, both with and without a 1.5 multiplier to the Framingham risk score, and to assess demographic, CV, and rheumatologic clinical characteristics associated with discordant risk scores.

**Methods:** A cross-sectional study was conducted using SLE and RA subjects drawn from the University of California, San Francisco, Arthritis, Body Composition, and Disability project. 10-year Framingham risk scores, modified Framingham risk scores (with a 1.5 multiplier), and 2013 ACC/AHA risk scores were calculated. As per Adult Treatment Panel-III (ATP-III) recommendations, a subject with a Framingham risk score (or modified Framingham risk score)≥10% was defined as high-risk by that score, whereas a subject with a Framingham risk score (or modified Framingham risk score)<10% was defined as low-risk. A subject with a 2013 ACC/AHA risk score >7.5% was defined as high-risk by that score, whereas a subject with a 2013 ACC/AHA risk score ≥7.5% was defined as low-risk. A subject with a discordant risk score was defined as one who had a Framingham risk score (or modified Framingham risk score) that characterized him/her as low-risk and a 2013 ACC/AHA risk score that characterized him/her as high risk. Associations of demographic, CV, and rheumatologic characteristics with discordant risk scores were analyzed using chi-squared tests for categorical variables and using independent t-tests for continuous variables.

**Results:** 11 (7.0%) of the 157 SLE subjects and 11 (11.5%) of the 96 RA subjects had discordant CV risk scores with low Framingham risk scores but high ACC/AHA risk scores. When the 1.5 multiplier was applied to the Framingham risk score, the number of subjects with discordant risk scores did not significantly change. Rheumatologic disease duration, CRP levels, African American race, diabetes, current use of anti-hypertensive medication, higher age, and higher systolic blood pressure were all significantly associated with discordant risk scores.

**Conclusions:** Approximately 10% of SLE and RA subjects had discordant 10-year CV risk scores with low Framingham risk scores but high ACC/AHA risk scores, even when a 1.5 multiplier was applied to the Framingham risk score. Prospective studies are needed to address the ability of different CV risk assessment tools, such as the 2013 ACC/AHA risk score, Framingham risk score, and modified risk scores, to predict CV events in rheumatologic patients, especially those with risk factors associated with discordant risk scores.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1171

**FR0712**

**DRIVERS OF UNREFRESHING SLEEP IN PEOPLE WITH MUSCULOSKELETAL PAIN**

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**Background:** Waking feeling unrefreshed is associated with poor health outcomes including an increased risk of cardiovascular death. Pain is a robust predictor of waking feeling unrefreshed. Pain is a complex disorder and it is not clear whether the pain itself, or associated somatic symptoms, mental health conditions and lifestyle factors, predicts waking unrefreshed.

**Objectives:** To investigate whether reporting pain was an independent predictor of waking unrefreshed among people with musculoskeletal pain.

**Methods:** Participants in a population study completed the Estimation of Sleep Questionnaire (ESPS), a 3-item scale (ESPS), which represents the number of days in the past month participants have experienced unrefreshing sleep, problems with sleep onset, maintenance and night awakenings. Pain assessments (body map and duration >3 months) were used to classify participants as having no pain, acute pain, chronic pain and CWP (ACR criteria: pain lasting ≥3 months in the axial skeleton and ≥6 weeks in the peripheral joints). Participants also reported demographics (date of birth, sex, English Index of Multiple Deprivation); somatic symptoms (Chalder Fatigue Scale (CFS) 11) and Inflammatory Bowel Syndrome (IBS); mental health (Hospital Anxiety and Depression (HAD) scale); disability (Stanford Health Assessment Questionnaire (HAQ)) and lifestyle factors (average number of
of alcoholic drinks per week, smoking status and Rapid Assessment of Physical Activity (RAPA). Univariable ordinal logistic regression tested the relationship between pain and waking unrefreshed. The model was then cumulatively adjusted for sleep, somatic symptoms, mental health, disability and lifestyle domains. All models were age, sex and deprivation adjusted. The results of a complete case analysis were comparable to those which used multiple imputation for missing data and the results of the complete case analyses are shown. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI).

**Results:** Of 1913 people who had complete data, 1376 (72%) woke unrefreshed on at least one day in the past month (41% ± 7 days; 31% ± 8 days). Compared to those with no pain, people with acute pain and chronic pain were two (OR 2.0, 95% CI (1.5–2.6) and 2.2 (1.9–2.7), respectively) times more likely to wake unrefreshed; those with CWP were five (5.0 (4.0–6.3)), times more likely to wake unrefreshed. Following adjustment for all other variables, the relationship between reporting chronic pain (1.5 (1.2–1.8)) or CWP (1.9 (1.4–1.5)) and waking unrefreshed was attenuated, but remained statistically significant. The reporting of acute pain was not an independent predictor of waking unrefreshed (1.4 (0.98–1.9)). Problems with sleep onset (±8 days vs 0: 2.9 (2.0–4.1) and maintenance (±8 days vs 0: 5.9 (4.1–8.4)), night awakenings (±8 days vs 0: 2.5 (1.7–3.7), IBS (2.2 (1.2–4.0)), current smoking (vs never: 1.5 (1.02–2.1)) and engagement in activities such as stretching and yoga (vs none: 0.8 (0.6–0.97), physical (1.3 (1.2–1.3)) but not mental (0.99 (0.9–1.1)) fatigue, and anxiety (definite vs no: 2.4 (1.8–3.1)), but not depression (definite vs no: 1.5 (0.8–2.6)), were associated with waking unrefreshed.

**Conclusions:** This study suggests that among people with chronic pain, the risk of waking feeling unrefreshed may be reduced through interventions that target factors such as smoking cessation, IBS management, physical fatigue and anxiety.

**Acknowledgements:** J. Anderson, M. Mulvey, A. Rashid

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1798

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**FRID0714 LUPUS NEPHRITIS AND PROGNOSIS. EFFECT OF MEMBRANOUS AND OTHER COMPONENTS OF THE HISTOLOGY**

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**Background:** In 1983 Austin et al. informed a series of prognostic factors (including histology) associated with the development of renal failure in patients with lupus nephritis (LN). Differences in actual therapies may have different hazard ratios of renal failure than the described by Austin et al. 1

**Objectives:** To evaluate histological factors associated with a decline in kidney function (DKF) in patients with SLE.

**Methods:** We evaluated all the patients in whom a kidney biopsy was performed. DKF was defined as a glomerulat filtration rate (GFR) of less than 60 ml/min/m² in two determinations in the follow-up. Histology was graded according to Austin et al. 1 (activity and chronicity) by a renal pathology specialist. Factors associated with the development of DKF were evaluated through Kaplan-Meier curves and Cox regression analysis (bivariate and multivariate).

**Results:** At this moment, we have followed 170 patients with LN and kidney biopsy. 130 (76.5%) women, mean age at kidney biopsy was 29.7±13.2 years; classes of LN were: 71 patients (41.8%) class IV, 30 (17.6%) class V, 22 (12.9%) class III/V, 19 (11.2%) class IV/V, 16 (9.4%) class III, and other classes 12 patients; 135 patients (79.5%) have a minimum follow-up of 12 months. There were statistically significant differences in four groups of LN: pure proliferative classes (III/IV/V), the combination with membranous (III/IV/V), pure membranous (V) or other classes (Figure1).

**Table 1. Factors associated with a DKF**

<table>
<thead>
<tr>
<th>Histological feature</th>
<th>Bivariate HR (CI)</th>
<th>Multivariate HR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerular abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellular proliferation</td>
<td>1.01 (0.83–1.22)</td>
<td>0.920 NA NA</td>
</tr>
<tr>
<td>Karyothesis</td>
<td>0.94 (0.76–1.17)</td>
<td>0.566 NA NA</td>
</tr>
<tr>
<td>Cellular crescents</td>
<td>1.09 (0.96–1.22)</td>
<td>0.179 0.95 (0.82–1.10) 0.501484</td>
</tr>
<tr>
<td>Hyaline thrombi</td>
<td>0.85 (0.64–1.12)</td>
<td>0.248 0.65 (0.47–0.90) 0.008837</td>
</tr>
<tr>
<td>Leukocyte infiltration</td>
<td>1.23 (0.97–1.57)</td>
<td>0.9848 1.03 (0.77–1.40) 0.815447</td>
</tr>
<tr>
<td>Glomerular sclerosis</td>
<td>1.79 (1.41–2.26)</td>
<td>&lt;0.001 1.67 (1.23–2.25) 0.008383</td>
</tr>
<tr>
<td>Fibrous crescents</td>
<td>1.71 (1.27–2.29)</td>
<td>&lt;0.001 1.55 (1.11–2.16) 0.009917</td>
</tr>
<tr>
<td>Membranous</td>
<td>0.50 (0.30–0.85)</td>
<td>0.015 0.44 (0.28–0.87) 0.017001</td>
</tr>
</tbody>
</table>

| Tubulointerstitial abnormalities | | |
|----------------------|------------------|
| Interstitial cell infiltration | 1.31 (1.13–1.56) | <0.001 1.18 (0.95–1.47) 0.126099 |
| Interstitial fibrosis | 0.80 (0.62–1.07) | 0.162 0.74 (0.47–1.16) 0.194012 |
| Tubular atrophy | 1.33 (1.02–1.74) | 0.035 1.10 (0.47–1.17) 0.613154 |
In the bivariate analysis, factors statistically significant associated with the development of DFK were: glomerular sclerosis, fibrous crescents, interstitial cell infiltration and tubular atrophy; having membranous component resulted as a "protector" factor for the development of DFK. The Cox regression model included all the factors with a p-value less than 0.25 in the bivariate analysis: independent factors associated with increased HR of DFK were glomerular sclerosis and fibrous crescents; however, hyaline thrombi and presence of membranous nephritis were associated with a decreased HR of DFK. (Table 1).

Conclusions: We describe factors associated with a DFK. We found that the proliferative LN in combination with membranous have a better prognosis than pure proliferative LN. Our study could help to evaluate the effects of therapies in LN.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4156

FRI0715 BEING A WOMAN AND HAVING KNEE OSTEOARTHRITIS INCREASES THE LIKELIHOOD OF COMORBIDITIES
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Background: Young adults with acute myocardial infarction are a critical group to examine for the purpose of risk factors stratification and modification [1].

In the setting of underlying systemic autoimmune diseases, premature cardiovascular disease deserves even more attention in these conditions, such as antiphospholipid syndrome (APS), the most common acquired thrombophilia.

Objectives: In this study we aimed to assess the clinical utility of the adjusted Global Antiphospholipid Syndrome Score (aGAPSS)[2] for the risk stratification of acute myocardial infarction in a cohort of young APS patients with thrombotic events.

Methods: The analysis included 83 consecutive APS patients (<50 years old) who presented with arterial or venous thromboembolic events. Data on cardiovascular risk factors and antiphospholipid antibodies (aPL) positivity were retrospectively collected. The aGAPSS was calculated for each patient by adding the points corresponding to the risk factors, based on a linear transformation derived from the β regression coefficient as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for aCL IgG/IgM, 4 for anti-b2 glycoprotein I IgG/IgM and 4 for LA.

Results: Demographic, clinical and laboratory characteristics of the cohort are summarized in Table 1. Higher aGAPSS values were observed in patients with acute myocardial infarction when compared to the others [mean aGAPSS 11.9 (S.D. 4.15, range 4–18) Vs. (mean aGAPSS 9.2, S.D. 5.1, range 1–17); T test: p < 0.05]. Significantly higher aGAPSS values were also seen in patients with acute coronary syndrome compared to patients with a history of peripheral or cerebrovascular arterial thrombotic events [mean aGAPSS 11.9 (S.D. 4.15, range 4–18) Vs. (mean aGAPSS 6.7, S.D. 5.7, range 1–17); T test: p < 0.005]. When separating for cardiovascular risk factors and aPL positivity, hypercholesterolemia was significantly higher in the group that developed myocardial infarction compared with patients with a history of any thrombosis and patients with a history of peripheral or cerebrovascular arterial thrombotic events (Chi square test: p < 0.0001 and p < 0.0001) and significantly higher rate of multiple positivity.

References:
[1] FRI0715

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3494

FRI0716 RISK STRATIFICATION IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION USING THE ADJUSTED GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE (aGAPSS)
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1Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases, Torino, Italy; 2Department of Rheumatology and Haemophilia, Guy’s and St Thomas’ Hospital, London, United Kingdom; 3S. Giovanni Bosco Hospital, Torino, Italy; 4Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom.

Background: Young adults with acute myocardial infarction are a critical group to examine for the purpose of risk factors stratification and modification [1].

In the setting of underlying systemic autoimmune diseases, premature cardiovascular disease deserves even more attention in these conditions, such as antiphospholipid syndrome (APS), the most common acquired thrombophilia.

Objectives: In this study we aimed to assess the clinical utility of the adjusted Global Antiphospholipid Syndrome Score (aGAPSS)[2] for the risk stratification of acute myocardial infarction in a cohort of young APS patients with thrombotic events.

Methods: The analysis included 83 consecutive APS patients (<50 years old) who presented with arterial or venous thromboembolic events. Data on cardiovascular risk factors and antiphospholipid antibodies (aPL) positivity were retrospectively collected. The aGAPSS was calculated for each patient by adding the points corresponding to the risk factors, based on a linear transformation derived from the β regression coefficient as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for aCL IgG/IgM, 4 for anti-b2 glycoprotein I IgG/IgM and 4 for LA.

Results: Demographic, clinical and laboratory characteristics of the cohort are summarized in Table 1. Higher aGAPSS values were observed in patients with acute myocardial infarction when compared to the others [mean aGAPSS 11.9 (S.D. 4.15, range 4–18) Vs. (mean aGAPSS 9.2, S.D. 5.1, range 1–17); T test: p < 0.05]. Significantly higher aGAPSS values were also seen in patients with acute coronary syndrome compared to patients with a history of peripheral or cerebrovascular arterial thrombotic events [mean aGAPSS 11.9 (S.D. 4.15, range 4–18) Vs. (mean aGAPSS 6.7, S.D. 5.7, range 1–17); T test: p < 0.005]. When separating for cardiovascular risk factors and aPL positivity, hypercholesterolemia was significantly higher in the group that developed myocardial infarction compared with patients with a history of any thrombosis and patients with a history of peripheral or cerebrovascular arterial thrombotic events (Chi square test: p < 0.0001 and p < 0.0001) and significantly higher rate of multiple positivity.

References:
[1] FRI0716

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3494
for LA, aCL (IgG/IgM), anti-¿GPPI antibodies (IgG/IgM) were present in the group that developed myocardial infarction (Chi square test: p < 0.05 for all aPL) (Table 2).

Conclusions: The aGAPSS is based upon a quantitative score and could aid risk stratifying APS patients younger than 50 years for the likelihood of developing coronary thrombotic events and may consequently guide pharmacological treatment for high-risk patients.

References:

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1600

FRIO718 POSITIVE CONVERSION OF TUBERCULOSIS SCREENING RESULTS AND INCIDENCE OF ACTIVE TUBERCULOSIS INFECTION IN PATIENTS RECEIVING BIOLOGIC TREATMENT

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Background: Previous studies reported active tuberculosis infections can occur during biologic treatment in patients with negative baseline LTBI screening. Current recommendations suggesting the annual testing for latent tuberculosis infections are mainly issued for patients with rheumatoid arthritis (RA) receiving anti-TNF inhibitors and there are lacking evidence for patients receiving non-TNF biologic agents and for patients with ankylosing spondylitis (AS) or psoriatic arthritis (PsA).

Objectives: The study was performed to investigate the conversion rate of initially negative tuberculosis screening test results during biologic treatment and the usefulness of repeated screening test for detecting unexpected tuberculosis infection in patients with RA, AS, and PsA.

Methods: A total of 95 patients (43 with RA, 50 with AS, and 2 with PsA) who had negative baseline interferon-y releasing assay (IGRA) results, which were assessed using QuantiFERON-TB Gold in tube (QFT-GIT), prior to initiation of biologic treatment were enrolled in this study. All patients received biologic agents for the treatment of their diseases and rescreening with QFT-GIT were performed in all patients after median 12 months from baseline test. Clinical characteristics were compared between converters and non-converters and incidence of active tuberculosis infection was evaluated.

Results: Patients were treated with different biologics (23 with etanercept, 50 with adalimumab, 5 with infliximab, 4 with golimumab, 1 with certolizumab pegol, 3 with abatacept, and 9 with tocilizumab). Positive conversions of initially negative IGRA were found in 13 (6% in patients with etanercept, 4 patients with adalimumab, 2 patients with tocilizumab and 1 patient with abatacept) of 95 patients (13.7%) after initiation of biologic treatment. Age over 50 years and diagnosis of RA were more common in converters. Multivariate analysis showed that age over 50 was an independent risk factor for IGRA conversion with OR 4.36 (95% CI 1.10 – 17.34, p=0.038). During biologic treatments, active tuberculosis infections were found in 3 of 13 converters (23%).

Conclusions: Although initial screening test showed negative results, the serial follow-up of tuberculosis screening test should be considered during biologic treatment in patients with rheumatic diseases to prevent unexpected tuberculosis infection.

References:

Acknowledgements: This study was supported by a grant of the Korean Health Technology R&D Project, Ministry for Health and Welfare, Republic of Korea (HI14C1174).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1286

FRIO718 PREVALENCE AND PATTERN OF COMORBIDITIES IN CHRONIC RHEUMATIC AND MUSCULOSKELETAL DISEASES: THE COMORD STUDY

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Background: Rheumatic and musculoskeletal diseases (RMD) frequently coexist with other conditions, resulting in multimorbidity, which may compromise arthritis management and lead to diminished quality-of-life and increased mortality. In 2016, EULAR published “Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases”, used to guide this study.

Objectives: The primary objective is to evaluate the prevalence and pattern of comorbidities in selected RMD in Lebanese patients. The secondary objective is to evaluate the gap between recommendations and routine comorbidities’ screening.

Methods: COMORD is an observational, cross-sectional, multicentric national study. Consecutive RMD patients (Rheumatoid Arthritis (RA), Osteoarthritis (OA), Systemic Lupus Erythematosus (SLE), Axial Spondyloarthritis (AxSpA) and Peripheral Spondyloarthritis (pSpA)) as diagnosed by the rheumatologist) were recruited at 6 practices from university hospitals and private clinics in Lebanon. Six axes of comorbidities (Cardiovascular, Malignancies, Infections, Gastrointestinal, Osteoporosis, Depression) were investigated using a case report form (patient interview). Optimal comorbidities screening was defined according to current recommendations and compared with monitoring in practice. Prevalences were presented descriptively. The number of comorbidities was correlated with predictive factors using Poisson Regression. Finally, Latent Class Analysis (LCA) was used to identify patterns of multimorbidity. All analysis were performed on IBM SPSS Statistics 23 and XLSTAT 18.07.

Results: 515 patients were recruited (196 RA, 161 OA, 75 AxSpA, 45 SLE, 40 pSpA). Mean age was 56y, 76% were female. There was no difference in the disease distribution between centers. The most common comorbidities were cardiovascular risk factors and diseases, followed by depression and osteoporosis. The number of comorbidities was significantly associated with age (p < 0.001), obesity (p < 0.001) and biotherapies (p = 0.05). LCA analysis identified 3 main clusters of multimorbidity: OA, RA, AxSpA (Fig 1). The most optimal screening was found for cardiovascular risk factors (84%). DXA was prescribed in 69% of correct indications. As for malignancies, mammograms and pap smears were the most optimally prescribed (26% and 28%). Colonoscopy and dermatology visit were prescribed in 22% and 18%. Correct vaccination (influenza and pneumococcal) was found in 17% and 8%. Predictive factors for optimal screening were age, university setting, social coverage, disease duration and biotherapy.

Conclusions: Comorbidities are prevalent in RMDs and follow specific multimorbidity patterns, with a predominance for cardiovascular, depression and osteoporosis. They are more frequent with age and obesity. Optimal screening needs to be improved.

References:
BURDEN OF HEPATITIS E VIRUS INFECTION IN PATIENTS WITH RHEUMATIC DISEASES

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Background: Hepatitis E virus (HEV) is considered an emerging pathogen in developed countries, potentially causing chronic hepatitis.

Objectives: This cross-sectional analysis was undertaken to determine the seroprevalence of HEV in patients with autoimmune or inflammatory arthritis. This subgroup of patients is often treated with immunosuppressive drugs, and is generally considered more susceptible to infections.

Methods: Serum samples were obtained from 449 consecutive patients consulting at the department of Rheumatology between October and November 2015. Patient characteristics with respect to diagnosis and treatment were collected. HEV IgM and IgG were measured by ELISA (Wantai Hepatitis E Virus IgG and IgM ELISA, Sardar SV). Positive or borderline samples were further analyzed for HEV RNA (RealStar® HEV RT-PCR Kit, Alton Diagnostics NRC WIV).

Results: A total of 449 patients were included, 211 men and 238 women. HEV IgG was positive in 82 samples (16.2%), 6 were borderline, and 5 were non-determinable (not enough serum). IgM was positive in only 2 samples (0.45%). These 2 patients had normal liver function tests. Additional PCR was performed on all positive and borderline samples, which turned out negative in all samples. Of the 88 IgG positive and borderline samples, 86 patients had a known diagnosis of chronic inflammatory arthritis, of which 50 patients had previously been diagnosed with rheumatoid arthritis, 18 with spondyloarthritis, 8 with psoriatic arthritis. Fifty patients were treated with biologics (37 TNF inhibitors), 43 patients were treated with methotrexate (mean dose 12.5mg weekly), and 20 were treated with corticosteroids (mean daily dose 5.9mg prednisolone equivalent).

Conclusions: In a consecutive cohort of patients with known diagnosis of autoimmune or inflammatory arthritis, seroprevalence of HEV IgG was 18.2%. No active HEV infection could be detected. We found this to be comparable to a historical cohort of healthy patients from the departments of Orthopedics and obstetrics1, where prevalence of HEV IgG was 14%.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5115

CHARACTERISTICS OF PATIENTS WITH GOUT TREATED TO SUA TARGET THAT CONTINUE TO EXPERIENCE FLARES:

BACKGROUND, JOB RELATED, HEALTH RELATED AND PSYCHOSOCIAL FACTORS AND THREE DIFFERENT MEASURES OF PRESENTEEISM: RESULTS FROM EULAR-PRO AT-WORK PRODUCTIVITY STUDY

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Background: Several measures of at-work productivity loss (i.e. presenteeism)
exist, varying in concept, recall period, and attribution. As a consequence, the contribution of contextual factors may vary which has important implications when considering these factors in studies evaluating the impact of inflammatory arthritis (IA) and osteoarthritis (OA) on presenteeism.

**Objectives:** To determine demographic, job related and health related factors associated with three different global measures of presenteeism in patients with IA or OA.

**Methods:** This large cross-sectional international EULAR-PRO study (n=8 countries) includes patients with RA, PsA, AS or OA in paid employment. Data collection included: demographics, job characteristics, health related and psychosocial factors. Patients also completed three global measures of presenteeism, varying in content, attribution and recall period. The Work Productivity Scale–Arthritis (WPS-A) measuring the affect of arthritis on productivity during the last 7 days, the Work Productivity and Activity Impairment Questionnaire (WPAI) measuring interference of arthritis on productivity in the last month, and the Work Ability Index (WAI) a generic scale measuring current ability to work. For interpretation purposes the scale of the WAI was reversed in this study. Due to skewed data, univariable median regression analyses were performed to assess the association between independent variables with each individual presenteeism instrument.

**Results:** 503 patients with IA/OA were recruited in this study with a mean age of 47 (SD=10) yrs and disease duration of 12.6 (SD=10) yrs. Except for male patients reporting a lower WPS-A score, no other demographics were significantly associated with presenteeism (Table). Being neutral/unsatisfied about the job, not being able to organize one’s own work, reporting higher VAS well-being and disability scores, and experiencing reduced quality of life were all significantly associated with higher presenteeism, a result observed for all three instruments. Furthermore, those with higher anxiety and depression scores also reported having more problems at work due to ill health. Differences between instruments were especially observed between the WPAI (affect of ill health on productivity)/WPS-A (interference of illness on productivity) and WAI (generic scale on ability to work) in relation to job demands, receiving help from colleagues and the option to postpone work.

**Conclusions:** This is the first study investigating the association of many contextual factors with three commonly used global measures of presenteeism. Overall, job satisfaction and the ability to organize one’s own work are the most important job characteristics associated with presenteeism and should be considered when measuring presenteeism.

**References:**


**Acknowledgements:** Funding: EULAR, AbbVie, BMS.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.5161

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**FR10723 TEMPORAL PATTERNS OF SEDENTARY BEHAVIOUR AND PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid Arthritis (RA) is associated with increased risk of cardiovascular disease (CVD). Recent evidence suggests sedentary behaviour (waking behaviour ≤1.5 metabolic equivalents whilst sitting/lying) may contribute towards the progression of RA outcomes, including heightened CVD risk. Sedentary behaviour occupies the majority of waking hours among people with RA (1). However, the proportion of time spent sedentary is likely to fluctuate over the course of the day, with periods of high sedentarity representing more optimal opportunity for intervention, and thus potentially higher intervention efficacy.

**Objectives:** The aims of this study were: 1) to explore temporal patterns of sedentary behaviour (and physical activity) among RA patients, and 2) to examine associations between temporal sedentary patterns and predicted 10-year risk of CVD.

**Methods:** Patients with RA (N=97) wore a GT3x accelerometer for 7 days to assess habitual sedentary time (<100 counts/min) and physical activity (PA; light =100–2000 counts/min). Accelerometer data were analysed separately for each hour (valid hour criteria; 60-minutes of data on ≥3 days, including a weekend day). To evaluate 10-year risk of CVD (Q-risk2), patients reported their medical history, provided a fasted blood sample and underwent assessments of blood pressure and body-mass index.

**Results:** Temporal patterns of sedentary time and PA are reported in Figure 1. Sedentary time declined throughout the morning (08:00–12:00). During the afternoon, sedentary time increased by 4.5 minutes (12:00–18:00; M =34.95±6.76 to M =39.06±7.91). A more marked increase in sedentary time was observed during leisure time (18:00–22:00; M =39.06±7.91 to M =47.90±6.30). Repeated measures analysis of variance (ANOVA) revealed sedentary time was significantly higher during leisure time (M =46.20±5.46) compared to the morning (M =36.89±5.81), and afternoon (M =39.50±6.7). Significant differences remained even after controlling for employment status (i.e., employed vs. unemployed/student, F(2,23)=1.40, p=0.27). Patients who accumulated M =45.31 sedentary minutes during their leisure time (18:00–23:00; median split), had significantly higher 10-year risk of CVD (M =22.93±13.85) compared to those accumulating M =45.31 sedentary minutes (M=6.09±7.62) [t(41)=3.92, p<0.01]. Finally, hourly patterns for light PA were the reverse of those observed for sedentary time. Hourly MVPA engagement was consistently <3 minutes (peak MVPA at 09:00–10:00, M =24.7±4.16).

**Conclusions:** Interventions targeting leisure time sedentary behaviour (18:00–23:00) may be more effective than interventions targeting work or travel time sedentary behaviour (08:00–18:00). Patients who accumulated higher sedentary time during leisure time may have the greatest potential for sedentary time reduction and associated improvements of CVD risk profile. Due to inverse patterns of engagement, replacing leisure time sedentary behaviour with light PA may offer an effective intervention approach.

**References:**


**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.5901
**FR0724** PREDICTORS OF PRESENTEEISM AND ABSENTEEISM IN PATIENTS COMMENCING TREATMENT WITH METHOTREXATE MONOTHERAPY OR BIOLOGIC THERAPY FOR RHEUMATOID ARTHRITIS

S. Leggot 1, M. Lunt 1, A. Barton 2, K. Hyrich 1, K. Walker-Bone 3, S.M. Verstappen 1 on behalf of RAMS and BRAGGSS co-investigators. 1Arthritis Research UK Centre for Epidemiology; 2Arthritis Research UK Centre for Genetics and Genomics, The University of Manchester, Manchester, UK; 3Arthritis Research UK/MRC Centre for Musculoskeletal Health and Work, The University of Southampton, Southampton, United Kingdom

**Background:** The adverse effects of RA on absenteeism (i.e. days absent from work) and presenteeism (at-work productivity loss) are increasingly recognised as an important issue. Research suggests the reasons are multifactorial with many factors such as disease severity, quality of life and psychological well-being, amongst other factors, can predict improvements in presenteeism and absenteeism at one year in patients on either MTX or biologics for the first time.

**Objectives:** To identify predictors of presenteeism and absenteeism over one year in patients with RA commencing treatment with methotrexate (MTX) or biologics for the first time.

**Methods:** Patients recruited to the Rheumatoid Arthritis Methotrexate Starters study (RAMS) or the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS), and in full or part-time paid employment were included in this analysis. Demographic (e.g., age), clinical (e.g., DAS28), and psychological data (e.g., Hospital Anxiety and Depression scale (HADS)) were collected at baseline. Indicators were followed up at six months and one year in both cohorts. Absenteeism in the last month (days missed), and presenteeism (0 = no interference – 10 = complete interference), were measured at all three points using the RA specific Work Productivity Survey (WPS-RA). Patients with at least one follow-up post baseline were included in this analysis. Due to excessive zeros in the WPS-RA, a repeated measure zero inflated negative binomial regression (ZINB) was used to test the association between baseline demographic, clinical and psychological variables and presenteeism and absenteeism over one year.

**Results:** Data was available for 191 patients in BRAGGSS and 308 in RAMS. In BRAGGSS, 51% of patients (n = 98) reported >1 days absent from work at one year, median symptom duration was 8 years (IQR 5–13); 78% female. In RAMS, the mean age was 52 years (SD 9.6), median symptom duration was 8.5 months (IQR 5–23); 66% female. At baseline, 26% (BRAGGSS) and 27% (RAMS) reported ≥1 days absent from work, and the median presenteeism scores were 5 (IQR 3–7) and 4 (IQR 1–7) for BRAGGSS and RAMS respectively. Presenteeism scores significantly improved over one year in both cohorts (BRAGGSS: median 2 [IQR 0–5], RAMS: median 2 [IQR 0–4] ). Kruskal-Wallis p < 0.001), as did absenteeism for both cohorts although non-significant. The ZINB revealed similar predictive patterns in both cohorts for presenteeism and absenteeism (Table 1). For example, for every 0.06 increase in EQ-SD (clinically important difference), the odds of being in the zero presenteeism group (i.e. no at-work productivity loss) over one year increased by a factor of 1.2 in BRAGGSS, and was similar in RAMS. In RAMS, a one unit increase in VAS fatigue decreased the odds of having no absenteeism over one year by a factor of 0.97.

**Table 1:** Demographic, clinical, and psychological predictors of presenteeism and absenteeism over one year

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fitted Beta</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.005</td>
<td>0.004</td>
<td>0.006</td>
</tr>
<tr>
<td>Gender (female = 1)</td>
<td>0.039</td>
<td>0.021</td>
<td>0.043</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>-0.013</td>
<td>0.012</td>
<td>0.060</td>
</tr>
<tr>
<td>Rapid ESX (ESX ≥ 28)</td>
<td>-0.058</td>
<td>0.034</td>
<td>0.029</td>
</tr>
<tr>
<td>VAS fatigue (0–10)</td>
<td>-0.074</td>
<td>0.039</td>
<td>0.007</td>
</tr>
<tr>
<td>VAS anxiety (0–10)</td>
<td>-0.045</td>
<td>0.035</td>
<td>0.037</td>
</tr>
<tr>
<td>EQ-5D (≥ 0.5)</td>
<td>-0.039</td>
<td>0.020</td>
<td>0.037</td>
</tr>
</tbody>
</table>

**Conclusions:** The results from this analysis support the notion of a multifactorial relationship between RA and work outcomes. The results suggest that greater quality of life and psychological well-being, amongst other factors, can predict improvements in presenteeism and absenteeism at one year in patients on either MTX or biologics for RA.

**Acknowledgements:** Funding: Pfizer I-CRP

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5077

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**FR0726** LONG TERM USE OF ANALGESICS AND NSAIDS IN EARLY RA: LESSONS FROM THE CARERA STUDY

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**Background:** One might consider pain accompanying musculoskeletal conditions as a separate illness entity deserving specific treatment. A subgroup of early Rheumatoid Arthritis (RA) patients has remaining pain despite adequate disease control and this might be reflected in the use of analgesics and NSAIDs.

**Objectives:** To investigate the usage of analgesics and antiphlogistics prospectively in the pragmatic randomized controlled CareRA trial and describe the users of such drugs taking into account body mass index (BMI), VAS pain and disease activity.

**Methods:** This study utilized data from the CareRA trial, a 2-year prospective randomized controlled trial investigating the use of conventional disease-modifying anti-rheumatic drugs (possibly/definitely RA-related or other). Meaningful sub-classifications were made (analgesics, cox2-selective and non-selective NSAIDs). We defined two dose classes of each drug, defined by the number of tablets, dose, frequency/timing, continuous/intermittent use, start/end date and indication.

**Results:** Of the total population, 15, 5% (53 patients) started long-term analgesics/NSAIDs before/at BL (pre-induction group) and 13% (45 patients) from w28-w52 (post-induction group).

**Conclusions:** Risk factors of ILD in MCTD are DLOC less than 60% of predicted, high titer RNP antibodies, no previous arthritis and increasing age.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1841

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**FR0725** PREDICTION OF INTERSTITIAL LUNG DISEASE IN MIXED CONNECTIVE TISSUE DISEASE

S. Reiser 1, R. Gunnarsson 2, T.M. Aalekken 3, M.B. Lund 4, J. Corander 5, P. Verschueren 1,2 on behalf of MRC and Clinical Research Centre, KU Leuven; 2Sk...
A detailed distribution of on-demand/daily analgesic/NSAID use is provided in the table below.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Group of long-term users</th>
<th>NSAIDs</th>
<th>Paracetamol</th>
<th>Opioids</th>
<th>Combined therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-selective</td>
<td>Selective</td>
<td>COX2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-induction (n=53)</td>
<td>26% (17%/d)</td>
<td>11% (4%/d)</td>
<td>45% (8%/d)</td>
<td>9% (6%/d)</td>
<td>9% (2%/d)</td>
</tr>
<tr>
<td>Post-induction (n=45)</td>
<td>33% (16%/d)</td>
<td>20% (7%/d)</td>
<td>33% (4%/d)</td>
<td>13% (7%/d)</td>
<td>0%</td>
</tr>
</tbody>
</table>

Proportionally more patients were using NSAIDs in the post-induction group and paracetamol in the pre-induction group. Mean DAS28CRP (BL-w104) in the pre-induction group was 3.11 (±0.70) and mean VAS pain 32.7 (±16.3). In this group 62.3% had sustained low disease activity while taking continuous analgesics/NSAIDs. Results in the post-induction group were comparable.

Analgesics/NSAID use was not significantly associated with mean (BL-w104 BMI) DAS28CRP or VAS pain.

Conclusions: Analgesics/NSAID intake in early RA was high (90%) and remarkably about 30% continued using these drugs, despite overall low disease activity. This high consumption might be explained by the ambiguous nature of arthritis-related pain and the lack of differentiation between nociceptive and non-nociceptive pain. Therefore pain management in early RA deserves more attention.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3399

FRI0727 IMPACT OF MATERNAL SYSTEMATIC AUTOIMMUNE RHEUMATIC DISEASES ON NEONATAL OUTCOMES: A POPULATION-LEVEL ANALYSIS

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Background: The impact of systemic autoimmune rheumatic diseases (SARDs) on peripartum outcomes is not well described at a population level despite the potential for active disease in this period.

Objectives: We examined the association between SARDs and neonatal outcomes in a contemporary pregnancy cohort in the province of Alberta, Canada.

Methods: The patient population consisted of women giving birth between January 1, 2005 to December 31, 2014 (n=312,081). For women with multiple births after January 1, 2009), and neonatal outcomes among women with and without SARDs were compared.

Results: Compared to women with no SARDs (n=311,755), women with SARDs (n=326; 0.1%) were slightly older (SARDs 31.3 vs No SARDs 29.3 years (p<0.01)) but did not differ in terms of rural residence, ethnicity, median household income or nulliparity. However, rates of pre-term delivery, emergent cesarean section, induction, hypertensive disorders/ecplampsia and mortality were higher among women with SARDs than those with no SARDs (Table 1). Offspring of women with SARDs had lower birth weights, were more likely small for gestational age (SGA), and had longer stays in neonatal ICU (Table 1). Among women with SARDs, prescription rates in the 270 days prior to delivery were highest for anti-malarials (Table 2). After multivariable adjustment, both NSAIDS use (OR (95% CI); 5.24 (1.57, 17.52), p<0.01) and steriod use (OR (95% CI); 3.15 (1.31, 7.59), p<0.01) were significantly associated with a higher risk of preterm delivery.

Conclusions: Women with SARDs are at an increased risk of adverse outcomes during pregnancy. The association between corticosteroid and NSAID use and preterm delivery requires further investigation. Our findings suggest the need for closer monitoring and coordinated care with obstetrics and perinatology in these high risk women.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4561

FRI0728 OSTEOARTHRITIS AND GOUT: REAL-WORLD EVIDENCE EVALUATING PATIENT CHARACTERISTICS, TREATMENT PATTERNS, AND HEALTHCARE UTILIZATION

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Background: Gout and osteoarthritis (OA) are common in the United States, but little is known about potential associations of OA and hyperuricemia/gout with clinical outcomes.

Objectives: This study examined variations in gout severity, management, and healthcare utilization among gout patients with and without OA.

Methods: Data were assessed from a survey of US physicians and patient chart audits. Participating physicians managed the care of >50 patients with gout annually; chart audits were of their most recent 5 consecutive adult patients with confirmed gout. Gout severity was measured by physician global assessment, flares, organ/joint damage, and tophi. Treatment characteristics, presence of clinician-confirmed OA, and sociodemographic factors were identified. Descriptive and multivariate (stepwise logistic regression) statistics analyzed the differences among gout patients with and without clinician-confirmed comorbid OA, and assessed urate-lowering therapy (ULT) use and gout control.

Results: Overall, 1159 charts of gout patients were abstracted (230 w/ OA, 929 w/o; 81% male; 71% white); the proportion of patients aged >61 was greater for those with gout and OA than those with gout but without OA (63% vs 32%; P<0.001). Patients with gout and OA had longer mean duration of gout (63 vs 41 months), were more likely to have tophi (44% vs 19%), joint damage (31% vs 11%), and clinician-rated severe gout (31% vs 12%) than those without OA (all P<0.01). Patients with gout and OA were also more likely to receive ULT (89% vs 70%; P<0.01), and among those receiving ULT, OA patients treated with allopurinol received a higher average daily dose (325 mg vs 286 mg; P<0.001). Gout patients with OA were more likely to have additional comorbidities (cardiovascular disease, kidney disease, COPD, depression, diabetes, hyperlipidemia, hypertension, obesity, prostate problems [men]) and have chronic pain than those without OA (all P<0.05). Gout patients with OA reported more office visits (4.0 vs 3.5), were more likely to have an emergency (31% vs 17%), and hospital (17% vs 11%) admission, and more likely to require surgery for gout in the past 12 months (3% vs 0.3%) (all P<0.01). In both groups, ULT use was associated with better gout control, but the specific factors predictive of ULT use and disease control varied between those with and without OA.

Conclusions: Gout patients with OA were more likely to have a greater impact on health system spending, with additional comorbidities and more severe gout than those without OA. These data suggest that gout patients with OA constitute a less healthy group in need of more careful monitoring and more aggressive gout management.

Acknowledgements: This study was sponsored by AstraZeneca.


DOI: 10.1136/annrheumdis-2017-eular.5030
DEFINITION OF REMISSION AND MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: In psoriatic arthritis (PsA) a state of minimal disease activity (MDA) or remission are the target of treatment [1], but due to the heterogeneity of disease manifestations, it is still an unmet need. Coates et al [2] have developed and validated a composite score for MDA that encompasses most disease domains. However, for disease remission there is no accepted definition, whereas studies “borrowing” measures from rheumatoid arthritis or using their own criteria.

Objectives: The objective of this study was to analyse existing data on the definition of MDA and remission in studies on PsA.

Methods: A systematic literature review was performed. Studies evaluating remission or minimal disease activity in PsA either as a primary or secondary outcome, published between 2007–2017, were identified using the terms (“psoriatic arthritis”) AND (“remission” OR “low disease state” OR “low disease activity” OR “minimal disease state” OR “minimal disease activity”). Studies assessing disease activity in general, without specifically mentioning remission or MDA were not included; reviews and case-reports were also excluded.

Results: Two hundred and thirty-five publications were identified, of which 56 were included in the final analysis. The majority were observational studies (65.5%) and there were no RCTs identified. In total, 10843 PsA patients were analysed: 8779 in observational studies and 2064 in intervention trials; 4823 patients fulfilled the CASPAR criteria [3] and 6667 (31 studies) were taking a biologic drug at their inclusion. The majority of the studies assessed either MDA (65.5%) or remission (60%), but only 14 studies (25.5%) assessed both of the two outcomes. MDA or remission were mainly used as a secondary outcome (52.7% of the studies).

MDA was assessed mainly in observational studies (61.7%) and in almost all cases (89.9% of the studies) the definition used was the one proposed by Coates et al [2]. Remission was also assessed mainly in observational studies (63.8%). The most used definition (57.6%) was based on the disease activity score (DAS28), with values less than 2.6 considered as “remission”. Articular (63.8%). The most used definition (57.6%) was based on the disease activity outcome (52.7% of the studies).

Conclusions: None declared


THE NEED FOR HOSPITAL ADMISSION FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN WESTERN AUSTRALIA LEADS TO A DOUBLING OF THE ALL-CAUSE MORTALITY RISK AS SEEN IN CONTROLS, ESPECIALLY FOR MEDICARE RELIANT AND MALE PATIENTS

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Background: Hospitalisation for Systemic Lupus Erythematosus (SLE) is a significant event.

Objectives: We aimed to understand the factors leading to an incident admission and its impact on long term outcome in SLE patients in Western Australia (WA).

Methods: Using whole-population data linkage of hospital admissions, cancer registrations and death records in WA from 1980 to 2015, we performed a retrospective comparative analysis for all patients admitted with a first ever primary diagnosis of SLE (ICD-9-CM 695.4, 710.0, ICD-10-L93.0 & M32). For SLE patients, we analysed annual incident hospitalisation rates and compared patient characteristics, all-cause mortality and cancer risk (by Kaplan-Meier and Cox regression) versus age- and gender-matched controls free of rheumatic disease.

Results: The incident hospitalisation rate for SLE (mean 20.9/million/year; CI: 11–35) showed little variation. SLE patients were younger, more likely to be indigenous, uninsured, have kidney and cardiovascular disorders and to die during their first hospitalisation (Table 1). Cancer risk was equivalent, but a first admission for SLE doubled the risk of subsequent death (OR=1.99, CI: 1.5–2.7, p<0.001) (Figure 1/Table 2). Medicare reliance (OR 1.7, CI: 1.4 – 1.9, p<0.001) and male gender (OR 1.4, CI: 1.0 – 1.8, p<0.001) were the strongest independent predictors of death.

Conclusions: Hospitalisation rates for SLE in WA have not decreased over 25 years. Once hospital-based management for SLE was required, the risk of all-cause mortality doubled compared to age and gender-matched controls. This risk was greatest in Medicare reliant or male SLE patients and not due to increased cancer risk.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5813

ARE THERE ANY IMPACT OF RAPID RADIOLOGIC PROGRESSION ON MORTALITY IN HUNGARIAN RHEUMATOID ARTHRITIS PATIENTS?


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Background: Prognosis of rheumatoid arthritis (RA) should be assessed early during the disease course. Rapid radiological progression (RRP) has been defined as a ≥1% unit increase in van der Heijde-Spear score within a year. The RA risk model has been developed by Vastesaeger et al in 2009. This tool calculates RRP based on non-radiographic indicators such as baseline CRP, RF and swollen joint count.

Objectives: We wished to test the matrix prediction model in the very first Hungarian cohort study.

Methods: In this non-interventional, cross-sectional retrospective study carried out in 11 Hungarian arthritis centres, we assessed high risk (≥40%) of RRP in biologic-naïve RA patients with active disease. In order to obtain a representative sample, patients were selected from each centre by a random technique. RRP was calculated according to the matrix model described by Vastesaeger et al. As a secondary endpoint, we compared methotrexate (MTX) responders vs non-responders with respect to RRP.

Results: We screened data of 1843 RA patients. Finally, data obtained from 1356 patients could be used for RRP prediction and MTX responsiveness. The mean age of patients was 55.5 years, 84.7% were women. The mean disease duration was 8.4 years. At the time of the assessment, mean CRP was 17.7 mg/l, RF was 139.3 IU/ml, mean DAS28 was 5.00 and mean swollen joint count was 6.56. High risk (≥40%) of RRP could be determined in 18.2% of patients. Among continuous variables other than those used for calculation of RRP risk, RA patients with the risk of RRP>40% (n=247) had significantly lower age than those with RRP<40% (n=1109) (53.33±12.31 vs 56.02±13.50 years; p=0.001).

With respect to binary variables, the risk of RRP>40% was significantly associated
with non-response to MTX (OR: 17.82), male gender (OR: 1.53), ACPA positivity (OR: 2.11), the presence of erosions (OR: 1.37) and current smoking (OR: 1.66). Binary logistic regression analysis revealed that MTX non-response (OR: 16.84), male gender (OR: 1.67) and ACPA positivity (OR: 2.18) were independent predictors of high-risk RRP (≥40%). With regards to MTX responsiveness, binary logistic regression analysis confirmed that both male gender (OR: 5.20) and the presence of erosions (OR: 7.98) were independent predictors of high RRP risk in the MTX responder subpopulation.

Conclusions: In the first biologic-naive Hungarian RA cohort assessed for RRP, RRP occurs in almost one-fifth of the patients. These patients differ from others in various clinical and serological parameters. RRP has also been associated with non-response to MTX.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3199
Lack of obesity-related features in adipocytes

Methods:

Results:

Obesity affects IFP.

Conclusions:

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particles are targeted by autotagonistic antibodies from RA and other systemic rheumatic diseases.

Methods: Using a protein macroarray we identified JKTBP in humans and animal models of inflammatory rheumatic diseases. Bacterially expressed recombinant JKBFP proteins were used to confirm the obtained data. Epitope, TLR7/9 and DNA methylation inhibitors determined by ELISA. JKTBP expression in cultivated cells and synovial tissue was analysed by indirect immunofluorescence, immunoblot and immunohistochemistry.

Results: Anti-JKTBP autoantibodies were detected in 46% of the patients with systemic lupus erythematosus (n=103), in 20–30% of the patients with rheumatoid arthritis (n=286), in 10% of the patients with mixed connective tissue disease (n=20) or spondyloarthropathy (n=20), and in <10% of patients with other autoimmune disorders (n=382). Sera positive to JKTBP as well as hNRNP-B1, revealed nearly two thirds of the RF IgM/CCP2-seronegative patients as early RA patients. Combining sensitivities to all autoantigens tested (JKTBP, AUF1, hNRNP-B1), it was possible to identify 92% of the early RA patients (n=91).

In the MRL/lpr mouse model of SLE, mice deficient of MyD88 and TLR7/9 lacked anti-JKTBP autoantibodies, whereas mice deficient of SIGIR/TIR8 showed enhanced anti-JKTBP autoantibody production. These results show that autoantibody generation against JKTBP, AUF1, hNRNP-B1 is dependent on TLR 7 and TLR 9 rheumatoid factor different to TLR 7 dependent generation of snRNPs. For all tested autotagons either their titter or generation are dependent on the activation of innate immune genes MyD88 and SIGIRIR/TIR8 gene.

Conclusions: These data identify SG as targeted particle in RA and JKTBP as a novel autoantigen in RA patients. JKTBP autoantibodies are also found in patients with models of inflammatory rheumatic diseases and autoimmune disorders.

Phagocytosis was superior in M2 (IL10) and M2 (IL4) activated MDM than in M1 MDM. Anti-TNF agents but not TCZ or RTX induced an increase of phagocytosis in M1 MDM.

**Conclusions:** Anti-TNF agents upregulate M2 alternative pro-resolving markers and downregulate M1 inflammatory markers in macrophages. Our results need to be extended by transcriptional analysis and evaluated in RA patients.

**References:**

**Disclosure of Interest:** Y. Degboe Grant/research support from: Société Française de Rheumatologie, B. Rauwel: None declared, M. Baron: None declared, J.-F. Boyer: None declared, A. Cantagrel: None declared, A. Constantin: None declared, J.-L. Davignon: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2408

**SAT0007**

**GROUP 3 INNATE LYMPHOID CELLS NUMBERS IN PERIPHERAL BLOOD PREDICT USTEKINUMAB (STELARA) THERAPY RESPONSIVENESS IN PSORIATIC DISEASE CASES WITH SUBCLINICAL IMAGING ENTHESOPATHY**

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**Background:** Ustekinumab targets the common p40 sub-unit of interleukin-12 (IL-12)/interleukin-23 (IL-23). In patients treated with Ustekinumab for psoriasis where patients were selected on the basis of subclinical imaging enthesopathy, we have noted an improvement in subclinical imaging enthesopathy (Savage LJ et al submitted), raising the possibility that it may be possible to find a biomarker for predicting response to therapy in psoriatic disease. Innate lymphoid cells may be centrally involved in the pathogenesis of psoriatic skin and joints disease, since they express IL-23R receptor and are associated with IL-17/IL-22 production.

**Objectives:** This work was performed to test the hypothesis that peripheral blood ILC perturbations may be useful in defining response in psoriasis cases with imaging confirmed subclinical enthesopathy.

**Methods:** Peripheral blood collected at baseline (before therapy, 24 weeks, 54 weeks) from patients in the MUSTEK trial (Ustekinumab in psoriasis cases selected on the basis of subclinical imaging enthesopathy) was analysed. ILC3s were identified as lineage negative (CD3- TCR- CD14- CD11c- CD1a- CD303- FcεRI- CD34- CD123-) with positive expression of CD127, IL22, and CCR6. ILC2 cells were identified as Lineage- CD127+ and CRTH2 positive, while ILC1 were identified as Lineage- CD127-, CD127+ and CCR6 positive. No correlation was found with total ILCs (ILC1,2, AND 3) (R=0.104, p>0.05).

**Results:** No correlation was found with total ILCs (ILC1,2, AND 3) (R=0.104, p>0.05). ILC3s were inversely correlated with the reduction in the PASI score (R =0.404, p=0.038). Interestingly, those patients with reduction below 90% of PASI score has a significantly higher absolute numbers of ILC3+ cells in peripheral blood at the baseline than PASI (n=6/23) than super-responder group (n=17/23).

**Conclusions:** The data obtained indicate that, IFN-DCs from RA patients at baseline ILC3s was inversely correlated in with the reduction in the PASI score (R =0.404, p=0.038). No correlation was found with total ILCs (ILC1,2, AND 3) (R=0.104, p>0.05).

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1249

**SAT0008**

**DRUG THERAPY ENHANCES TOLEROGIC PROPERTIES OF DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control auto-reactive T-lymphocytes, the enhancing of tolerogenic properties of DCs seems to be a new important strategy in treatment of RA. The experimental research in animals and human in vitro studies revealed the capacity of anti-rheumatic drugs to inhibit stimulating activity and to enhance tolerogenic functions of DCs. The aim of this work was to investigate the role of different drug therapies on DC functions in RA patients.

**Objectives:** The aim of our study is to investigate, whether drug therapies influence the properties of monocyte-derived DCs generated in the presence of IFNs (IFN-DCs) in RA patients, and if the effect of disease-modifying anti-rheumatic drugs differ from that of biological/pulse steroid therapy.

**Methods:** Thirty nine patients with RA with high and moderate activity of disease were recruited in this study. All patients fulfilled ACR/EULAR criteria (2010). Nineteen patients received methotrexate, lefunomide, sulfasalazine or their combination (RA1). Twenty patients were at pulse therapy (methypredinsolone 500mg No. 3) or biological drugs (adalimumab or rituximab) (RA 2). All studies were performed after receiving informed consent. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α in the absence and presence of dexamethasone, applied on third day (LPD) or as maturation stimuli added on fourth day. The expression of CD14, CD83, CD 86, B7H1, HLA-DR, TLR-2 on the surface of DCs was measured by flow cytometry. The functions of DCs were evaluated by measuring cytokine production and DC allostimulatory activity in mixed lymphocyte reaction (MLR).

**Results:** Both DC-RA1 and DC-RA2 where shown to display impaired maturation evidenced by elevated expression of CD14 and decreased number of mature (CD14+CD83+) DCs. Whereas, DCs-RA2 demonstrated several additional differences, including increased number of intermediate CD14+CD83+ cells (compared with donors DCs), higher expression of inhibitory molecule B7-H1 (PD-L1) (compared with donors DCs and DCs-RA1) and tendency to lower expression of CD86 and higher expression of TLR-2. Besides, DCs-RA2 produced higher concentrations of IL-6 and had 2-fold lower allostimulatory activity then DCs-RA1. These differences together with phenotypic changes suggested more pronounced tolerogenic properties of DCs-RA2. Despite the revealed DC differences in RA1 and RA2 patients both types of DCs preserved in vitro sensitivity to dexamethasone, that suppressed the production of TNF-α and reduced allostimulatory activity. The data obtained indicate that, IFN-DCs from RA patients at drug treatments are characterized by tolerogenic properties, which are more pronounced in patients with biological or pulse steroid therapy.

**Disclosures of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5347

**SAT0009**

**DISTRIBUTION AND INTRACELLULAR SETTING OF GRANULYSIN IN WOMEN WITH KNEE OSTEOARTHRITIS**

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**Background:** The role of the cell-mediated immune response is recently recognized in osteoarthritis (OA) (1). Granulysin (GLY) is mediator of cellular immunity and cytotoxic molecule expressed in T and NK cells in regulatory (15 kDa) and cytotoxic (9 kDa) forms (2). Cytotoxic 9 kDa form of GLY mediates apoptosis of eukaryotic cells (3) and might be responsible for silent unscheduled apoptosis of joint tissue cells in patients with OA without clinically recognized

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2408
systematic immune reaction, as measured by erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (4). We investigate GNLY distribution and intracellular setting in peripheral blood lymphocytes of patients with OA.

Objectives: Women with knee OA (17), and age and sex appropriated control (17) were tested. All of them signed informed consent before sampling of peripheral blood lymphocytes.

Methods: Medical history, clinical examination, X-ray and routine laboratory testing (ESR, CRP) were used for diagnosing OA. Peripheral blood mononuclear cells (PBMC) were isolated by gradient density centrifugation and used for multiple, simultaneous intracellular [total GNLY, 9 kDa GNLY, 15 kDa GNLY and Lyso-02-like membrane protein-1 (LAMP-1)] and surface antigens (CD3 and CD56) detection by immunofluorescence. Data were analyzed by flow cytometry or confocal microscopy.

Results: In OA and control samples the percentage of total GNLY+ cells and GNLY expressing NK and T cells did not significantly differ and correlate with ESR and CRP. The frequency of GNLY+ cells was always higher in natural killer (NK) then in T cells and 9 kDa GNLY dominated over 15 kDa GNLY. However, 9 kDa GNLY co-localized more with the marker of cell degranulation, LAMP-1 in polarized granules of OA patients when compared to the control or to the 15 kDa GNLY.

Conclusions: The increase in the expression of cytotoxic (9 kDa) over regulatory (15 kDa) GNLY form in PBMC and its intracellular setting in polarized exocytic granules suggests the involvement of activated GNLY+ lymphocytes in the immunopathogenesis of knee OA, indispensable of ESR and CRP.

References:

Acknowledgements: The experiments were financed by the University of Rijeka (No.13.06.1.0.06) and “Thalassotherapia- Opatija”, Opatija, Croatia.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5499

SAT0010 | THE DAMP PROTEIN S100A8/A9 IS CRUCIALLY INVOLVED IN MYELOID-DERIVED SUPPRESSOR CELL (MDSC) DIFFERENTIATION AND FUNCTION IN COLLAGEN-INDUCED ARTHRITIS

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Background: Over the last years, the differentiation and activation of MDSC under tumor conditions has been studied extensively. Various tumor-derived factors have been identified in promoting the accumulation of this suppressive cell population. Recently, we determined the two ligands S100A8 and S100A9 as important factors in the differentiation of MDSC during tumor conditions. However, little is known about the S100A8/A9 driven expansion and activation, as well as the relevance of these cells in autoimmune diseases such as rheumatoid arthritis.

Objectives: We therefore analyzed the mechanisms involved in S100A8/A9 driven MDSC accumulation and their functional importance in a mouse model of rheumatoid arthritis.

Methods: To investigate the effect of S100A8/A9 on MDSC differentiation, bone marrow cells from wild type (wt), S100A8 knockout (A9ko) and S100A9 transgenic (A9tg) mice were analyzed. Accumulation of MDSC and their phenotypical characterization was performed by FACS analysis and functional characterization including arginase activity, NO- and ROS-production and T cell proliferation assays.

Results: The role of S100A8/A9 and MDSC in arthritus was investigated using the collagen-induced arthritis (CIA) mouse model. Accumulation of MDSC in different organs was analyzed by FACS and systemic S100A8/A9 levels were measured by ELISA. Ex vivo functional analysis of purified MDSC was performed to assess the potential of these MDSC to inhibit T cell responses.

Conclusions: Our in vitro studies reveal that, in the presence of S100A8, myeloid progenitor cells differentiate to immature cells that phenotypically as well as functionally resemble MDSC. These cells are characterized by co-expression and up-regulation of arginase activity, NO- and ROS-production, and exhibit strong inhibitory effects on the proliferation of both CD4- and CD8-positive T cells. Furthermore, accumulation of MDSC by extracellular S100A8 was found to be mediated via the Toll-like receptor 4 signaling pathway. In addition, lack of intracellular S100A8/A9 results in a decreased number of MDSC as well as a reduced suppressive activity of these cells, implying a dual role of these proteins for MDSC differentiation and function.

Investigating the role of S100A8/A9 and MDSC in a mouse model of CIA, a clear correlation between disease scores, MDSC numbers and systemic S100A8/A9 levels was observed. Furthermore, disease activity was reduced in wt and A9tg mice compared to A9ko mice and was in line with an increased accumulation of MDSC in the lymph nodes. Next to an enhanced suppressive activity of MDSC isolated from lymph nodes of wt and A9tg mice, these MDSC promoted the accumulation of regulatory T cells (Treg) whilst suppressing the differentiation of TH17 cells. In contrast, MDSC isolated from lymph nodes of A9ko mice had no effect on Treg differentiation and did not inhibit TH17 emergence.

Conclusion: Our in vitro data and results clearly show a S100A8/A9 dependent accumulation of cells that phenotypically as well as functionally resemble MDSC also under non-tumor conditions. In vivo data strongly support the importance of these findings. By influencing MDSC accumulation and function, S100A8/A9 is critically involved in regulating the disease outcome in rheumatoid arthritis, implying an important role for S100A8/A9 derived MDSC in regulating immune reactions during autoimmune diseases.

Disclosure of Interest: None declared.


SAT0011 | THE ACTIVATION OF MUSCARINIC ACETYLCHOLINE RECEPTORS INFLUENCES THE ONTOGENY OF NEUTROPHILS

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Background: There is growing evidence that nervous and immune system communicate with each other through soluble mediators.1 Immune cells such as neutrophils express muscarinic acetylcholine receptors (mACHR), which are neuroimmune receptors and highly prevalent in the nervous system.2 Aberrant neuroimmune functioning plays an important role in various autoimmune diseases. Dysregulation of neutrophil immune responses such as oxidative burst and migration is one of the key mechanisms leading to tissue damage in autoimmune diseases.3 However, the impact of mACHR activation on neutrophils remains understudied.

Objectives: We aimed to determine effects of muscarinic receptor activation on development and functions of neutrophils.

Methods: Neutrophils were isolated from peripheral blood of healthy donors by dextran sedimentation. After one hour in the absence or presence of the natural ligand acetylcholine (Ach) (10nM-100μM) or the muscarinic agonist oxotremorine-m (oxo-m) (10nM-100μM), neutrophil respiratory burst was analyzed by dithyrodhodamine (DHR) flow cytometry assay and migration assessed by transwell assay in response to N-formylmethionyl-leucyl-phenylalanine (fMLP). Cells that migrated were quantified by flow cytometry. To analyze the effects mACHR activation on the development of neutrophils, HL-60 cells were incubated in the presence of DMSO (1%), oxo-m (100μM) or DMSO plus oxo-m. After 6 days, cells were harvested and expression of maturation markers (CD15, CD63 and CD16) as well as mACHR (M1-M5) were measured by flow cytometry.

Results: We observed no effects of mACHR activation on the respiratory burst of neutrophils. However, both Ach and oxo-m inhibited neutrophil migration in a dose-dependent manner, but with peculiar differences. By increasing acetylcholine concentrations, we observed a reduction of neutrophil migration in a directly proportional manner. On the other hand, while the lowest dose (10nM) of oxo-m inhibited migration of HL-60 cells, the increase of oxo-m showed inversely proportional effects on neutrophil migration. Thus, we aimed to investigate, if the highest dose of oxo-m has a different effect on neutrophils ontogeny. In agreement with the results obtained with neutrophils, the incubation of HL-60 cells with the highest dose of oxo-m showed no effect on oxidative burst and migration and induced no changes in the expression of mACHRs (M1-M5), CD16 and CD63 in HL-60 cells. However, we observed that it resulted in significantly increased surface levels of the neutrophilic lineage marker CD15.

Conclusions: Our data indicate a differential activation of mACHR affecting different steps of neutrophil ontogeny. Considering this finding, abnormalities in the activation of muscarinic receptors as have been observed in autoimmune diseases might contribute to neutrophil dysfunction and need further investigation.

References:

Disclosure of Interest: None declared.


SAT0012 | S100A8/A9 INCREASES THE MOBILIZATION OF LY6C HIGH MONOCYTES TO THE SYNOVIAL DURING EXPERIMENTAL OSTEARTHROPATHY

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Background: It is increasingly recognized that part of the pathology in osteoarthri-
RESULTS: Injection of S10A9 into the knee joints of naive mice resulted in an elevated expression of monocyte-related markers (Ly6C, CCR2, and CX3CR1) within the synovium after 1 and 3 days, suggesting that S10A9/A9 is directly involved in the activation of monocytes. At CioA day 7 in WT mice, numbers of Ly6C+ monocytes, but not Ly6Chigh monocytes, were strongly increased (7.6-fold) in the synovium as compared to saline-injected control joints. In contrast, S10A9 KO mice showed a significant increase in Ly6Chigh monocytes (2-fold), whereas the number of Ly6C+ monocytes remained unaffected. Concurrently, a strong upregulation of several monocyte cell adhesion molecules (ICAM-1, ICAM-2, ICAM-1, KC, and MIP1α) was observed locally in the synovium, of which only the Ly6Chigh mobilization marker CX3CL1 was significantly higher in S10A9 KO mice, corresponding with the increased Ly6Chigh monocytes in the synovium of S10A9 KO mice. This could however not explain the local increased number of Ly6C+ monocytes at CioA day 7 in WT mice, and therefore we next investigated the major source of the monocytes, which is the BM. We observed a decrease of 14% of myeloid cells (consisting partly of Ly6Chigh monocytes) in the BM of WT mice at CioA day 7, whereas there were no changes in the BM of S10A9 KO mice, suggesting that S10A9/A9 affects the release of myeloid populations from the BM. In line with that, expression of adhesion molecules (LFA-1, VCAM, VE-cadherin, PECAM1, and L-selectin) was lower at CioA day 7 in the BM of S10A9 KO mice when compared to WT mice.

Conclusions: Local induction of OA leads to S10A9/A9 production, and therefore we next investigated the main source of the monocytes, which is the BM. We observed a decrease of 14% of myeloid cells (consisting partly of Ly6Chigh monocytes) in the BM of WT mice at CioA day 7, whereas there were no changes in the BM of S10A9 KO mice, suggesting that S10A9/A9 affects the release of myeloid populations from the BM. In line with that, expression of adhesion molecules (LFA-1, VCAM, VE-cadherin, PECAM1, and L-selectin) was lower at CioA day 7 in the BM of S10A9 KO mice when compared to WT mice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6181

Background: Dendritic cell (DC) are a heterogeneous group of antigen presenting cells that can be subdivided into CD1c+ and CD141+ DC. CD141+ DC are a rare population of DC that were first discovered in 2010 in human peripheral blood. Due to their rarity very little is known about the function of these cells in other tissue or in disease. These newly described DC subset have thus never been described in Inflammatory Arthritis (IA) or any of the rheumatic diseases.

Objectives: To identify DC in IA synovium and functionally assess if these cells play a pathogenic role in IA.

Methods: CD141+ DC were magnetically purified from synovial fluid mononuclear cells (SMFC) and peripheral blood mononuclear cells (PBMC) stimulated and stained with a panel of fluorochrome conjugated antibodies for multicolour flow cytometry. CD141+ DC isolated and purified from IA synovial fluid were subsequently cocultured with allogeneic CD3+ T cells for 6d after which intracellular cytokine production was assessed by flow cytometry. Supernatants from this CD141+ DC cell cultures were used to treat synovial fibroblasts & the expression of adhesion molecules, cytokines & MMPs was measured. Finally, using sorted populations of CD141+ DC from SFMC and PBMC, RNA sequencing was performed and differentially expressed genes and interaction network analysis were identified using the DeSeq2 R package, Ingenuity Pathway Analysis (IPA) and Innate and Cytoscape. 78 DC1+ T cells. The IA synovium consists of a complex interplay of multiple cell types. Therefore next we examine the effect of this CD141+ DC-T cell interaction on the key invasive cells in the synovium – synovial fibroblasts. Supernatants from CD141+ activated T cells were cultured with fibroblasts & induced expression of ICAM-1, IL-6, IL-8, MMP1 & MMP3. SF CD141 expressed significantly higher levels of IFNγ and IL-17a. Using the hyperxision TREM1 activation of which induces further expression of CD80, CD86 and CD40. Coculture of these TREM1 activated CD141 with CD3+ T cells increases IFNy and IL-17a production. Finally RNASeq analysis revealed that there are 2089 differentially expressed genes between SF CD141+ DC & WB CD141+ DC. These genes are involved in a number of key pathways such as energy metabolism, chemokine & cytokine signalling. Principal Component Analysis (PCA) revealed that CD141+ DC with the synovium are distinctly different from blood CD141+ DC.
Disclosure of Interest: None declared

SAT0015 ANCA-ASSOCIATED VASCULITIS- AND SYSTEMIC LUPUS ERYTHEMATOSUS-INDUCED NEUTROPHIL EXTRACELLULAR TRAPS HAVE INTRINSICALLY DIFFERENT FEATURES

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Background: Neutrophil extracellular traps (NETs) are immunogenic, extracellular DNA structures, thought to play an important role in the pathogenesis of many systemic autoimmune diseases including ANCA-associated vasculitis (AAV) and systemic lupus erythematosus (SLE). However, the pathogenic role of NETs is poorly understood. NETs are thought to play a pivotal role in the pathogenesis of many systemic autoimmune diseases including ANCA-associated vasculitis (AAV) and systemic lupus erythematosus (SLE). They are formed by the release of a net-like structure composed of extracellular DNA, histones, and various other proteins. NETs have been shown to be involved in the pathogenesis of various autoimmune and inflammatory diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis, and lupus nephritis.

Objectives: To investigate the characteristics of NETs induced by sera of AAV and SLE patients.

Methods: The present study involved 101 AAV patients, 59 SLE patients, and 10 healthy controls. Healthy neutrophils were stimulated with 10% serum of these patients to induce NETs. Quantity of NET induction was measured by a novel, highly sensitive NET quantification assay using 3D-confoval laser scanning microscopy. Qualitative characteristics of NETs were investigated by immunofluorescence microscopy that detected co-localisation of several established autoantigens on AAV- and SLE-induced NETs, including citrullinated histone-3 (CitH3), neutrophil elastase (NE), high mobility group box-1 (HMGB1), myeloperoxidase (MPO) and proteinase-3 (PR3).

Results: Quantitative NET induction demonstrated that AAV sera induced significant more NETs (median [Q1 - Q3]: 20.74 [9.56 – 74.14]), compared to SLE sera (5.02 [1.88 – 14.33]). Also qualitatively, NETs induced by AAV or SLE sera were distinct. In both cases, NETs showed co-localisation of MPO and PR3 with extracellular DNA. However, AAV-induced NETs had significantly higher CitH3 expression than SLE-induced NETs. Interestingly, the opposite was observed for other markers as HMGB1 was exclusively expressed on SLE-induced NETs and NE was also higher expressed on SLE-induced NETs compared to AAV-induced NETs. Intriguingly, the distinction between AAV and SLE NETs was further corroborated by live imaging demonstrating differences in morphology and chronology of NET induction: in SLE NET-clusters were induced within the 1st hour while in AAV non-clustered NETs composed of long, thin DNA-fibres were induced in 2–4 hours through lytic effusion.

Conclusions: The present study demonstrates that NET induction in AAV and SLE results in quantitative and qualitative distinct NETs indicating that NET formation in AAV and SLE is likely based on intrinsically different processes. These data increase our understanding of the pathophysiologic relevance of NETs and how they could be considered as a common pathway underpinning different autoimmune diseases.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3804

SAT0016 A NEW SUBSET OF NK CELLS, WITH ENHANCED CYTOTOXIC FUNCTION, IS INCREASED IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Natural killer cells (NK cells) are granular lymphocytes that belong to the innate immune system. Their primary function is the lysis of virus-infected or tumoral cells. These functions are regulated by activating (NKG2D, NKp46, NKP30, NKG2C, NKP44) and inhibitory (KIRs) receptors. The lysis of tumor cells is mediated by the release of perforin and granzymes, which damage the plasma membrane of target cells.

Objectives: To analyze the phenotype of circulating NK cells as well as its function in SLE patients.

Methods: Sixty SLE patients and fifty-five controls were included in this study. Diagnosis was made according to ACR criteria. Activity of disease was measured by SLEDAI index. The expression of NKG2A, IL-10, NKG2D, NKG2C, NKG2D, NKP30, NKP46, NKP44, CD155, CD16, HLA-DR, CD11c+ was evaluated in NK cells (CD3-CD56+) from peripheral mononuclear cells. NK cell function was assessed by the percentage of monocyte-derived DC lysis by NK cells.

Results: Diminished levels of circulating NK cells were found in SLE patients (p=0.0439) compared to healthy subjects. NK cells from SLE showed higher levels of the inhibitory receptor ILT2 (p=0.0024), and the costimulatory molecules CD86+ (p=0.0113) and CD14+ (p=0.0238); in addition, SLE patients displayed a higher expression of MHC-class II molecule, HLA-DR+ (p<0.0001). Interestingly, higher levels of atypical NK cells CD11c+HLA-DR+ (p=0.0075) were found in SLE patients compared with healthy subjects. Furthermore, we found that SLE patients showed a significant increase level of monocyte-derived DC lysis by NK cells.

Conclusions: In this study, we show for the first time that NK cells in SLE have an altered phenotype, expressing receptors, which are characteristic of dendritic cells (CD134, CD86 and HLA-DR). The expression of these receptors may provide NK cells with the ability to activate T cells, which together with their higher capacity to lyse immature or tolerogenic DCs could contribute to SLE pathogenesis. It is known that NK cells could have a dual role in autoimmune diseases, here we propose that the lysis of DC mediated by NK cells could be important to modulate the pathogenesis in SLE patients. Even more, in this report we identify a new subset of NK cells, CD11c+HLA-DR+, reported previously in a mouse lupus model. It is essential to highlight that these NK cells with DC-like phenotype could be crucial for the development of SLE.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3565

SAT0017 INVESTIGATING NOVEL AUTOANTIBODIES IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS

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Background: Granulomatosis with polyangiitis (GPA) is a disease characterized by inflammation in small blood vessels, leading to significant organ damage and ultimately great morbidity and mortality. The presence of anti-neutrophil cytoplasmatic antibodies (ANCA) is a hallmark of the disease, and thought to directly play a role in pathogenesis by activating primed neutrophils. The two major antigens that ANCA are believed to recognize are myeloperoxidase (MPO) and proteinase 3 (PR3). Although anti-MPO antibodies are directly pathogenic when transferred or induced in animal models, the evidence is less clear for PR3. Clinically, it is debated whether levels of anti-PR3 correlate with disease activity. Therefore, we believe that anti-PR3 antibodies are not the primary drivers of disease in patients with PR3+ ANCA-vasculitis (i.e. GPA), and that novel autoantibodies may play a role in disease pathogenesis.

Objectives: The objective of this work is to identify novel human autoantigen targets of novel autoantibodies identified in GPA, and to test their association with disease. The goal is to discover novel autoantigens that will ultimately lead to new diagnostics and therapeutics.

Methods: Cell-barcode-enabled antibody repertoire sequencing was performed on blood plasmablasts (antibody-producing cells formed during an immune response) from five PR3+ ANCA-vasculitis patients with GPA treated with rituximab in the RAVE trial. Phylogenetic trees were bioinformatically created in order to identify clonal families of plasmablasts. Antibodies representing clonal families of plasmablasts were recombinantly expressed and are being tested using human protein arrays and ELISAs to determine their antigen specificity.

Results: All five PR3+ ANCA-vasculitis patients sequenced from the RAVE trial achieved complete remission but subsequently flared. Plasmablasts were isolated at the baseline flare, at remission and at the post-rituximab flare. Phylograms of the antibody repertoire revealed clonal families of affinity-matured antibodies that share heavy and light chain VJ usage. A total of 24 representative antibodies were selected for recombiant expression, including representative antibodies derived from clonal families: (1) shared across patients at baseline flare and/or post-rituximab flare (n=5), (2) present at baseline flare and post-rituximab flare (n=7) [persistent clone or same clone came back], (3) present at baseline flare or post-rituximab flare (n=6), (4) present in remission and post-rituximab flare (n=5) [achieves remission despite clone presence], (5) present in remission (but not flare) (n=1) [patient in remission despite clone presence]. None of the 24 antibodies bind PR3 in an ELISA and thus these antibodies do not represent...
EFFECTS OF ANTI-TNF ALPHA THERAPY ON B CELLS IN RHETUMOGRHITIS (RA) PATIENTS

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Background: Our laboratory has previously characterized defects in humoral B cell responses of aged mice and humans. These defects include: the reduction in activation-induced cytokine deaminase (AID), required for the generation of class-switched memory B cells and the reduction in the percentage/number of the subset of switched memory B cells (1). AID and switched memory B cells have been proposed to be effective predictive biomarkers of vaccine responses (2). Moreover, we have shown that aging is characterized by increased systemic inflammatory which induces intrinsic B cell inflammation, measured by intracellular (ic) TNF-α, and this significantly decreases the capacity of the same B cells to make protective antibodies in response to vaccination (3). Other marker of B cell intrinsic inflammation is micro-RNA (miR) expression, particularly miR-16 and miR-155, which is increased in elderly B cells and negatively correlated with B cell function (4).

Objectives: Our goal for this study was to evaluate B cell phenotype and function in RA patients treated Methylxenate (MTX), alone or together with anti-TNF-α. We hypothesized that patients treated with anti-TNF-α will show improved B cell function due to reduction in icTNF-α.

Methods: We recruited 9 RA patients, 5 patients on MTX and 4 on MTX/anti-TNF-α. We measured the relevant B cell subsets in blood (Naive, switched memory, IgM memory and late memory) by flow cytometry. Staining was performed with antibodies specific for CD19, CD27 and IgD. In addition, we isolated blood B cells using magnetic beads, and measured the expression of miR-16 and miR-155 on blood B cells by qPCR.

Results: Preliminary data showed that the percentages of switched memory (IgD-CD27+) B cells are significantly higher (p < 0.003) in patients undergoing MTX/anti-TNF-α therapy. We also observed a significant decrease in naive B cell percentages (p < 0.028). Preliminary results also showed a decrease in the mRNA expression of both miR-16 and miR-155 in patients on combination therapy compared to MTX alone.

Conclusions: These results support the hypothesis that therapy with anti-TNF-α is beneficial for improving B cell function in RA patients, as compared to MTX therapy alone. Future experiments will seek to evaluate intrinsic B cell TNF levels in these patients and correlate them with measurements of B cell function. Treatment with anti-TNF-α may be able to block the excessive amounts of systemic TNF-α and in turn B cell TNF-α which could improve the antibody responses and the risk of infections in RA patients undergoing therapy.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4331

SAT0019 ESTROGEN INFLUENCES THE SIALYLATION PROFILE AND INFLAMMATORY PROPERTIES OF B CELLS – A POTENTIAL EXPLANATION FOR THE SEX DIFFERENCES AND INCREASED RISK FOR RA IN POSTMENOPAUSAL WOMEN

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Background: Rheumatoid arthritis preferentially affects women. RA has its peak over 50 years coincidencing with the decrease in sex hormones in menopause. Recently, the transition from asymptomatic autoimmunity to RA has been shown to essentially depend on the glycosylation status of antibodies affecting the binding affinity to Fc gamma receptors. Hence a decrease in the sialylation of antibodies resulting from a decrease in the activity of the sialylation enzyme β-galactosidase α2,6-sialyltransferase (ST6GAl1) was shown to trigger the onset of RA.

Objectives: To test whether estrogen influences the glycosylation status of antibodies and ST6GAl1 expression explaining why postmenopausal women are particularly prone to develop RA

Methods: In the experimental part we tested the influence of estrogen on anti-citrullinated protein antibodies (ACPAs) sialylation and ST6GAl1 expression. Ovariectomized mice, which were either left without estrogen supplementation or were supplemented with estrogen (hormone replacement), were immunized with ovalbumin (OVA) to induce antibody production. Immunoglobulin G (IgG) levels were analyzed by ELISA and the glycosylation of the Fc-part of total and OVA-specific IgG was determined using lectin ELISA and MALDI-TOF, respectively. ST6GAl1 expression in plasma cells was determined by RT-PCR and FACS. Inhuman part we measured the effects of estrogen treatment on autoantibody levels and IgG glycosylation in a cohort of postmenopausal RA patients over 2 years.

Results: Ovariectomy and loss of estrogens was associated with a lower sialylation of OVA-specific IgG. Conversely estrogen treatment significantly increased the sialylation level of newly formed OVA-specific and total IgG as well as enhanced the expression of ST6GAl1 enzyme in plasma cells suggesting a shift towards an anti-inflammatory pattern of IgG. These results were confirmed with patients treated protective estrogens and RA patients showing that hormone replacement therapy significantly increased antibody glycosylation, while in a control RA population not exposed to estrogens no such increase in sialylation of IgG was found. Estrogens however, did not influence the CCP autoantibody levels.

Conclusions: These findings indicate that estrogen regulates ST6GAl1 and increases the glycosylation of IgG. Lack of estrogen decreases IgG glycosylation and results in pro-inflammatory properties of IgG which may explain the increase prevalence of RA in postmenopausal women.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6287

SAT0020 THE CITRULLINOME IN TISSUE AND BIOFLUIDS OF HUMAN AND MOUSE ORIGIN

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Background: Protein citrullination is fundamental to several essential processes in apoptosis and antimicrobial defense, however, also linked to multiple pathogenic endpoints. This post-translational modification (PTM), by conversion of arginine to citrulline residues, is mediated by peptidylarginine deiminase (PAD) enzymes found in specific cells and tissues. In polymorphonuclear cells (PMNs) these enzymes enable NETosis, a specialized form of programmed necrosis and the formation of NETs (neutrophil extracellular traps). Also, these enzymes are expressed in the synovium of patients with rheumatoid arthritis (RA) thereby triggering the production of autoantibodies against citrullinated proteins (ACPAs). Objectives: Our objective was to optimize methodology for characterization of this PTM and determine the citrulline in tissue and biofluids of human and mouse origin. The clinical relevance of autoantibodies against citrullinated proteins (OA), Spondyloarthritis (SpA) as well as presence of ACPAs and NETs

Methods: Synovial fluid (SF) and plasma was collected from patients diagnosed with RA, OA, SpA (n=120). Inflammation levels patients were characterized with plasma C-reactive protein (CRP), and circulating anti-CCP levels as well as 10 most relevant proinflammatory cytokines. Intestinal tissue (colon mucosa) from RA patients (n=10) and joint lysate from collagen-induced arthritis mouse model (n=24). All samples were analyzed by citrulline specific sample preparation and high-end mass spectrometric analysis. Follow-up studies were performed by multiple techniques including confocal microscopy and cell-free DNA measurement.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.775
Rheumatoid arthritis (RA) is a chronic autoimmune disease established in vitro in this complex microenvironment has yet to be characterised. Therefore, we investigated the functional relationship linking fibroblasts and T lymphocytes.

Objectives: Our deep proteome based analysis of tissue and biofluids have enabled an extended catalogue of citrullinated proteins and sites relevant to RA patients. Human CD4 T cells were stained with a proliferation-tracking dye after 17a and RANKL after 5 days. Lastly, co-culture of T cells and synovial fibroblasts resulted in proliferation of CD4 T cells (P<0.05), and decreased IgM+CD21-/low memory B cells and Tfh percentage associated with an increase in Tregs frequency (P=0.03), and positively correlated with regulatory T cells (Tregs) (P=0.03), and negatively correlated with B lymphocyte stimulator receptor 3 and programmed death-ligand 1 (35.7% ± 6.1% versus 14.9% ± 3.8%, and 12% ± 1.3% versus 8% ± 0.9%, respectively). B lymphocyte stimulator receptor 3 and programmed death-ligand 1 (35.7% ± 6.1% versus 14.9% ± 3.8%, and 12% ± 1.3% versus 8% ± 0.9%, respectively). B lymphocyte stimulator receptor 3 and programmed death-ligand 1 (35.7% ± 6.1% versus 14.9% ± 3.8%, and 12% ± 1.3% versus 8% ± 0.9%, respectively).

Methods: 27 HCV-CV patients treated with DAA therapy, 12 healthy donors (HD) and 12 HCV were included. We investigated the effects of DAA-based therapy on cellular and cytokine abnormalities in HCV-CV patients by flowcytometry, cytokine/Immunomarker multiplex and ex vivo gene expression.

Results: Compared with HD and HCV, pre-DAA abnormalities in HCV-CV patients.

Conclusions: Our results highlight genes that may drive the pathogenic activity of B cells in RA and suggest shared methylation patterns with SLE.

Disclosure of Interest: None declared


SAT0022 | EPIGENOME-WIDE ASSOCIATION STUDY OF RHEUMATOID ARTHRITIS IDENTIFIES DIFFERENTIALLY METHYLATED LOCI IN B CELLS

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Background: Epigenetic regulation of immune cell types could be critical for the development and maintenance of autoimmune diseases like Rheumatoid Arthritis (RA). B cells are highly relevant in RA, since patients express autoantibodies and depleting this cell type is a successful therapeutic approach. Epigenetic variation, such as DNA methylation, may mediate the pathogenic activity of B cells.

Methods: We performed a genome-wide association study (EWSA) for RA with three different replication cohorts, to identify disease-specific alterations in DNA methylation in B cells.

Results: Genomic DNA from B lymphocytes was assayed on the Illumina HumanMethylation450 BeadChip, assaying ~450,000 different CpG sites. Differential methylated positions (DMPs) were identified in a discovery cohort using a single-point analysis using logistic regression, as well as a pathway-level analysis using a newly developed permutation-based method. A discovery cohort of 50 RA patients and 75 healthy controls from Spain was used to identify the most differentially methylated regions after multiple test correction. Using an independent sample of 15 patients and 15 controls from the same population we performed a replication analysis of the most significant CpG sites and pathways.

Conclusions: Our results highlight genes that may drive the pathogenic activity of B cells in RA and suggest shared methylation patterns with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6294

SAT0021 | HUMAN CD4 T CELLS AND SYNOVIAL FIBROBLASTS COOPERATE TO PROMOTE INFLAMMATION IN THE RA SYNOVIAL JOINT

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by synovial tissue proliferation and degradation of articular cartilage. Activated synovial fibroblasts proliferate and express matrix-degrading proteases, adhesion molecules and proinflammatory cytokines, which contribute to cartilage and joint destruction. Moreover, synovial cell activation correlates with infiltration of inflammatory lymphocytes and monocytes which in turn contribute to synovioctye activation, thus further exacerbating inflammation.

Objectives: The functional relationship linking fibroblasts and T lymphocytes in this complex microenvironment has yet to be characterised. Therefore, we established an in vitro model to examine the outcomes of co-cultured activated human CD4 T cells with RA synovial fibroblasts.

Methods: Co-culture assays were carried out using immortalised K4M RA synovial fibroblasts or synovial fibroblast cells derived from arthroscopy biopsies of RA patients. Human CD4 T cells were stained with a proliferation-tracking dye and co-cultured with pre-seeded synovial fibroblasts for 5 days. The resulting cell cultures and supernatants were examined for proliferation, cytokine production, secretion of matrix metalloproteinases and expression of adhesion molecules.

Results: We found that CD4 T cells and K4M RA cells reciprocally induced an increased expression of adhesion molecules ICAM and VCAM. Furthermore, co-culture of CD4 T cells and synovial fibroblasts resulted in proliferation of CD4 T cells expressing increased levels of the proinflammatory cytokines INFγ and IL-17a and RANKL after 5 days. Lastly, co-culture of T cells and synovial fibroblasts resulted in secretion of IL-6, IL-8, INFγ and IL-17a and matrix metalloproteinases MMP-1 and MMP-3.

Conclusions: These results indicate that CD4 T cells work mutually with synovioctyes to create an inflammatory microenvironment likely to promote joint destruction. Future studies will characterise the role of glucose metabolism in these cells and investigate if metabolism is intrinsically coupled to effector functions in both cell types.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6294

SAT0023 | DIRECT-ACTING ANTIVRAL-BASED THERAPY RESTORES IMMUNE TOLERANCE IN HEPATITIS C-INDUCED CRYOGLUBULINEMIA VASCULITIS

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Objectives: Interferon-free direct-acting antiviral (DAA)-based therapy has proven to be very effective in patients with hepatitis C virus-cryoglobulinemia vasculitis (HCV-CV). However, their mechanisms of action and their effects on cellular immunity remain poorly defined.

Methods: 27 HCV-CV patients treated with DAA therapy, 12 healthy donors (HD) and 12 HCV were included. We investigated the effects of DAA-based therapy on cellular and cytokine abnormalities in HCV-CV patients by flowcytometry, cytokine/Immunomarker multiplex and ex vivo gene expression.

Results: Compared with HD and HCV, pre-DAA abnormalities in HCV-CV patients included a decreased percentage of CD4+CD25+FoxP3+ regulatory T cells (P<0.01) with increases in IgM+CD21+ (P<0.05), CD4+INFγ (P<0.01), CD4+IL17A (P<0.001) and CD4+CXCR5+IL12+ follicular helper T cells (Tfh) (P<0.01), IgM+CD21low memory B cells were negatively correlated with regulatory T cells (Tregs) (P>0.03), and positively correlated with Tfh (P<0.03) and serum cryoglobulin levels (P<0.01). DAA-based therapy was associated with an increase in Treg frequency (1.5% ± 0.18% versus 2% ± 0.18%, and 12% ± 1.3% versus 8% ± 0.9%, respectively). B lymphocyte stimulator receptor 3 and programmed death-ligand 1 staining expression on B cells increased in HCV-CV after DAA-based therapy (MFI 37±2.4 versus 47±2.6, P<0.01; and 29±7.3 versus 48±9.3, P<0.05 respectively).

Conclusions: Our results indicate that DAA-based therapy effectively normalizes many of the disturbances in peripheral B and T lymphocyte homeostasis of HCV-CV patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3911

SAT0024 | ALTERATIONS OF PERIPHERAL BLOOD B-CELL SUBSETS IN EARLY RHEUMATOID ARTHRITIS


Background: Alterations of B-cell subgroup have been described in the...
Peripheral blood of rheumatoid arthritis (RA) patients (pts), but differences between B-cell subsets distributions in early and later onset RA (LORA) are still unclear [1,2].

Objectives: To examine B-cell subsets in peripheral blood of healthy donors, early disease duration (<6 months) RA (ERA) and LORA pts by flow cytometry, and to analyze differences between B-cell subsets and RA activity.

Methods: 24 active ERA pts (20F/4M); median age 54 years (range) (38–64); disease duration 5 months (4–6); DAS28 score 5.2 (4.7–5.9); RF+75%, ACCP+87.5% and 20 LORA pts (16F/4M); median age 58 years (range) (44–62); disease duration 12 years (4.5–17.5); DAS28 score 5.3 (4.6–6.2); both RF+ and ACCP+ 80%, were assessed for B-cell subpopulations and laboratory data. In ERA, CRP, LORA pts were treated with DMARDs (anti-TNF-α, Methotrexate), glucocorticoids, and NSAIDS; ERA pts received NSAIDS only. CD19+B cells, memory B cells (CD19+IgD+CD27+), double-negative (CD19+IgD+CD27−), transitional (CD19+IgD+CD10+CD38++CD27−) B cells, and plasmablasts (CD19+CD38+++IgD−CD27−CD20−) were analyzed using multicolor flow cytometry.

Results: The median percentages (range) of non-switched memory B cells (CD19+IgD+CD27+) were lower in ERA and LORA RA cohorts compared to donors: 3.0% (1.6–5.5) and 6.2% (2.4–10.2) vs 7.4% (3.7–11.1), respectively; p<0.05 for both cases. In LORA pts, the median percentages (range) and absolute numbers of switched memory B cells (CD19+IgD+CD27+) were higher compared to ERA pts (CD19+IgD+CD27+), naïve (CD19+IgD–CD27−), double-negative (CD19+IgD+CD27−), transitional (CD19+IgD+CD10+CD38++CD27−) B cells, and plasmablasts (CD19+CD38+++IgD−CD27−CD20−) analyzed were using multicolor flow cytometry.

Conclusions: In ERA pts, immunophenotyping showed increased frequencies of naïve B cells and decreased frequencies and absolute numbers of switched memory B cells compared to LORA cohort.

References:


Disclosure of Interest: None declared

AIOLOS OVEREXPRESSION IN SYSTEMIC LUPUS

BREACH OF AUTOREACTIVE B-CELL TOLERANCE BY

1,2, M. Bucchia 3, M. Néel 2, M. Rimbert 2,4, C. Agard1, M. Hourmant 5,

References:

further developing MGD010 as a therapeutic modality for autoimmune diseases.

delivers an immunomodulatory effect that effectively counters B-cell function.

CD79B component, a single dose administration of either 3 or 10 mg/kg MGD010

the activity of the checkpoint molecule CD32B in combination with the BCR

G.E. Ringheim

CD27+IgD- switched memory, CD27+IgD+ nonswitched memory, and CD27-IgD-

HAV-specific IgG levels in subjects treated with MGD010 compared with placebo

decreased surface BCR and CD40 expression as well as a moderate decrease

prior observations (1), ex vivo flow cytometric analysis confirmed dose-dependent

in total serum IgM levels. Reduced HAV seroconversion rates were observed in

to follow study procedures. There were no severe adverse events in subjects who

seroconversion rate of HAV and quantification of serum HAV IgG concentration.

DOI:


SAT0029 | B CELL DEPLETION AFFECTS CD8 T CELLS IN ANCA-ASSOCIATED VASCULITIS

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Background: In anti-neutrophil cytoplasmic antibodies associated vasculitis (AAV), several clues suggest that the efficacy of B cell depletion therapy lies beyond the suppression of ANCA-producing cells and may involve the suppression of B-T cell crosstalk. However little if any data are available regarding the impact of rituximab on CD4, regulatory T and CD8 T cells in this setting.

Objectives: To compare the effects of conventional immunosuppressants (CIS) and rituximab (RTX) on 3 T cell compartments in AAV. To assess the impact of patients B cells and that of B cell depletion on CD8 T cell cytokine production.

Methods: Thorough cross-sectional immunophenotypic analysis of CD4, regulatory T and CD8 cells of 53 patients with AAV, using polychromatic flow cytometry. A marker of endogenous immunosuppressive cytokine/chemokine production of in vitro stimulated CD8 T cells. Active untreated AAV patients’ B cells and/or CD8 T cells were cocultured for 72h with Staphylococcal Enterotoxin (Autoologus and cross-population experiments), and CD8 T cells cytokine production was then assessed by flow cytometry.

Results: Among CD4 T cells, we found that frequency of naive and memory subsets and the expression of CCR5, CCR4 and CD62L were not influenced by maintenance treatment type. Similarly, total Treg frequency and Treg subsets including CD62L+ Helios+ resting (CD45RA+) and memory (CD45RA-FoxP3) Tregs were comparable among RTX and CIS treated patients. By contrast, the type of maintenance treatment markedly influenced the CD8+ T cell compartment. Patient under B cell depletion therapy had less TEMRA (CD45RA+CCR7+) and more TEM cells than those receiving CIS, and resembled those in long term remission off therapy. CMV seropositivity did not explain the observed differences. Longitudinal data confirmed that B cell depletion significantly decreased TEMRA (CD45RA+CCR7-) CD8 T cell frequency (p<0.0001), whereas CIS had the opposite effect. Furthermore, we found that in vitro stimulated CD8 T cells from B cell depleted patients produced less pro-inflammatory cytokine/chemokine than those from patients treated with CIS. In coculture with B cells and SEB, patients CD8 cells coculture produced higher level of inflammatory cytokines than those from controls, but only when they were stimulated with patients’ B cells.

Conclusions: B cell depletion therapy has a significant impact on the CD8 T cell compartment in terms of phenotype and function. B cell can promote pro-inflammatory function of CD8 T cell in vitro. CD8 T cell are found in vasculitides lesions. These observations raise the question whether the disruption of B cell help to CD8 T cells could contribute to the dramatic efficacy of RTX. Further studies are needed to demonstrate the implication of patients’ CD8 T cell in tissue damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6894

SAT0030 | BREACH OF AUTORESTRICTIVE B-CELL TOLERANCE BY POST-TRANSLATIONALLY MODIFIED FOREIGN PROTEINS

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Background: Autoimmunity in Rheumatoid arthritis (RA) patients is characterized by a reduced expression of anti-protein antibody proteins (AMPAs). Much less is known about the occurrence and aetiology of other AMPA responses in RA such as autoantibodies directed against post-translationally modified (PTM) proteins. The best-known AMPA in RA are anti-citrullinated protein antibodies (ACPA). Less is known about the occurrence and aetiology of other AMPA responses in RA such as autoantibodies directed against post-translationally modified (PTM) proteins. The best-known AMPA in RA are anti-citrullinated protein antibodies (ACPA).

None declared

DOI: 10.1136/annrheumdis-2017-eular.6894
leading to the formation of these autoantibodies. At present it is unknown how AMPa are generated and how autoreactive B-cell responses against PTM proteins are induced.

Objectives: To investigate how PTM proteins, more specifically carbamylated proteins, could contribute to a breach of B-cell tolerance.

Methods: Proteins towards five different carbamylated proteins was determined for 160 RA-patients and 40 healthy individuals. Anti-CarP antibody cross-reactivity was studied by inhibition experiments. Mass spectrometry was performed to identify carbamylated self-proteins in human rheumatic and osteoarthritic joint tissue. Mice were immunized with carbamylated- or non-modified foreign (Cova) and self-antigens (mouse Albumin). Serum of immunized mice and monoclonal antibodies were analyzed for antigen reactivity.

Results: We show that anti-CarP antibodies in RA are highly cross-reactive towards multiple carbamylated proteins, including modified self- as well as modified non-self proteins. Immunization with carbamylated foreign proteins (Ca-OVA) induced a strong anti-CarP response against both carbamylated foreign- and self-proteins. Similar to murine serum anti-CarP antibodies, murine monoclonal anti-CarP antibodies were highly specific and cross-reactive to multiple carbamylated (auto)antigens. Although citrulline greatly resembles homocitrullines residues in structure, murine anti-CarP antibodies differ in antigen recognition profile from ACa as they are able to discriminate between citrullinated and homocitrullinated forms of the same protein. Interestingly, we were able to identify carbamylated-albumin, in RA synovial tissue, indicating that albumin is present in carbamylated forms in the inflamed joint.

Conclusions: Self-reactive AMPA-responses can be induced by exposure to foreign proteins containing PTM. Our findings show that autoreactive B-cell responses against PTM specific self proteins can be induced by exposure to PTM proteins and provide new insights on the breach of autoreactive B-cell tolerance by foreign proteins.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5984

SAT0031 DETECTION AND ISOLATION OF ANTIGEN-SPECIFIC B CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The majority of autoimmune diseases, e.g. rheumatoid arthritis (RA), are characterized by autoantibodies that are produced by B cells. We have identified several novel post-translationally modified epitopes in collagen type II (CII), a major cartilage constituent that are autoreactive. In mouse models, autoantibodies that bind to these epitopes can either induce or protect against inflammatory arthritis. However, very little is known about the frequencies or phenotype the B cells that produce these autoantibodies in humans.

Objectives: The aim of this project is to study the B cells that produce autoantibodies reactive to these epitopes in patients with RA.

Methods: Clinical data and peripheral blood were collected from patients with RA (n=100). Titres of CII-reactive serum-autoantibodies were determined by Luminex. Titres of CII-reactive serum-autoantibodies were determined by Luminex. The different subsets of B cells that expressed a CII-reactive B cell receptor (n=100). Titres of CII-reactive serum-autoantibodies were determined by Luminex. Serum of immunized mice and monoclonal antibodies were analyzed for antigen reactivity.

Results: We show that anti-CarP antibodies in RA are highly cross-reactive towards multiple carbamylated proteins, including modified self- as well as modified non-self proteins. Immunization with carbamylated foreign proteins (Ca-OVA) induced a strong anti-CarP response against both carbamylated foreign- and self-proteins. Similar to murine serum anti-CarP antibodies, murine monoclonal anti-CarP antibodies were highly specific and cross-reactive to multiple carbamylated (auto)antigens. Although citrulline greatly resembles homocitrullines residues in structure, murine anti-CarP antibodies differ in antigen recognition profile from ACa as they are able to discriminate between citrullinated and homocitrullinated forms of the same protein. Interestingly, we were able to identify carbamylated-albumin, in RA synovial tissue, indicating that albumin is present in carbamylated forms in the inflamed joint.

Conclusions: Self-reactive AMPA-responses can be induced by exposure to foreign proteins containing PTM. Our findings show that autoreactive B-cell responses against PTM specific self proteins can be induced by exposure to PTM proteins and provide new insights on the breach of autoreactive B-cell tolerance by foreign proteins.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2796

SAT0032 EX Vivo ANALYSIS OF AUTOANTIGEN-SPECIFIC T CELL RESPONSES USING A MULTI HLA-CLASS II TETRAMER APPROACH

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Background: HLA class II tetramers allow the direct ex vivo enumeration and phenotypic characterization of antigen-specific T cells and have proven a useful tool in different settings, e.g. allergy and vaccination.

Objectives: Based on flow cytometry we developed a multi HLA-class II tetramer approach that renders it possible to look at numerous specificities simultaneously and is sufficiently sensitive at the same time as auto-reactive T cells are likely to be rare. We focused on validated citrullinated T cell epitopes previously studied in RA, namely a-enolase, fibrinogen and CILP.

To test the robustness and sensitivity of our multi-tetramer assay, we performed repeated experiments on PBMCs of HLA-DRB1*04:01-positive healthy controls and HLA-DRB1*04:01-positive RA patients.

Results: We first, we examined the sensitivity of the panel by assessing PBMC from healthy donors and we could detect low frequencies of auto-reactive T cells in these samples (1–10 per million CD4), mostly displaying a naïve phenotype, which was in sharp contrast to influenza-specific T cells in the same donors which were 10–20 fold higher in numbers. Moreover, we detected the robustness of the panel by running technical repeats of all healthy donor samples, which yielded similar frequencies. Thereafter, we focused on RA patient PBMC obtained from repeated blood draws (2–4 weeks apart). Also in these samples, frequencies ranged between 10–20 tetramer-positive cells per million CD4 T cells, i.e. similar as in healthy controls. Moreover, not all T cell specificities were present in all patients. Still, we found the frequencies to be stable in the repeated blood draws in approximately half of the individuals, implicating that frequencies close to 1 cell per million CD4+ T cells is borderline of what we can stably detect. Importantly, the patient samples utilized were not taken from time points of active disease, where we hypothesize frequencies to be elevated. This may be the case also in synovial fluid and as a proof of principle, we assessed synovial fluid samples of HLA-DRB1*04:01+ RA patients and were able to detect auto-reactive T cells at frequencies comparable to the ones found in peripheral blood.

Conclusions: In conclusion, we developed a sensitive tetramer panel allowing the simultaneous enumeration and phenotypic characterization of antigen-specific T cells in ex vivo samples from RA patients that can be used for monitoring and in-depth studying of these cells during the course of disease and treatment in individual patients.


SAT0033 SMOOKING CONTRIBUTES TO EXHAUSTED STATE OF CD4+ T CELLS IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) has recently been linked to an exhausted state of CD4+ T cells in peripheral blood of patients [1]. Exhaustion of CD4+ T cells limits their proliferation and increases cell death. In CD8+ T cells smoking counteracts exhaustion, which may lead to increased cytotoxic activity exemplified by targeting of cells with high expression of the anti-apoptotic protein survivin [2]. Exhaustion of CD4+ T cells coincides with expression of interferon (IFN) response genes [3], referred to as the IFN signature. The development of the IFN signature has been linked to smoking status [4].

Objectives: We investigated how smoking affect the CD4+ T cell population in peripheral blood of RA patients with focus on the exhaustion marker programmed cell death-1 (PD-1).

Methods: Blood samples were collected from RA patients and healthy women with different smoking status and analysed for PD-1 and survivin expression using flow cytometry and qPCR. Sorted Th17 cells from peripheral blood were analysed for expression of 18 genes upregulated during exhaustion [3], herein referred to as the exhaustion set, and serum levels of survivin were assessed by ELISA. Peripheral blood CD4+ cells were analysed for their expression of seven IFN response genes [4]. The role of survivin in the formation of exhausted CD4+ T cells was studied in collagen-induced arthritis (CIA), where mice were treated with nicotine or vaccinated with survivin peptides.

Results: High frequency of exhausted PD-1+CD4+ cells was found in smoking RA and the numbers of PD-1+CD4+ cells correlated to the IFN signature expression by cytotoxic CD8+CD107+ cells (r=−0.62, p=0.01). Additionally, the frequency of PD-1+CD4+ cells increased with reduction of the IFN signature population (r=0.71, p=0.002). The IFN signature was found exclusively among smoking RA patients. The patients with the IFN signature all had CD4+ cells with low survivin
analysed. Th17 cells from RA patients with high serum survivin were enriched in genes of the exhaustion set. CD4+ cells with high survivin expression were negative for PD-1, while PD-1+ cells had low expression of survivin. In CIA mice the survivinPD−1− CD4+ cells were reduced by nicotine treatment (p=0.03) or survivin vaccination (p<0.009).

Conclusions: Elevated survivin expression associates with exhaustion of CD4+ T cells in RA by increasing the frequency of PD-1+CD4+ cells and supporting the IFN signature. Balancing T cell exhaustion and preventing the IFN signature are potential future treatment strategies for RA.

References:

Disclosure of Interest: None declared

SAT0034 ANALYSIS OF THE T-CELL SUBSET COMPOSITION IN ANKYLOSING SPONDYLITIS PATIENTS WITH LONG-STANDING ANTI-TNF THERAPY

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Background: Ankylosing spondylitis (AS) is a chronic, progressive, immune-mediated inflammatory disease, driven primarily by Th1 and Th17 cells. Anti-TNF therapies are successfully used in AS to achieve and maintain remission. However, their influence on the composition of the T-cell repertoire is not clear, and, in particular, the few published studies involve mostly patients with anti-TNF treatment of short duration.

Objectives: We aimed to characterize the changes in several T cell subsets after long-term anti-TNF treatment in AS patients.

Methods: Twenty-two AS patients on long-term anti-TNF therapy were evaluated (15 anti-TNF-responders and 7 non-responders). A wide range of cell subtypes were analysed with flow cytometry and compared with therapy-naive and short-term data.

Results: Key findings include decreased proportions of naive CD4 and CD8 cells, increased frequencies of Th1 and Th17 cells and higher Th1/Th2 and Th17/Treg ratios in the long-term anti-TNF-treated patients (responders, non-responders and total), which was found to be significant not only when compared with healthy controls, but also with therapy-naive and short-term anti-TNF-treated AS patients. We have found several alterations within the various activated T-cell subsets – increase in CD4HLADR cells in responders, in CD8HLADR cells in the whole AS group and in responders, and in CD4CD25 cells in responders, and decrease in CD4CD69 cell percentages in long-term treated patients – becoming evident only after long-term anti-TNF therapy.

Conclusions: This study provides a comprehensive assessment of the impact of anti-TNF therapy on the T cell repertoire in AS, and indicate that these therapies induce profound changes within T-cells. Changes in T cell phenotype seem to develop progressively during therapy, even in inactive disease, and reflect an ongoing effector T-cell differentiation and activation, and a normalization of Tregs development.

Disclosure of Interest: None declared

SAT0035 INHIBITION OF PROTEIN KINASE C THETA BY THE SELECTIVE INHIBITOR CC-90005 INDUCES T CELL ANERGY


Background: Protein Kinase C theta (PKC-θ), a member of the PKC family of serine/threonine kinases, is essential in T cell receptor (TCR) signaling and T cell activation [1]. Inhibition of PKC-θ activity may provide new therapeutic options for autoimmune diseases with a T effector cell dependent pathology. CC-90005 is a selective inhibitor of PKC-θ and may be a co-expression profile specific to IL-17 expressing T cells. This work was funded in part by the King’s Health Partners R&D Challenge Fund (R140080) and in part by research support from Novartis.

Disclosure of Interest: K. Steel: None declared. E. Chan: None declared. B. Kirkham: MSD, Pfizer, Roche. L. Taams Grant/research support from: Novartis, UCB, Abbvie, Bristol Myer Squibb, Celgene, Janssen, MSD, Pfizer, Roche. L. Taams Grant/research support from: Novartis and UCB.


Results: CC-90005 anergy induction was shown to require only short initial exposures of as little as 2 h and to maintain anergy for as long as 48–96 h post CC-90005 washout. However, T cells pre-treated with the inhibitor in the absence of concomitant TCR stimulation were able to respond to stimulus after as little as 1 h washout, indicating a rapid recovery of PKC-θ activity and T-cell function. CC-90005 upregulated an anergy-related E3 ubiquitin ligase, G质, was a possible downstream mediator of CC-90005 effect on T cell anergy.

Conclusions: CC-90005, a specific inhibitor of PKC-θ, significantly inhibits TCR-mediated T cell activation, proliferation, and cytokine production. Moreover, inhibition of these T-cell functions persists after drug withdrawal and restimulation of T-cells, but only if the primary T cell activation event occurs in the presence of CC-90005. Thus, CC-90005 induces a functional unresponsiveness anergic state in T cells if present during TCR activation, which may have long-term therapeutic benefit in the treatment of T-cell mediated autoimmune and allergic inflammatory conditions.

References:

Disclosure of Interest: None declared

SAT0036 IL-17+CD8+ T CELLS ENRICHED IN THE SYNOVIAL FLUID OF PSA/SPA PATIENTS EXHIBIT A PRO-INFLAMMATORY CYTOKINE PHENOTYPE

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Background: Seronegative spondyloarthropathies (SpA) share common clinical and immunological characteristics, including a common association with MHC class I, suggesting a role for CD68+ T cells. In contrast, rheumatoid arthritis (RA) is associated with MHC class II. We previously showed that IL-17+CD8+ T cells are increased in the synovial fluid (SF) of patients with psoriatic arthritis (PsA) but not RA, compared to peripheral blood (PB). This study extends this analysis to other SpA types, and phenotypes the SF IL-17+CD8+ T cells to further elucidate their potential pathogenic role.

Methods: Paired PB and SF were collected from patients with RA, PsA and other SpA types (ankylosing spondylitis (AS), reactive arthritis (ReA), enteropathic arthritis (EA) and peripheral SpA (pSpA)) from Guy’s Hospital Rheumatology clinic with informed consent. PB from healthy controls (HC) was collected at King’s College London. PBMC and SFMC were isolated and stimulated ex vivo with PMA/ionomycin before analysis of surface marker and cytokine expression by flow cytometry.

Results: The percentage of IL-17+CD8+ T (Tc17) cells was increased in the SF of PsA (median 0.9%, p=0.0012, n=13) as well as other SpA patients (0.34%, p=0.0009, n=14), but not RA patients (0.07%, p=0.3, n=7) compared to matched PB (median 0%, n=10, no significant differences between disease and control PB). The percentage of SF IL-17+CD8+ T (Tc17) cells was increased in patients with SpA (2.14%, p=0.004, n=14), RA (2.31%, p=0.016, n=7) and to a lesser extent PsA (0.97%, p=0.057, n=13), compared to PB (median 0.61%, no significant differences between disease and control PB).

Phenotypically, most SF IL-17+CD8+ T cells expressed CD38 (89%, n=7) and CD161 (75%, n=8), known markers of IL-17+CD8+ T cells. A high percentage also expressed CD103 (69%, n=9), which was not observed in the synovial IL-17+CD8+ T cells (2%, n=10). A high frequency of IL-17+CD8+ T cells co-expressed a range of pro-inflammatory cytokines including IFN-γ (72%, n=12), GM-CSF (58%, n=7), TNF-α (48%, n=12) and to a lesser extent IL-21 (20%, n=6) and IL-22 (5%, n=6). IL-10 was usually co-expressed at very low levels (1%, n=7), although 2 samples showed co-expression of IL-10 (33%, n=2). CRCR6, CD161, GM-CSF and IL-21 were not significantly co-expressed by either IL-17A negative CD8+ or IFNγ+CD8+ (Tc1) T cells from the SF, indicating this may be a co-expression profile specific to IL-17 expressing T cells.

Conclusions: These findings confirm the presence of an IL-17A+CD8+ T cell subset in the SF of PsA patients and extend this to other SpA types. The expression of the integrin CD103 by these cells indicates they may represent a tissue resident memory (Trm) population in the synovial joint. In addition to IL-17A, the co-expression of several pro-inflammatory cytokines combined with low expression of IL-10, suggests a pro-inflammatory role for these cells.

Disclosure of Interest: None declared.
SAT0037 | THE EFFECTS OF B CELL DIRECTED THERAPY ON DISEASE RELEVANT BIOMARKERS IN SUBJECTS AT RISK OF RHEUMATOID ARTHRITIS

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Background: Exploration of the mechanism underlying the delay of development of clinical signs of seropositive rheumatoid arthritis (RA) observed after B cell directed therapy in individuals at risk of developing autoantibody positive RA may offer insights into the mechanism of disease and may assist the development of preventive strategies.

Objectives: To explore the effects of a single infusion of rituximab (anti-CD20 antibody) on the observed delay of the onset of clinically manifest arthritis in individuals at risk of developing autoimmune positive RA.

Methods: In a study of 81 subjects positive for both anti-citrullinated protein antibody (ACPA) and rheumatoid factor (RF) with arthralgia who never had clinically manifest arthritis and never used disease-modifying antirheumatic drugs, a 55% reduction of the risk of developing arthritis was observed 12 months after receiving a single iv infusion of 1000 mg rituximab when compared to placebo. In this group there was a delay in the development of arthritis of 12.0 months (12 months placebo vs 24 rituximab group) at the 25% quartile (75% free of arthritis of the arthritis-free survival). Explorative analysis of disease-related biomarkers was performed in subgroups to better understand the mechanisms of the observed delay of clinical disease onset.

Results: Baseline levels of ESR (mm/h; HR 1.03; p=0.016), the total number of B cells in peripheral blood (HR 1.49; p=0.047), the presence of anti-CD45-RO CD45RA+ CD8 memory lymphocytes (HR 1.38; p=0.048), and the percentage of regulatory B cells (HR 1.19; p=0.001) were related to arthritis development over time. Importantly, genetic analysis of 100 RA associated SNPs showed that the top SNP associated with arthritis development in the rituximab-treated group (OR=1.33, confidence interval 1.03-1.71) that is a common polymorphism not associated with arthritis in the placebo group. Explorative analysis showed trends for multiple biomarkers in the B cell compartment that appeared predictive of the development of arthritis.

Conclusions: A single infusion of 1000 mg rituximab significantly affects B cell memory and subsets of memory and regulatory B cells as well as a reduction of disease-related antibodies and immunoglobulin levels in individuals at risk of RA. The changes coincide with a decrease in risk and a delay in development of arthritis in this population. PLC2L2 gene polymorphism was associated with arthritis development in rituximab-treated individuals.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1316

SAT0039 | LARGE TENDER JOINTS HAVE THE GREATEST IMPACT ON LONGITUDINAL TRAJECTORIES OF FUNCTION IN EARLY RHEUMATOID ARTHRITIS

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Background: Physical function remains suboptimal in patients with early rheumatoid arthritis (ERA) despite adequate disease control. Hence, factors impacting function need further evaluation. Large weight bearing joints are more likely to influence overall function than small non-weight bearing joints although the magnitude of impact may be task dependent. By weighting large joints more than small joints, the Lansbury Articular Index (LAI) may have stronger associations with function than standard joint counts that give equal weight to small and large joints.

Objectives: 1) To compare the correlations of weighted and non-weighted arthritis joint measures with physical function over time; and 2) to determine the impact of large compared to small joint involvement on the trajectory of HAQ in ERA.

Methods: ERA participants had <1 year symptom duration at enrolment in a 6 joint early Arthritis Cohort and were told nine large joints (time-varying) on the HAQ trajectory were estimated with a series of generalized estimating equations (GEE). GEE models were adjusted for baseline age, sex and education.

Results: ERA subjects (n=2125, 73% female; baseline mean (SD) age 53 (15) years, DAS28 5.1 (1.4)), were followed for median (IQR) 24 (10,48) months. At their last visit 44% were in remission (DAS28 < 2.6). HAQ over time was highly correlated with the following: DAS28 (r=0.83), LT28 (r=0.70), TJC28 (r=0.89), SJC28 (r=0.90) and moderately with the LS28 (r=0.59) and SJC28 (r=0.61) trajectories. Each increase in joint involvement was associated with increase in HAQ: large tender joint (0.110 (95% CI 0.102–0.119)), large swollen joint (0.109 (0.099–0.120)), tender hand joint (0.036 (0.032–0.039)), swollen hand joint (0.035 (0.032–0.039)).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5650

SAT0038 | SERUM B LYMPHOCYTE CHEMOATTRACTANT PROTEIN 13 (CXC13) AND MUSCULOSKELETAL ULTRASONOGRAPHIC FINDINGS IN EARLY RHEUMATOID ARTHRITIS

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Background: Patients in clinical remission may continue to have synovitis detected by the musculo skeletal ultrasonography (MSUS). Recently B-lymphocyte chemotactic protein (CXCL13) has reported to be upregulated and risen to be a possible new marker of disease inflammation in RA.

Objectives: to detect early synovitis by grey scale and power Doppler MSUS, measure serum levels of CXCL13 and to correlate these levels with both clinical and ultrasonographic disease activity in early RA patients

Methods: CXCL13 serum was assessed by the modified ELISA kit and were follwed for clinical and ultrasonographic disease activities measures (DAS28, tender joint count (TJC28), swollen joint count (SJC28), function (Health Assessment Questionnaire: HAQ) were captured at each visit. The LAI weighted 28 joint count (LT28) and swollen joint count (LS28) were calculated based on the standard 28 joint sites. Correlations of trajectories were calculated using joint modeling for each of the following: DAS28, TJC28,SJC28,LS28 LT28 with the HAQ (2 trajectories/model). Unadjusted effects of large joints (shoulders, elbows, hips, knees, ankles) and hand joints (time-varying) on the HAQ trajectory were estimated with a series of generalized linear mixed models (GEE). GEE models were adjusted for baseline age, sex and education.

Results: ERA subjects (n=2125, 73% female; baseline mean (SD) age 53 (15) years, DAS28 5.1 (1.4)), were followed for median (IQR) 24 (10,48) months. At their last visit 44% were in remission (DAS28 < 2.6). HAQ over time was highly correlated with the following: DAS28 (r=0.83), LT28 (r=0.70), TJC28 (r=0.89), and moderately with the LS28 (r=0.59) and SJC28 (r=0.61) trajectories. Each increase in joint involvement was associated with increase in HAQ: large tender joint (0.110 (95% CI 0.102–0.119)), large swollen joint (0.109 (0.099–0.120)), tender hand joint (0.036 (0.032–0.039)), swollen hand joint (0.035 (0.032–0.039)).
In multivariable modeling, after adjusting for age, sex, and education, large joints had greater effects (tender 0.074 (0.065–0.084), swollen 0.027 (0.014–0.04) on HAQ than hand joints (tender 0.013 (0.009–0.017), swollen 0.008 (0.003–0.013)).

Conclusions: Both Lansbury and standard joint count trajectories correlate similarly with HAQ in ERA. The weighting of large joints in LAI was insufficient to reflect the importance of joint inflammation. Furthermore, HAQ probably bespeaks HAQ questions emphasize large joint activities. The effects of large joint swelling may be under recognized due to difficulty in measuring hip, shoulder or elbow swelling. Overall, tender joints had a greater impact on swollen joints and large tender joints had the most impact on function.


SAT0040 ASSESSING 5-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS WITH MODERATE DISEASE: FINDINGS FROM A UK MULTI-CENTRE PROSPECTIVE OBSERVATIONAL STUDY

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Objectives: To investigate the long-term progression of radiographic joint damage in these patients and moderate disease activity states can help reduce radiographic progression and consequently joint destruction, minimising the risk of disability in the long-term.

Results: Of 316 and 328 pts in the ADA and ABA groups, respectively, 38 and 45 pts had all specified baseline characteristics (Cohort 1) and 280 and 283 pts had an absence of at least 1 of the specified characteristics (Cohort 2). Overall, the baseline characteristics, including anti-cyclic citrullinated peptide titres, were well balanced between the groups, with the exception of weight. For Cohort 1, the adjusted mean change (95% CI) from baseline DAS28 (CRP) with ADA vs ABA was −2.18 (−2.61, −1.75) vs −1.56 (−2.01, −1.11) at Week 26, −2.58 (−2.99, −2.17) vs −1.68 (−2.10, −1.25) at Week 52 and −2.50 (−2.97, −2.03) vs −2.0 (−2.49, −1.50) at Week 104. Similar trends of increased efficacy with ABA vs ADA were observed for changes from baseline CDAI SDAI, HAQ-DI, pain and fatigue; no differences in radiographic progression were observed. For Cohort 2, no differences in clinical outcomes between ADA and ABA groups were observed. Given the differences in baseline weight between ADA and ABA groups in Cohort 1, sensitivity analyses that excluded pts >100 kg and adjusted for baseline weight were performed and demonstrated minimal effect of weight on treatment efficacy.

Conclusions: This post hoc analysis seems to indicate a trend of increased efficacy for abatacept in pts with seropositive, erosive early RA compared with the TNF inhibitor adalimumab. Given the small sample size, additional pre-specified randomized studies are needed to compare the benefit of biologic DMARDs with different MOAs in pts with early, rapidly progressing RA.

References:

This study provides support on the importance of tight treatment control with early and aggressive therapy according to T2T principles. Preventing sustained moderate disease activity states can help reduce radiographic progression and consequently joint destruction, minimising the risk of disability in the long-term.


SAT0041 EFFICACY OF ABATACEPT VERSUS ADALIMUMAB IN PATIENTS WITH SEROPOSITIVE, EROSIVE EARLY RA: ANALYSIS OF A RANDOMIZED CONTROLLED CLINICAL TRIAL (AMPLE)


Background: Patients (pts) who are anti-citrullinated protein antibody (ACPA) positive tend to develop more severe erosive disease than ACPA-negative pts.1 The presence of seropositivity and erosions have been noted in EULAR treatment guidelines as poor prognostic factors to identify pts with RA who require early and aggressive clinical intervention.2 Since the disease in pts with seropositive, erosive early RA is mostly driven by immunological features, response to RA therapy may vary based on therapeutic mechanism of action (MOA).

Objectives: To investigate the efficacy of abatacept (ABA) vs adalimumab (ADA) in pts with seropositive, erosive early RA.

Methods: AMPLE (NCT00929864) was a 2-year, Phase IIIb study in which biologic-naive pts with RA were randomized 1:1 to either SC ADA 125 mg weekly or SC ADA 40 mg biweekly, both with background MTX. This post hoc analysis of AMPLE compared clinical outcomes between treatment groups in a subgroup of pts with specified baseline criteria: disease duration >6 months, RF or ACPA seropositivity and -1 radiographic erosion. Disease activity and patient-reported outcomes were evaluated at Weeks 26, 52 and 104. Endpoints were compared between ABA and ADA groups using chi-square test for categorical variables, analysis of covariance model (ANCOVA) controlling for baseline covariates and DAS28 (CRP) stratification for continuous variables.

Results: Of 316 and 328 pts in the ADA and ABA groups, respectively, 38 and 45 pts had all specified baseline characteristics (Cohort 1) and 280 and 283 pts had an absence of at least 1 of the specified characteristics (Cohort 2). Overall, the baseline characteristics, including anti-cyclic citrullinated peptide titres, were well balanced between the groups, with the exception of weight. For Cohort 1, the adjusted mean change (95% CI) from baseline DAS28 (CRP) with ADA vs ABA was −2.18 (−2.61, −1.75) vs −1.56 (−2.01, −1.11) at Week 26, −2.58 (−2.99, −2.17) vs −1.68 (−2.10, −1.25) at Week 52 and −2.50 (−2.97, −2.03) vs −2.0 (−2.49, −1.50) at Week 104. Similar trends of increased efficacy with ABA vs ADA were observed for changes from baseline CDAI SDAI, HAQ-DI, pain and fatigue; no differences in radiographic progression were observed. For Cohort 2, no differences in clinical outcomes between ADA and ABA groups were observed. Given the differences in baseline weight between ADA and ABA groups in Cohort 1, sensitivity analyses that excluded pts >100 kg and adjusted for baseline weight were performed and demonstrated minimal effect of weight on treatment efficacy.

Conclusions: This post hoc analysis seems to indicate a trend of increased efficacy for abatacept in pts with seropositive, erosive early RA compared with the TNF inhibitor adalimumab. Given the small sample size, additional pre-specified randomized studies are needed to compare the benefit of biologic DMARDs with different MOAs in pts with early, rapidly progressing RA.


This study provides support on the importance of tight treatment control with early and aggressive therapy according to T2T principles. Preventing sustained moderate disease activity states can help reduce radiographic progression and consequently joint destruction, minimising the risk of disability in the long-term.


This study provides support on the importance of tight treatment control with early and aggressive therapy according to T2T principles. Preventing sustained moderate disease activity states can help reduce radiographic progression and consequently joint destruction, minimising the risk of disability in the long-term.

Conclusions: The present study shows that radiographic destruction over peripheral joints, which directly reflects cumulative inflammatory burden, is a strong independent risk factor for plaque development that is associated with CV events and mortality.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5985

SAT0043 FACTORS AFFECTING THE NEED FOR ORTHOPAEDIC SURGERY IN PATIENTS WITH RHEUMATOID ARTHRITIS. RESULTS FROM 1010 PATIENTS DIAGNOSED WITH RA FROM 1972-2009

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Background: Surgery still comprises a necessary part of treating RA patients, when medication fail to prevent joint destruction. Orthopaedic corrective procedures are considered a reliable and objective proxy for a destructed joint, and is an important outcome measure in RA.

Objectives: To investigate how patient characteristics, time of diagnosis and treatment affect the need for orthopaedic surgery in patients with rheumatoid arthritis (RA).

Methods: We reviewed the medical history of 1544 patients diagnosed with RA at Haukeland University Hospital in Bergen, Norway from 1972 to 2009, of which 1010 (mean age 57, 69% women) were included in the study. Relevant orthopaedic procedures were obtained from the Norwegian Arthroplasty Register and the hospital’s administrative patient records. 693 procedures (joint synovectomies 22%, arthrodeses 21%, prostheses 41% and forefoot procedures 12%) were performed in 315 patients. Survival analyses were completed to evaluate the impact of age, sex, radiographic changes and year of diagnosis, on the risk of undergoing surgery.

Results: Patients diagnosed in 1972–1985 and 1986–1998 had a relative risk (RR) of 2.4 and 2.2 (p<0.001) respectively, of surgery compared to patients diagnosed in 1999–2009. Radiographic changes at diagnosis and female sex were also significant risk factors. Disease activity at baseline did not affect the outcome. Anti-rheumatic medication was significantly different in the three time periods.

Disclosures: None declared
DOI: 10.1136/annrheumdis-2017-eular.3521

SAT0042 SEVERITY OF RADIOGRAPHIC DESTRUCTION ON PERIPHERAL JOINTS IS A STRONG INDEPENDENT RISK FACTOR FOR CAROTID ATHEROSCLEROSIS


Background: In our previous study, we identified that cumulative inflammatory burden contributes to the development of carotid atherosclerosis through a synergistic interaction with conventional cardiovascular (CV) risk factors in patients with rheumatoid arthritis (RA). However, it is controversial whether the presence of joint destruction which result from inflammatory burden may be a risk factor for carotid atherosclerosis.

Objectives: To investigate whether intima-media thickness (IMT) and plaques of carotid artery are influenced by radiographic joint destruction in patients with RA.

Methods: A total of 186 patients with RA were included in the present study. Plain X-ray of the hands and feet were used to assess the severity of joint destruction. We developed a new radiographic scoring system, named Rheumatoid Arthritis-Radiographic Severity Score (RA-RSS), which scores 21 joint groups with the modified Steinbrocker method. The following joint groups were included: 2 proximal interphalangeal (PIP) joint group, 2 metacarpophalangeal (MCP) joint group, 2 wrist joint group, 2 elbow joint group, 2 shoulder joint group, 1 atlantoaxial joint group, 2 hip joint group, 2 knee joint group, 2 ankle joint group, 2 tarsometatarsal (TMT) joint group, and 2 metatarsophalangeal (MTP) joint group. The grade was determined by the worst changes in each joint group of PIP, MCP, TMT, and MTP joints. RA-RSS groups are assigned as follows: 0 = No radiographic changes; 1 = mild destruction of bone and cartilage; 2 = moderate destruction of bone and cartilage or joint deformities; 3 = Severe destruction of bone and cartilage or bony ankylosis (Score ranges from 0–63). We performed carotid ultrasound to detect the presence of carotid atherosclerosis.

Results: Among 186 patients who were graded using RA-RSS, 110 patients had carotid plaques (59.1%). RA-RSS was significantly higher in patients with plaques compared to patients without plaques (11.2±8.79 vs. 7.6±7.72, p=0.004). Patients were divided into two groups by the cut-off value of plaque development as determined using receiver operating characteristic (ROC) curves: 11.5 (61.8%) patients with RA-RSS ≥10 and 71 (38.2%) with RA-RSS <10. There was a significant difference between the groups with respect to the presence of plaques (48.7% vs. 76.1%, p<0.001), while there was no difference in mean carotid IMT (0.87±0.19 vs. 0.89±0.14, p=0.684). The mean age, the presence of conventional CV risk factors, Korean version of the modified HAQ (mHAQ), DAS28-ESR, and RA-RSS >10 were significantly associated with plaque development. Multivariate logistic regression analysis showed that RA-RSS ≥10 (OR 2.94 [95% CI 1.48–5.84]) and the presence of conventional CV risk factors (OR 2.30 [95% CI 1.21–4.35]) were independent risk factors for plaque development.

Disclosures: None declared

References:
A 10-YEAR FOLLOW UP STUDY OF EARLY SERONEGATIVE ARTHRITIS DIAGNOSED AT AN ADULT AGE

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Background: Up to 20–30% of patients enrolled into RA cohorts and clinical trials are seronegative. However, in studies examining predictors, prognosis, and response to treatment, seropositive and seronegative groups of patients seem to behave differently. Only a few studies have focused on the long term follow up of seronegative arthritis.

Objective: To investigate long-term outcomes of patients with seronegative arthritis during a 10-year follow-up period including clinical outcomes and reclassification of diagnosis when applicable.

Methods: A total of 1046 patients were classified as early RA in 1997–2005 at single rheumatology center and scheduled for a ten year follow-up, including 434 seronegative patients who are subjects of the present analysis. Follow-up examinations were carried out for at least 2 years and then at 5 and 10 years by the treating specialist including complete clinical examination and patient reported outcomes. In addition, case–reviews were performed, with re-classification of the cases when applicable.

Results: Among the 434 seronegative patients (69.4% women, mean age 58), 271 subjects were seen for the 10 year visit with the mean disease activity index (DAS28 of 2.3 (SD 1.02) and the mean HAQ of 0.71 (SD 0.72). Out of the remaining 146 patients, 88 had died and 53 did not attend the 10-year visit due to altered diagnosis, refusal or mortality. Five patients had dropped out and files of 17 patients were missing. During the follow-up of 10 years, 12/434 (2.7%) patients could be classified as seropositive or erosive RA: 4 turned seropositive (2 for ACPA and 2 for RF [-2x normal level]) and 8 developed erosions typical for RA. Reclassification revealed 70 (16.1%) cases of gout, 24 (5.5%) cases of osteoarthritis without evidence of inflammatory disease, 47 (10.8%) cases of psoriatic arthritis, 9 (2.1%) cases of spondyloarthritides and 16 (3.7%) cases of plausible reactive arthritis. Few cases were reclassified as gout (11 cases (2.5%)) and pseudogout (3 cases (0.7%). Also paraneoplastic arthritis (6 cases (1.4%)), juvenile arthritis (5 cases (1.2%), hemochromatosis (2 cases (0.5%)), ankylosing spondylitis (2 cases (0.5%) and temporal arthritis (2 cases (0.5%)) were revealed during follow up. One case of each reflex sympathetic dystrophy, trauma-induced arthritis, meniscal injury, optional Nasu Hakola disease, microscopic polyangiitis (MPA), granulomatous polyangiitis (GPA), antiphospholipid syndrome and cases of Collins ulcer were also found. The remaining 147 patient (33.8%) could not be reclassified in any clear new diagnosis. A total of 44 of these undifferentiated cases had transient arthritis, 43 cases had features of seronegative spondyloarthritides and 57 cases remained totally unspecified, while three patients had features of inflammatory connective tissue disease (SLE and Sjögren’s syndrome), but they did not meet available classification criteria. In addition, files of 17 (3.9%) patients were missing from the analyses.

Conclusions: Over a 10-year period, 97% of seronegative patients remained seronegative and did not develop RA-like erosions. Reclassification revealed significant heterogeneity in the diagnosis of seronegative RA. Therefore, seronegative arthritis should not be studied as a homogenous disease entity.

References:

Disclosure of Interest: None declared


11 YEARS’ FOLLOW-UP OF A DANISH 2-YEAR TREAT-TO-TARGET RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: BASELINE PREDICTORS OF FUNCTIONAL AND RADIOGRAPHIC OUTCOMES


Background: Up to 20–30% of patients enrolled into RA cohorts and clinical trials are seronegative. However, in studies examining predictors, prognosis, and response to treatment, seropositive and seronegative groups of patients seem to behave differently. Only a few studies have focused on the long term follow up of seronegative arthritis.

Objective: To investigate long-term outcomes of patients with seronegative arthritis during a 10-year follow-up period including clinical outcomes and reclassification of diagnosis when applicable.

Methods: A total of 1046 patients were classified as early RA in 1997–2005 at single rheumatology center and scheduled for a ten year follow-up, including 434 seronegative patients who are subjects of the present analysis. Follow-up examinations were carried out for at least 2 years and then at 5 and 10 years by the treating specialist including complete clinical examination and patient reported outcomes. In addition, case–reviews were performed, with re-classification of the cases when applicable.

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Conclusions: Over a 10-year period, 97% of seronegative patients remained seronegative and did not develop RA-like erosions. Reclassification revealed significant heterogeneity in the diagnosis of seronegative RA. Therefore, seronegative arthritis should not be studied as a homogenous disease entity.

References:

Disclosure of Interest: M. L. Hetland Grant/research support from: AbbVie, BMS, MSD, Pfizer, Orion, Novartis, Biogen, Eli Lilly, K. Stengaard-Petersen: None declared, P. Junker: None declared, H. Lindegaard: None declared, T. Ellingsen: None declared, J. Pødenphant: None declared, H. Skjødt: None declared, A. Vestergaard: None declared, B. Ejbjerg: None declared, S. Jacobsen: None declared, N. S. Krogh: None declared, M. Østergaard Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, K. Hørslev-Petersen: None declared

DOI: 10.1136/annrheumdis-2017-eular.1720
comparison of the data obtained, the adverse events reported for each drug were normalized using the number of treatments for the same period. The reporting odds ratio (OR) and its 95% confidence intervals (CI) were calculated regarding the different categories of adverse events. The incidence of serious adverse events, serious infections, withdrawals due to adverse events and deaths were also evaluated.

**Results:** The EudaVigilance database contains 851,882 adverse events reported for IFX, ETN, and ADA. During this period, the different TNF antagonists have shown almost the same safety profile. The reported adverse events were classified by systems organ class (SOC) and the most frequent were administration site reactions (22.8%) and infections and infestations (11.2%). Safety was not statistically different. The comparison between IFX originator and its biosimilar did not show statistically significant differences in safety (ROR 1.08 (0.80,1.46)) during the initial 3-years after launch for both drugs. However, a small non-significant increase in adverse reactions was noted for IFX-biosimilar, which might reflect increasing attention for this class of drugs.

**Conclusions:** The comparison of reference IFX and IFX-biosimilar did not demonstrate statistically significant differences in safety. This pharmacovigilance study provides the first analysis of TNF antagonists from the EudaVigilance database and offers a framework for safety comparison between originators and biosimilar TNF antagonists.

**Acknowledgements:** We would like to acknowledge EudraVigilance for providing access to the database.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5884

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**PREDICTING MAINTENANCE OF RESPONSE BASED ON DISEASE CHARACTERISTICS AND EARLY CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS UPON WITHDRAWAL OF ADALIMUMAB**

J.S. Smolen1, P. Emery2, H. Zhang3, X. Wang4, J. Suboticki3, I. Sainsbury3, A. Kavanaugh4, 1Medical Univ of Vienna, Vienna, Austria; 2Leeds Inst of Rheumatic & Musculoskeletal Medicine, Leeds, United Kingdom; 3AbbVie, N Chicago, IL; 4Univ of California, San Diego, CA, United States

**Background:** Some patients (pts) with rheumatoid arthritis (RA) achieve low disease activity (LDA) after treatment with adalimumab (ADA) plus methotrexate (MTX) and can maintain LDA after ADA withdrawal1. However, others experience a flare in disease activity. The factors associated with loss or maintenance of response are not understood.

**Objectives:** To identify disease characteristics and early clinical responses, which predict maintenance of LDA upon ADA withdrawal in individual RA pts.

**Methods:** Data from the OPTIMA trial were used in this post hoc analysis. In period 1 (P1), pts were treated for 26 weeks (wks) with ADA+MTX or placebo (PBO)-MTX. Pts on ADA+MTX who achieved DAS28-CRP ≤ 3.2 at wks 22 and 26 (responders) were randomized to ADA withdrawal, or ADA+MTX continuation up to Wk 78. Responders to PBO-MTX in P1 continued on PBO-MTX up to Wk 78 (PBO continuation). Data from the ADA withdrawal arm were used to predict LDA at Wk 78 by DAS28-CRP (≤ 3.2) or SDAI (≤ 11). Potential factors including baseline (BL) disease characteristics and Wk 26 responses, including DAS28-CRP, SDAI, ACPA reactivities toward 13 different citrullinated peptides (fillagrin, fibrinogen, alpha-enolase, vimentin, histone) (1).

**Results:** A regression tree method3 was established by the LASSO method, which performs variable selection by penalizing unduly complicated models, with/without incorporating the speed of DAS28-CRP or SDAI response as an individual predictor. Logistic regression on the LASSO-selected factors yielded coefficients used to derive individual scoring equations and prediction scores for Wk 78 outcomes (fig footnote). Prediction score cutoffs were established by the regression tree method. The results were validated in data from the PBO continuation arm.

**Conclusions:** For the prediction of DAS28-CRP LDA at Wk 78, BL physician global assessment (PhGA) and health-assessment questionnaire-disability index (HAQ-DI), and Wk 26 DAS28-CRP, HAQ-DI, SDAI and CRP were selected by LASSO, and used to calculate the prediction score. Including speed of response did not affect the predictors chosen. Of 9 pts predicted not to have DAS28-CRP LDA at Wk 78, 0 had LDA (NPV=100%) (fig 1). Out of 66 pts predicted to have DAS28-CRP LDA at Wk 78, 63 predictions were correct (PPV=96.5%). Results were comparable for most cutoff categories in the validation arm (PPV=82%); however, no pts were predicted to have a non-response at Wk 78. For the prediction of SDAI LDA at Wk 78, the NPV was 86% (1/7 predictions incorrect); PPV was 98% (39/41 predictions correct); in the validation arm, the PPV was 82%.

**References:**


**Disclosure of Interest:** J. Smolen Grant/research support from: from Pfizer, MSD, AbbVie Inc., BMS, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., Consultant for: from MSD, AbbVie Inc., BMS, UCB, Roche, Novartis, Sandoz, and Lilly., Hans Smolen Grant/research support from: from Pfizer, MSD, AbbVie Inc., BMS, UCB, Roche, Novartis, Samsung, Sandoz and Lilly. Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation; and writing, reviewing, approval of final version. Medical writing: Naina Barretto of AbbVie.
Background: The rheumatoid arthritis (RA) Treat to Target (T2T) recommendations\(^1\) defined in 2010 aimed to support clinicians to achieve optimal therapeutic outcomes for their patients.

**Objectives:** 38 hospitals prospectively audited management of newly diagnosed RA patients to determine compliance with the T2T recommendations and therapeutic outcomes achieved.

**Methods:** From April 2012 to September 2016 and upon diagnosis of RA, data on disease history, management and clinical outcomes were collected prospectively in a web-based tool. Follow-up to date provides data for up to 24 months from diagnosis (baseline).

**Results:** 1571 patients were recruited in 38 centres, with 12 months’ follow-up for 713 patients and of these 269 also had 24 months’ follow-up. 1021 (65%) patients were followed for the subset of patients with available DAS28 scores at the relevant time points, stratified by those who did/did not achieve their remission target and those with/without sustained remission at 24 months. Of the 108 eligible patients required to receive biologic therapy, according to NICE guidance, 39 (36%) received a biologic within their first 24 months of treatment.

**Conclusions:** The results suggest that more patients with a target set at baseline in 12 months do not appear to affect the proportion of patients in remission at 24 months, but active management in the first 12 months (4 visits, <4 DAS28 scores) does appear to be associated with more patients in remission at 24 months. Thus we conclude that treating RA early and aggressively, in line with the T2T guidelines, leads to sustained clinical improvement.

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**References:**

CITRULLINATION OF ADENOSINE DEAMINASE ISOFORMS IN SYNNOVIAL FLUIDS (SFs) OF RA PATIENTS AND PREDICTION OF TREATMENT SUCCESS

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1 H.C. Buniatian Institute of Biochemistry of Armenian NAS; 2 “Yerevan” Medical Center, Yerevan, Armenia

Background: One of the most important discoveries in rheumatology is the characterization of citrulline containing auto-antigens [1]. The identification of citrullinated proteins as auto-antigens and the development of new assay based on the detection of anti-citrullinated protein antibodies (ACPAs) become a breakthrough in the diagnosis and treatment of rheumatoid arthritis (RA). Matsui and coauthors in vitro identified adenosine deaminase (ADA) as an ACPA antigen [2]. Earlier we have reported the enhanced ADA activity in synovial fluids (SFs) of RA patients [3]. This increasing was in correlation with the ratio of small isoenzyme (SADA) from SFs with high ADA activity (100–190 IU/L) were used. Earlier we demonstrated a negligible level of SADA at activity can serve as new citrulline containing ACPA antigen. This finding can be used as an independent predictor of disease activity. In our cohort, 105 (30.1%) ERA patients were treated with biological disease modifying anti-rheumatic drugs (bDMARDs) over time. Biotechnological therapy was less frequently started by subjects in CDC, both after 12 months (p=0.003) and at the time of last FU (p=0.0001). At the multivariate analysis, not achieving CDC at the 12th month of FU [OR (95% CI): 2.69 (1.59–4.57)] and a normal BMI (95% CI): 2.05 (1.23–3.42) were the variables significantly associated to bDMARD therapy over time.

Conclusions: The simultaneous achievement of symptom control, inhibition of radiographic progression and normalization of function, is a feasible target in real world EAC. Having a VERA and a normal weight are associated to a high chance of “deep” remission.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5496

SAT0053 THE INCIDENT IMMUNOLOGICAL STATUS PREDICTS DRUG-FREE DISEASE FLARE IN RHEUMATOID ARTHRITIS PATIENTS ACHIEVING STRINGENT CLINICAL AND ULTRASONOGRAPHIC CONTROL OF THE PERIPHERAL INFLAMMATORY PROCESS

A. Manzo, S. Bugatti, F. Benaglio, B. Vitolo, G. Sakellariou, R. Caporali, C. Montecucco, Rheumatology and Translational Immunology Research Laboratories (LaRIT), Division of Rheumatology, IRCCS Policlinico San Matteo Foundation/University of Pavia, Pavia, Italy

Background: The development of predictive tools to evaluate health risks and make the optimized health plans in patients with rheumatoid arthritis (RA) achieving remission still represents a major unmet need. In this perspective, the relative weight of clinical, ultrasound and immunological assessment of disease characteristics for predicting recurrence of the inflammatory process under drug-free conditions remains unclear.

Objectives: To investigate the predictive value of baseline clinical remission stringency, synovial power Doppler (PD) ultrasound indices and the incident autoimmune status, as predictors of flare under drug-free conditions after a DAS28-driven treatment strategy with methotrexate (MTX) in early RA.

Methods: 85 RA patients achieving remission and candidate to MTX withdrawal were recruited according to the following criteria: 1) introduction of MTX within 12 months from symptoms onset, 2) at least 24 months of MTX treatment with a DAS28-driven protocol targeting low disease activity (LDA), 3) DAS28 ≤ 2.6 for ≥ 6 months in the absence of corticosteroids. Following treatment withdrawal, patients were followed for three months intervals across 24 months through clinical, ultrasound (hands-feet-axillary lymph nodes), radiographic and immunologic screenings (ACPAs, CRP status, CXC1L3 circulating levels and FACS analysis for quantification of KB67/ regulatory-T B cell subsets). Treatment was re-introduced in case of DAS28 > 3.2 or stable LDA.

Discipline: Other
DOI: 10.1136/annrheumdis-2017-eular.1433
Results: At baseline, 84% of the patients were in remission according to the SDAI (median 84.8 vs. 205.6 ng/mL, p=0.0006), and in the dead group than in the alive group. Univariate analyses revealed that age ≥ 75 years and those who died after AE (dead group), and identified variables significantly associated with AE occurrence and survival using Cox hazard analyses. A rapid and meaningful reduction in pain is important to quality of life in patients (pts) with rheumatoid arthritis (RA). Baricitinib (bari) is a selective inhibitor of Janus kinase (JAK) 1/2 in development for pts with active RA, regardless of the pt population. Significant improvements in pain for bari vs PBO and bari vs ADA were sustained through week 24.

Conclusions:

Background: Acute exacerbation (AE) is recently recognized as deterioration of respiratory status in idiopathic pulmonary fibrosis. It is reported that AE also occurs in other interstitial lung diseases (ILD) such as collagen vascular diseases associated ILD (CVID-ILD). However, the characteristics and risk factors of AE in CVID-ILD are not clearly identified.

Objectives: To clarify the characteristics of patients with rheumatoid arthritis-associated interstitial pneumonia (RA-IP) and to investigate the risk factors associated with AE and its survival of RA-IP.

Methods: We examined the clinical features of 60 RA-IP patients admitted to our hospital between July 2010 and September 2016. We compared the characteristics between patients who developed AE (AE group) and those who did not (non-AE group), and between patients who survived after AE (alive group) and those who died after AE (dead group), and identified variables significantly associated with AE occurrence and survival using Cox hazards analyses.

Results: Thirty-six (60%) were female. Twenty-two (36.7%) developed AE and 22 (36.7%) died after AE. The mean age at RA diagnosis was 61.1 ± 16.3 years in the AE group and 61.5 ± 13.1 years in the non-AE group. Sex, smoking habit and high-resolution computed tomography (HRCT) pattern were not significantly different between two groups. Although there was no significant difference, more patients in the AE group received methotrexate (MTX) treatment than those in non-AE group (40.9% vs. 18.9%, p=0.12), and MTX use was significantly associated with occurrence of AE in a Cox hazard analysis (Hazard ratio [HR] 1.09, 95% confidence interval [CI] 1.01–1.18). Further, age (median 70 vs. 82 years, p=0.002) and matrix metalloproteinase-3 (MMP-3) level (median 84.8 vs. 205.6 ng/mL, p=0.003) on admission were significantly higher in dead group than in alive group. Univariate analyses revealed that age ≥ 75 years (HR 10.53, 95% CI 1.26–88.15), MMP-3 ≥ 200 ng/mL (HR 15.58, 95% CI 1.38–175.8), and 3L or more oxygen use (HR 8.46, 95% CI 1.02–70.49) on admission were significantly associated with death (Table 1).

Table 1. Percent Pain Improvement in RA-BEAM and RA-BEACON

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<th>RA-BEAM</th>
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<tr>
<td>PBO (N=488)</td>
<td>27</td>
<td>27</td>
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<tr>
<td>Bari 4 mg</td>
<td>49**</td>
<td>49**</td>
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<td>ADA (N=330)</td>
<td>47***</td>
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<td>PBO (N=176)</td>
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<td>Bari 2 mg</td>
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<td>ADA (N=177)</td>
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<td>PBO (N=487)</td>
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<tr>
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* p<0.05 vs PBO; ** p<0.01 vs PBO; *** p<0.001 vs PBO; **p=0.05 vs ADA; ***p=0.01 vs ADA; p-values based on logistic regression model. ADA = adalimumab; Bari = baricitinib; PBO = placebo.

Conclusions: Bari-treated pts reported significantly greater and more rapid reductions in pain severity as measured by the pain VAS compared to PBO or ADA; improvements were sustained throughout 24 weeks. The results were similar regardless of the pt population.

References:

Disclosures of Interest: P. Taylor: None declared, B. Faurel Consultant for: AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Lilly, Novartis, Pfizer, Roche, SOBI pharma, UCB.

DOI:10.1136/annrheumdis-2017-eular.36441

Baricitinib showed rapid and greater reduction in pain compared to adalimumab or placebo in patients with rheumatoid arthritis

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Background: A rapid and meaningful reduction in pain is important to quality of life in patients (pts) with rheumatoid arthritis (RA). Baricitinib (bari) is a selective inhibitor of Janus kinase (JAK) 1/2 in development for pts with active RA.

Objectives: To evaluate the effect of bari treatment on pain reduction compared to adalimumab (ADA) or placebo (PBO) in pts with inadequate response to methotrexate (MTX) or biologic disease-modifying antirheumatic drugs (bDMARDs).

Methods: In RA-BEAM (NCT01710358), 1305 pts with inadequate response to MTX were randomised 3:3:2 to PBO QD, bari 4 mg once daily (QD), or ADA 40 mg biweekly. In RA-BEACON (NCT01721044), 527 pts with inadequate response or intolerance to bDMARDs were randomised 1:1:1 to PBO or bari (2 or 4 mg) QD. This post-hoc analysis reports the pts’ assessment of pain using a visual analogue scale (VAS, range: 0 to 100 mm). The proportion of pts who achieved ≥30% pain improvement of ≥30%, ≥50%, and ≥70% on their baseline pain score, baseline joint erosion status (RA- BEAM only), and history of bDMARD at screening (RA-BEACON only). Missing data were imputed using modified last observation carried forward.

Results: Mean baseline pain scores were 60, 62, and 61 for PBO, bari 4 mg, and ADA, respectively, in RA-BEAM and 65, 62, and 66 for PBO, bari 2 mg, and bari 4 mg, respectively, in RA-BEACON. A significantly greater proportion of pts treated with bari 4 mg achieved ≥30%, ≥50%, and ≥70% pain improvement as early as week 1 compared to PBO (both studies) and as early as week 4 compared to ADA (RA-BEAM) (Table). A significant pain improvement of ≥70% was achieved at week 12 for pts treated with bari 4 mg compared to PBO (both studies) and ADA (RA-BEAM). Pain improvement of ≥30%, ≥50%, and ≥70% with bari 2 mg was significant compared to PBO by week 12 (RA-BEACON). Significant improvements in pain for bari vs PBO and bari vs ADA were sustained through week 24.

Table 1. Pain improvement in RA-BEAM and RA-BEACON

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* p<0.05 vs PBO; ** p<0.01 vs PBO; *** p<0.001 vs PBO; **p=0.05 vs ADA; ***p=0.01 vs ADA; p-values based on logistic regression model. ADA = adalimumab; Bari = baricitinib; PBO = placebo.

Conclusions: Baricitinib showed rapid and greater reduction in pain compared to adalimumab or placebo in patients with rheumatoid arthritis.
**SAT0056** RHEUMATOID ARTHRITIS MAGNETIC RESONANCE IMAGING SCORE (RAMRIS) CAN PREDICT DAS28 THERAPY RESPONSE AFTER 6 MONTHS: RESULTS OF THE GERMAN ARTHROMARK COHORT

P. Sewerin1, S. Vordenbäumen1, C. Schleich2, R. Sengewein2, R. Brinks3, G. Pongratz2, J. Lesch2, L. Le4, U. Mansmann1, M. Schneider1, B. Ostendorf1 on behalf of ArthroMark Studygroup. 1Department for Rheumatology; 2Department for Diagnostic and Interventional Radiology; 3Hilger-Research-Center for Rheumatology, University Hospital Düsseldorf, Düsseldorf; 4Institute for Medical Information Sciences, Biometry and Epidemiology, Ludwig Maximilian University of Munich, Munich, Germany

Background: Remission is the ultimate goal in rheumatoid arthritis (RA). The absence of rheumatoid factors (RF) and/or anti-citrullinated protein (CCP) antibodies, no morning stiffness, low conventional disease activity and no erosions are considered to have low disease activity, and early therapeutic intervention are established good prognostic markers. Magnetic resonance imaging (MRI) is a well evaluated imaging technique and is increasingly used in daily practice. In this study, we prospectively investigated the prognostic performance of high-field MRI and serological biomarkers 6 months after initiation of methotrexate in patients with early RA (eRA).

Objectives: To evaluate the value of high-resolution MRI of the hand as a prognostic marker for EULAR-response and remission after 6 month of MTX therapy in early RA patients.

Methods: Prospective study on the ArthroMark cohort using 3T MRI of the hand at baseline (V0) before initiating an MTX-therapy in eRA patients, after 3 months (V3) and after six months (V6). 28 patients (Ø 56.8 years) with RF and/or CCP positive RA and a disease duration ≤6 months (mean±16.3 weeks) fulfilling the 2010 ACR/EULAR criteria were examined. EULAR core set of variables were recorded: patient’s global assessment of disease activity, number of tender and swollen joints, ESR and CRP. The following biomarkers were assessed by ELISA: Dkk-1, Osteoprotegerin, IL-22, MMP-3, TNF-Alpha and Neopteriptide-Y. Remission was defined as DAS28 <2.6 according to the ACR/EULAR remission criteria. MRI-scan was performed by using the OMERACT RA-MRI scoring system (RAMRIS) to assess disease activity.

Results: A low RAMRIS subscore for erosions (p=0.019) or total RAMRIS score (p=0.0001) were significant results found for the MRI markers assessed for response prediction at either V3 or V6. Concerning remission, low levels of RAMRIS at baseline were significantly associated with EULAR remission at V6 (p=0.033). The other markers assessed did not show significant results at either V3 or V6. In multivariate analyses, response was predicted more accurately with the inclusion of either RAMRIS (p value LR-test =0.035), RAMRIS synovitis subscore at MCP-2 (p value LR-test =0.035) or a combination of the two (p value LR-test =0.042). Remission was more accurately predicted when RANKL was considered with low RANKL improving the chance of remission. In contrast to response-prediction, MRI did not significantly add to the prediction model for remission.

Conclusions: Low RAMRIS scores or RAMRIS synovitis subscorer at MCP-2 were predictive for therapy response after 6 months in our generalised mixed model. Baseline RAMRIS was able to significantly predict remission. Our data suggests that MRI and/or serological markers may did disease activity prediction and facilitate patient selection for intensified therapy in the future.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3808

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**SAT0058** EFFECTS OF BARICITINIB ON PATIENTS WHO STOP METHOTREXATE MONOTHERAPY AND SWITCH TO BARICITINIB MONOTHERAPY

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Background: Baricitinib (bari) is a reversible oral Janus kinase (JAK) inhibitor with selectivity for JAK1/JAK2 in development for treatment of patients (pts) with active rheumatoid arthritis (RA). In the 52-week (wk) Phase 3 RA-BEGIN study of MTX-naïve pts, there were 3 arms: bari 4 mg once daily (QD), meloxicam (MET) 7.5 mg QD, up to 20 mg weekly (QW), and the combination of bari plus MTX (bari+MTX). Nonresponders were rescued from week 24 onwards by receiving bari+MTX, regardless of original treatment. Bari monotherapy showed superior efficacy compared to MTX monotherapy and similar clinical efficacy to bari+MTX.

Methods: In RA-BEGIN, 588 pts were randomised 4:3:4 to MTX, bari monotherapy 4 mg QD and bari+MTX. At wk 24, 27% of pts who had entered the LTE; all pts received bari 4 mg monotherapy, MTX could be added in the LTE by investigator decision. Seventy-seven percent of pts (451/588) enrolled in the LTE, of whom 423 had not been rescued in RA-BEGIN. This post hoc analysis evaluated clinical efficacy of pts who continued bari monotherapy compared to those in whom MTX was added within the first 24 wks of the LTE.

Results: Of these 423 pts, 202 (47%) remained on monotherapy at Wk 24 of the LTE and 223 pts started on MTX before wk 24. Most (193) had initiated MTX within 4 wks of starting the LTE study, evenly balanced from the 3 original arms. Acros stance of pts who had MTX added in the LTE had worse disease control upon entry and during the LTE. Through 24 wks, statistically significant improvement in disease state was observed in the MTX-to-bari-group regardless of whether or not MTX was added back. In the bari-to-bari monotherapy group, the addition of MTX led to lowered disease activity, which was statistically significant. No statistically significant changes in disease activity were observed in the pts who were switched from bari+MTX to bari monotherapy regardless of additional MTX therapy (Table 1). Exposure-adjusted incidence rates for total treatment-emergent adverse events, including non-serious infections, were lowest in the MTX-to-bari group. Clinically significant or consistent differences in SIE,
SAEs, or AEs leading to study drug discontinuation were not seen in any of the arms, whether MTX was added or not.

Conclusions: Switching from MTX to bari monotherapy, maintaining bari monotherapy was associated with improvements in depths of disease control during the initial 24 wks post-switch. Disease control did not significantly change after withdrawal of MTX from combination therapy. Pts who entered the LTE with suboptimal disease control after treatment with bari monotherapy may benefit from the addition of MTX. Discontinuation of MTX in pts treated with combination during the index study was associated with maintenance of response. There were no differences in important measures of safety including events that are serious or led to discontinuation.


Background: In rheumatoid arthritis (RA), several autoantibody characteristics, including specificity, levels and isotypes, may influence their pathogenic properties and clinical and laboratory outcomes of the disease (1,2). Furthermore, particular, classical IgM rheumatoid factor (RF) may boost inflammation triggered by anti-citrullinated protein antibodies (ACPAs) (3).

Objectives: To investigate whether RF impacts on disease characteristics and response to therapy in ACPA-positive early RA patients treated with conventional synthetic disease modifying drugs (csDMARDs).

Methods: 574 early RA patients consecutively enrolled in our Early Arthritis Clinic between 2005 and 2014 were included. Patients had symptoms’ duration ≤12 months, were glucocorticoid- and DMARD-naive, and fulfilled RA criteria at inclusion. IgM RF and IgG ACPA were determined in baseline sera by immunonephelometry and a second-generation ELIA CCP assay respectively. Autoantibody levels were considered high when >3 times the upper limit of normal (ULN). Patients were treated with incremental doses of methotrexate according to a treat-to-target strategy aiming at low disease activity (LDA, DAS28<3.2). The associations between autoantibody specificity and levels and the achievement of LDA and disease remission (DAS28<2.6) over 6 months were investigated by Cox regression.

Conclusions: High peak radiographic progression is a rear phenomenon that gets less frequent in patients over the last years of observation. This may be an effect of modern therapy. Among the patients with high radiographic progression, (1) a greater delay between diagnosis and first symptoms was found and (2) the use of biologic agents was less frequent. These data suggest that the decreasing frequency of very high radiographic peak progression in the Swiss RA patients reflect a more effective therapeutic approach in the last years.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4232
selected for outcome analyses. Among seropositive patients, both LDA and remission were less frequently achieved in case of RF-potency. Relevantly, in ACQA-positive patients (n=273), the co-occurrence of RF dose-dependently influenced clinical outcomes. After 6 months of treatment, LDA and disease remission were achieved respectively by 69.6% and 47.8% of single ACPA-positive patients (chi-square for trend p=0.18 for LDA; p=0.05 for remission). After adjusting for confounders (age, gender, symptoms’ duration, baseline disease activity, use of prednisone, recruitment period), high levels of RF independently predicted failure to achieve LDA with an HR (95% CI) of 0.61 (0.39 to 0.95) and failure to achieve remission with an HR (95% CI) of 0.63 (0.35 to 0.99) (Figure 1). In contrast, ACQA levels did not show any significant predictive value, neither for thresholds of -3 ULN nor >100 U.

Conclusions: Among ACQA-positive RA patients, disease characteristics may vary in association with the extent of overall humoral autoimmunity. In particular, the concomitant presence of high levels of IgM RF seems associated with lower response rates to csDMARDs. Collectively, these findings highlight the importance of further subclassifying patients with autoantibody-positive RA in order get deeper insights into disease mechanisms and clinical outcomes.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5778

SAT0061  | HAQ SCORE IS AN INDEPENDENT PREDICTOR OF SUSTAINED REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: We compared remission rates, according to different definitions of remission in rheumatoid arthritis (RA) and investigated the potential predictors of sustained remission at the 2-year follow-up.

Methods: We obtained data on 291 RA outpatients, seen from July 2009 to September 2012. Sociodemographic data and answers to questionnaires were collected at each interview. Remission was defined according to the Disease Activity Score in 28 joints (DAS28-ESR), DAS28-CRP, Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), and ACR/EULARARLar definition. Sustained remission was defined as when the patient fulfilled the definitions at two consecutive annual assessments. Predictors of sustained remission according to the DAS28-CRP were assessed by univariate and multivariate analyses.

Results: For the 291 RA patents, the remission rates of RA were 17.9% (DAS28-ESR), 54.3% (DAS28-CRP), 10.3% (SDAI), 10.0% (CDAI), and 8.6% (Boolean). On follow-up for 2 years, the sustained remission rates of RA were 46.5% (DAS28), 55.0% (DAS28-CRP), 37.5% (SDAI), 32.0% (CDAI), and 30.8% (Boolean). RA patients who achieved sustained remission according to the DAS28-CRP were younger, and had more education, higher monthly income, lower patient global assessment, lower patient pain assessment, and had less joints with grade 3 signals (p=0.04). Specifically, patients with a low CRP, and a high 14–3-3 level had a higher likelihood of flaring versus those with a low 14–3-3, 22% versus 12%.

Conclusions: Baseline 14–3-3 and increases in its levels are associated with worse radiographic outcomes in patients who achieve clinical remission and discontinue ADA. To reduce the risk of flare in patients who are candidates for discontinuation of ADA, CRP and 14–3-3 measurements should be considered in combination as markers of flare prediction.

Disclosure of Interest: S. Hira: None declared, A. Marotta Employee of: A)urex Life Sciences Corp., K. Hanami: None declared, Y. Tanaka: None declared
DOI: 10.1136/annrheumdis-2017-eular.5429

SAT0063  | A PROSPECTIVE STUDY ON COMPARISON OF COMPOSITE INDICES WITH ULTRASOUND FOR DETECTING REMISSION AND PREDICTION OF FLARE IN 2 YEARS


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Background: Treat-to-target (T2T) approach suggests using a composite index patient’s remission status. To compare two ultrasound indices for RA patients in remission taking Ultrasound Global Synovitis Score (GLOESS) as a gold standard and their predictive value for flares in 2 years.

Methods: RA patients who were considered to be in clinical remission according to the clinician were recruited. Disease activity was assessed using DAS28-CRP, CDAI, SDAI and Rapid-3 and 38 joints from 2007 to 2011. The total GLOESS score was calculated in 2 consecutive visits of the following 2 years, whenever available.

Results: Ninety-six consecutive patients (80.2% females) were recruited. Patients were more frequently categorized as being in remission using DAS28 (80%) as compared to CDAI (50%), SDAI (45.2%) and Rapid-3 (37.5%). Patients that were in remission according to CDAI had lower GLOESS scores on 28 joints (p=0.05) and had less joints with ≥2 signals (p=0.04) (table). For SDAI patients in remission had less number less number of joints with grade ≥2 signals (p=0.03) than to have lower GLOESS scores on 28 joints as well as lower number of joints with ≥2 signals (p=0.06). None of the US scores were able to differentiate different disease states according to DAS28-CRP or Rapid. Flare data was available in 76 patients, 22 of whom had flares. Patients that had flare had higher GLOESS scores on 28 joints at baseline (p=0.03) and tend to have higher number of joints with grade ≥3 signals (p=0.06). Although numerically higher, none of the clinical indices were able to predict flares based on remission status (remission vs non remission: CDAI: 22.5% vs 36.1, p=0.2; SDAI: 22.9 vs 38.6, p=0.2; DAS28: 25.4% vs 50%, p=0.1; RAPID3: 20% vs 34.8%, p=0.2).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2363
Background: Anti-citrullinated protein/peptide antibodies (ACPA) have been suggested to identify a more severe phenotype of rheumatoid arthritis (RA).

Objectives: In this study in a recruitment cohort of early RA we have assessed a number of antibodies against different citrullinated and/or mutated peptides using a multiplex platform in relation to the patients disease inflammation and radiological disease progression.

Methods: Patients with early RA (<12 m of symptoms) fulfilling the 1987 ARA criteria (n=1022, 629/393, mean age 56.7±14.0 years) were sampled at the time of diagnosis and assessed using disease activity score (DAS28) at baseline, 1, 2, 12 and 18 months. Radiographs were graded using Larsen score (baseline and at 24 m). Plasma sampled at baseline was analysed for presence of antibody reactivities against 21 different citrullinated and mutated peptides/proteins; Fibronectin (Fib), -α2 (36–52), -β2 (573, Fib)-α2, Fib-α2, Fib β2 (62–78, 72), Fib-β2 (78–72), Filaggrin (Fil307–324), -α-Enolase peptide 5–21 (CEP-1), Vimentin ( Vim) 2–17, Vim60–75, F4-R-Cit, F4-Cit-Cit, F4-Cit-R, or mutated proteins (Blaz2, Pept1, Pept5, Pept21, Pept22) and type II Collagen citrullinated or not using a custom-made microarray assay based on the ImmunoCAP ISAC system (Phadia AB, Sweden). Cut-off levels were at the 98th percentile of controls (n=477). Anti-CCP2 was analysed using ELISA (EuroDiagnostic, Sweden).

Results: The most frequent appearing ACPA were: Fib-β2 (60–74) (56.6%), Fib-β2 (536–52) (55%); Fib-β2 (573, Fib)-α2 (54.9%), Fil307–324 (51.7%); CEP-1 (53.7%) and Pept5 (52.0%). Antibodies against CEP1 (76%), Fib-β2 (62–78) (72%), Fil307–324, F4-R-Cit antibodies with significant correlation between radiological progression and antibodies against Vim-2–17, Fib-β2 (36–52), CEP1, Fib-β2 (621–635) and CCPRP and between DAS28 and Vim60–75, F4-R-Cit, Pept21 (74%, F4-R-Cit antibodies vs. being negative).

Conclusions: Analyses at baseline, of the ACPA specificity profiles allowed different patterns of disease activity and radiological progression during the first 24 months of the disease to be identified.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5085
UPIA, Rheumatoid Arthritis (RA), Spondyloarthritis (SpA) or Psoriatic Arthritis (PsA), respectively.

Results: During the follow-up (6 (14.3%) UPIA reached a defined diagnosis (2 RA, 2 SpA and 2 PsA, respectively). At baseline, UPIA who differentiated had higher GSUS (p=0.01) and PDUS scores (p=0.02) compared to patients who remained as UPIA. At follow-up 1 year, UPIA who differentiated to arthritis had higher histological scores for lining and sublining CD68⁺ (p=0.005 and p=0.04 for lining and sublining, respectively), sublining CD3⁺ cells (p=0.002) and CD31⁺ vessels count (p<0.001) than patients who remained as UPIA. In addition, there were direct correlations between baseline GSUS and PDUS scores with lining CD68⁺ cells scores (p<0.001 for GSUS and p=0.02 for PDUS scores respectively), sublining CD68⁺ cells scores (p=0.02 for GSUS and p=0.03 for PDUS scores respectively), sublining CD3⁺ cells score (p=0.02 for GSUS and p=0.002 for PDUS scores respectively) and CD31⁺ vessels count (p<0.001 for CD31⁺, p<0.001 for GSUS scores respectively). Finally, the areas under the receiver operating characteristic (ROC) curves CD31⁺ vessels count (cut-off value: 24.3), GS score (cut-off value: 1.5) and PDUS score (cut-off value: 1.5) were calculated to assess the best cut-off points to identify the differentiation likelihood during the follow-up in UPIA patients. The logistic regression analysis, demonstrated that having baseline GSUS and PDUS scores >1.5 [OR:13.64 (95% CI: 0.98–242.59); p=0.05] and CD31⁺ vessels count >24.3 [OR:51.13 (95% CI: 3.15–829.16); p=0.01] were independent factors associated with the achievement of defined arthritis.

Conclusions: Histological and US assessment may help in the identification of patients with seronegative UPIA with high likelihood of clinical differentiation towards defined arthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4841

FURTHER TREATMENT INTENSIFICATIONS IN UNDIFFERENTIATED AND RHEUMATOID ARTHRITIS PATIENTS OVER TIME. PATIENTS IN LOW DISEASE ACTIVITY HAVE LIMITED BENEFIT TOWARDS PHYSICAL FUNCTIONING

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Background: It is recommended to optimize treatment as long as a predefined treatment target is not met, but should we aim at remission if patients are in low disease activity (LDA)?

Objectives: To assess if RA or undifferentiated arthritis (UA) patients who achieved LDA benefit with better functional ability from treatment intensification aimed at DAS remission.

Methods: In the IMPROVED study 610 patients with early RA (ACR 2010) or UA were “treated to target” aimed at DAS remission, assessed 4-monthly. Initial treatment was methotrexate (MTX) + tapered high dose prednisone. Patients with DAS ≤ 1.6 tapered treatment. Patients with DAS > 1.6 were randomized to MTX + tapered high dose prednisone or to MTX + adalimumab. Over 5 years, patients with DAS > 1.6 were required to increase, change or restart medication. HAQ was measured 4-monthly. A linear mixed model analysis with confounders.

Results: Overall, over 5 years DAS (baseline mean (SD): 3.2 (1.7) and HAQ (1.2 (0.7)) showed a statistically significant and clinically relevant decrease (ΔHAQ -0.59, 95% CI -0.61; -0.57; ΔDAS -1.77, 95% CI -1.79; -1.75). The number of patients in LDA per visit ranged from 88 to 146, of which 26% to 73% (increasing over time) had no treatment change due to protocol violations. We found a statistically significant but not clinically relevant effect of treatment change on ΔHAQ, corrected for baseline HAQ, age, gender and treatment arm (model 1, β -0.085, 95% CI -0.13; -0.044). When ΔDAS was added (model 2), the effect of treatment change was partly explained by ΔDAS and no longer statistically significant (β -0.002; 95% CI -0.006; 0.015). The effect of treatment intensification on HAQ improvement became less over time, as demonstrated by a statistically significant interaction between change in HAQ and time in follow-up model 3 (β 0.0098, 95% CI 0.0010; 0.019) (table 1).

Conclusions: Treatment intensification in early RA or UA patients who already achieved low disease activity is associated with a statistically significant decrease in HAQ, but not with a clinically meaningful improvement in functional ability. The effect on ΔHAQ decreased with increasing follow-up time. Therefore not remission or low disease activity, but good functional ability may be the optimal treatment target at which to steer treatment adjustments. These results suggest that, whereas remission may be the optimal goal, when patients in low disease activity have acceptably low HAQ, further treatment intensification may only have downsides such as side effects and costs.

Disclosure of Interest: None declared

THE TIME UNTIL PERFORMING TIGHT CONTROL AS A TREAT-TO-TARGET STRATEGY AND THE TOLERABILITY OF METHOTREXATE STRONGLY INFLUENCE THE ACHIEVEMENT OF CLINICAL REMISSION IN RHEUMATOID ARTHRITIS

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Background: Clinical remission (CR) is the first targeted outcome of early treatment for rheumatoid arthritis (RA). Therefore, a consensus is needed for achieving CR by using the treat-to-target (T2T) strategy in RA treatment. However, in patients who received long-term insufficient treatment for RA, achievement of CR becomes increasingly difficult, especially if there is delay in the treatment. We believe that making primary-care physicians aware of treatment results will increase the remission rate of RA.

Methods: We examined 388 patients with RA who were observed between January and October 2016 and who had not received new disease-modifying anti-rheumatic drugs (DMARDs) more than 3 months before the observation day. We investigated their age at RA onset, sex, Steinerbrock radiographic stage and functional class, activity level, rheumatoid factor (RF), the anti-cyclic citrullinated peptide antibody and DMARDs prescribed at the first consultation (Prescribed Before), disease activity, status of methotrexate (MTX), glucocorticoids (GCs), and biologic agent use at the last observational day.

Results: We analysed the assumed remissions by using the Boolean-based definition (Boolean remission) as a purpose variable for these factors. Furthermore, we examined the odds ratio (OR) and 95% confidence interval (95% CI) by using a multiple logistic regression analysis for the statistically significantly different factors.

As for the time-related factor, we recognized that each factor had distinct multiplex collinear characteristics. Therefore, we adopted the time required for the first consultation as disease duration with the most effective values as the analysis object. The representative factor for the functional assessment adopted class according to the number of effective analyses.

Results: We recognised the statistically significant differences in disease duration, stage, class at the time of the first medical examination, RF, Prescribed Before, and state of MTX and GCs use at the last observation day for the achievement of Boolean remission.

We examined the multiple logistic regression analysis with the previously mentioned results and obtained the following results.

- Disease duration (per 1 year); OR 1.110, 95% CI 1.048–1.175, p<0.001.
- MTX (state; using vs no using); OR 2.522, 95% CI 1.560–4.076, p<0.001.
- GCs (state; no using vs using); OR 1.803, 95% CI 0.912–3.565, p=0.090.
- Disease duration (≥ 1.605y vs > 1.605y); OR 2.233, 95% CI 1.437–3.470, p<0.001.
- MTX (state; using vs no using); OR 2.566, 95% CI 1.644–4.291, p<0.001.
- Class at 1st interview; OR 1.589, 95% CI 1.181–2.136, p=0.01.
- Class at 1st visit; OR 1.512, 95% CI 1.126–2.029, p<0.01.
- GCs (state; no using vs using); OR 1.883, 95% CI 0.956–3.711, p=0.067.

Conclusions: Our results indicated the importance of the time required for consultation facilities with the T2T strategy treatment, tolerability for MTX use, and mild dysfunction at the first interview. The window of opportunity to achieve remission for patients with RA has less time than expected. Therefore, we recommend that physicians should introduce patients with RA to a rheumatologist following the T2T strategy promptly when the primary care provided by the family physician is insufficient.
A RAPID3-LIKE INDEX DOCUMENTS SUPERIOR EFFICACY OF BARICITINIB VERSUS ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: RAPID3 (Routine Assessment of Patient Index Data) indicates differences in efficacy of active versus control treatments at levels similar to DAS28 and CDAI (Disease Activity Score 28-Erythrocyte Sedimentation Rate) and CDAI (Clinical Disease Activity Index) in clinical trials of adalimumab, abatacept, certolizumab.

Objectives: To compare improvement according to RAPID3, DAS 28-ESR, and CDAI in the RA-BEAM trial of baricitinib vs adalimumab and placebo.

Methods: Post-hoc analyses were performed of the RA-BEAM trial, in which patients with moderately to severely active rheumatoid arthritis and an inadequate response to methotrexate (MTX) were randomized to baricitinib, adalimumab, or placebo. All patients were to continue stable background MTX and other DMARDs, as well as stable low-dose prednisone and/or NSAIDs, if indicated. A RAPID3-like index was computed from 3 measures: physical function (FN), pain (PN), and patient global assessment (PATGL). FN on a HAQ (Health Assessment Questionnaire) of 20 items [rather than MDHAQ (multidimensional HAQ) of 10 items] was recalculated from 0–3 to 0–10; PN and PATGL (visual analog scales) were recalculated from 0–100 to 0–10, for a 0–30 total score, hence “RAPID3-like”.

Conclusions: RAPID3-like documented greater efficacy of baricitinib versus adalimumab and placebo in the RA-BEAM trial, with results in similar ranges to DAS28-ESR and CDAI. RAPID3 is feasible to provide quantitative, standard medical history data; almost of the time and effort is by the patient rather than a health professional, assuring quantitative data in the infrastructure of usual clinical care.


SAT0069

SAT0070

A RAPID3-LIKE INDEX DOCUMENTS SUPERIOR EFFICACY OF BARICITINIB VERSUS ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Conclusions: RAPID3-like documented greater efficacy of baricitinib versus adalimumab and placebo in the RA-BEAM trial, with results in similar ranges to DAS28-ESR and CDAI. RAPID3 is feasible to provide quantitative, standard medical history data; almost of the time and effort is by the patient rather than a health professional, assuring quantitative data in the infrastructure of usual clinical care.


SAT0071 RHEUMATOID ARTHRITIS (RA) REGISTRY IN AKITA PREFECTURE, WHERE AGING IS THE MOST ADVANCED IN JAPAN

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Background: The rate of aging (percentage of population aged 65 years and over) in Akita Prefecture is 33.8% (26.6% for the whole of Japan), the highest throughout Japan. The Akita Orthopaedic Group on Rheumatoid Arthritis (AORA) was established in 2010. Since then, patients have been enrolled every year to prepare the registry.

Objectives: To compare patient characteristics as well as clinical effectiveness between the treatments with and without use of methotrexate (MTX) and a biological (BIO) using the data of the AORA registry.

Methods: The subjects were 2,016 patients enrolled in the Akita registry in 2015. The subjects included 403 men and 1,613 women. According to the use of MTX and BIO, 2,016 patients were divided into the group treated with no use of MTX or BIO (group A), that treated with BIO, but no use of MTX (group B), that treated with MTX, but no use of BIO (group C), and that treated with MTX and BIO (group D).

Results: The subjects were grouped into group A (n=873), B (n=153), C (n=805), and D (n=385). MTX was used in 59.2% and BIO was used in 26.7% of all patients. The mean ages were 69.6 years (group A), 67.5 years (group B), 65.6 years (group C), and 62.6 years (group D). The aging rates were 67.9% (group A), 55.6% (group B), 56.8% (group C), and 48.3% (group D), which shows that aging was more advanced in group A.

The results of patients with a complication of hypertension, diabetes, respiratory disease, cerebrovascular disease, heart disease or malignant tumour were 52.0% (group A), 54.2% (group B), 45.3% (group C), and 40.8% (group D). The incidence of complication was the lowest in group D.

The rates of patients who received one or more of conventional synthetic disease-modifying antirheumatic drugs (cs DMARDs) other than MTX were 79.0% (group A), 42.5% (group B), 39.9% (group C), and 19.2% (group D). Although bucillamine and salazosulfapyridine were frequently used in any group, concomitant use of tocilizumab was remarkable in group A, and C, while that of iguratimod was remarkable in groups C and D. The rate of use of a prednisolone (PSL), was significantly higher in group B. The dose of PSL was significantly higher in group A. In regard to BIO, three drugs of etanercept, tocilizumab, and abatacept accounted for 90% in group B. In group D, etanercept and tocilizumab were also frequently used, followed by infliximab, adalimumab, golimumab and abatacept. In DAS28ESR, the rate of combined low disease activity and remission was significantly higher in group D. The mean values of C-reactive protein (CRP) (mg/dL) were 0.61 (group A), 0.52 (group B), 0.47 (group C), and 0.35 (group D), which shows that the mean value was significantly higher in group A than group D.

Conclusions: Using the AORA registry, we compared patient characteristics as well as clinical effectiveness between the treatments with and without use of MTX and BIO. Since in group A, neither MTX nor BIO could be used in most patients, one had to practically rely on PSL. The study suggests that remission needs to be achieved prior to increase in complication due to aging.

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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2560
or remission. Rescue rates were 7.3% for bari 4mg, 17.1% for bari 2mg. Most rescued patients could regain LDA or remission. Dose reduction was associated with a lower rate of non-serious infections; rates of SAEs and AEs leading to discontinuation were consistently seen with dose reduction from 4mg to 2mg in well-controlled pts. However, after step-down most pts could maintain LDA or remission, or recapture control with return to 4mg if needed. Attempted dose taper may be a reasonable consideration for some pts following induction of sustained disease control with bar 4mg.


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2840

**SAT0074 PERSISTENCE WITH METFORMIN TREATMENT AND ONSET OF RHEUMATOID ARTHRITIS**

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**Background:** Several studies have suggested that metformin, an oral hypoglycemic agent, possess an anti-inflammatory property and may have a role in the treatment of rheumatoid arthritis (RA)1,2, but little is known on its preventive effects.

**Objectives:** To examine the association between persistence with metformin and the onset of RA.

**Methods:** Using the computerized medical database of a large health organization in Israel (Maccabi Healthcare Services, MHS) we have identified incident RA cases among new users of metformin between 1998 and 2014. Included were patients aged 18 or above with one year of follow up before and after the therapy initiation. RA was defined according to physician diagnoses. Participants were followed until the earliest of the following dates: onset of RA, leaving MHS, death, end of follow up (1.1.2016). Persistence with metformin was assessed by calculating the mean proportion of follow-up days covered (PDC) with metformin during the study period.

**Results:** A total of 113,749 eligible patients were included. During the study follow up period (794,386 person-years) we identified 600 incident cases (incidence rate of 75 cases per 100,000 PY). The incidence of RA in women (111 per 100,000 PY) was higher compared to men (42 per 100,000 PY). In a multivariable model, persistence with metformin (PDC≥80%) was associated with lower risk of RA (hazard ratio (HR) 0.66; 95% confidence interval (CI) 0.53–0.82) compared to non-persistent participants (PDC<80%). Figure 1 shows the hazard function according to persistence with metformin treatment. Similar risk reduction was observed among men but did not reach statistical significance (HR=0.85; 95% CI 0.54–1.32).

**Table 1 - Characteristics of patients with and without carotid plaque**

<table>
<thead>
<tr>
<th>Carotid Plaque</th>
<th>Absence</th>
<th>Presence</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=50)</td>
<td>(n=10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>55 ± 10</td>
<td>61 ± 8</td>
<td>0.03</td>
</tr>
<tr>
<td>Male</td>
<td>58%</td>
<td>50%</td>
<td>0.18</td>
</tr>
<tr>
<td>CRP/ml</td>
<td>15 ± 27</td>
<td>38 ± 13</td>
<td>0.001</td>
</tr>
<tr>
<td>FRS</td>
<td>12.8±11.6</td>
<td>5.7±6.8</td>
<td>0.008</td>
</tr>
</tbody>
</table>

**Conclusion:** In the present study, we observed an association between high persistence to metformin therapy and reduced risk of developing RA in women.
Doe Early Remission Lead to Better 5-Year Outcomes Than Low Disease Activity? Results from the Real Life Nor-Dmard Study


Background: When initiating therapy with synthetic disease-modifying anti-rheumatic drugs (sDMARDs) in patients with rheumatoid arthritis (RA), the recommended target is remission or low disease activity (LDA). Limited data exist on the impacts of reaching remission rather than LDA on long-term outcomes. Objectives: To compare RA-patients who achieved Simplified Disease Activity Index (SDAI) remission versus LDA 6 months after initiating sDMARD therapy, with regard to physical function, Health Related Quality of Life (HRQoL) and disease activity during 5 years of follow-up in a routine clinical setting. Methods: Data were provided NOR-DMARD, a prospective multicentre longitudinal observational study. We selected DMARD-naive patients with RA enrolled between December 2000 and April 2009 who had a registered visit with available SDAI status 6 months after initiating sDMARD therapy. Data on each patient were collected at baseline, after 3, 6 and 12 months, and yearly thereafter, including the Modified Health Assessment Questionnaire (MHAQ), the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) with Physical and Mental Components Summary scores (PCS and MCS, respectively) and SF-6D, and assessments that allowed the calculation of the composite disease activity scores SDAI, Clinical Disease Activity Index (CDAI) and the Disease Activity Score based on 28 joint counts (DAS28), Multivariate linear mixed models were used to explore the effect of SDAI status at 6 months on physical function (MHAQ), HRQoL (SF-36 PCS and MCS, SF-6D) and disease activity (SDAI, CDAI, DAS28) during 5 year follow-up. The statistical models were adjusted for age, gender, disease duration and baseline disease activity. Furthermore, we performed mixed model analyses separately for patients in LDA, MDA and HDA at baseline, exploring the impact of SDAI status at 6 months on long-term disease activity in each sub-group. Results: Of 1148 eligible patients, 867 patients (75.5%) started with methotrexate in monotherapy and 281 (24.5%) started with another sDMARD or sDMARD combination. Patients in SDAI remission (n=145; 16.6%) rather than LDA (n=454; 39.5%) 6 months after initiating therapy had better physical function (MHAQ), estimated mean difference 0.11–0.20, p<0.002, higher SF-36 PCS (4.13–8.16, p<0.003) and SF-6D (0.06–0.12, p<0.0001), and lower disease activity (SDAI, DAS28, CDAI, DAS28) 5 years after follow-up. The statistical models were adjusted for age, gender, disease duration and baseline disease activity. Furthermore, we performed mixed model analyses separately for patients in LDA, MDA and HDA at baseline, exploring the impact of SDAI status at 6 months on long-term disease activity in each sub-group. Conclusions: The achievement of SDAI remission 6 months after initiating DMARD-therapy was associated with favourable long-term outcomes compared with the achievement of SDAI low disease activity. The results from the study support that stringent remission is the optimal treatment target in patients with RA.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4226

Serum Level of Syndecan-4 And Its Correlation With Clinical Parameters In Rheumatoid Arthritis Patients

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Background: Heparan sulfate proteoglycan syndecan-4 plays an important role in inflammation. However, the role of syndecan-4 in rheumatoid arthritis (RA) has not yet been elucidated. Objectives: To detect serum level of syndecan-4 in RA patients and investigate its correlation with RA clinical parameters. Methods: The concentration of serum syndecan-4 was assayed by enzyme-linked immunosorbent assay (ELISA). 43 patients' serum samples from our RA cohort study between 2014 and 2016, and 20 age- and gender-matched osteoarthritis (OA) patients' serum samples were collected and analyzed. Compared the serum syndecan-4 levels in RA patients with DAS28 ≥3.2 and DAS28 ≥3.2 by Wilcoxon signed rank test. The relationships between serum syndecan-4 levels and RA clinical parameters (DAS28, rheumatoid factor (RF), erythrocyte sedimentation rate, C-reactive protein, etc.) were analyzed. Results: Baseline serum syndecan-4 levels of RA patients were significantly higher than the matched OA patients (1101.56 pg/mL vs 281.41 pg/mL, p<0.0001). In RA patients who had sera both at the point of DAS28 ≥3.2 and DAS28 ≥3.2 (n=13), we found that the former syndecan-4 levels were higher than the latter (1666.22 pg/mL vs 1378.34 pg/mL, p<0.05). The levels of serum syndecan-4 and RF were significantly and positively correlated in RA patients (r=0.696, p=0.008). Furthermore, there is a tendency that serum syndecan-4 levels were higher in the RF-positive (n=31) than in the RF-negative (n=12) RA patients (1344.43 pg/mL vs 971.27 pg/mL, p=0.078).

Conclusions: Compared with age- and gender- matched OA patients, serum syndecan-4 concentration is significantly higher in RA patients. Serum syndecan-4 level is positively correlated with RF. Syndecan-4 may play an important role in the pathogenesis of RA. Further investigation is required to study the mechanism of syndecan-4 in RA.

References:

Acknowledgements: We are indebted to all the patients who kindly participated in this study. This study was partly supported by Peking University Clinical Research Institute.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.1091

Clinical Features and Perforin A91V Gene Analysis in SOJA Children With Macrophage Activation Syndrome

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Objectives: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening syndrome. Here we aim to review the precipitating events, clinical features, treatment, outcome and perform A91V gene analysis in systemic onset juvenile idiopathic arthritis (SoJIA) children with MAS.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3874
Methods: Retrospective review of cases of MAS from a collected database of fourteen children with SoJIA from 2003 to 2008. Gene-specific polymersase chain reaction (PCR) primers were used to analyze the perforin A91V gene polymorphism.

Results: Fourteen patients (nine boys) were considered to have evidence of MAS, with age ranged from 4 months to 12 years. The primary diagnosis was systemic onset juvenile idiopathic arthritis. No medication was identified as trigger. Eleven had infections prior to MAS, specific infectious agents were identified in four. High fever, new onset hepatosplenomegaly, lymphadenopathy, liver dysfunction, abnormal lipid metabolism and hemophagocytosis were common clinical features. Two cases were with acute respiratory distress syndrome (ARDS), multiple organ failure (MOF) in three and three died. The perforin A91V (NCBI:SNP rs35947132) variant gene was detected in seven systemic onset juvenile idiopathic arthritis complicated with MAS cases, but no mutation were found. Glucocorticoid, intravenous immunoglobulin, immunocompressive therapy were effective and HP (Plasmasphere) used in one serious case was also effective.

Conclusions: MAS is a rare and potentially fatal complication of childhood rheumatoid diseases, especially systemic onset juvenile idiopathic arthritis. Most of our patients were male, and most cases were preceded by infection. Bone marrow studies support the diagnosis. MOF may be a poor prognostic sign. Aggressive early therapy is essential.

Disclosure of Interest: None declared


SAT0078 MAGNETIC RESONANCE IMAGING OF THE HANDS IN RHEUMATOID ARTHRITIS: UNILATERAL OR BILATERAL?

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Background: MRI had higher sensitivity of detecting inflammation than physical examination and higher examination of detecting bone damage than X-rays. Physical examination and X-rays are usually performed on bilateral hands of RA patients, however, MRI evaluation of unilateral hand was recommended by OMERACT at the very beginning when RA MRI score (RAMRIS) was validated in the databases.

Objectives: To explore the advantages of bilateral hands MRI on RA.

Methods: Consecutive hospitalized RA patients were recruited from April 2014 to April 2016 at Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University. Together with assessing swelling and tenderness of 28 joints essential for DAS28, bilateral wrists and MCPJ2–5 of each patient were scanned simultaneously on 3.0T MRI system. MRI synovitis, osteitis and bone erosion were scored referred to the definitions and atlas of RAMRIS system.

Results: (1) Among 120 RA patients were included, 79% were female, age (median and IQR, similarly hereinafter) was 52 (44–61) years, disease duration was 48 (12–120) months and DAS28-crp was 5.9 (4.7–6.9). The mean imaging time for the entire MRI examinations including the time of patient positioning and contrast agent injection was 23 minutes. The mean scoring time was 10 minutes for RAMRISbilateralhands and 7 minutes for RAMRIS unilateral-hand. Interreader ICC for RAMRIS_bilateral_hands was 0.852 in synovitis, 0.739 in osteitis and 0.815 in bone erosion. (2) The mean imaging evaluation time was 23 minutes. The other 50 patients had equally severe involvement at physical examination. (3) Of wrists with MRI synovitis, osteitis and bone erosion per joint or bone were shown in figure 1A. For MCPJ2–5, 27%–42% of RA patients showed unilateral synovitis, 45%–53% showed unilateral osteitis and 51%–69% showed unilateral bone erosion (Figure 1B).

Conclusions: Performing MRI of bilateral hands yields additive information compared with imaging only unilateral hand.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6106

SAT0079 ASSOCIATION OF ALCOHOL CONSUMPTION AND DISEASE ACTIVITY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: ANALYSIS OF THE IORRA COHORT

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Background: While the results of several observational studies suggest that light-to-moderate alcohol consumption may decrease the risk of susceptibility to or severity of rheumatoid arthritis (RA) (1–3), findings regarding the effect of alcohol consumption on RA disease activity are conflicting. Furthermore, there are few reports of longitudinal studies regarding the effect of alcohol consumption on RA disease activity. In addition, although alcohol consumption in the Japanese general population was lower than that in European countries, according to the 2011 World Health Organization’s Global Status Report on Alcohol and Health, there are few reports specifically concerning alcohol consumption in Japanese RA patients.

Objectives: To examine the longitudinal relationship between alcohol consumption and changes in disease activity in patients with RA using the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort database.

Methods: Subjects were RA patients who participated in the IORRA cohort study between October 2014 and October 2015. Patients were assigned to one of 5 groups according to alcohol-drinking status at baseline: the non-drinking group, drinking group 1 (0 g < Alco-drink ≤ 14 g), drinking group 2 (14 g < Alco-drink ≤ 28 g), drinking group 3 (28 g < Alco-drink ≤ 50 g), and drinking group 4 (50 g < Alco-drink). Multiple regression analyses were used to examine the relationship between alcohol consumption and baseline DAS28, and change in DAS28 between baseline and 1 year.

Results: Data from a total of 4,695 Japanese patients with RA (female: 86.6%, mean age: 61.3 years old, mean disease duration: 15.2 years, and mean DAS28: 2.5) were utilized. The main characteristics of the database were: male, mean age, mean disease duration, mean DAS28 at baseline/after 1 year in the non-drinking group, and drinking groups 1, 2, 3, and 4 were 2.735 (92.8%, 64.0 years old, 16.1 years, 2.7/2.7), 646 (89.9%, 58.7 years old, 14.8 years, 2.4/2.5), 497 (82.5%, 56.7 years old, 13.8 years, 2.3/2.3), 444 (71.6%, 56.4 years old, 13.0 years, 2.3/2.3) and 373 (58.2%, 57.5 years old, 13.7 years, 2.2/2.3), respectively. Baseline DAS28 in drinking groups 2 (p=0.02), 3 (p<0.01), and 4 (p<0.01) was significantly lower than that in the nondrinking group. Multivariate regression analysis revealed that there was no association between alcohol-drinking status and the change in DAS28 at 1 year, after adjusting for DAS28 at baseline.
SAT0080 | CLINICAL SIGNIFICANCE OF SOLUBLE CD163 IN REFRACTORY SYSTEMIC-ONSET IDIOPATHIC ARTHRITIS

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Objectives: The present study explored the correlation of soluble CD163 with refractory systemic-onset juvenile idiopathic arthritis (refractory So-JIA) as well as the clinical significance of soluble CD163 in (refractory So-JIA).

Methods: A total of 33 young patients diagnosed with So-JIA in the active period and 30 young patients diagnosed with So-JIA in the inactive period at Guangzhou Women and Children's Medical Center (Guangzhou, China) from January 2010 to January 2012 as well as 40 age-matched healthy individuals, who had visited the hospital for medical examination in the same time-period were enrolled in the present study. Flow cytometry was used to determine the lymphocyte count and ELISA was adopted for determining the levels of soluble CD163 in serum

Results: The levels of soluble CD163 and their correlation with indexes of disease activity were observed. In patients with So-JIA in the active period, the levels of soluble CD163 and the TOEL count were significantly higher than those in the inactive So-JIA and healthy individuals (P < 0.05). Furthermore, the levels of soluble CD163 were positively correlated with C-reactive protein, ferritin, erythrocyte sedimentation rate, white blood cell count and immunoglobulin E as indexes of disease activity (P < 0.05).

Conclusions: Soluble CD163 is a more valuable index for early recognition refractory active So-JIA, which can provide a basis for active period development and clinical observation. Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2340

SAT0082 | THE INVESTIGATION FOR THE INFLUENCE OF SILASTIC ARTHROPLASTY OF METACARPOPHALANGEAL JOINT ON THE ACTIVE EXTENSION RANGE OF PROXIMAL INTERPHALANGEAL JOINT IN THE RHEUMATOID HAND


Orthopedic Surgery, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Background: The ulnar deviation (UD) deformity of the metacarpophalangeal (MCP) joints is a typical deformity in the patients of rheumatoid arthritis (RA). Joint replacement arthroplasty can be indicated for the treatment of severe UD deformity, silastic prostheses being widely used with generally good results [1]. There are few, however, previous reports focusing on the relationship between the range of motion (ROM) of the MCP and PIP joints after the surgery.

Objectives: The objective of this study was to investigate the relationship of silastic replacement arthroplasty of MCP joint replacement on post-operative extension range of PIP joint of the same finger.

Methods: RA patients who underwent silastic replacement arthroplasty of at least 1 MCP for the treatment of UD deformity were reviewed. There were 80 hands of 65 patients, average age of whom was 70.1 (32.4 - 86.1) years old, 56 patients being female and 9 being men. The ROM of the PIP joints before and after surgery was recorded from the medical records, and the relationship between the post-operative change of ROM in PIP joints and post-operative ROM of the MCP joint of same finger was examined. Paired t-test and the correlation coefficient were used for statistical analysis.

Results: The mean active extension range of PIP joints in index to little finger changed from -0.68° (-56.3-30.0) to 0.92° (-52.3-30.0) [P < 0.05], -6.4° (-104.0 to -30.0) to 8.41° (-56.3-112.0) [P < 0.05]. Non-PIP joint (T1FI as reference) changed from 0.29° (0-30.0) to 0.12° (-76.0-30.0) [P < 0.05]. Methotrexate use 0.084 0.12 0.51

Conclusions: In our multicenter study using a linear mixed-effect model including between-institution variation as a random effect, RF positivity, in addition to some well-known variables, was found to be independently associated with decreased effects of bDMARDs treatment in bio-naive RA patients. Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1508

SAT0081 | RELATIONSHIP BETWEEN RHEUMATOID FACTOR POSITIVITY AND TREATMENT EFFECT WITH A FIRST BIOLOGIC AGENT IN RHEUMATOID ARTHRITIS: MULTICENTER STUDY USING A MIXED-EFFECT MODEL

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Background: Although the presence of rheumatoid factor (RF) may be a risk factor for the onset and progression of rheumatoid arthritis (RA), sufficient literature does not exist to support the clinical relationship between RF positivity and the effects of treatment with biologic disease-modifying antirheumatic drugs (bDMARDs). This multicenter study aims to explore the association of RF positivity with the effects of bDMARDs treatment in bio-naive RA patients using a linear mixed-effect model.

Objectives: In a multicenter study, patients are clustered within institutions, therefore results of adjustment models are likely to be biased by random, unobserved between-institution differences. Such bias could lead to inaccurate prediction and interpretation of outcomes. We used a linear mixed-effect model including between-institution variation as a random effect, which would improve the performance of this multicenter study.

Methods: In total, 625 bio-naive RA patients registered in the Tsurumai Biologics Cooperative Clinical Registry (biologics Japan), a multi-institution registry of 15 affiliated institutions in Japan, who received bDMARDs treatment during the study period (2006–2016) were eligible for inclusion. Demographic information and disease characteristics were assessed at baseline. DAS28 using erythrocyte sedimentation rate was recorded at baseline and following 24 weeks of therapy, in order to predict DAS28 improvement at 24 weeks, a linear mixed-effect model including between-institution variation as a random effect, controlling for RF positivity, age, sex, stage, methotrexate (MTX) use, prednisolone (PSL) use, tumor necrosis factor inhibitor (TNFi) or non-TNFi, and DAS28 at baseline, was developed.

Results: Of the 625 patients, 513 showed RF positivity and 112 were antibody negative. Mean ± SD age at baseline was 56.9±14.0 years; 509 patients were women (81.4%). The mean ± SD DAS28 score at baseline was 5.9±1.24. Proportion of MTX and PSL use were 79.3% and 58.1%, respectively. Following adjustment for relevant covariates, RF positivity was associated with a decrease biologic treatment effect (β = −0.33±0.12, p < 0.05). In another model including an additional interaction term of RF status and TNFi or non-TNFi, the influence of RF status on treatment effect was persistent (β = −0.26±0.14, p < 0.01). These two models had comparable AIC. A model excluding RF positivity term had larger AIC than these two models, suggesting that RF positivity is crucial for predicting the effect of bDMARDs treatment.

Conclusions: In our multicenter study using a linear mixed-effect model including between-institution variation as a random effect, RF positivity, in addition to some well-known variables, was found to be independently associated with decreased effects of bDMARDs treatment in bio-naive RA patients. Disclosure of Interest: None declared

SAT0083  TOCLIZUMAB INDUCED CLINICAL REMISSION IN RHEUMATOID ARTHRITIS PATIENTS: RESIDUAL DOPPLER SIGNALS IN COMPARISON WITH OTHER BIOLOGICS

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Objective: To study the residual Power Doppler (PD) signals for assessing synovitis in CRP negative patients with rheumatoid arthritis (RA) treated with biological agents.

Methods: Biologics treated RA patients who were maintained normal CRP for more than 6 months (34 TNF inhibitors, 37 Tocilizumab, 23 Abatacept) were assessed by ultrasonography. Residual PD signals were assessed in MCP, PIP, and wrist joints with both hands. We assumed patients who had any PD signals in assessed joints were “residual PD signals”.

Results: All treated patients with biologics maintained normal CRP for a half year (n=94). 35.1% of patients treated with biologics had positive PD signals. The remission rates of DAS28-ESR, CDAI, and Boolean were 68.7%, 62.8%, and 48.9% respectively. 28.1% of patients who achieved DAS28-ESR remission had residual PD signals, 22.0% in CDAI, and 21.7% in Boolean. 23.8% of patients treated by TNF inhibitors who achieved DAS28-ESR remission had residual PD signals, 34.6% in Tocilizumab, and 20.0% in Abatacept. In case of setting the DAS28-ESR remission less than 3.0, 30.2% of patients who achieved DAS28-ESR remission had residual PD signals, 29.0% in less than 2.0, and 12.5% in less than 1.5. The patients who have no tender or swollen joints and the excellent patient oriented global health assessment (VAS score was zero) had fewer residual PD signals (23.4% vs 68.6% in tender joints, 26.7% vs 66.7% in swollen joints, and 13.3% vs 44.4% in patient VAS).

Table 1. Rate of remission and residual PD signals

<table>
<thead>
<tr>
<th>Patients number</th>
<th>All biologics</th>
<th>TNF inhibitors*</th>
<th>Tocilizumab</th>
<th>Abatacept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual PD signals**</td>
<td>94</td>
<td>33/34 (31.5%)</td>
<td>37/34 (11%)</td>
<td>23/34 (6.8%)</td>
</tr>
<tr>
<td>DAS28-ESR remission</td>
<td>78/94 (83.0%)</td>
<td>32/34 (94.1%)</td>
<td>31/34 (94.1%)</td>
<td>5/23 (21.7%)</td>
</tr>
<tr>
<td>Residual PD signals</td>
<td>22/37 (59.7%)</td>
<td>21/32 (65.6%)</td>
<td>21/37 (56.8%)</td>
<td>18/23 (78.3%)</td>
</tr>
<tr>
<td>CDAI remission</td>
<td>57/94 (60.2%)</td>
<td>21/34 (62.1%)</td>
<td>21/34 (62.1%)</td>
<td>22/34 (64.7%)</td>
</tr>
<tr>
<td>Residual PD signals</td>
<td>15/37 (40.5%)</td>
<td>9/31 (28.1%)</td>
<td>6/31 (19.4%)</td>
<td>11/34 (32.4%)</td>
</tr>
<tr>
<td>Boolean remission</td>
<td>59/94 (62.8%)</td>
<td>26/34 (76.5%)</td>
<td>23/35 (66.7%)</td>
<td>26/34 (76.5%)</td>
</tr>
<tr>
<td>Residual PD signals</td>
<td>15/39 (38.5%)</td>
<td>12/29 (41.4%)</td>
<td>3/19 (15.8%)</td>
<td>2/14 (14.3%)</td>
</tr>
</tbody>
</table>

*TNF inhibitors (Infliximab n=6), Eularcept (n=14), Adalimumab (n=7), Golimumab (n=4), Certolizumab pegol (n=3). ** Residual PD signals: patients who had any PD signals in assessed joints. ***Achieved: remission rate in biologics treated patients who were maintained normal CRP for a half year.

Conclusions: The patients who achieved clinical remission had residual PD signals. Patients with Tocilizumab induced remission had more residual PD signals compared with TNF inhibitor or Abatacept induced remission. More strict criteria of clinical remission may reduce residual PD signals in patients treated by Tocilizumab.

Disclosure of Interest: None declared


SAT0084 A STUDY ON CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS ACHIEVING DEPRESSION REMISSION WITH 6 MONTHS OF BIOLOGIC AGENT TREATMENT

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Background: Approximately 15% of RA patients also suffer from depression, with an odds ratio of 1.42 (95% CI 1.3 - 1.5) compared to the general population [1]. A previous study reported that biological agents can improve the depression status in RA patients [2]. Although previous studies have been cross-sectional, there were no reports that analyzed factors that led to depression remission.

Objective: To examine the relationship between baseline factors and depression remission after six-month biologic agent treatment in rheumatoid arthritis (RA) patients.

Methods: The subjects were 384 RA patients treated with biologic agents. The following patient’s characteristics were investigated: age, gender, number of visits, disease duration, previous biologic agents, baseline steroid dosage, methotrexate dosage and serum matrix metalloproteinase-3 (MMP-3) levels. For evaluation, we used the Simplified Disease Activity Index for RA disease activity; the Health Assessment Questionnaire Disability Index (HAQ-DI) score for activities of daily living; the Short Form-36 for non-specific health-related quality of life; and the Hospital Anxiety Depression Scale (HAD-S) scores.

Depression remission was defined by HAM-D <7 after 6 months of treatment. The subjects were divided into two groups according to the presence or absence of depression, and a retrospective study was performed.

Results: We included 152 patients in the analysis. Two hundred thirty-two

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2498
patients were excluded due to primary and secondary failure, complications, loss to 6-month follow-up, incomplete data, etc. Compared with a group of RA patients with depression remission (n=124), a group of patients with no depression remission (n=126) (regression coefficient 1.35; 95% CI 0.39–2.31; p=0.006).

Conclusions: Our results demonstrated that the rate of discontinuation due to adverse events by biologics was significantly high in RA patients over 75 years and above.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1443
SAT0088 | HDL CHOLESTEROL EFFLUX CAPACITY IN RHEUMATOID ARTHRITIS PATIENTS: CONTRIBUTING FACTORS AND RELATIONSHIP WITH SUBCLINICAL ATHEROSCLEROSIS

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Background: Lipid profiles appear to be altered in rheumatoid arthritis (RA) patients due to disease activity and inflammation. Cholesterol efflux capacity (CEC) has not only been linked to cardiovascular events in the general population, but also to be impaired in RA patients.

Objectives: To analyze whether CEC is related to subclinical atherosclerosis, as determined by the presence of carotid plaque or increased levels of carotid intima-media thickness (cIMT) in RA patients. Secondarily, we aimed to describe the disease-contributing factors that are related to CEC as an expression of the abnormalities in the lipid profile associated with the disease.

Methods: Cross-sectional study that encompassed 401 individuals; 178 patients and 223 sex-matched controls. CEC was measured using an in vitro assay, lipoproteins serum concentrations, and standard lipid profile were assessed in patients and controls. Carotid intima-media thickness and carotid plaques were assessed in RA patients. A multivariable analysis was performed to evaluate the relation of CEC with RA-related data, lipid profile and subclinical carotid atherosclerosis.

Results: Mean CEC was not significantly different between RA patients (18.9 ± 5.90) and controls (18.6 ± 10.44), p=0.11. Demographic variables were not associated with CEC except for a correlation with male gender that was only found in RA patients, but not in controls. Systolic blood pressure inversely correlated with CEC in controls (beta coefficient -0.01 [0.20–0.01], p=0.025). In RA patients, a similar trend was found although a statistically significant difference was not reached. Neither the traditional cardiovascular risk factors nor the cardiovascular co-morbidity-related data were associated with CEC. Similarly, lipid profile did not show any relationship with CEC in patients or controls. ESR tended to be associated with a lower CEC although it did not reach statistical significance. RA patients with low (beta coeff. -5.2 [-10.0–0.3], p=0.039) and moderate disease activity (beta coeff. -4.6 [-8.5–0.7], p=0.020) were associated with inferior levels of CEC when compared to patients in remission. CEC was not found to be associated with cIMT in RA patients. However, higher CEC was associated with a protective effect for the presence of carotid plaque in RA patients. This relationship was maintained even after multivariate analysis (OR 0.94 [0.93–0.99], p=0.015).

Conclusions: Our study, which includes the largest series of RA patients ever assessed for CEC, reveals for the first time that CEC is related to subclinical atherosclerosis in RA patients. The fact that CEC is also associated with disease activity reinforces the idea that CEC may be a mediator between disease activity and subclinical atherosclerosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular4100

SAT0089 | COMPARATIVE CARDIOVASCULAR SAFETY OF ABATACEPT AND TUMOR NECROSIS FACTOR INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT TYPE 2 DIABETES: A POPULATION-BASED COHORT STUDY

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Background: Patients with rheumatoid arthritis (RA) are at high risk of developing cardiovascular disease (CVD) and may benefit from potent disease-modifying anti-inflammatory drugs such as biologics. Since diabetes mellitus (DM) is a major risk factor for CVD, RA patients with DM constitute a high CVD risk subgroup calling for particular attention. However, there is a lack of knowledge on the comparative cardiovascular safety of different biologics in RA patients with DM.

Objectives: To examine the comparative cardiovascular safety of abatacept versus TNF inhibitors in RA patients with and without DM.

Methods: RA patients enrolled in both public (Medicare) and commercial (Truven MarketScan) health plans in the U.S. who newly initiated abatacept or TNF inhibitors were eligible. The primary outcome of interest was a composite CVD endpoint of myocardial infarction (MI), stroke/transient ischemic attack (TIA), and coronary revascularization. The secondary outcomes included each component of the composite CVD endpoint and heart failure (HF). After 1 year of exposure, Cox proportional score (PS) matching between two exposure groups, Cox proportional hazard model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for each outcome, comparing abatacept to TNF inhibitors. PS matching was separately done in subgroups with or without baseline DM in each database. PS-matched hazard ratios were compared between the two databases were pooled using an inverse variance–weighted fixed-effect model.

Results: We identified 31,899 Medicare enrollees (6,107 new users of abatacept and 25,792 new users of TNF inhibitors) and 71,956 commercial enrollees (6,942 new users of abatacept and 65,464 new users of TNF inhibitors) with RA. Among RA patients, abatacept may be associated with a reduced risk of coronary events compared to TNF inhibitors, particularly in patients with DM. The risk of HF was not different between these two groups.

Conclusions: Among RA patients, abatacept may be associated with a reduced risk of coronary events compared to TNF inhibitors, particularly in patients with DM. The risk of HF was not different between these two groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular2407
Clinical arthritis is always preceded by subclinical inflammation? A longitudinal study at joint level in patients with arthralgia that developed arthritis.

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**Background:** The clinical phase of Rheumatoid arthritis (RA) is preceded by a phase with subclinical inflammation. MRI can detect subclinical inflammation and, at patient level, this is predictive for the development of clinical arthritis. However, at joint level it is unknown how arthritis develops. It is unknown how frequently joints with subclinical inflammation progress to clinical arthritis, and vice versa, how often joints that developed clinical arthritis had local subclinical inflammation during the preceding phase of arthralgia. A longitudinal MRI study in patients that developed arthritis can unravel if arthritis development is restricted to some locations in which the severity of inflammation increases over time or, alternatively, if the process is more generalized with a weak association between the locations of subclinical inflammation and subsequent clinical arthritis.

**Objectives:** This longitudinal study at joint level during progression from pre-RA to RA determined the relation between the location of subclinical inflammation and clinical arthritis over time.

**Methods:** 290 small joints (4 MCPs, 1 wrist, 5 MTPs per person) of 29 patients that presented with arthralgia and developed clinical arthritis were studied with 1.5T MRI at both time-points. MRIs were evaluated for BME, synovitis and tenosynovitis by three readers (ICCs 0.98, 0.96 and 0.97) that were blind to clinical data and the time in order. Subclinical inflammations was defined as presence of BME, synovitis and/or tenosynovitis.

**Results:** The median time between presentation with arthralgia and clinical arthritis development was 17 weeks. At presentation with arthralgia 68 joints had subclinical inflammation and no significant association was found between joint tenderness and the presence of local MRI-detected subclinical inflammation (OR 0.98; 95% CI 0.48–1.9). Over time, 21% of 68 joints had resolution of subclinical inflammation, 60% had persistent subclinical inflammation and 19% developed clinical arthritis. At arthritis development 37 joints were swollen. Of these, 24 (65%) had no prior subclinical inflammation at the time of presentation with arthralgia (Figure).

**Conclusions:** This first longitudinal MRI-study on joint level in pre-RA suggested that the majority of joints that developed clinical arthritis had no (long-lasting) preceding phase with subclinical inflammation.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6583
poorly understood. The study of lipid profiles in RA has been biased towards lipoprotein levels, whereas those of triglycerides (TG) and lipoprotein functionality have been neglected.

Objectives: since recent findings point to an emerging role for TG and TG-rich lipoproteins (TRL) on inflammation, we aimed to evaluate a combined lipid profile clustering. How high TG and low HDL levels (TGhighHDLlow) in RA.

Methods: lipid profiles were analyzed in 113 RA patients, 113 healthy controls (HC) and 27 dyslipemic subjects (DL). A group of 13 biological-naïve RA patients was prospectively followed for 3 months upon TNFα-blockade. Serum levels of inflammatory mediators were assessed by immunoassays. PON1 activity and Total Antioxidant Capacity (TAC) were quantified in serum. PON1 rs662 status was evaluated by RT-PCR.

Results: the prevalence of the TGhighHDLlow profile was similar among RA patients (29/113), HC (30/113) and DL (11/27), linked to higher TRL levels in all groups. However, this profile was associated with increased CRP (p=0.012), TNFα (p=0.004), MCP-1 (p=0.004), IP-10 (p=0.018) and leptin (p<0.001) serum levels in RA, where decreased PON1 activity and TAC were found (both p<0.001). TRL serum levels were positively correlated to inflammatory mediators, whereas a negative association was found for PON1 activity (r=-0.203, p=0.036). These findings remain after excluding patients with previous CV events or those under statins. No associations were observed in the HC and DL groups. When RA patients were stratified by PON1 rs662 status, these associations were restricted to the low activity genotype (QQ) (TNFα: p<0.002, MCP-1: p=0.013, EGF: p=0.047, IP-10: p<0.018 and leptin: p<0.002), whereas no effect of the lipid profile was observed in the QQ/patients harboring the TC or CC genotypes (all p>0.205). As expected, QQ-patients exhibited a lower PON1 activity compared to the other genetic variants (both p<0.010). The TGhighHDLlow prevalence was related to a decreased anti-TNFα usage in the cross-sectional sample (p=0.004). A poor clinical response was associated with an increased TRL levels (p<0.042).

Conclusions: the TGhighHDLlow profile is associated with systemic inflammation, increased TRL levels, decreased PON1 activity and a poor clinical outcome upon TNFα-blockade in RA. Overall, these findings support the link between inflammation and lipid profile, oxidative status and TRL having a pivotal role. The TGhighHDLlow profile can be proposed as a surrogate marker of HDL dysfunction in RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4380

SAT0094 METABOLIC AND CARDIO-VASCULAR BENEFITS OF HYDROXYCHLOROQUINE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS
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Background: Cardiovascular disease (CVD) is the leading cause of mortality in rheumatoid arthritis (RA) patients (1). Hydroxychloroquine (HCQ) has been shown to improve major outcomes like survival rates in other inflammatory diseases, like systemic lupus (2).

Objectives: The aim of our study was to access currently available literature on the cardiovascular impact of hydroxychloroquine (HCQ) in patients with RA.

Methods: We systematically searched literature (via PubMed, Embase and abstracts from recent ACR and EULAR congresses) for studies evaluating the effects of HCQ, either in monotherapy or in combination with other conventional synthetic disease modifying antirheumatic drugs (csDMARDs) on cardiovascular outcomes or known risk factors for CVD in RA patients (lipid profiles, diabetes incidence and vascular events), and incidence of CVD). A meta-analysis was performed with Review Manager Software, with random effects models, whenever methodologically possible and relevant. Data were extracted by one investigator and independently checked by another.

Results: The IL discussed the 185 articles and abstracts of potential interest, and further examination resulted in 16 studies fulfilling required criteria for pre-planned analyses regarding the cardiovascular impact of HCQ in RA. For lipid profiles, the mean difference (mg/dL) between HCQ users versus nonusers was -9.82 (95% confidence interval [95% CI] 14.03, 5.60) for total cholesterol, -10.61 [14.17, -7.04] for low density lipoprotein, -18.15 [27.20, 11.10] for triglycerides and +4.13 [2.22, 6.04] for high density lipoprotein (figure 1); with respectively a decrease (mg/dL) of 13.15 [20.96; 5.34], 12.35 [10.14; 4.36], 12.54 [28.94; 3.86] and an increase of 1.67 [0.96, 4.31] after HCQ initiation. Diabetes incidence was reduced in HCQ ever users versus patients who never used HCQ (with a hazard ratio of 0.59 [0.49; 0.70]). In addition, HCQ seems to decrease insulin resistance and incidence of cardiovascular events but data were too scarce for meta-analysis.

Conclusions: Beside its limited efficacy on disease activity, this study supports the interest of HCQ on lipid profiles, and diabetes incidence, and to a lesser extent on cardio-vascular events and insulin resistance in RA patients. These data strongly suggest that HCQ may be of some interest in RA, in combination with other csDMARDs.

References:
B. Secura1, A. de Vera-González2, A. González-Delgado2, J.M. Olmos3, J.L. Hernández2, R. López-Mejías4, B. Ulía4, M.A. González-Gay5,6, I. Ferraz-Amaro1, 1Division of Rheumatology; 2Central Laboratory Division, Hospital Universitario de Doctor Queralt; 1Division of Internal Medicine; 2Division of Rheumatology; 3Division of Rheumatology, IDIVAL. Hospital Universitario Marqués de Valdecilla, Santander, Spain; 6Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, University of the Witwatersrand, Johannesburg, South Africa

Background: Rheumatoid arthritis (RA) patients have higher levels of resistance to the action of insulin (IR) compared to healthy subjects. The increase in IR, is related to beta-cell dysfunction and it can be a consequence of chronic low-grade inflammation, and insulin resistant state that is in turn a risk factor for atherosclerosis. The increase in IR is associated with increased CRP (p=0.010), IP-10: p=0.018, and leptin: p=0.002), whereas no effect of the lipid profile was observed in the QQ/patients harboring the TC or CC genotypes (all p>0.205). As expected, QQ-patients exhibited a lower PON1 activity compared to the other genetic variants (both p<0.010). The TGhighHDLlow prevalence was related to a decreased anti-TNFα usage in the cross-sectional sample (p=0.004). A poor clinical response was associated with an increased TRL levels (p<0.042).

Conclusions: the TGhighHDLlow profile is associated with systemic inflammation, increased TRL levels, decreased PON1 activity and a poor clinical outcome upon TNFα-blockade in RA. Overall, these findings support the link between inflammation and lipid profile, oxidative status and TRL having a pivotal role. The TGhighHDLlow profile can be proposed as a surrogate marker of HDL dysfunction in RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2048

Figure 1. Forest plot for the mean difference (mg/dL) between HCQ users and non-users of total cholesterol (A), low-density-lipoprotein (B), high-density-lipoproteins (C), and triglycerides (D).

In RA patients, biventricular systolic-diastolic function of the heart was impaired compared to FM (Table 2). Over the study period, myocardial function improved (Table 2) and DAS28-CRP declined (3.5±1.1 vs 2.3±1.0; p<0.001). Only RA patients had LGE, with no improvement over time (67%).

Table 2. Cardiac magnetic resonance findings in RA and FM patients

<table>
<thead>
<tr>
<th>RA patients</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EF%</td>
<td>59±4</td>
<td>59±3</td>
<td>0.477</td>
</tr>
<tr>
<td>LV ESV, ml/m²</td>
<td>34±6</td>
<td>33±8</td>
<td>0.449</td>
</tr>
<tr>
<td>LV EDV, ml/m²</td>
<td>82±11</td>
<td>81±11</td>
<td>0.645</td>
</tr>
<tr>
<td>LV EF%, ms</td>
<td>472±99</td>
<td>445±106</td>
<td>0.035</td>
</tr>
<tr>
<td>RV EF%</td>
<td>59±6</td>
<td>60±6</td>
<td>0.065</td>
</tr>
<tr>
<td>RV ESV, ml/m²</td>
<td>34±9</td>
<td>32±8</td>
<td>0.009</td>
</tr>
<tr>
<td>RV EDV, ml/m²</td>
<td>81±12</td>
<td>79±11</td>
<td>0.034</td>
</tr>
</tbody>
</table>

LV = left ventricle, RV = right ventricle, ESV = end-systolic volume, EDV = end-diastolic volume, EF = ejection fraction, TPRF = time to peak filling rate.

Conclusions: Myocardial function was impaired in RA patients with active RA compared to FM controls, although the latter group had worse classical CV risk factor profile. After one-year DMARD-treatment targeting to remission, myocardial function improved in parallel with decreasing RA activity. Inflammation seems to be deleterious to the myocardium. Tight control of RA activity may improve myocardial function.

References:
POLYPHARMACY IS ASSOCIATED WITH AN INCREASED RISK OF ADVERSE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

A.D. Amarilla Vallejo, A. Rutherford, M. Filkova, M. Molokhia,

E. Nikphorou, S. Norton, K. Hyrich, J. Galloway

Background: In the general population, polypharmacy (PP) is associated with increased risk of adverse events. The relationship between adverse outcomes and PP in Rheumatoid Arthritis (RA) has not been studied in depth. The mantra of RA management encourages PP through combination therapy to deal with the comorbidity associated with RA. The aim of this study was to study the relationship between PP and adverse events in RA, including the influence of DMARDs within the PP count.

Methods: Data from the British Society for Rheumatology Biologics Register were analysed. PP was defined as number of drugs co-prescribed at baseline, with two models: (1) including DMARDs (excluding DMARDs from the medication count). PP was stratified by 0–5, 6–9 and >10. Patients were studied from initiation of at least one biologic until 1st serious adverse event (SAE), 3 years of follow up, or last available visit, whichever came first. A Cox-proportional hazard model was used, with adjustment for a priori selected confounders.

Results: This study included 15,004 patients commencing biologics. The demographics are shown in Table 1. Excluding DMARDs from the PP cohort comprised patients who previously or concurrently started TMP-SMX with biologic treatment with biologics. PP is common in patients with RA and is associated with adverse events especially when patients are on >10 drugs. Excluding or including DMARDs from the PP model had negligible impact on findings. The relationship between PP and comorbidity is worthy of further research, as PP represents a potentially simple but valuable predictor of adverse outcomes, and a suitable surrogate for comorbidity in epidemiological analyses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2262

SAT0099

POLYPHARMACY IS ASSOCIATED WITH AN INCREASED RISK OF ADVERSE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. D. Amarilla Vallejo, A. Rutherford, M. Filkova, M. Molokhia

E. Nikphorou, S. Norton, K. Hyrich, J. Galloway

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6862

SAT0100

ACPA AND ABDOMINAL ADIPOSITY ARE INDEPENDENT PREDICTORS OF INCREMENTS IN BASAL INSULIN IN PATIENTS WITH RA

C. A. Rutherford, M. Filkova, M. Molokhia

Results: We retrospectively analyzed patients classified with RA per ACR 1987 and ACR/EULAR 2010 criteria with at least one year of follow-up in a cohort of RA patients without comorbidities from Hospital Civil ‘Juan I. Menchaca’. Patients who developed IR during follow-up had a mean increase of DAS-28 of 1.27 (P < 0.005 vs patients who improved or never developed IR). Patients positive for ACPA had a greater increase in IR during follow-up. Multivariate analysis revealed that ACPA, increments in WHR and ST4 were independent predictors of basal insulin increases during follow-up.

Conclusions: ACPA and abdominal adiposity (WHR) are independent predictors of IR development in RA

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6862

SAT0101

POSSIBILITY OF BACTERIAL INFECTION PROPHYLAXIS OF TRIMETHOPRIM-SULFAMETHOXAZOLE IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TREATMENT WITH BIOLOGICS: A SINGLE-CENTER, RETROSPECTIVE, CASE-CONTROL STUDY

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Background: Trimethoprim-sulfamethoxazole (TMP-SMX) is widely used for the prophylaxis of Pneumocystis jiroveci pneumonia (PCP) in immunocompromised patients, but data about the prophylactic effect of TMP-SMX against bacterial infections are insufficient.

Objectives: To analyze the prophylactic effect of TMP-SMX against severe bacterial infections in elderly patients with rheumatoid arthritis undergoing treatment with biologics.

Methods: Data were retrospectively collected from the medical records of patients with rheumatoid arthritis at our center. We divided the elderly patients (65 years or above) who took biologic agents into two groups. The first group (TMP-SMX+) comprised patients who previously or concurrently started TMP-SMX with biologic

Abstract SAT0099 – Table 1

<table>
<thead>
<tr>
<th>All Patients</th>
<th>0–5 drugs</th>
<th>&gt;6 drugs</th>
<th>10 drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=15,004</td>
<td>n=7,115</td>
<td>n=6,019</td>
<td>n=1,870</td>
</tr>
<tr>
<td>Baseline characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Age in years</td>
<td>56.3</td>
<td>54.0</td>
<td>57.6</td>
</tr>
<tr>
<td>Mean DAS 28 (SD)</td>
<td>4.30 (1.76)</td>
<td>4.17 (1.79)</td>
<td>4.51 (1.67)</td>
</tr>
<tr>
<td>Mean HAQ (SD)</td>
<td>1.93 (0.64)</td>
<td>1.85 (0.65)</td>
<td>2.10 (0.56)</td>
</tr>
<tr>
<td>Mean Disease Duration (SD) in years</td>
<td>12.59 (9.72)</td>
<td>11.96 (9.32)</td>
<td>13.79 (10.26)</td>
</tr>
<tr>
<td>Comorbidity (SD)</td>
<td>1.87 (0.80)</td>
<td>1.65 (0.74)</td>
<td>2.29 (0.73)</td>
</tr>
</tbody>
</table>

Analysis of Serious Adverse Events

| Exposure time (person-years) | 14.200 | 9.690 | 3.706 | 804 |
| Event count (single failure model) | 3261 | 2002 | 1251 | 368 |
| Incidence rate (95% CI) | 25.5 (24.7–26.3) | 20.6 (19.7–21.5) | 33.7 (31.9–35.6) | 45.7 (41.3–50.7) |

Adjusted for age, sex, DAS, HAQ, disease duration and comorbidities.
agents for the purpose of PCP prophylaxis and continued with it throughout the treatment with biologics. The second group (TMP-SMX+) comprised patients who were not prescribed TMP-SMX throughout the treatment with biologics. We analyzed the retention rate of each group by Kaplan-Meier curves and the Wilcoxon test. The primary end point was the 18-month retention rate of biologics without severe infection (defined as hospitalization or multiple days of intravenous antibiotic treatment in the clinic, including suspected cases).

**Results:** The TMP-SMX+ group included 30 patients with a mean age of 76.7±7.0 years. The rate of ACPA positivity was 80.0%, MTX use was 73.3%, oral steroid use was 43.3%, and bio-naive patients was 73.3%. The number of patients treated with abatacept, certolizumab pegol, etanercept, golimumab, infliximab, and tocilizumab was 13, 7, 7, 1, and 1, respectively. The cumulative retention rates at 12 and 18 months were 1.000 and 0.941, respectively. Prophylactic doses of TMP-SMX were between TMX 20mg/SMX 100mg/day and TMX 91mg/SMX 457mg/day.

The TMP-SMX- group included 113 patients with a mean age of 73.6±5.6 years. The rate of ACPA positivity was 79.3%, MTX use was 70.8%, oral steroid use was 54.9%, and bio-naive patients was 80.5%. The number of patients treated with abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and tocilizumab was 15, 15, 4, 41, 7, 18, and 13, respectively. The cumulative retention rates at 12 and 18 months were 0.812 and 0.790, respectively. There was a significant difference between the retention rates in the two groups (p =0.038, Wilcoxon test). Five patients were enrolled in both groups because another biologic agent was used in different periods.

In the TMP-SMX+ group, only one patient was hospitalized for probable bacterial pneumonia (causative bacteria not detected). In the TMP-SMX- group, nine patients were hospitalized for pneumonia, three for septic arthritis, two for urinary tract infection, and two for soft tissue infection. The causative bacteria were Escherichia coli, Klebsiella oxytoca, Enterococcus faecalis and others.

Furthermore, seven patients in the TMP-SMX- group were treated for PCP, whereas no patients contracted PCP in the TMP-SMX+ group. Furthermore, seven patients in the TMP-SMX+ group were treated for PCP, whereas no patients contracted PCP in the TMP-SMX+ group.

**Conclusions:** Prophylactic administration of TMP-SMX may reduce the risk of bacterial infection in elderly patients with rheumatoid arthritis undergoing treatment with biologics.

**References:**

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4650

**SAT0102**

**THE EFFECT OF LACTATION ON THE ACTIVITY OF RHEUMATOID ARTHRITIS**

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**Background:** It has been reported that rheumatoid arthritis (RA) onset in females is often associated with post-partum period and lactation. Moreover, flares of disease were more frequent, than in non-breastfeeding women during 3 to 6 months period of the follow-up (FUP). RA exacerbations were more frequent in lactating women than in non-breastfeeding women during 3 to 6 months period of the FUP. RA flare was documented based on changes in DAS28CRP score values vs the previous visit following EULAR recommendations.

**Objective:** To assess the prevalence of nocturnal hypertension and its associations in patients with RA.

**Methods:** 62 patients with RA (EULAR 2010) without known cardiovascular disease were examined (73% females, age 58.5±15.4 (M±SD) years, 13% months post-partum. Pts’ median age was 29 (20–37) years, disease duration 8 (1–28) years. RF (62.1%) and ACPA (58.6%) seropositive, of radiographic stage 2–3 (72.4%) and functional class 1–2 (86.2%) prevailed. At each control visit DAS28CRP score and the number of between the visits flares were obtained among breastfeeding and non-breastfeeding women. RA flare was documented based on changes in DAS28CRP score values vs the previous visit following EULAR recommendations.

**Results:** 6 pts were lost for follow up (FUP; the 1 after Mo 37, 5 after Mo 5–6 post-partum). Lactation immediately after birth was suppressed in 5 (15.6%) pts. 27 (84.4%) pts were breast-feeding their babies for the period from 2 weeks to 16 months (Mo=2.5 [1.6] months). All relevant data on the study population during the FUP is summarized in the Table1.

**Conclusions:** Lactation and breastfeeding is associated with 4-fold higher risk of RA exacerbation as compared to non-breastfeeding population (RR=4; 95% CI=1.8;9.2; p=0.0002). Increased RA exacerbation rates among nursing mothers is partially explained by postponement of active therapy. The majority of pts refused initiation of therapy for the sake of breastfeeding.

Approaches to breastfeeding practices in RA mothers should be individual. Nursing is acceptable during RA remission or low disease activity given the patient continues on the recommended drugs, compatible with breast-feeding.
smokers, 61% with AH, 34% with dyslipidemia). Median duration of RA was 8 years (IQR 3–17), Seropositive RA was diagnosed in 69% of patients. Median CRP was 12.1 mg/l (IQR 2.2–23.4 mg/dl), median rheumatoid factor (RF) was 32.5 IU/ml (IQR 8.3–173 IU/ml). All patients received disease-modifying antirheumatic drugs, 22% (38%) - biological treatment. Median duration of AH was 6.1 years (IQR 0–10) years. All patients with AH received antihypertensive treatment. 24h peripheral and central BP monitoring was performed (BenLab Vasotens, “Petr Telegin”). Arterial stiffness was assessed by applanation tonometry (Sphygmocor, AtCor). P<0.05 was considered significant.

Results: Mean office BP was 130±15/82±10 mmHg. Mean pulse wave velocity (PWV) was 8.6±2.8 m/s. Reverse dipping state was as follows: non-dipping in 37% (62.9%) patients, dipping in 7 (11.3%), extreme dipping – in 5 (8.1%) and reverse dipping in 11 (17.7%). Median of nocturnal fall in systolic BP was 3.5% (IQR 0–9%). Isolated nocturnal AH was observed in 12 (19.4%) pts. Patients were divided in three groups according to nocturnal fall of BP: G1 (non-dipping >10%) – 42 (67.7%) pts and G2 (dipping <10%) – 16 (32.3%) pts. Non-dippers were older (56.7±16.2 vs 49±12.5 years), more often were smokers (20 vs 0%), had higher BMI (25.4±6.0 vs 22.3±5.1 kg/m²), median duration of AH (1.5, IQR 0–11 vs 0; min, max 1 year), median duration of RA (10, IQR 7–19 vs 2.5; IQR 2–6.5 years), PWV (8.6±2.8 vs 7.2±2.1 m/s), nocturnal BP (120.4±12.6/69.8±10.4 vs 103.8±8.2/55.4±4.4 mmHg), <0.05 for trend. Spearman analysis revealed significant correlations between nocturnal fall in SBP and RA duration (r=-0.3), reverse dipping and age (r=0.21), age and CRP (r=0.21), and disease duration and prednisone dose. Conclusion: The majority of patients with rheumatoid arthritis are characterized by non-dipping state. Diastolic nocturnal hypertension is a significant predictor of non-dipping in this patient population.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5131

SAT0104 | THE IMPACT OF DISEASE ACTIVITY ON PATIENT REPORTED COGNITIVE Dysfunction (“brain fog”) IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic, inflammatory disease and its burden extends beyond joint disease. In recent years, there has been significant advances in treating joint disease but we need a greater understanding of physical and especially psychosocial comorbidities to improve quality of life in RA patients. In particular, patients often report “brain fog” meaning a diminished ability to think, learn, remember and perform other mental tasks. Doctors have long recognized that patients with certain physical conditions can experience cognitive dysfunction. Limited information is available in the literature with regard to the prevalence of cognitive dysfunction and factors associated with the condition in RA.

Objectives: To characterize the association of disease activity with patient reported cognitive dysfunction in patients with RA overall and stratified by age.

Methods: We identified patients with RA aged ≥ 18 years who were enrolled in the Canadian registry who were rheumatoid arthritis naïve at their last follow-up visit (October 2010–June 2016). We compared those who reported cognitive dysfunction (responded “yes” to the question asking if they had “problems with thinking”) to those who did not with respect to disease activity based on the Clinical Disease Activity Index (CDAI). Unadjusted and adjusted logistic regression models controlling for demographic (age, gender, race, education), comorbidity/lifestyle (diabetes, fibromyalgia, body mass index, smoking) and RA disease characteristics (disease duration, disability and prednisone dose) were conducted. We further examined whether the relationship between disease activity and cognitive dysfunction varied based on patients age (≤ 55 vs > 55 years) testing the modest effect using a likelihood ratio test.

Results: There were 10,401 patients who met inclusion criteria of whom 883 (8%) reported cognitive dysfunction. Those who reported cognitive dysfunction were more likely to be women (83% vs. 73%, p<0.001), younger (62 vs 64 years, p<0.001), disabled (16% vs. 11%, p<0.001) with higher levels of disease activity based on the CDAI (51% vs. 31%, p<0.001). In adjusted models, the likelihood of cognitive dysfunction increased with higher levels of disease activity in the total population (Table). The impact was more pronounced in those age ≤ 55 (p=0.007; Table).

Conclusions: HBV occult infection seems to influence negatively the effectiveness

<table>
<thead>
<tr>
<th>Disease activity OR (95% CI)*</th>
<th>Total population</th>
<th>Age ≤ 55**</th>
<th>Age ≥ 55**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Low</td>
<td>2.70 (2.13–3.45)</td>
<td>3.97 (2.34–6.75)</td>
<td>2.42 (1.84–3.20)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3.56 (2.75–4.61)</td>
<td>5.93 (3.45–10.19)</td>
<td>3.01 (2.24–4.05)</td>
</tr>
<tr>
<td>High</td>
<td>3.90 (2.92–5.21)</td>
<td>7.82 (4.99–13.98)</td>
<td>2.90 (2.04–4.12)</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, race, disability, education, smoking status, body mass index, diabetes, fibromyalgia, disease duration and prednisone dose.
**Adjusted for gender, race, disability, education, smoking status, body mass index, diabetes, fibromyalgia, disease duration and prednisone dose.
of biological therapies in RA patients. However, being a real-life setting, unknown confounding factors might generate an apparent association or mask a true correlation between the HBCab status and clinical outcomes.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2032

SAT0107 FURTHER “WELLNESS” CAN BE ACHIEVED BY SURGICAL INTERVENTION IN THE IMPAIRED HAND EVEN FOR PATIENTS WITH WELL-CONTROLLED RHEUMATOID ARTHRITIS
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Background: The hand is the most frequently involved site in rheumatoid arthritis (RA). The treatment aim of RA is achieving and maintaining remission (REM) or low disease activity (LDA) via tight medical control. However, despite remarkable advances in medication, progressive deterioration and/or deformity of the hand, if adequate medication is not administered in the early stage. Surgical reconstruction is still required in hands with functional loss and/or a grotesque appearance caused by joint deterioration or tendon rupture. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and wellness.

Objectives: The objective of this study was to clarify the systemic effects of surgical intervention in the impaired hand, even in patients with well-controlled disease who have achieved REM or LDA.

Methods: A prospective cohort study was performed in 119 hands of 119 patients with functional loss and/or a grotesque appearance due to RA who underwent primary elective surgery between October 2012 and September 2014. A total of 42 hands in 42 patients (males: 2; females: 40) had a disease activity of REM or LDA just before surgery. In the REM/LDA group, the average (range) age was 61 (29–82) years, and the average (range) disease duration was 15 (2–35) years. The procedures performed included Darrach procedure (ulnar head resection) in 17 hands, radiolunate arthrodesis in 10, extensor tendon reconstruction in 6, thumb/index metacarpophalangeal joint arthroplasty (Swanson) in 14, proximal interphalangeal (interphalangeal) joint fusion in 4, and thumb CM joint arthroplasty (Thompson) in 4 and so on. The patient-reported outcome (PRO) was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), Patient’s General analogue scale (PS-VAS), modified Health Assessment Questionnaire Disability Index (mHAQ). Drugs administered for patient had been checked at the time of consultation.

Results: On the whole, the physical function (HAQ-DI, DASH, GP), QOL (HAQ-DI, EQ-5D, Pt-GH), mental wellness (BDI-II, Pt-GH), and disease activity (DAS28-CRP) were significantly improved at 6 and 12 months after surgery compared to baseline (p < 0.05). In the REM/LDA group, a significant improvement was noted in the upper-extremity function (DASH), QOL (EQ-5D), and disease activity (DAS28-CRP) at 6 and 12 months after surgery; however, we did not observe any significant changes in any other items (Table 1).

Table 1: Outcome of surgical intervention in the impaired hand for patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th></th>
<th>HAQ-DI</th>
<th>EQ-5D</th>
<th>DASH</th>
<th>GP</th>
<th>DAS28-CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n=19</td>
<td>0.17</td>
<td>0.72</td>
<td>13.4</td>
<td>36 (23)</td>
<td>42.1 (33.5)</td>
</tr>
<tr>
<td>POIF 6mos</td>
<td>0.97 (0.76)</td>
<td>0.76 (0.14)</td>
<td>11.7 (8.6)</td>
<td>24.1 (21)</td>
<td>37.1 (21.7)</td>
</tr>
<tr>
<td>POIF 12mos</td>
<td>0.91 (0.76)</td>
<td>0.76 (0.14)</td>
<td>11.9 (9.1)</td>
<td>24.5 (21)</td>
<td>37.5 (25.3)</td>
</tr>
<tr>
<td>REM/LDA n=42</td>
<td>0.65 (0.63)</td>
<td>0.75 (0.14)</td>
<td>11.0</td>
<td>15 (8.1)</td>
<td>34.6 (21.8)</td>
</tr>
<tr>
<td>POIF 6mos</td>
<td>0.80 (0.68)</td>
<td>0.60 (0.14)</td>
<td>10.1</td>
<td>16 (8.1)</td>
<td>30.2 (19.6)</td>
</tr>
<tr>
<td>POIF 12mos</td>
<td>0.81 (0.70)</td>
<td>0.79 (0.16)</td>
<td>10.8</td>
<td>16 (14)</td>
<td>30.5 (21.0)</td>
</tr>
</tbody>
</table>

Mean(SD); *p<0.05 compared to baseline, **p<0.01 compared to baseline

Conclusions: Achieving REM or LDA is not the ultimate goal of treatment for patients with functional loss and/or a grotesque appearance of their hands. Further “wellness” can be achieved by surgical intervention in the affected hand, even for patients with well-controlled RA. Such intervention can also ameliorate the disease activity.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4213

SAT0108 CLINICAL SIGNIFICANCE OF ANTI-ACTIN ANTIBODIES IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES
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Background: Anti-actin antibodies (AAA) are well-described as the major component of smooth muscle autoantibodies (microfilament antibodies). They are specially detected in patients with chronic active hepatitis (CAH) and celiac disease (CD). AAA have also been found less frequently in various other autoimmune disorders including systemic lupus erythematosus (SLE), Sjogren’s syndrome, and myasthenia gravis, as well as in primary biliary cirrhosis and alcoholic liver disease.

Objectives: to study clinicobiological characteristics of patients with AAA in autoimmune inflammatory rheumatic diseases (AIRD).

Methods: From January to December 2016, we have collected all cases of patients with AAA presenting for symptomatology of AIRD. The presence of AAA was detected fortuitously by indirect immunofluorescence (IF) in accordance with its characteristic fluorescence pattern in Hep2 cells (BioRad®). The specificity for F-actin was confirmed by IIF on rat liver-kidney-stomach sections (Biosystem®) and/or Immunodot (Euroimmun). Coeliac disease related antibodies were performed in all patients with AAA.

Results: Six patients were included: 5 women and a man with a mean age of 43.5 years. AIRD have been suspected in these patients and the mean clinical features were inflammatory polyarthritis and fever. AIRD was diagnosed in three (50%), SLE and five (75%) in patients with rheumatoid arthritis (RA). Hepatic function was disturbed with elevated serum ALT and AST activities in one case highly suspected of CAH. CD was diagnosed in one case. The sixth patient had positive antinuclear antibodies, hypocomplementemia and anti-Ro52, anti-SSB and anti-DFS antibodies associated with FR but didn’t
fulfilled SLE criteria. The immunological tests showed anti-nuclear antibodies among all patients with high titre and anti-DNA antibodies in SLE and CAH patients respectively. One RA patient had anti-Ro60 antibodies.

**Conclusions:** During our study, AAA were found fortuitously in AIRD. This association is rarely described in the literature. Hepatic involvement can be seen as fibromyalgia, depression, etc.). However, DAM and STR may affect clinical management and outcomes of treatment in many RA patients. For example, an RA patient with well-controlled INF who has secondary fibromyalgia may have 0 swollen joints (SJc) and an ESR<15, but nonetheless have a DAS28 of 5.1, CDAD of ≥22, and RAPID3 of ≥16 (indicating high activity), based on 14/28 tender joints and a patient global assessment of 80/100. Therefore, quantitative estimates of DAM, and STR, as well as INF may clarify patient status and clinical management decisions.

**Objectives:** To analyze physician quantitative estimates for the proportion of management decisions attributed to INF, DAM, or STR (total=100%) in RA patients seen in routine care.

**Methods:** At one academic rheumatology center, the rheumatologist completes 0–10 visual analog scales (VAS) for overall global assessment (DOCGL), tender joints and a patient global assessment of 80/100. Therefore, quantitative estimates of DAM, and STR, as well as INF may clarify patient status and clinical management decisions.

**Results:** Among the 77 RA patients, >40% of clinical management decisions were attributed to INF in only 31 (40%), versus >40% to DAM in 33 (43%), and >40% to STR in 17 (22%) (Table). No category of INF+DAM or INF+STR included >60% attributed to INF. Cross-tabulations were computed for various phenotypes in 5 INF+DAM and INF+STR categories, 0, 1–20%, 21–40%, 41–60%, and 61–100%.

**Conclusions:** Physician quantitative estimates of the proportion of clinical management decisions attributed INF, DAM, and STR may help clarify RA patient status and document a basis for clinical decisions. High levels of DAM and/or STR may explain in part why a target of RA remission often is not met in many patients seen in routine clinical care.

**References:**

value -0.05 and \( t = -0.486 \), \( p \) value <0.01 respectively), depressed bronchial resistance SGaw (\( t > 0.773 \), \( p \) value <0.01) and increased RV (\( t = -0.736 \), \( p \) value <0.01), which determined BO severity.

**Conclusions:** More than half of patients with RA have BO predominantly in terminal bronchioles. Accepting significant decrease of Clara cell protein CC16 in patients with RA we suppose pathogenic relationship between functional depression of Clara cell anti-inflammatory activity and BO in this category of patients.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4585

**SAT0112 PREVALENCE AND INCIDENCE OVER 3 YEARS OF DIFFERENT COMORBIDITIES IN RHEUMATOID ARTHRITIS (RA): A 3 YEAR LONGITUDINAL STUDY IN 769 ESTABLISHED RA PATIENTS**


**COMEDRA working group, Paris, France**

**Background:** Comorbidities including cardiovascular (CV) risk, cancer and osteoporosis are frequent in RA.

**Objectives:** To quantify at baseline and 3 years later, the prevalence (at baseline) and incidence (over 3 years) of some selected comorbidities.

**Methods:** This was an open long term (3 years) extension of the COMEDRA 6-month randomized controlled trial in which patients with definite, stable RA were visiting a nurse for comorbidity counselling.[2] Comorbidity status was assessed through face-to-face interviews and nurses provided advice on screening and management, at baseline and 3 years later. The frequency of comorbidities was assessed at both timepoints and incidence of new cases was assessed as overall % of patients and as relative increase in the given comorbidity.

**Results:** Of the 970 recruited patients, 776 (80%) were followed up at 2–4 years (15, 1.5%, had died) and 769 (79%) had available data for comorbidities at both timepoints: at baseline, mean (±SD) age 57 (±11) years, mean disease duration (14, ±10) years; 614 (80%) were women and 538 (70%) were receiving a biologic.

**Table:** frequency of comorbidities at baseline and 3 years later

**Conclusions:** Comorbidities are frequent in RA though screening does not always address the most frequent or severe comorbidities. Efforts must be pursued to improve comorbidity screening and prevention.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2978

**SAT0113 OBESITY AND METABOLIC SYNDROME INFLUENCE ON N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN RHEUMATOID ARTHRITIS PATIENTS**

L. Kondratyeva, T. Popkova, I. Kirillova, D. Novikova, A. Novikov, E. Alexandrova, E. Nasonov. V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

**Background:** N-terminal pro-brain natriuretic peptide (NT-proBNP) is a recognized myocardial injury marker, a known predictor of heart failure and cardiovascular death. Rheumatoid arthritis (RA) patients (pts) were shown to have higher than in general population NT-proBNP concentrations, proportional to serum C-reactive protein (CRP) levels.

**Objectives:** To find out whether obesity/overweight or MS may modify NT-proBNP levels in RA pts.

**Methods:** A total of 68 early RA pts (72% females, 28% males) was enrolled in the study. Mean disease duration was 6 [4;8] months, and RA activity using DAS28 calculator was 5.6 [5.1;6.4] scores. The majority of pts had positive RF (87%) and ACPA (88%). All pts were glucocorticoid and disease-modifying antirheumatic drugs - naïve prior to inclusion. The overweight/obesity was determined by WHO criteria in patients with body mass index (BMI) >25 kg/m2. National Cholesterol Education Program/Adult Treatment Panel III criteria were used to confirm MS. Serum levels of NT-proBNP (pg/mL) were measured using electrochemiluminescence test Elecsys proBNP II (Roche Diagnostics, Switzerland).

**Results:** Overweight and obesity were established in 54,4% RA pts. Overweight/obese RA pts were older than pts with normal BMI (57 [53;61] years vs 48 [34;61] years, \( p <0.02 \)), had higher DAS28 scores (5.65 [5.20;6.57] vs 5.28 [4.76;5.69], \( p <0.01 \)), higher CRP (38.8 [14.3;47.9] mg/L vs 12.8 [2;22.8] mg/L, \( p <0.01 \)). Elevated NT-proBNP concentrations were found in 62.2% overweight/obese pts vs 29.0% pts with normal weight (\( p <0.01 \)). Median NT-proBNP concentrations in overweight/obese pts were 153 [75;226.8] pg/mL vs 72.2 [40;147.4] pg/mL, respectively (\( p <0.02 \)). MS was established in 62.2% pts with BMI >25 kg/m2 and in 25.8% pts with BMI <25 kg/m2 (\( p >0.01 \)). Median NT-proBNP concentrations did not vary significantly in pts with and without MS, whether they were overweight/obese (\( p >0.75 \)), or had normal BMI (\( p >0.27 \)). In 2011, we started a cardiovascular (CV) risk management program for rheumatoid arthritis (RA) patients visiting Reade in the Netherlands. We previously reported the presence of under treatment of hypercholesterolemia and hypertension [1].

**Objectives:** To assess the effectiveness of our CV risk management program in RA patients, using new CV risk stratification tools.

**Methods:** CV risk screening was performed at baseline and informed the general practitioner (GP) about the results, including advices regarding the initiation of cardio preventive drugs. In high risk patients, antihypertensives were prescribed and, if indicated, lipid-lowering drugs. In low risk patients, preventive medication was left to the GP. CV risk screening was repeated after 12 months.

**Results:** Of the 266 patients 202 (76%) were female, the mean age was 58±11 years. After one year, 88 out of 134 patients who received inadequate or no treatment at baseline were still untreated or undertreated. Of the 188 (71%) patients who were at high CV risk and who did have an indication to start therapy, only 7.5% was contacted by their GP and another 6.8% arranged an appointment themselves. While the 10-year CV risk did not decrease in the whole population, a risk reduction was found in the patients that started medication. Remarkably, 42% of patients reported lifestyle changes, including more exercise (20%), diet adaption (16%) and weight loss (9%).

**Conclusions:** It is striking that one year after the introduction of our CV risk management program for rheumatoid arthritis (RA) patients visiting Reade in the Netherlands, we previously reported the presence of under treatment of hypercholesterolemia and hypertension [1].

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3731

**SAT0114 POOR CARDIOVASCULAR RISK MANAGEMENT IN RHEUMATOID ARTHRITIS PATIENTS DESPITE AN EXPLICIT CARDIOVASCULAR RISK MANAGEMENT PROGRAM**

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1Amsterdam Rheumatology and immunology Center | Reade, Amsterdam; 2Antonius Hospital Zuidwest Friesland, Sneek; 3VU University Medical Center; 4Amsterdam Rheumatology and immunology Center | VU University Medical Center, Amsterdam, Netherlands

**Background:** In 2011, we started a cardiovascular (CV) risk management program for rheumatoid arthritis (RA) patients visiting Reade in the Netherlands. We previously reported the presence of under treatment of hypercholesterolemia and hypertension [1].

**Objectives:** To assess the effectiveness of our CV risk management program among RA patients.

**Methods:** CV risk screening was performed at baseline and informed the general practitioner (GP) about the results, including advices regarding the initiation of cardio preventive drugs. In high risk patients, antihypertensives were recommended when systolic blood pressure >140 mm/Hg and statins were recommended when low-density lipoprotein >2.5 mmol/l. The decision to start preventive medication was left to the GP. CV risk screening was repeated after one year. Patients completed a questionnaire about the actions that were taken following the results of the initial screening.

**Results:** Of the 266 patients 202 (76%) were female, the mean age was 58±11 years. After one year, 88 out of 134 patients who received inadequate or no treatment at baseline were still untreated or undertreated. Of the 188 (71%) patients who were at high CV risk and who did have an indication to start therapy, only 7.5% was contacted by their GP and another 6.8% arranged an appointment themselves. While the 10-year CV risk did not decrease in the whole population, a risk reduction was found in the patients that started medication. Remarkably, 42% of patients reported lifestyle changes, including more exercise (20%), diet adaption (16%) and weight loss (9%).

**Conclusions:** It is striking that one year after the introduction of our CV risk management program for rheumatoid arthritis (RA) patients visiting Reade in the Netherlands, we previously reported the presence of under treatment of hypercholesterolemia and hypertension [1].
**SA0115** EFFECT OF BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (bDMARDS) ON CARDIOVASCULAR DISEASE (CVD) RISK IN RA PATIENTS: THREE YEARS RESULTS FROM A CANADIAN COHORT

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**Background:** RA patients have a higher risk for developing CV Diseases (e.g. IHD and stroke) than the general population. We reported previously (ACR, EULAR) the results CV risk in our patients treated with bDMARDS for 1 & 2 years.

**Objective:** To assess the effect of bDMARDS treatment on 10-year CV disease risk in patients with RA after 36 months and evaluate the impact of their use on the incidence of CV events.

**Methods:** A cohort of RA patients was followed prospectively. Demographics, disease activity parameters, inflammatory markers, CV events, CVD 10 year risk assessment (Framingham Risk Score (FRS)) were ascertained at the baseline and every six months, up to 36 months. Statistical analysis utilized SPSS (IBM version 24) software.

**Results:** 321 patients were included, of those 270 patients were followed for three years. Eight bDMARDS were included evaluating their effect on disease activity and CV risk in 233 patients who continued on their prospective biologic for the three years.

Significant overall reduction in disease activity in all groups was obtained as compared to baseline. The whole group DAS improved from 3.996 to 3.118.

The HAQ also improved significantly (1.201 to 0.857) and the CRP improved significantly (12.91 mg/L to 7.3).

Overall, Total cholesterol (TC) changed from 5.195 mmol/L at baseline to 4.992 (P 0.001). High Density Lipoprotein Cholesterol (HDL-C) decreased significantly at 36 months from 1.336 to 1.376. The Atherogenic Index (AI) for the whole cohort changed from 3.636 to 3.845. The overall 10 year risk of cardiovascular event increased from 12.878 to 13.8.

The cohort included 321 patients. Eight bDMARDS were evaluated to assess their effect on disease activity and CV risk. The outcomes in 233 patients who continued their prospective biologic for the three years were reported (Table). 77% were females, median RA duration was 11 yrs. Significant reduction in disease activity in all groups was achieved vs. baseline. The DAS improved from 3.996 to 3.118, the HAQ improved significantly (1.201 to 0.857) and the CRP also improved significantly (12.91 mg/L to 7.3).

**Conclusions:** The bDMARDS studied were effective in controlling the disease activity of RA. Although the overall CV risk was not reduced in the group as a whole at 36 months, bDMARDS may still play a role in reducing the CV risk in these patients.

**Disclosure of Interest:** M. Hirose: Grant/research support from: Roche Canada, C. Moro: None declared, A. Lewis: None declared

DOI: 10.1136/annrheumdis-2017-eular.3188
Conclusions: Pain is a frequent and relentless suffering during the long-term course of rheumatoid arthritis. In this study, 34% of the patients had unacceptable pain 15 years after diagnosis indicating unsatisfactory treatment. Unacceptable pain also occurred in patients in remission indicating that pain in RA is multifactorial. Therefore, the cause of pain should be identified and treatment initiated accordingly.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3641

SAT0117 RETENTION RATES OF ADAHILUMAB, ETANERCEPT, AND INFLIXIMAB AS 1ST OR 2ND-LINE BIOThERAPY FOR RHEUMATOID ARTHRITIS PATIENTS IN DAILY PRACTICE IN AUVERGNE

M. Soubrier1, B. Pereira2, T. Frayssac1, A. Fan1, M. Couderc3, S. Malochet-Guinamand1, S. Mathieu1, Z. Tatar1, A. Tournadre3, J.-J. Dubost1.

Methods: We have conducted a retrospective cohort study among patients to investigate the safety and efficacy of an alternate-day corticosteroids (CORT) as first-line therapy for rheumatoid arthritis (RA) and is as effective as a daily corticosteroid dose for treating rheumatoid arthritis. The retention rates of the initial anti-TNF treatment (etanercept [ETN], adalimumab [ADA], and infliximab [IFX]) initiated as first-line biotherapy for rheumatoid arthritis (RA) and is as effective as a daily corticosteroid dose for treating rheumatoid arthritis.

Results: Among the 346 patients analyzed, 201 received ETN, 82 ADA, and 63 IFX. The first anti-TNF was interrupted in 151 cases. The retention rates were 82.8%, 67.6%, 46.5%, 28.1%, and 22.5% at 1, 2, 5, 10, and 15 years, respectively, with a median retention duration of 59.2 months (ETN: 59.3 [19.1–104.2], ADA: 79.9 [19.3–136.2], and IFX: 72.7 [17.5–134.5]). The predictive factors of discontinuation were active RA (DAS28-CRP HR: 1.22 [1.03–1.45]), inflammatory syndrome (ESR HR: 1.01 [1.00–1.02], CRP HR: 1.00 [1.00–1.01]), absence of MTX treatment (HR: 0.60 [0.43–0.83]), and corticosteroid use (HR: 1.91 [1.31–2.78]). The patients who switched to another anti-TNF treatment had an inferior retention than those who switched to a non-anti-TNF treatment (HR: 0.39 [0.17–0.87]; p=0.02).

Conclusions: In real-life conditions, the retention rates of the initial anti-TNF treatment (etanercept [ETN], adalimumab [ADA], and infliximab [IFX]) initiated as first-line biotherapy for rheumatoid arthritis (RA) and is as effective as a daily corticosteroid dose for treating rheumatoid arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3676

SAT0118 SAFETY AND EFFICACY OF ALTERNATE-DAY CORTICOSTEROIDS AS ADJUNCTIVE THERAPY IN RHEUMATOID ARTHRITIS

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Background: Corticosteroids are often used for treating rheumatoid arthritis. However, minimizing adverse events while maximizing efficacy remains challenging. An alternate-day corticosteroid dose is known to decrease adverse events.

Objectives: To investigate the safety and efficacy of an alternate-day corticosteroid dose for treating rheumatoid arthritis.

Methods: We have conducted a retrospective cohort study among patients over 18-year-old who started oral corticosteroids (prednisolone and methylprednisolone) as treatment of rheumatoid arthritis from 2005 to 2014 at St. Luke’s International Hospital, a tertiary-level community teaching hospital in Tokyo, Japan. Patients were included if they met the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for rheumatoid arthritis, and had positive anti-cyclic citrullinated peptide antibody. They were excluded for a history of corticosteroid use for other diseases, or if they were lost to follow-up within 1 year after starting corticosteroids. We divided patients into a daily corticosteroid group (QD) and an alternate-day corticosteroid group (QOD). Patients received both daily and alternate-day corticosteroids were assigned to the daily group. We investigated the percentage of patients without any infection within 1 year after starting corticosteroids. We have conducted multivariate logistic regression model analysis to calculate adjusted odds ratio for QD/QOD to the outcome. We also investigated the mean decrease in C-reactive protein (CRP) at 1 month as a marker of short-term effectiveness, and the percentage of patients free from corticosteroid at one year, using student’s t-test.

Results: In total, 139 patients were analyzed (69 in the QD group, 70 in the QOD group). The maximum dose of corticosteroid in one year was not significantly different in both groups. However, the percentage of patients without any infection within 1 year after starting corticosteroids was 82.8%, 67.6%, 46.5%, 28.1%, and 22.5% at 1, 2, 5, 10, and 15 years, respectively, and the mean daily dose of corticosteroid in one year was significantly higher in the QD group (6.1±4.4 mg/day vs 3.9±1.7 mg/day; P<0.01). The percentage of patients without any infection within 1 year after starting corticosteroids at one year was 26.1% in QD group, and 58.6% in QOD group (P<0.01). Kaplan-Meier plot showed that QD group patients were more difficult to become free from corticosteroid (log-rank test: P<0.01).

Conclusions: Alternate-day corticosteroid dose has a lower adverse event rate and is as effective as a daily corticosteroid dose for treating rheumatoid arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4160
was more common in women with RA, but did not differ significantly between pregnancies prior to and after RA diagnosis. A total of 41% of the post-RA pregnancies had an adverse pregnancy outcome (miscarriage, preterm delivery, or infant abnormalities), compared to 13% of pre-RA pregnancies (p<0.01) and 20% of control pregnancies (p=0.01).

Conclusions: Women with RA, overall, had similar rates of miscarriage, stillbirth, and ectopic pregnancy compared to healthy women, but pregnancies that occurred after RA diagnosis had higher rates of these adverse outcomes. More pregnancies in women with RA were planned, leading to a lower rate of elective termination.

Acknowledgements: This study was funded by Pfizer.

Disclosure of Interest: M. Closwie Grant/research support from: Pfizer, Jansen, Consultant for: UCB, G. McDaniel: None declared, A. Eudy: None declared

DOI: 10.1136/annrheumdis-2017-eular.6333

**SAT0120 EVALUATION OF THE RISK OF OVERALL MALIGNANCY AND MALIGNANT LYMPHOMA WITH METOTREXATE AND BIOLOGICAL AGENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE IORRA COHORT DURING A 14-YEAR OBSERVATION PERIOD**

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Background: While dramatic progress has been made in this decade with treatments for rheumatoid arthritis (RA), such as methotrexate (MTX) and biological agents, concern about the safety, including the occurrence of malignancy, of these highly effective drugs still exists in daily clinical practice. There has not been an evident association between the use of biological agents and the occurrence of malignancy in most reports from clinical trials1 and observational studies2, although MTX use might be associated with the development of malignant lymphoma, called MTX-associated lymphoproliferative disorder3, in patients with RA. In an analysis of risk factors for overall and site-specific malignancies in Japanese patients with RA, higher disease activity was identified to be a risk factor for overall malignancies (hazard ratio [HR] 1.10, 95% CI 1.02–1.19), suggesting that tight control of RA disease activity would reduce the occurrence of malignancies in patients who were on MTX therapy4,5. However, it is still uncertain whether MTX and biological agents were risk factors for overall malignancy and malignant lymphoma using a marginal structural Cox proportional hazards model5 confirmed by medical records. Data for malignancies occurring in patients who were on biological agents) in a large observational cohort of Japanese patients with RA over a long-term period.

Methods: Among Japanese patients with RA enrolled in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort from April 2000 to September 2013, data for all malignancies were extracted from patients’ self-reports and confirmed by medical records. Data for malignancies occurring in patients who died of other causes during the study were also collected from medical information from affiliated hospitals. We analysed whether MTX and biological agents were risk factors for overall malignancy and malignant lymphoma using a marginal structural Cox proportional hazards model5 adjusted for age, gender, smoking history, body mass index, RA disease duration, rheumatoid factor positivity and disease activity (28-joint disease activity score).

Results: Among 11,106 Japanese patients with RA representing 68,483 person-years, 507 overall malignancies, including 68 malignant lymphomas, were confirmed. Neither MTX nor biological agent use was a significant risk factor for overall malignancy with a HR (95% CI) of 1.18 (0.77–1.81) and 1.01 (0.69–1.53), respectively, or for malignant lymphoma, with a HR (95% CI) of 1.17 (0.55–2.48) and 1.26 (0.43–3.64), respectively.

Conclusions: The use of MTX and biological agents was not significantly associated with the occurrence of overall malignancy or malignant lymphoma during long-term longitudinal observation of Japanese patients with RA.

References:

**SAT0121 COMORBIDITIES AND DISEASE ACTIVITY ARE RELEVANT FOR FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS**

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Background: Health status in rheumatoid arthritis (RA), as measured by Health Assessment Questionnaire - Disability Index (HAQ-DI), has been established as a relevant quantitative measure to assess and monitor the disease (1). Current RA therapy has shown improvement in patient-reported outcomes, but more data on specific factors influencing health status are needed (2).

Objectives: To assess the relationship between functional disability and clinical factors in patients with RA, using the HAQ score.

Methods: Cross-sectional study in patients with RA according to the ACR classification criteria from three Brazilian University Hospitals. Demographic and comprehensive clinical data, including components of metabolic profile were collected at the time of assessment. Blood pressure, weight and height were determined in the assessment visit and recent laboratory data were assessed from medical records. Disease activity was evaluated by the Disease Activity Score in 28 joints (DAS28) and functional disability was assessed by the HAQ-DI, considering an index < 0.5 as disability. All analyses were performed using Stata for MAC 12.0 software. Variables that achieved a p-value < 0.05 in the univariate analysis were considered as candidates to take part of a multivariate binominal logistic model, and in this model, variables were considered as statistically significant at the 0.05 level (3).

Results: 453 patients were included, 380 (83.9%) women, mean age 55.7 ±12 years, 356 (79.1%) Caucasian, and mean disease duration of 13.3 ±9 years. Methotrexate were used by 73.5% of the sample. Mean DAS28 was 3.9 ±1.4, mean HAQ score was 1.11 ±0.77, and 23.9% of the patients had HAQ score >0.5. Dyslipidemia, high blood pressure (HBP) and family history of premature cardiovascular disease occurred in 28.6%, 12.8%, 51% and 21.4% of the patients, respectively. Mean body mass index (BMI) was 27.1 ±4.9 kg/m². In multivariate analysis age, DAS28, tobacco use, and diabetes mellitus were independently associated with HAQ >0.5 (TABLE 1).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01 (1.01,0.03)</td>
<td>0.001</td>
</tr>
<tr>
<td>DAS28</td>
<td>1.01 (1.04,0.45)</td>
<td>0.001</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.37 (1.06,1.77)</td>
<td>0.016</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1.83 (1.82,8.13)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

DAS28 – disease activity score in 28 joints; BMI – body mass index; OR – odds ratio.

Conclusions: Our results depicted that distinct factors could reflect in the functional status response in RA patients. This is relevant since it may influence the clinically important difference when evaluating the HAQ response in populations with diverse cultural features and different comorbidities prevalence.
WHICH MULTIMORBID CONDITIONS ARE MORE PREVALENT AROUND THE TIME OF EARLY RA DIAGNOSIS AND HAVE THE GREATEST IMPACT ON TRAJECTORIES OF DISEASE ACTIVITY IN THE FIRST YEAR? RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

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Background: Multimorbidity (MM) is highly prevalent in early RA (ERA), and higher counts of conditions are associated with poorer disease control 1. It is important to understand the number of, and which specific conditions most affect disease presentation, early therapies and disease activity over time.

Objectives: To estimate the prevalence of MM conditions at the time of ERA diagnosis and associations with ERA clinical characteristics, early treatment, and trajectory of disease activity in the 1st year of follow up.

Methods: Data were from ERA patients (<1-year of symptoms) enrolled in CATCH (Canadian Early Arthritis Cohort) who met 1987 or 2010 RA criteria, and had at least two DAS28 measures in the first year. We examined baseline prevalence of: 1) cardiovascular disease (CVD), 2) diabetes, 3) cancer, 4) pulmonary disease, 5) bowel disease, 6) other rheumatic diseases, and 7) psoriasis, obtained from patient-reports of physician-diagnosed medical conditions, 8) obesity (BMI ≥30), and 9) depressive symptoms (RAND-12 <42). We compared baseline demographic and clinical characteristics in ERA + each condition vs. ERA alone. We estimated adjusted effects of each condition on early use of RA therapies with logistic regression and adjusted effects of each condition on DAS28 trajectory over the first year of follow up with linear growth models.

Results: The sample included 1,595 patients, 1,153 (72%) were female, with a mean (sd) age of 54 (15) years and 6 (3) months of symptoms. At baseline, 1,434 (92%) were treated with conventional DMARDs (mostly methotrexate (76%) and 33 (2%) with a biologic. More than 70% of ERA patients reported at least one MM, and over 30% reported 2+ MMs. Patients with MM were often older and had higher disease activity at baseline, with variations by condition. Patients with RA+CVD or depressive symptoms had a 60% and 90% higher adjusted odds of baseline steroid use, respectively (p <0.01). In fully adjusted growth models, relative to patients with ERA only, patients with: a) diabetes, other rheumatic diseases or depressive symptoms had higher baseline DAS28 scores and less improvement over time; b) pulmonary disease, bowel disease, psoriasis or obesity had similar baseline DAS28 scores but less improvement over time; and c) CVD or cancer had higher baseline DAS28 scores but similar improvement over time (all p<0.05).

Conclusions: Multimorbidity is common in ERA patients seen in routine practice and associated with higher disease activity at baseline, less improvement over time, or both, and a greater likelihood of prescribing steroids for certain conditions. Integrating MM in to current RA care strategies may help achieve better patient outcomes.

References:

Disclosure of Interest: None declared.

Bristol-Myers Squibb Canada, F Hoffmann-La Roche Inc, Janssen Inc, Pfizer Pharmaceuticals, UCBS, Amgen, D. Tin: None declared. C. Thorne: None declared. V. Bykerk: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5444

SAT0123 MULTIDIMENSIONAL EVALUATION OF PAIN IN RHEUMATOID ARTHRITIS

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Background: Although pain in rheumatoid arthritis (RA) is frequently thought to be inflammatory in nature, some studies reported clinically significant pain despite relatively low rheumatoid arthritis (RA) disease activity. Less than 50% of patients are satisfied by the management of pain.

Objectives: to report a recent multidimensional evaluation of pain in a large RA population.

Methods: Patients with RA were enrolled in 7 French Rheumatology Centers during a visit or a hospitalization in a transversal observational study. Socio-demographic data, previous and prescribed medications, disease duration, immunologic status, DAS28 score were assessed. Patients completed the multidimensional pain questionnaire from french health autority, the health assessment questionnaire (HAQ), the Beck depression scale and the anxiety scale STAI. Joint damage was evaluated by a simple erosion narrowing score.

Results: Of the 299 screened patients, 296 were included with a mean age of 58.4±11.7 years, 80.3% of female, a mean disease duration of 13.2±9.6 years, positivity of rheumatoid factors in 76.4%, anti-citrullin antibodies in 74% of cases. Concerning medications, 42.7% were treated by corticoids (mean dose=6.4 mg/d), 66% by analgesics drugs (64.1% with acetaminophen, 45.6% weak opioids, 7.1% strong opioids) and 24.4% with NSAID. The RA treatments were DMARDs in 69.1% and biotherapies in 82.7% of cases. The mean DAS28 score was 3.1±1.3 with 38.7% of patients in remission and 15.4% in low disease activity. The verbal scale for satisfaction about pain management showed that a third of patients was very satisfied, the half satisfied, 16% weakly or not satisfied. The mean pain visual analog scale (VAS) for the last 8 days was 33.6 ±26.5/100. 39% of patients had a pain VAS >40 mm/100. The Beck scale showed a moderate to severe depression in 34.3% of patients. Anxiety was present in 57.5%. The impact of pain on daily behaviors were more important on work. The pain VAS for the 8 days was correlated with the score of depression et with the DAS28 score (p=0.0001). The population with a pain VAS >40 mm had a significant more important Beck score, anxiety score, HAQ, DAS28 score and had more impacts of pain on daily behaviors.

Discussion: there was no difference between the populations with VAS ≤40 or >40 mm in terms of IL-6, IL-17 and IL-33 serum levels. The multidimensional evaluation of pain wasn’t different between treatment groups (DMARDs, biotherapies) and between the different biotherapies. Multivariate analysis with principal component analysis
found statistically significant associations between pain VAS and depression score, impacts of pain on daily behaviors and between pain VAS and DAS-28.

Conclusions: Almost 40% of patients had moderate to severe pain in a population of severe RA followed in hospital centers and treated with biotherapies in more than 80% of cases. Therefore, pain is still a major outcome to consider in RA. But a low proportion of patients with moderate to severe pain is less important than that one published by Taylor et al. Pain is associated with the DAS-28 score, but also with the depression score.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3287

SAT0124 HIGHER BMI AND SHORTER DISEASE DURATION ARE ASSOCIATED WITH “FIBROMYALGIC” RHEUMATOID ARTHRITIS – EVALUATION USING POWER DOPLPER ULTRASONOGRAPHY

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Background: Power Doppler ultrasonography (PDUS) can differentiate RA patients who truly have active disease. Patients with persistent joint tenderness may not necessarily have true inflammation; yet composite disease activity indices remain high, leading to treatment escalation. These patients are often referred to have “fibromyalgic RA” where tender joints far exceed that of swollen joints.

Objectives: We evaluated the predictors of “fibromyalgic RA” (FMRA), defined as patient-reported tender joint count (TJC) at least 7 greater than PDUS joint count. Methods: Consecutive RA patients were recruited in a tertiary rheumatology centre in Singapore. Patients self-assessed 28 joints for tenderness, followed by blinded PDUS assessment of the corresponding joints. Patients were grouped into either, (i) PDUS joint count > patient-reported TJC, (ii) PDUS joint count = patient-reported TJC (iii) patient-reported TJC > PDUS joint count, (difference >7). Group (iv) defined as FMRA. Predictors of FMRA were evaluated by multinomial logistic regression.

Results: Of the 101 patients, 81% were female, 72% Chinese, median age of 52 (IQR 48-59) and mean disease duration of 6.2 (1.9-8.8) years. Median BMI was 23.6 (8.0-27.0) and DAS28 was 3.2 (2.5-4.2). FMRA patients (15%) had a high median patient-reported TJC of 13 (10-18) but low median PDUS joint count of 1 (0-4). Compared to the other groups, they had higher median DAS28 of 4.6 (3.3-5.2), shorter mean disease duration of 2.3 (0.4-6.8) years, and higher median BMI of 26.9 (23.7-32.2). No differences in mean ESR or proportion of patients with serositis disease were observed. Using Group (i) as the reference, patients with FMRA were more likely to have a higher BMI (adjusted OR=1.6, 95%CI 1.2; 2.1,p=0.001 for every unit increase) and shorter disease duration (adjusted OR=0.8, 95% CI 0.7;0.98,p=0.03 for every additional year). Age, gender, ethnicity, disease activity (PDUS score) and serositis were not significant predictors of FMRA.

Conclusions: Higher BMI and shorter disease duration were independent predictors of FMRA. Use of PDUS would be useful in this group, rather than becoming treatment escalation on composite disease activity indices alone.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1598

SAT0125 TENOSYNOVITIS IN RHEUMATOID ARTHRITIS: PREVALENCE AND DETERMINANTS OF TENOSYNOVITIS DETECTED IN THE SONAR-ULTRASONOGRAPHY EXAMINATION IN THE SCQM COHORT

R. Micherell1, A. Scherrer2, L. Brulhardt2, L. Ziswiler4, P. Zufferey5, B. Möller6, R. Micheroli7

Background: Tenosynovitis is one of the common features of rheumatoid arthritis (RA). The diagnosis of tenosynovitis is frequently made clinically and erosive progression in RA is more sensitive. US and MRI detected tenosynovitis is a predictor for unstable remission and erosive progression in RA.

Objectives: The aim of this study was to assess the prevalence and determinants of TS detected in the SONAR (Swiss Sonography Group in Arthritis and Rheumatism) examination in patients with Rheumatoid Arthritis in the SCQM Cohort.

Methods: The SONAR ultrasound examination consists of a semi-quantitative score employing both multiplanar grey scale (B-mode) and Doppler-mode (PWo) and a TS composite score (grade 0–3). Pathologic TS was defined as TS grade 2–3. Characteristics of patients with and without TS are shown using standard descriptive methods. In a longitudinal sub-group the change in TS from no TS to pathologic TS or vice versa and DAS28 over time was categorized as “worse”, “same” and “better” (ΔDAS28 >2.1). The correlation between change DAS28 and in tenosynovitis was evaluated.

Results: 941 RA patients with TS score were available. 20% of included patients showed signs of TS. The presence of TS was associated with male gender and higher values of disease activity and physical function disability. Furthermore, 15% of patients in DAS28 Remission had sonographic TS. TS was less frequently observed in patients on biologic therapies (Table 1). The longitudinal subgroup consisted of 348 patients. The correlation between change in DAS28 and change in TS was poor (polychoric correlation 0.28 [0.14, 0.43]).

Table 1. Patient Characteristics at first Tenosynovitis measurement

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tenosynovitis</th>
<th>OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>Yes (N=184)</td>
<td>No (N=757)</td>
</tr>
<tr>
<td>Mean age in years</td>
<td>67</td>
<td>56</td>
</tr>
<tr>
<td>Mean disease duration in years</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>RF positive, n (%)</td>
<td>123 (68)</td>
<td>511 (70)</td>
</tr>
<tr>
<td>Anti-CCP positive, n (%)</td>
<td>109 (65)</td>
<td>477 (70)</td>
</tr>
<tr>
<td>DAS28 Remission, n (%)</td>
<td>24 (15)</td>
<td>232 (38)</td>
</tr>
<tr>
<td>Mean DAS28</td>
<td>3.9</td>
<td>3.1</td>
</tr>
<tr>
<td>Mean B-Mode SONAR Score</td>
<td>12.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Mean PD-SONAR Score</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mean Physician Global Assessment</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Mean HAQ Score</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>On biologic, n (%)</td>
<td>61 (33)</td>
<td>399 (53)</td>
</tr>
<tr>
<td>On synthetic DMARD, n (%)</td>
<td>110 (60)</td>
<td>500 (66)</td>
</tr>
</tbody>
</table>

Conclusions: In the SCQM RA cohort TS is associated with male gender and an overall higher disease activity. One should actively look for TS even in RA patients in DAS28 remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4006

SAT0126 MENTAL HEALTH BENEFITS ASSOCIATED WITH REDUCTION IN DISEASE ACTIVITY AMONG RHEUMATOID ARTHRITIS PATIENTS: A SYSTEMATIC REVIEW OF THE LITERATURE

V. Strand1, R. Rendas-Baum2, M. Kosinski3, D. Brooks4, R. Ganguly4

Background: The association between physical functioning and rheumatoid arthritis (RA) disease activity is well established. In randomized controlled trials (RCTs) of RA treatment, reductions in disease activity result in improved physical functioning. The mental health benefits associated with reductions in disease activity are less well recognized.

Objectives: Investigate the association between reductions in RA disease activity and measures of mental health status.

Methods: A systematic review of the published literature of RCTs in RA was conducted. The search was limited to those published in the last 10 years that included the Short-Form (SF)-36 Health Survey as an outcome measure.

Results: The search strategy yielded 77 articles of which 38 were excluded for the following reasons: not RCT (23); focus exclusively on early RA (9); psychometric evaluation (4); review study (1); and off topic (1). Of the 39 articles reporting mean changes in scores on the SF-36 mental health (MH) and role emotional (RE) domain, treatment by group analysis also presented these changes in association with reductions in RA disease activity measures.1-3 In relation to American College of Rheumatology (ACR) response criteria, small to moderate (0.2–0.5 standard deviation [SD]) effect size changes in RE and MH domain scores were observed among RA patients whose ACR responses ranged from 20–49%. Moderate to large effect sizes (0.5–0.8 SD) were reported in RE and MH domain change scores among ACR50 responders. Similar changes in RE and MH domain scores were reported by patients with reductions in Simplified Disease Activity Index (SDAI) of ≤10 points.

Conclusions: The benefits of clinically meaningful reductions in disease activity among RA patients not only include improved physical functioning but also meaningful improvements in overall mental health status. The improvement in mental health is positively associated with reduction in disease activity, with only small to moderate improvements associated with less than ACR responses. Additional work is needed to investigate the incremental effects of RA therapies on mental health beyond the effects related to reductions in disease activity.

References:


DOI: 10.1136/annrheumdis-2017-eular.3568
**SAT0127**

**UNFAVORABLE BODY COMPOSITION ALREADY AT THE ONSET OF CLINICAL ARTHRITIS**

S.A. Turk, D. van Schaardenburg, M. Boers, S. de Boer, C. Fokker, W.F. Lems, M.T. Nurmosahmed, Amsterdam Rheumatology and Immunology Center; Reade; Amsterdam Rheumatology and Immunology Center; Academic Medical Center; Amsterdam Rheumatology and Immunology Center; VU University Medical Center, Amsterdam, Netherlands

**Background:** Rheumatoid arthritis is associated with an increased cardiovascular (CV) risk. There is mounting evidence that inflammation is involved in the pathogenesis thereof (1). An unfavorable body composition is, independently, associated with an increased CV risk, and often present in established arthritis patients. This unfavorable composition is a loss of muscle mass (sarcopenia), in the presence of a stable or even increased (abdominal) fat mass (sarcopenic obesity). However, their applicability in ethnic RA subsets is unknown.

**Objectives:** Currently it is unknown when this unfavorable body composition develops. Therefore, we compared body composition in DmARD-naive early arthritis patients with non-arthritis controls and explored the association with disease activity and traditional CV risk factors.

**Methods:** A total of 317 consecutive early arthritis patients and 1268 age, gender and ethnicity matched non-arthritis controls (3) had a Dual-energy X-ray absorptiometry scan to assess lean (muscle) mass index (LMI), fat mass index (FMI), fat mass distribution (arms and legs versus trunk) and android to gynoid fat mass ratio. For the obesity definition, the cut offs based on the control group were applied (mean minus two times SD). In addition, a disease activity score, erythrocyte sedimentation rate, lipid profile (total cholesterol, LDL, HDL, triglycerides) and blood pressure assessments were done.

**Results:** Early arthritis patients (84% fulfilling the 2010 ACR/EULAR criteria) had a significantly lower mean LMI (p < 0.01) compared with controls. Female patients had a higher mean BMI (p = 0.01) and more fat was distributed to the trunk in patients (females p = 0.01, males p = 0.07) (table). The prevalence of an unfavorable body composition (i.e. sarcopenia and sarcopenic obesity) was higher than in controls, for females 5.0% versus 1.3%, OR: 4.2, p < 0.01 and for males 8.2% versus 1.5%, OR: 5.7, p < 0.01 (figure). A higher BMI, more android fat and more fat distributed to the trunk were associated with higher blood pressure and lipid levels (and lower HDL levels). There was no clear relationship between body composition parameters and disease activity.

**Table 1. Body composition of early arthritis patients and non-arthritis controls**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Arthritis females</th>
<th>Control females</th>
<th>Arthritis males</th>
<th>Control males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat mass index (mean, SD)</td>
<td>27.6 (3.5)</td>
<td>26.4 (4.6)*</td>
<td>26.8 (4.4)</td>
<td>27.4 (3.6)</td>
</tr>
<tr>
<td>% of fat distributed to the trunk (mean, SD)</td>
<td>52.6 (3.5)</td>
<td>49.7 (6.5)*</td>
<td>58.8 (6.4)</td>
<td>57.6 (5.6)</td>
</tr>
<tr>
<td>Android to gynoid fat mass index (mean, SD)</td>
<td>0.5 (0.2)</td>
<td>0.5 (0.0)</td>
<td>0.7 (0.2)</td>
<td>0.8 (0.2)*</td>
</tr>
<tr>
<td>Lean mass index (mean, SD)</td>
<td>6.6 (0.9)</td>
<td>6.7 (0.8)*</td>
<td>8.0 (1.1)</td>
<td>8.6 (1.0)*</td>
</tr>
<tr>
<td>Obesity (n,%)</td>
<td>99 (45.2)</td>
<td>334 (34.8)</td>
<td>50 (52.1)</td>
<td>222 (57.7)</td>
</tr>
<tr>
<td>Sarcopenia (n,%)</td>
<td>11 (5.0)</td>
<td>11 (1.3)*</td>
<td>8 (8.2)</td>
<td>6 (1.5)*</td>
</tr>
<tr>
<td>Sarcopenic obesity (n,%)</td>
<td>2.0 (0.9)</td>
<td>2.0 (0.2)</td>
<td>4.4 (3.8)</td>
<td>3.0 (0.8)*</td>
</tr>
</tbody>
</table>

n = number, SD = standard deviation, % = percentages *p-value < 0.05 between arthritis and non-arthritis controls.

**Conclusions:** Patients at the clinical onset of arthritis more often have an unfavorable body composition (sarcopenia and sarcopenic obesity) than non-arthritis controls. An unfavorable body composition was associated with higher blood pressure and lipid levels (and lower HDL levels).

**References:**


Disclosure of Interest: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2174

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**SAT0128**

**CLINICAL FEATURES AND EVOLUTION OF PULMONARY FUNCTION IN A SINGLE-CENTER COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS RELATED INTERSTITIAL LUNG DISEASE**


**Background:** Interstitial lung disease (ILD) is an extra-articular manifestation of Rheumatoid Arthritis (RA), has been related with a poor prognosis. However, there is a lack of clinical data regarding its evolution with different treatment approaches.

**Objectives:** Our aim was to assess clinical features and evolution of ILD in a cohort of RA patients from a tertiary hospital

**Methods:** Single-centre retrospective observational study including all patients diagnosed with ILD with a previous or posterior diagnosis of RA evaluated from January 2007 to December 2016 in the Rheumatology Department of a university hospital.

**Results:** Twenty-one patients (18 women) were included, mean age 68.4±11.9, mean RA duration 12.3±8.2 years. 9.5% were current smokers and 33.3% former smokers. 61.9% were ACPA+ (52.4% with high basal titers, median ACPA titers: 699; IQR 321–811) RF+ (47.3%), with high titers (median RF: 71.4%) 68% had extra-articular manifestations, mainly rheumatoid nodules. RA diagnosis was made after that of ILD in 4 patients; mean elapsed time 1.56±1.26 years. In the other 17 patients, the mean duration of RA until ILD diagnosis was 11.2±7.2 years. Currently 17 subjects (85%) receive GC; 4 (19%) in monotherapy and 11 (57.9%) synthetic DmARDs (5 methotrexate, 3 leflunomide (LEF), 1 hydroxychloroquine (HCQ) and 2 with double therapy (HCQ/AZA and HCQ/LEF)).

Four patients are currently treated with biological therapy (2 abacetap (ABA), 1 infliximab and 1 etanercept (ETN), all of them in monotherapy. Five patients received TNFI prior to ILD diagnosis (3 ETN, 1 infliximab and 1 adalimumab). Biological therapy was withdrawn in 3 cases and switched to ABA in the two remaining ones.

The median duration of EPID was 2.5 (range 0.7–11.9) years. HRCT patterns were: non-specific interstitial pneumonia (NSIP) 52.9%, usual interstitial pneumonia (UIP) 17.6%, cryptogenic organized pneumonia (COP) 11.8%, and other patterns 17.7%.

1 patient had baseline and follow-up PFT; 9 (64.3%) remained stable; 3 (21.4%) improved and 2 (14.3%) worsened (1 had received previous ETN). There was a trend for worsening of PFT in patients with UIP pattern.

No patient died from ILD during this period

**Conclusions:** In our RA-ILD cohort, NSIP was the most common HRCT pattern and PFT remained stable in most patients during follow-up. Five patients (23.8%) had received TNFI prior to ILD diagnosis and only one of them showed worsening of PFT during ETN treatment, with clinical improvement after withdrawal.

**References:**


Disclosure of Interest: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3284

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**SAT0129**

**EXPLORATION OF COMORBIDITY INDICES IN AN ETHNIC RHEUMATOID ARTHRITIS SUBSET**

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**Background:** Comorbidity is common in ethnic patients with rheumatoid arthritis (RA) and often impact choice of DMARD therapy and clinical outcomes. In addition to the complex sum of comorbidities, comorbidity indices have been proposed as better predictors of poor clinical outcomes in patients with rheumatoid arthritis. However, their applicability in ethnic RA subsets is unknown.

**Objectives:** To compare composite to mean comorbidity indices in ethnic subsets with rheumatoid arthritis.

**Methods:** Patients enrolled in the Ethnic Minority RA Consortium (EMRAC), with at least 6 months of follow-up data were analyzed. At enrollment, sociodemographic data and RA disease status, rheumatic disease comorbidity index (RCDI) and comorbidity count (COUNT) were analyzed amongst ethnic subsets. Spearman correlation was estimated between RCDI and COUNT while Poisson regression
was used to model the differences in the comorbidity indices between race groups.

Results: 453 EMRAC subjects were analyzed; 342 (81.4%) were female, average age was 58.9 (±15.1) years, average duration 13.3 (±11.1) years and average follow-up length 2.1 (±1.4) years. Individual comorbid frequencies as well as comorbid associations included in Table 1. The median nerve thickness was overall RDCI and COUNT was 0.90 (95% CI [0.88, 0.91], P <0.001). Hispanics, however, had significantly lower comorbidity indices scores than other race groups (RDCI Hispanic vs White P=0.003, Hispanic vs Black P=0.004, Hispanic vs Other P=0.038; COUNT Hispanic vs White P=0.012, Hispanic vs Black P=0.004, Hispanic vs Other P=0.157).

Objectives: To establish the median nerve thickness (measured by ultrasound) in RA and its relation to renal impairment.

Methods: 120 RA patients were recruited through a specialized rheumatology clinic. The US measurements were performed by the same person. Patients were sitting with their forearms resting in a supinated position on a small table. The US probe (an 8–16 MHz linear array transducer) was held as lightly as possible to avoid disturbing the anatomy of the nerve. The median nerve was examined at the entrance of the carpal tunnel, between the pisiform bone and the tubercle of the scaphoid bone, where the distal volar carse is an external pisiform landmark. A continuous trace was made just within the hyperechogenic boundary of the nerve. The cross-sectional area of the median nerve was calculated directly by the software of the US equipment. Each median nerve was measured three times, and the mean value was used for further analyses. Modification of Diet in Renal Disease (MDRD) equation used to estimate the Glomerular Filtration Rate (GFR). The average of the right and the left areas of the median nerve were used when exploring bivariate correlations to the renal variables (Pearson’s correlation coefficients). All statistics were performed using USTAT program.

Results: the average median nerve thickness was 9.72±2.6 mm² (Range 1.5–22.25). The average GFR was 122±20 ml/min (95.6–248). Thickness of the median nerve was positively associated with the age of the participants (p=0.03, CI: 0.00, 0.08), body mass index (p=0.04, CI: 0.00, 0.21), uric acid level (p=0.033, CI: 0.00, 0.01), and urine microalbumin (p=0.04, CI 0.00, 0.01). GFR showed no significant relation the thickness of the median nerve.

Conclusions: RA patients without symptoms or clinical signs have a median nerve thickness that is positively correlated to the level of microalbumin and uric acid. Whether sonographic examination of the median nerve would be helpful in predicting who is going to have a deteriorated renal function need to be explored in a larger study.

Background: Disease flares in RA are common. The RA Flare Questionnaire (RA-FQ) can be used to identify and quantify flares in rheumatoid arthritis (RA).

Objectives: To further explore the psychometric properties of RA-FQ, we used Rasch analysis and reviewed results with RA patients research partners (PRPs) to gain additional insight into the interpretability, meaningfulness, and utility of results. Ten PRPs first completed the questionnaire for the robust psychometric properties of the RA-FQ. RUMM2030 was used to evaluate unidimensionality, targeting of items to people, reliability, response options, redundancy, local dependence, and model fit was excellent ($\chi^2 = 31.6$, df=45; $p=0.935$). There was little evidence of differential item functioning by sex, age, or country/language. Items suggest flare symptoms and impacts increased together showing a consistent story of how individuals experience worsening RA disease activity. Among PRPs, scores ranged from 10 to 41. There was unanimous agreement from the patients that the RA-FQ could also enhance communication between doctors and patients at routine visits. Several noted potential applicability in monitoring day-to-day status and with self management. Thresholds for clinically important worsening to identify flare varied by setting, patient population, and context of use.

Conclusions: Taken together, results from classical and Rasch analyses support for the robust psychometric properties of the RA-FQ. The 5-item measure is easy to complete and simple to score. Feedback from RA PRPs and clinicians increase confidence in the relevance, meaningfulness, and easy interpretation of RA-FQ results for clinicians, researchers, and patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5593
conventional cardiovascular risk factors. Exclusion criteria were smoking, diabetes mellitus, symptomatic AH, cardiovascular diseases (except AH). DMAS was measured by using the BPlab with technology VASOTENSE (Russian). An index of arterial stiffness (ASI), a daily index of arterial stiffness (AASI), an aortic pulse wave velocity (PWVao), augmentation index (Alx) were measured. All indexes were estimated at day and night hours. Statistics was performed with STATISTICA 7.0 (StatSoft, USA).

**Results:** Hypertensive RA patients and AH patients without RA had comparable DMAS parameters (ASI, PWVao, Alx). The AASI index was higher in RA patients without AH versus controls (0.48±0.2 and 0.29±0.17, respectively, p=0.00001) and the AASI index was higher in hypertensive RA patients versus AH patients (0.5±0.2 and 0.38±0.15, respectively, p=0.01). AASI >0.77 revealed at RA patients more often than in controls: at 13.15% of hypertensive RA patients and at 16.6% of RA patients without AH, respectively, p<0.05. The increase of PWVao observed at RA patients frequently than in controls (p<0.05). Daily index ASI100 was higher in RA patients without AH than in healthy controls (121 [109.5; 139] mmHg vs. 107 [103; 115] mmHg, p=0.014). The increased of Alx75 was registered in 25% of RA patients without AH and in 9.09% of controls (p=0.08). PWVao and average Alx75 correlates with ESR (r =0.38 and r =0.36, respectively, p<0.05) in RA patients with AH; AASI correlates with level C-reactive protein (r=0.36, p<0.05). ASI and AASI in RA patients with AH correlates with age (Spearman's r =-0.41 and r =-0.36, respectively, p<0.05), systolic blood pressure (r =0.76 and r =0.65, respectively, p<0.05); pulse blood pressure (r =0.77 and r =-0.43, respectively, p<0.05).

**Conclusions:** Arterial stiffness, according to daily monitoring, in RA patients is higher than in hypertensive patients without RA and healthy controls. Arterial stiffness in patients with RA and AH is higher than in patients with RA without AH. Age, systolic blood pressure, pulse blood pressure, high levels of ESR and C-reactive protein associated with increased arterial stiffness in RA patients.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5683

**SAT0136** ASSOCIATION OF GENOTYPES FOR BCLI POLYMORPHISM IN THE GLUCOCORTICOID RECEPTOR GENE WITH ISCHEMIC HEART DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** The objective is to study associations of genotypes for Bc1I polymorphism in the glucocorticoid receptor (GR) gene with ischemic heart disease (IHD) in patients with rheumatoid arthritis (RA).

**Methods:** 161 subjects with rheumatoid arthritis aged 40 years and older were examined by means of instrumental, clinical and laboratory examinations. Rheumatoid arthritis was diagnosed according to ACR/EULAR Classification Criteria (2010). The IHD diagnosis was verified by means of ACC/AHA guidelines (2012). BCL1 polymorphism in exon 2 was identified using polymerase chain reaction with subsequent analysis of restriction fragment length polymorphism by Fevery I. et al. (venous blood was used as the material for the study). Statistical analysis was performed using SPSS-17 program.

**Results:** It was revealed that 76 (47.2%) patients had isolated RA (group I), while 85 (52.8%) individuals had RA with concomitant IHD (group II). In group I, there were 29 (38.2%) patients with C/C genotype, 39 (51.3%) – with C/G genotype, and 8 (10.5%) – with G/G genotype. The distribution in group II was as following: 16 were homozygous for the C allele (18.8%), 40 were heterozygous (47.1%) and 29 were homozygous for the G allele (34.1%) (χ²=15.23; p<0.02). It was established that the risk of ischemic heart disease was 6.57 times higher in homozygotes for the G allele (OR=6.57; 95% CI=2.44–17.73; p<0.001) as compared with homozygotes for the C allele.

**Conclusions:** It was established that G/G genotype prevailed in RA patients with ischemic heart disease, while C/C genotype prevailed in patients with isolated RA. The risk of IHD development in patients with RA was associated with G/G genotype for Bc1I polymorphism in the GR gene.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3998

**SAT0137** BONE MINERAL DENSITY MEASUREMENT INTERVALS FOR SEROPOSITIVE RHEUMATOID ARTHRITIS PATIENTS NOT TREATED FOR OSTEOPOROSIS

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**Background:** Osteoporosis occurs more frequently in rheumatoid arthritis (RA) patients than in healthy individuals. However the appropriate interval for the bone mineral density (BMD) measurement in RA patients is not well established.

**Objectives:** This study investigated the effective BMD measurement interval and the risk factors associated with the development of osteoporosis for RA patients.

**Methods:** A retrospective study was performed on 511 RA patients aged more than 40 years old who had undergone BMD (DXA, GE LUNAR PRODIGY ADVANCE) testing more than once and who had normal BMD or osteopenia at the baseline BMD test and no history of any fracture of the spine or femur. The subjects were categorized into four subgroups: normal BMD (T-score > -1), mild (1 > T-score > -1.5), moderate (1.5 > T-score > -2), and advanced (≥ 2 T-score > -2.5) osteopenia. The BMD testing interval was defined as the estimated time for 10% of the RA patients to make the transition into osteoporosis without osteoporotic fracture or the administration of any osteoporosis drug.

**Results:** The observation period was 2,214 patient-years, with an average of 4.3 years. The estimated BMD testing interval was more than 10 years for normal, 4.3 years for mild, 2.5 years for moderate, and 1.5 years for advanced osteoarthritis in estimated the time for 10% of the RA patients to make the transition into osteoporosis without osteoporotic fracture or the administration of any osteoporosis drug.

**Conclusions:** Our study indicated that in normal or osteopenic RA groups, a baseline BMD T-score is the most important factor in estimating the interval in which osteoporosis is predicted to occur. In addition, we recommend that the BMD measuring interval should be greater than 10 years in normal BMD RA
SAT0138  OPTIMIZING TARGETED THERAPY: CAN PROMS FILL THE GAP BETWEEN PATIENTS’ AND PHYSICIAN-PERCEIVED REMISSION IN RHEUMATOID ARTHRITIS

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Objectives: 1. To compare the patient perspective on remission in RA in comparison to the rheumatologist perceived remission perspectives. 2. To determine the value of Patient Reported outcomes in identifying specific symptoms and aspects of disease ability to define remission in RA from the patient perspective.

Methods: RA patients diagnosed according to ACR/EULAR criteria were treated with biologics. Remission was measured in two ways: 1) patient perceived remission using the question “Would you say that, at this moment, your disease activity is as good as gone? (yes/no)”; and 2) Physician perceived remission was defined as a physician global assessment <1 on a 0–10 VAS, phrased as “How active do you think the rheumatoid arthritis of your patient is today?” The study included 188 RA patients (76 males, 112 females; mean age 52.4±11 years) and 87 rheumatologists (30 males, 57 females; mean age 48.7±11.7 years). All participants were asked to complete a questionnaire which was composed of all domains identified in relation to the disease remission. 10 cm visual analogue scale (scored 0–10) was used to illustrate the importance of each factor in an individual opinion. The list included joint pain, functional ability, quality of life, absence of morning stiffness, absence of fatigue, normal laboratory tests, no comorbidity risk, radiological remission. Disease Activity score and ability to work. In addition, patients were asked to complete a copy of the PROMs [1]. One-way analysis of variance was used for the comparison of independent variables. Spearman correlation coefficient was used to assess the correlation between variables.

Results: There were no significant differences in questionnaire answers in relation to patients’ demographics and present disease activity. Regarding the patient perceived remission, the top 4 were: pain (76%), functional ability (71%), quality of life (69%) and fatigue (43%). Regarding the physician perceived remission, the following factors were rated more relevant by rheumatologists than the patients (p<0.001): low disease activity score (88%), radiological remission and progression of erosions (76%), lab measurements (ESR/CRP) (57%) followed by difficulties in performing paid work (49%).

Conclusions: We observed that enthesis involvement was not seldom in patients with seronegative RA. Furthermore there were also similar frequency of enthesitis involvement in seropositive patients with RA. The value of enthesis sites evaluation for the differential diagnosis of patients with seronegative RA should be further investigated and the assessment of enthesis sites in seronegative and seropositive RA patients can be important to detect active and chronic changes in the enthesis region.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4491

SAT0139  ASSESSING ENTHESITIS BY ULTRASONOGRAPHY IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: In patients with seronegative rheumatoid arthritis (RA) there is a difficulty to make the differential diagnosis with the spondyloarthropathies. Objectives: To assess the presence of enthesitis in patients with seronegative rheumatoid arthritis in comparison with the healthy controls, patients with seropositive rheumatoid arthritis and ankylosing spondylitis.

Methods: In this cross-sectional study, seronegative and seropositive rheumatoid arthritis patients, who fulfilled the 2010 ACR/EULAR criteria, patients with ankylosing spondylitis and healthy controls have been assessed by grey scale and power doppler ultrasonography for the presence of enthesopathy at the achill, plantar fascia, proximal patella, distal patella, quadriceps, tibialis anterior, triceps, common flexor and extensor tendons. Clinical assessment of the patient groups included demographic findings, health assessment questionnaire and disease activity score.

Results: In our study, we recruited age and sex matched 27 seronegative RA, 17 healthy controls, 20 seropositive RA and 12 ankylosing spondylitis patients. We performed and analysed both right and left sides of the enthesis regions separately which have been indicated in the methods section. The mean DSAS28, mean ESR and mean CRP of the patients with seronegative RA were 3.6±1.28, 32.2±21.2 and 12.37±27.77 respectively (Table 1).

Median of Madrid sonographic enthesis index (MASEI) was 5 in patients with seronegative RA. 4 patients have severe scores. There were significant differences between seronegative RA and healthy controls (5, p=0.014) but no differences has been observed between seronegative seropositive RA (6) and ankylosing spondylitis (7) in MASEI scores.

Conclusions: We observed the presence of enthesitis involvement was not seldom in patients with seronegative RA. Furthermore there were also similar frequency of enthesitis involvement in seropositive patients with RA. The value of enthesis sites evaluation for the differential diagnosis of patients with seronegative RA should be further investigated and the assessment of enthesis sites in seronegative and seropositive RA patients can be important to detect active and chronic changes in the enthesis region.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4457

SATURDAY, 17 JUNE 2017

Rheumatoid arthritis - anti-TNF therapy

SAT0140  EFFECT OF OBESITY IN RESPONSE TO BIOLOGICS IN RHEUMATOID ARTHRITIS

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Background: Obesity epidemic has impacted practically every area of health including care of patients with RA. Adipose tissue is an active organ that produces pro-inflammatory molecules. A significant treatment challenge remains is the standard dose of RA medications may not attain same concentrations at sites of inflammation in obese vs non-obese patients thus making them less effective.

Objectives: The study aim was to determine whether obesity represents a risk factor for a poor remission in RA requiring biologic therapies. Obesity may be associated with more severe and refractory inflammation through increased levels of inflammatory adipocytokines leptin, resistin or visfatin or decreased levels of the anti-inflammatory adipocytokine adiponectin. We retrospectively analysed 178 patients diagnosed with RA at East Kent University Hospitals.

Methods: Data analysed for age, sex, disease duration, prior DMARD, positivity RF and CCP antibodies, median 28 (5-84) at diagnosis and at 6 months were analysed. Median of MPH was 28 (5-84) at diagnosis and at 6 months were analysed. Main aim was to analyse any difference between obese and non-obese patients in terms of their response to treatment. Obese patients were defined with a BMI of 30 or above.

Results: See Table 1.
Results suggested that there were significant differences between two groups for sex, duration of disease, RA and CRP. There was also some evidence of difference between groups in terms of their age and pre-treatment DAS28 score but these differences were only of borderline statistical significance. There was smaller proportion of males in the obese group with 20% male compared to 36% of non-obese patients. Obese patients had on average a longer disease duration with a median of 12 years compared to a median of 8 years for the non-obese group. The RA status also varied between groups with a much higher proportion of patients in the negative category for the obese group. CRP values were significantly lower in the obese group with a median of 24 compared to 35 in the non-obese group.

### Table 2. EULAR response between obese and non-obese patients

<table>
<thead>
<tr>
<th>EULAR response</th>
<th>Non-Obese N (%)</th>
<th>Obese N (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No response</td>
<td>9 (9%)</td>
<td>32 (39%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate response</td>
<td>40 (42%)</td>
<td>36 (43%)</td>
<td></td>
</tr>
<tr>
<td>Good response</td>
<td>46 (48%)</td>
<td>15 (18%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Non-obese had the best response with 48% good response compared to 18% of the non-obese group with post treatment mean DAS28 score of 3.2 and mean reduction of 2.4.

**Conclusions:** Obesity is important factor that impacts treatment and outcome in RA. Further clinical studies to elucidate the pharmacokinetics of specific biologic agents in relation to BMI should provide further clinical guidance.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4861

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**SAT0141**

**OPTIMAL CIRCULATING ADALEUMAB LEVELS RANGE ASSOCIATED WITH GOOD CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** TNF inhibitors have become an important part of healthcare worldwide for inflammatory diseases such as RA. Many publications show that responders (pts) have higher Adalimumab (Ada) serum trough levels (ATL) than non-responders. These factors are influenced by age, weight, gender or other factors that may predict a poor response to MTX.

**Objectives:** To identify predictors of MTX insufficient response (IR) and rapid radiographic progression (RRP) among pts with RA receiving 6 months of MTX therapy.

**Methods:** In OPTIMA, pts with RA -1 year were randomized to receive either adalimumab (ADA) 40 mg every other wk (EOW) + MTX weekly (wkly) or placebo (PBO) EOW + MTX wkly for 26 wks. In PREMIER, pts with RA -3 years were randomized to receive ADA 40 mg EOW + MTX wkly, ADA 40 mg EOW + PBO wkly, or PBO EOW + MTX wkly for 2 years. This post hoc analysis compared MTX-IR pts, defined as not reaching stable low disease activity at wks 22 and 26 in OPTIMA and wks 20 and 24 in PREMIER, with pts who responded to initial MTX monotherapy. Comparisons were also made between pts who did and did not have RRP and assessed by an increase in modified Total Sharp Score (mTSS) of >1.5 from baseline (BL) to 6 mos. In pts with available data, backward logistic regression was used to identify potential predictors of MTX-IR and RRP. Candidate predictors included BL demographics, time-averaged disease parameters for 3 time periods (through 4 wks, 8 wks, and 12 wks of MTX exposure), and BL disease characteristics for the 12-wk interval. Time-averaged variables were calculated as area under the curve standardized for length of time interval.

**Results:** This analysis included 525 MTX-IR and 162 MTX responders. Mean disease duration at BL was 6 mo for both groups. The mean Disease Activity Score 28 (DAS28) was 5.6 ± 1.5 for MTX-IR and 5.2 ± 1.4 for MTX responders. The mean mTSS at BL was 20.7 for pts who experienced RRP vs those who did not (12.4). Predictors of MTX-IR and RRP at 6 mos are shown in the Figure. Time-averaged HAQ-DI and DAS28 (CRP) through 12 wks were the strongest predictors of both MTX-IR and RRP. Additionally, early clinical response (time-averaged DAS28[CRP]) at both 4 and 8 wks was predictive of both MTX-IR and RRP; however, time-averaged HAQ-DI was not predictive until wk 12.

**Conclusions:** In the OPTIMA and PREMIER trials, post-BL measures of RA activity were predictive of MTX-IR and RRP. Pts who are likely to progress on MTX or have RRP may be good candidates for switching to earlier step-up therapy to reduce the likelihood of permanent bone damage.

**References:**


**Acknowledgements:** AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation; and (funded) writing, reviewing, approval of final version. Medical writing: Y.E. Barker, M.J. Thiesen, Complete Publication Solutions, LLC.
Disclosure of Interest: A. Kavanaugh Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, R. F. van Vollenhoven Grant/research support from: AbbVie, Amgen, BMS, GSX, Pfizer, Roche, and UCB, Consultant for: AbbVie, Biotec, BMS, Crescendo, GSX, Centocor-Janssen, Lilly, Merck, Pfizer, Roche, UCB, and Vertex, B. A. Wolfe Shareholder of: AbbVie, Employee of: AbbVie, S. Florentinus Shareholder of: AbbVie, Employee of: AbbVie, J. L. Suboticki Shareholder of: AbbVie, Employee of: AbbVie, J. S. Smolen Grant/research support from: AbbVie, Consultant for: AbbVie, Speakers bureau: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.1892

SAT0144 | TUMOR NECROSIS FACTOR-ALPHA INHIBITORS AND PSYCHIATRIC SIDE EFFECTS: RESULTS FROM THE FRENCH PHARMACOVIGILANCE DATABASE

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Background: Although Tumor Necrosis Factor alpha (TNF-α) is a major proinflammatory cytokine in the brain, potential psychiatric side effects of TNF-α inhibitors have been little investigated. Manic and psychotic disorders are not recognized as TNF-α inhibitors’ side effects even though few reports of such complications have been reported.

Objectives: This study reports cases with psychiatric symptoms (in the spectrum of psychotic and manic disorders) that occur during treatment with tumor necrosis factor alpha (TNF-α) inhibitors and aims to evaluate the role of these agents as causative factors.

Methods: We searched the French Pharmacovigilance Database for consecutive cases of positive psychiatric side effects reported during treatment with TNF-α inhibitors. Major psychiatric symptoms were defined according to DSM-V, as mania and psychosis, and minor psychiatric symptoms as psychomotor agitation, euphoria, hallucinations, personality distortion, and increased libido. Each case had one major symptom or at least one minor symptom.

Results: Among 7912 consecutive cases of side effects registered in the database for TNF-α inhibitors, 184 reported psychiatric symptoms, and of these, 71 met inclusion criteria, whereas 113 met an exclusion criterion. Depression was the most frequent cause for exclusion. TNF-α inhibitors were the only medication suspected in 56 cases (79%). The time between beginning TNF-α inhibitors and onset of symptoms varied from hours to months with a median time of 49 days (IQR=156); initial symptoms mostly worsened under treatment. TNF-α inhibitors were withdrawn in 42 (61%) cases. The improvement of symptoms was significant associated with treatment withdrawal (78% versus 22%, p<0.01). Relapses occurred after rechallenge of TNF-α inhibitors in three of four patients.

Conclusions: We report the first cohort of 71 cases with psychiatric symptoms in the spectrum of manic and psychotic disorders during treatment with TNF-α inhibitors. Our experience suggests that anti-TNFα therapy may cause manic or psychiatric side effects.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4818

SAT0143 | COMPARISON OF TREATMENT WITH GOLIMUMAB AND CERTOLIZUMAB-PEGOL IN ARTHRITIS- RESULTS FROM THE SOUTH SWEDISH ARTHRITIS TREATMENT GROUP (SSATG) REGISTER

C. Rosenma, E. Lindqvist, P. Geborek, M. C. Kapetanovic. Section of Rheumatology, Lund University. Department of Clinical Sciences Lund, Skåne University Hospital, Lund, Sweden

Background: “Head to head” studies comparing the efficacy and tolerability of different TNF inhibitors are scarce, in particular the comparison between certolizumab pegol and golimumab.

Objectives: To compare the efficaciousness, drug survival and tolerability of certolizumab-pegol and golimumab in adult patients with establish arthritis (RA, JIA, SpA or unspecified polyarthritis) starting these treatments between February 2010 and December 2013 at outpatient unit at the Skåne University Hospital, Department of Rheumatology Lund/Malmö and two associated private rheumatology units.

Methods: All patients starting treatment with biologics were consecutively included in the South Swedish Arthritis Treatment Group (SSATG) register and regularly followed up according the standard protocol including: SJC/TJC, CRP, ESR, physicians global assessment of disease activity, patients’ assessment of disease activity and pain (VAS global and VAS pain) and HAQ. Last follow up date was October 17th 2016. Kaplan–Meier survival analysis was used to estimate the drug survival. Possible predictors of drug survival were analysed using Cox regression model.

Results: In total, 352 patients (71% women, mean age 51 years, mean disease duration 12 years) started these treatments during study period. Of these, 168 received golimumab and 184 certulizumab-pegol. Mean treatment time was 31 months (range 0–77). Percentage of patients with RA, SpA, JIA and unspecified arthritis were 58.4%, 16.4%, 5.7%, and 19.5% respectively. Certolizumab-pegol was more used in RA (67% vs 49%) and JIA (8% vs 2%) while golimumab was more frequent among patients with SpA (21% and 12%) or PsA (23% and 10%, respectively). Only 7% of golimumab and 10% of certolizumab-pegol patients received these drugs as first biologic treatment and approximately 50% of patients received these drugs as ≥ 3 biological treatment.

In golimumab treated patients mean DAS28 decreased from 4.3 (baseline) to 3.3 (3 months); 2.8 (6 months) and 2.7 (12 months) but levelled off at 36 months follow up. Corresponding mean DAS28 levels in certulizumab-pegol treated patients were 4.6 (baseline); 3.2 (3 months); 2.8 (6 months) and 2.6 (12 months). The similar pattern was seen in changes in HAQ and CDAI over the study time. There were no statistically significant differences in DAS, HAQ or CDAI between treatments at any follow up visit. At the end of follow up 68% with golimumab and 60% (32%) of certulizumab-pegol patients remained on their treatment. No significant difference in drug survival was seen between the treatments (Figure). Patients with spondyloarthropathy had significantly better survival on golimumab compared to RA patients (p=0.005) which remained after adjustment for age, gender, CRP, number of previous biologics and concomitant methotrexate at baseline.
Influence of body mass index (BMI) on the disease

Randomised double-blind study shows comparable

long-term efficacy and safety between rituximab

biosimilar CT-P10 and innovator rituximab in

patients with rheumatoid arthritis: 48-week results


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Background: In phase 1 trials (NCT01534884 and NCT01873443), pharmacokinetic equivalence of CT-P10, biosimilar of rituximab, to innovator rituximab (RTX) was demonstrated. In the phase 3 study, equivalence of PK and efficacy up to week 24 were achieved between CT-P10 and RTX (US and EU sourced) 12. Objectives: To investigate the long-term efficacy, pharmacodynamics, immunogenicity and safety of CT-P10 up to week 48.

Methods: Patients with rheumatoid arthritis were randomly assigned to CT-P10, US-RTX or EU-RTX, in combination with MTX. The patients received 2 treatment courses at Week 0 and 24, each consisting of 2 infusions of 1000mg study drug every 2-week interval.

Results: A total of 372 patients were randomised, and 330 patients completed the 2nd course treatment. DAS28 scores through Week 48 were comparable between CT-P10 and US/EU-RTX (Figure), as well as the proportion of ACR responses at Week 48 between the CT-P10 and combined rituximab groups; 81.3% and 79.8% for ACR 20, 55.4% and 53.9% for ACR50, and 31.7% and 33.7% for ACR 70, respectively.

Figure 1. Efficacy Results – DAS28.

B-cell depletion was comparable from after the 1st infusion and up to Week 48. Number (%) of patients with positive anti-drug antibodies in the CT-P10, US-RTX, and EU-RTX was 7 (4.9), 13 (9.4), and 5 (8.6), respectively at Week 48. The safety profile was also similar across groups (Table).
SAT0147 | SERUM LEVELS OF THE ANTI-TNF BIOLOGICS CORRELATE WITH CLINICAL EFFICACY IN PATIENTS WITH INFLAMMATORY ARTHRITIS

C. C. Mok 1, B. Fong 1, L. Y. Ho 1, H. C. To 1, 2.

Background: The risk of infections, especially severe infections (SI), remains of particular interest in rheumatoid arthritis (RA), both defective immune response and therapeutic immunosuppression being responsible. The RABBIT Risk Score (RRS), an instrument developed and validated in the German Biologics Register RABBIT and replicated in other RA settings (British Register), allows the estimation of SI occurring during 12 months according to local guidelines, enveloped between 2008 and 2016 in a single academic center. Along with disease activity and therapeutic response, baseline RRS (http://www.biologika-register.de/en/home/risk-score/) was applied for each case, to evaluate the predictive value of the RRS. The study included patients with spondyloarthritis (SpA) and psoriatic arthritis (PSA) and were commenced on antitumor necrosis factor (anti-TNF) biologic according to the trough levels of the drugs. Low drug concentrations were significantly more patients withdrew treatment due to inefficacy at month 12 in this group of patients (33% vs 75%; p<0.001 by log rank test).

Results: The performance of RRS was previously established in a pilot study on 181 RA. Currently, the RRS was considered in 144 RA recruited to the first group and 128 to the second. The prescription pattern significantly changed (p<0.05 for patients enrolled in last years: RA were more likely to receive earlier biDMARDs, for lower activity and functional status; moreover, lower corticosteroids (dose, duration) and fewer synthetic DMARDS before starting biologics were reported (p<0.05).

Methods: Longitudinal study on 272 consecutive RA with moderate-to-severe active disease at baseline (defined as the BASDAI >4, CRP >5 mg/L and tender joint count >7), recruited at 32 academic centers from 2011 to 2014. The RABBIT Risk Score is a simple risk tool that allows the estimation of SI occurring during 12 months according to the baseline RRS.

Conclusions: The RABBIT Risk Score is a simple tool, able to predict serious infections in Romanian RA receiving biological therapy (TNF and non-TNF drugs), optimizing the selection of appropriate medication based of individual infectious risk profile in routine practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2774

SAT0148 | COMPARATIVE EFFECTIVENESS OF TOFACITINIB, BIOLOGIC DRUGS AND TRADITIONAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS

C. M. Moura 1, M. A. Machado 1, H. Behloul 1, J. R. Curtis 2, M. Abrahamowicz 1, S. Bernatsky 1.

Background: Most rheumatoid arthritis (RA) patients initiate therapy with methotrexate (MTX), but 1/3 will have low disease activity with this agent alone. Several therapeutic options are available for patients with MTX-resistant RA, including new Janus kinase (JAK) inhibitors (e.g. tofacitinib). Objectives: To compare the effectiveness of traditional disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs and tofacitinib for RA patients with inadequate response to MTX.

Methods: We used MarketScan® databases (2011–2014) to study adult RA individuals previously treated with methotrexate (oral or SQ) and newly prescribed one of the medications under study. The date of first filled prescription or infusion drug was defined as the cohort entry and a 12-month pre-period was used to exclude prior users of biologics or tofacitinib. We required subjects to be continuously enrolled in the medical and pharmacy plan 12 months before and after the cohort entry. Effectiveness was access through an algorithm previously validated, based on the following criteria: 1) non-adherence; 2) switching/adding a new biologic or tofacitinib; 3) switching/adding a new DMARD; 4) increasing of the dose of the starting therapy; 5) use of glucocorticoid joint injections; and 6) increasing the dose of oral glucocorticoid. A patient’s therapy was defined as not effective if at least one of the criterion occurred during the first year of follow-up.

Results: 16,305 RA patients were included; 2,879 began therapy with DMARD, 13,345 with biologics and 81 with tofacitinib. Among all patients, 77.5% were female and the mean age was 56.2 years (standard deviation 12.6). Table 1 shows the proportion of patients that meet the individual criterion and that achieved effectiveness at the end of the 12-month follow-up.

Conclusions: Similar rates of therapy effectiveness were observed among groups, although the rates for the individual criteria differed. Fewer patients initiating biologic agents were non-adherent compared to DMARD and tofacitinib therapy, but switching/adding and injections tended to be higher in this group.
Table 1. Proportion and 95% confidence interval (CI) of patients who achieved therapy effectiveness and the individual criteria

<table>
<thead>
<tr>
<th>Effectiveness criteria</th>
<th>DMARD</th>
<th>Biologics</th>
<th>Tolctilin</th>
</tr>
</thead>
<tbody>
<tr>
<td>% 95% CI</td>
<td></td>
<td>% 95% CI</td>
<td>% 95% CI</td>
</tr>
<tr>
<td>Non-adherence</td>
<td>75.1</td>
<td>73.5-76.7</td>
<td>54.5</td>
</tr>
<tr>
<td>Switch/add biologic or tocolitin</td>
<td>16.1</td>
<td>14.8-17.5</td>
<td>34.6</td>
</tr>
<tr>
<td>Switch/add tocolitin</td>
<td>13.0</td>
<td>11.7-14.6</td>
<td>16.6</td>
</tr>
<tr>
<td>Increase in dose or frequency</td>
<td>8.6</td>
<td>7.6-9.7</td>
<td>6.9</td>
</tr>
<tr>
<td>Glucocorticoid joint injection</td>
<td>7.8</td>
<td>6.9-8.9</td>
<td>14.0</td>
</tr>
<tr>
<td>Increase in dose of oral glucocorticoid</td>
<td>19.0</td>
<td>17.6-20.5</td>
<td>17.6</td>
</tr>
<tr>
<td>Effective therapy (none of the criteria)</td>
<td>15.5</td>
<td>14.2-16.8</td>
<td>17.9</td>
</tr>
</tbody>
</table>

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4992
SAT0152 REAL-LIFE INFliximab AND ADALIMUMAB TROUGH LEVEL AND ANTI-DRUG ANTIBODY MEASUREMENTS IN RHEUMATOLOGY: THE FINNISH EXPERIENCE
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1Research Programs Unit, Immunobiology, University of Helsinki; 2United Medix Laboratories Ltd, Helsinki; 3Pediatric Rheumatology, Kuopio University Hospital, Kuopio; 4Rheumatology, Helsinki University and Helsinki University Hospital, Helsinki, Finland

Background: Therapeutic drug monitoring of TNF inhibitors (TNFi) may optimize clinical benefits while at the same time reducing financial costs and risk of adverse events1,2. Monitoring the TNFi trough levels (TLS) and the anti-drug antibodies (ADAbs) can provide relevant information to make rational adjustments to therapy if indicated.

Objectives: To identify distributions and trends in infliximab (IFX) and adalimumab (ADL) TLSs and ADAbs from clinically requested, real-life samples from Finnish patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA), or juvenile idiopathic arthritis (JIA).

Methods: Samples for TL and ADAbs were taken on a clinical basis in daily practice from four university hospitals and 15 central hospitals in Finland and sent for analysis to United Medix Laboratories. Samples were collected and analyzed from January 2012 to February 2016. TL measurements were performed by enzyme-linked immunosorbent assay (either at Sanquin laboratories, Amsterdam, The Netherlands, or in Helsinki, Finland). Adalimumab, TLS from 2–10 μg/ml (IFX) or 5–10 μg/ml (ADL) were considered as general target ranges. ADAbs measurements were performed by radioimmunoassay (Sanquin). 1762 TL (1241 patients), 1598 ADAB (1203 patients), and 860 combined TL and ADAB samples (716 patients) were analyzed. Statistical analyses were performed by SPSS (IBM, Armonk, NY). p < 0.05 was considered statistically significant.

Results: The highest proportions of samples with very low TLS (< 0.1 μg/ml) were found in IFX-treated RA patients (14.5%) and ADL-treated SpA patients (12.6%). The proportion of all samples in the general target range was 51.3% (IFX) and 33.4% (ADL). Compared to reported data of RA and SpA samples had possibly supratherapeutic (<10 μg/ml) TLSs (RA: ADL, 22.9% vs IFX, 10.4%, p < 0.001 and SpA; ADL, 21.4% vs IFX, 15.0%, p < 0.05). A greater proportion of ADL JIA patients had TLS >10 μg/ml (ADL, 54.5% vs IFX, 36.3%, p < 0.001). Proportions of samples with ADAbs (≥12 AU/ml) ranged from 18.0% (IFX RA) to 28.6% (ADL, SpA). A greater proportion of ADL samples with TLS of 2–5 μg/ml and detectable ADAbs (≥12 AU/ml) (RA: ADL, 3.3% vs IFX, 0%; SpA: ADL, 5.6% vs IFX, 0%; JIA: ADL, 3.4% vs IFX, 0.9%) was observed.

Conclusions: IFX RA and ADL samples had the highest proportions of very low TLS and compared to IFX much greater proportions of ADL samples in IFX RA and ADL SpA had been reported through different ADL RA and SpA samples had possibly supratherapeutic (<10 μg/ml) TLSs. Furthermore, ADL ADAbs were lower compared to IFX ADAbs. RA and SpA patients monitored by IFX and ADL had TLS and ADAbs that differed considerably from the expected model. RA patients had higher TLS and ADAbs compared to SpA. RA ADAbs were lower compared to SpA ADAbs.

References:


SAT0154 EFFECTIVENESS AND SAFETY OF CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND PLACQUE PSORIASIS: OBSERVATIONAL STUDY IN REPUBLIC OF KOREA
D.-W. Kim1, T.-H. Kim1, S.R. Kwon2, E.Y. Lee3, C.-N. Son4, Y.S. Kim5, S.H. Kim7, Y.-B. Park8, J.-W. Hur9, H.-S. Lee10, S.J. Lee11, S.H. Lee11, 1Inje University Busan Paik Hospital, Busan; 2Hanyang University Hospital for Rheumatic Diseases, Seoul; 3Inha University Hospital, Incheon; 4Seoul National University College of Medicine, Seoul; 5Keimyung University Dongsan Medical Center, Daegu; 6Chosun University Hospital, Gwangju; 7Gwangmyeonggaeng Saeum Hospital, Gyeonggi-do; 8Yonsei University Severance Hospital; 9Eulji University Seongdong Hospital, Seoul; 10Hanyang University Guri Hospital, Gyeonggi-do; 11Celltrion Inc., Incheon, Korea, Republic Of

Background: CT-P13 is approved as a biosimilar of innovator infliximab for rheumatoid arthritis (RA), ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA) and Plaque Psoriasis (Ps)

Objectives: To evaluate the effectiveness and safety of CT-P13 under routine care in Republic of Korea.

Methods: This observational study included both biologic naïve patients (Naïve group) and patients who switched from other anti-tumor necrosis factor (TNFi) to CT-P13 (Switch group). Effectiveness was evaluated based on remission (DAS28≤2.6 in RA, BASDAI≤3 in AS and absence of swollen and tender joint counts in PsA), and response (BASDAI 20/50/75 in AS and PASI 50/75 in Ps). Adverse events (AEs) were collected over 6 month period.

Results: Total 940 patients (400 with RA, 531 with AS, 3 with PsA and 6 with Ps) were registered and 338 (36.0%) patients (108 with RA, 228 with AS, 2 with PsA) who switched to CT-P13 were included.

The proportion of patients achieving remission was similar between Naïve and Switch groups in both RA and AS during post-baseline visits (Table 1). In RA, the proportion of patients achieving each disease activity category by DAS28 was similar between Naïve and Switch groups (Figure 1). The proportion of patients significantly younger (53.3 vs 59.7 years), with lower disease duration of RA (8.8 vs 11.2 years) compared to low dose MTX group. Patients in the high dose group also had higher disease activity (mean CDAI: 20.8 vs 15.4) and more likely to be biologic-naïve (71.3% vs 55.4%), compared to the low dose group (all p < 0.05). Unadjusted and adjusted analyses found no sufficient evidence that patients on high dose MTX had a better improvement in the outcomes selected (table). Persistency of ADA did not differ between the two groups.

Table: Outcomes at 6 months among ADA plus low (<152 mg) vs high (≥152 mg) combination MTX therapy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Low MTX (n=114)</th>
<th>High MTX (n=105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achievement of Remission (DAS28≤2.6)</td>
<td>7.1 (15.7%)</td>
<td>7.4 (15.8%)</td>
</tr>
<tr>
<td>Achievement of LDA (BASDAI≤3)</td>
<td>28 (26.6%)</td>
<td>35 (43.9%)</td>
</tr>
</tbody>
</table>

Conclusions: In this real world study, improvements in PROs and achievement of LDA/remission at 6 months were similar in the groups initiating ADA in combination with either low dose or high dose MTX.

References:

Acknowledgements: This study is sponsored by Corrona, LLC. Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.

who achieved BASDAI 20/50/70 response gradually increased from week 6 to week 24 or 30 in Naive group with AS (Figure 1).

Fifty percent of naïve patients with PsA achieved clinical remission. The proportions of both PASI 50 and 75 responses were 50% at Week 22 in Naive group and were 100% and 50% in Switch group, respectively during post-baseline visit in 23 patients. Throughout this study, treatment-emergent adverse events (TEAE) and treatment-emergent serious adverse events (TSEAE) were reported as Table 2. Only 11% of patients experienced infection.

Table 1. Clinical remission in RA and AS

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-baseline</th>
<th>Baseline</th>
<th>Post-baseline</th>
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<tbody>
<tr>
<td>NAIVE</td>
<td>RA</td>
<td>DAS28 (ESR)</td>
<td>AS</td>
<td>BASDAI</td>
</tr>
<tr>
<td></td>
<td>0/181 (0.0%)</td>
<td>24/182 (13.1%)</td>
<td>0/25 (0.0%)</td>
<td>5/25 (20.0%)</td>
</tr>
<tr>
<td></td>
<td>DAS28 (CRP)</td>
<td>0/181 (0.0%)</td>
<td>43/179 (24.0%)</td>
<td>2/25 (8.0%)</td>
</tr>
<tr>
<td></td>
<td>AS</td>
<td>BASDAI</td>
<td>AS</td>
<td>BASDAI</td>
</tr>
<tr>
<td></td>
<td>2/292 (0.7%)</td>
<td>199/292 (68.2%)</td>
<td>112/209 (53.6%)</td>
<td>150/210 (71.4%)</td>
</tr>
</tbody>
</table>

Table 2. Summary of safety results

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
<th>RA</th>
<th>AS</th>
<th>PS</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAE</td>
<td>196/400 (49.5)</td>
<td>183/331 (54.5)</td>
<td>1/3 (33.3)</td>
<td>26/50 (52.0)</td>
<td></td>
</tr>
<tr>
<td>TESAE related with CT-P13</td>
<td>73/400 (18.3)</td>
<td>64/331 (19.3)</td>
<td>0/3 (0.0)</td>
<td>2/6 (33.3)</td>
<td></td>
</tr>
<tr>
<td>TESAE related with CT-P13</td>
<td>52/400 (13.0)</td>
<td>14/331 (4.2)</td>
<td>0/3 (0.0)</td>
<td>16/6 (26.7)</td>
<td></td>
</tr>
<tr>
<td>Infusion-related reactions</td>
<td>15/400 (3.8)</td>
<td>6/331 (1.8)</td>
<td>0/3 (0.0)</td>
<td>0/6 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Clinical response of RA and AS

Table 2. Week 24 Clinical and Functional Outcomes Among Patients Receiving Adalimumab in Combination with a Single csDMARD

<table>
<thead>
<tr>
<th></th>
<th>Adalimumab+MTX</th>
<th>Adalimumab+non-MTX csDMARD</th>
</tr>
</thead>
<tbody>
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<td>1/121</td>
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<tr>
<td></td>
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<td>0/180</td>
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Conclusions: MTX administered in combination with biologics, like ADA, leads to superior outcomes vs monotherapy. For pts who can’t tolerate MTX, non-MTX csDMARDs, specifically HCO and SSZ but not LIF, may be good alternatives, as outcomes were largely comparable with those of pts receiving MTX when combined with ADA. The limited sample size examined in this analysis should be confirmed in a larger pt population.

References:
2. Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation, and abstract writing, review, and approval. Medical writing: Ben Wolfe of AbbVie.


DOI: 10.1136/annrheumdis-2017-eular.1597
Our findings confirm specific CD4+ and CD8+ T-cell responses from patients with latent form of tuberculosis (LTBI) and active tuberculosis (TB) subjects, in which INF-γ in the tubes TB1 and TB2 was observed in 16 individuals and 15 non-responder individuals, respectively in 27.3% and 23.9% RA patients, and 27.4% and 23.5% PsA patients. MTX was not associated with an increased drug survival in both RA (p=0.09) and PsA patients (p=0.50), where 50% of MTX users survived for 2 years, compared to 48% of ADA treated patients achieving remission or low disease activity (LDA). Reasons for discontinuation were not associated with different ADA clinical response, as well as concomitant MTX.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eur.4292

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**SAT0158**

**EFFICACY OF SWITCHING FROM ETANERCEPT TO ADALIMUMAB IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS WHO EXPERIENCED A FIRST-LINE BIOLOGIC THERAPY FAILURE: THE FEARLESS STUDY**

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**Department of Rheumatology, Gaetano Pini Institute, Milano; 2Rheumatology Unit, AOUI, Vittorio Emanuele, Catania; 3Rheumatology, Azienda Ospedaliero Universitaria Città della Salute and della Scienza, Torino; 4Clinica di reumatologia, Dipartimento di scienze mediche e biologiche, ASULID, Udine; 5UOC di Reumatologia, Azienda Ospedaliero-Universitaria Sant’Anna Cona-Ferrara, Ferrara; 6SOS Reumatologia, Ospedale S. Giovanni di Dio, Firenze; 7Clinica Reumatologica, Università Politecnica delle Marche, Ancona; 8U.O.Rheumatico, ASL Taranto-PF OLO SS. Annunziata Taranto e Valle d’Itria, Taranto; 9Department of Clinical Sciences and Community Health, Division of Rheumatology, University of Milano and Gaetano Pini Institute, Milano, Italy.

**Background:** The strategy for the choice of the second biologic agent after the failure of the first TNF inhibitor (TNFi) is still an unclear aspect in the treatment of both rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Switching between structurally different TNFis (from etanercept [ETN] to monoclonal antibody [mAb] or vice versa) has been proposed as a more effective procedure than switching among different mAbs, but to date no study has been specifically focused on exploring this topic.

**Objectives:** To evaluate the comparative 2-year retention rate and the 12-month efficacy of adalimumab (ADA) as second biologic agent in etanercept (ETN) non-responder RA and PsA patients in a multicentre retrospective study.

**Methods:** All RA and PsA patients from 11 Italian Rheumatology Units treated with ADA after a first-course ETN failure and with at least 12-month follow-up were retrospectively collected in a multicentre registry. Data analysis was limited to the period from January 2002 to May 2016. Two-year ADA retention rate was calculated by Kaplan-Meier method. 12-month ADA response was defined as achievement of disease activity score 28 calculated by using erythrocyte sedimentation rate (DAS28-ESR) <2.6 (remission) or >2.6 and <3.2 (low disease activity, LDA). Sub-analyses according to reason for ETN discontinuation and concomitant methotrexate use in RA and PsA patients have been performed.

**Results:** The study population (219 patients) included 117 RA (female 85.5%, mean [± standard deviation, SD] age 53.2±13.5 years, mean [±SD] disease duration 10.1±7.7, positive rheumatoid factor 70.2%; positive anti-citrullinated peptide antibodies (ACPA) 59.6%; mean [±SD] baseline DAS28-ESR 4.97±1.3; MTX users 64.9% and 102 PsA patients [female 63.7%; mean [±SD] age 51.7±10.6; mean [±SD] disease duration 7.1±5.1; mean [±SD] baseline DAS28-ESR 4.4±1.1; MTX users 50%). The 2-year retention rate was 48.2% in RA and 56.5% in PsA patients, irrespective of reason for ETN discontinuation. Similarly, concomitant MTX was not associated with an increased drug survival in both RA (p=0.09) and PsA patients (p=0.50), where 50% of MTX users survived for 2 years, compared to 48% of ADA treated patients achieving remission or LDA. Reasons for ETN discontinuation were not associated with different ADA clinical response, as well as concomitant MTX.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eur.3747

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**SAT0159**

**IMPACT OF PARTICIPATION IN THE ADALIMUMAB PATIENT SUPPORT PROGRAM ON FUNCTIONAL AND CLINICAL OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: PASSION STUDY**


**Department of Medicine, University of British Columbia; 2Addenbrooke’s Hospital, Cambridge, United Kingdom; 3Rheumatazentrum, Ratingen, Germany; 4AbbVie Inc., North Chicago, United States; 5AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany.

**Background:** Patients (pt) with Rheumatoid arthritis (RA) who are treated with adalimumab (ADA) are offered participation in the Support Program for Patients (PSP) to access a wide variety of services. To date, no prospective study has been conducted to analyze the acceptance and the impact of these PSPs on treatment effectiveness and pt satisfaction.

**Objectives:** The purpose of this study was to examine the effectiveness of ADA in patients with rheumatoid arthritis (RA) attending a course in the context of PSP participation. **Methods:** PASSION (NCT01383421) was a 78-week (wk) post-marketing observational study of pts with RA receiving ADA in routine clinical care. Pts from the EU, Israel, Mexico, Puerto Rico, and Australia with an insufficient response to ≥ 1 disease-modifying antirheumatic drug (DMARD) newly initiating ADA (1 prior...
biologic DMARD was allowed) were enrolled. The primary endpoint was the % of pts achieving the minimal clinically important difference (MCID; improvement of ≥0.22 compared to baseline [BL] in the Health Assessment Questionnaire Disability Index (HAQ-DI) at wk 78. Non-responder imputation (NRI) was used to account for the missing values. Secondary clinical parameters included % of pts achieving MCID in HAQ-DI at wks 24, 52 and changes in the 28-joint DAS based on CRP (DAS28(CRP)), Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) at wks 24, 52, and 78 vs BL. Pts were categorized based on their participation in the PSP: ever (PSP users) vs never (PSP non-users) and outcomes were compared after adjusting for corresponding BL values.

Results: Overall, the primary endpoint, percentage of pts achieving the MCID for HAQ-DI, was achieved by 72.1% (as observed) and 42.8% (NRI) of pts at week 78 with the percentage of pts achieving the MCID for HAQ-DI significantly higher in PSP users vs PSP non-users (48.1% vs 37.8% [NRI]; P<0.001). From 1,025 pts, 48.7% pts were PSP users (BL: mean age, 54.3 years; % female, 77.1%; mean RA duration, 7.8 y; mean HAQ-DI, 1.5; mean DAS28(CRP), 5.3; mean SDAI, 35.6; mean CDAI, 33.3; 17.8% pts had received prior biologic DMARD. Significant changes (P<0.05) from BL to wk 78 were observed for pts using the PSP vs PSP non-users in HAQ-DI (0.53 vs 0.39), DAS28(CRP) (−2.33 vs −1.97), SDAI (−24.5 vs −19.8), and CDAI (−22.66 vs −18.55) scores (Figure). Study discontinuation rates were significantly (P=0.001) lower among PSP-users vs PSP non-users (25.5% vs 41.6%). Reasons for discontinuations are listed in the Table.

Figures: Changes from baseline in DAS28 (CRP) (A), SDAI (B), CDAI (C), and HAQ-DI (D) over time between PSP users and PSP non-users.

Significantly different between PSP users and PSP non-users (P<0.05). Log rank test (Mantel-Cox) for comparison of survival curves.

Table: All reasons for study discontinuation by PSP utilization category

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<thead>
<tr>
<th>Subject Disposition</th>
<th>All Patients N=1,025</th>
<th>Reference etanercept (n=515)</th>
<th>GP2015 (n=510)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UlC discontinued (%)</td>
<td>164 (15.9)</td>
<td>72 (13.9)</td>
<td>92 (17.9)</td>
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</tr>
<tr>
<td>Adverse event</td>
<td>56 (5.4)</td>
<td>24 (4.7)</td>
<td>32 (6.3)</td>
<td>0.12</td>
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<tr>
<td>Withdraw consent</td>
<td>37 (3.6)</td>
<td>15 (2.9)</td>
<td>22 (4.3)</td>
<td>0.10</td>
</tr>
<tr>
<td>Late to follow-up</td>
<td>46 (4.5)</td>
<td>17 (3.3)</td>
<td>29 (5.7)</td>
<td>0.14</td>
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<tr>
<td>Serum adverse events</td>
<td>24 (2.3)</td>
<td>11 (2.2)</td>
<td>13 (2.5)</td>
<td>0.82</td>
</tr>
<tr>
<td>Lack of efficacy</td>
<td>68 (6.6)</td>
<td>20 (3.9)</td>
<td>48 (9.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Others</td>
<td>32 (3.1)</td>
<td>18 (3.5)</td>
<td>14 (2.7)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Conclusions: The final study results showed that, in pts with moderate to severe RA who initiated ADA, significantly better improvement in functional and clinical outcomes was achieved in the PSP users vs the PSP non-users. Improvements were achieved at early timepoints and continued to increase throughout the study.

Acknowledgements: AbbVie funded the study and the analysis, and approved the abstract for submission. Medical writing assistance was provided by Gaurav Patki, PhD and Benjamin Wolfe, PhD from AbbVie.

Disclosure of Interest: F. Van den Bosch Consultant for: AbbVie, Celgene, Janssen, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene, Janssen, Pfizer, and UCB. A. Ostor Consultant for: Roche, Chugai, MSD, AbbVie, Pfizer, Novartis, Napp, and BMS. S. Wassenberg Consultant for: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen and UCB. J. K. Anderson Consultant for: AbbVie, Celgene, Janssen, Pfizer, MDC, Lilly, Janssen, and UCB. S. Wassenberg Consultant for: AbbVie, Celgene, Janssen, Pfizer, MDC, Lilly, Janssen, and UCB. A. Ostor Consultant for: Roche, Chugai, MSD, AbbVie, Pfizer, Novartis, Napp, and BMS. S. Wassenberg Consultant for: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen and UCB. J. K. Anderson Consultant for: AbbVie, Celgene, Janssen, Pfizer, MDC, Lilly, Janssen, and UCB.

Results: We screened 255 articles by title and abstract and 7 publications fulfilled our inclusion criteria. Three meeting abstracts were also included. Six studies assessed infliximab biosimilars (CT-P13 and SB2), three studies assessed etanercept biosimilars (SB4 and GP2015) and one study assessed an adalimumab biosimilar (ABP 501). All but two concerned phase III trials and seven were performed on rheumatoid arthritis patients. All biosimilars had comparable immunogenicity profiles in respect to their reference drugs, except for the etanercept biosimilar SB4, which presented significantly less ADA than the etanercept when compared to reference etanercept (0.7% vs 13.1% at 24 weeks and 1.0% vs 13.2% at 52 weeks, p<0.001 for both). As expected, infliximab had the highest incidence of ADA; the proportion of ADA in studies of infliximab and adalimumab was higher when compared to historical data. Only 4 studies reported nADA, which were highest in the infliximab biosimilar CT-P13 54-week study in ankylosing spondylitis patients. Electrochemiluminescence immunoassay was the preferred method to measure ADA. Table 1 summarizes the main findings in the included studies.

Table 1. Immunogenicity of biosimilars approved for the treatment of inflammatory rheumatic diseases. ADA: antidrug antibody; NA: not available; nADA: neutralizing antidrug antibody. *The EGAILITY study presented a four-arm design in which two arms were continuously treated with either reference etanercept or GP2015 and the other two arms were systematically switched. The results presented in this table concern the groups continuously treated with reference etanercept or GP2015.

Conclusions: Currently approved biosimilars for the treatment of rheumatic diseases have comparable immunogenicity profiles in respect to their reference drugs. The discrepancy in ADA between SB4 and reference etanercept did not correlate with efficacy or safety and did not preclude biosimilarity, according to the regulatory agencies. The higher proportion of ADA compared to historical data may be explained by the greater sensitivity of current immunogenicity assays, such as electrochemiluminescence immunoassay.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2486
**SAT0161**  PRELIMINARY REAL WORLD DATA ON SWITCHING PATTERNS BETWEEN ETANECETP, ITS RECENTLY MARKETED BIOSIMILAR COUNTERPART AND ITS COMPETITOR ADALIMUMAB, USING SWEDISH PRESCRIPTION REGISTRY

R. Alten1, P. Neregård1, H. Jones3, E. Singh3, C. Curiale4, T. Meng5, L. Luchesse6, C. Miglio6, J. Young7, G. J. Bergman7,1, Schlosspark-Klinik, Berlin, Germany;7Pfizer, Stockholm, Sweden;7Pfizer, Collegeville, United States;7Pfizer, Rome, Italy;7Pfizer, Berlin, Germany;7QuintilesMS, London, United Kingdom;7QuintilesMS, Solna, Sweden

**Background:** The increasing availability of biologic treatments over the past 10 years has revolutionized the management of chronic inflammatory autoimmune diseases such as rheumatic diseases. In April 2016, the first etanercept biosimilar (EtnBS) was launched in Sweden, which may represent a cheaper option to its innovator adalimumab (EtnI) against anti-TNF and other biologic agents. In this study, we evaluate early observations and investigate the reasons for switching back.

**Objective:** The objective of this study was to describe the position of etanercept innovator (EtnI) within the Swedish biologic market for rheumatic diseases, before and after the launch of its biosimilar. The study also provides early real-world data on the market penetration of EtnBS by evaluating switching dynamics to and from this drug since the date of launch.

**Methods:** The overall biologic market share across all type of rheumatic diseases was monthly tracked over the last year of available data in the Swedish Prescription Registry (100% coverage). The proportion of patients receiving a rheumatologists prescription for any biologic in each month, from November 2015 to October 2016 was recorded. In addition, switching dynamics of patients initiating EtnBS treatment between April 2016 and October 2016 were studied. The proportion of patients receiving no biologic treatment (naive) and of those on treatment with EtnI, adalimumab and other biologic agents in the 12 months prior to initiate EtnBS treatment was reported. Furthermore, patients who switched from EtnBS back to EtnI or adalimumab and the mean time to this second switch were also evaluated.

**Results:** EtnI and adalimumab dominate the biologic market for rheumatic diseases in Sweden, holding the 40% and 28% of market share, respectively, up to April 2016. However, in the 6 months after EtnBS was launched, the share of EtnI decreased constantly, dropping to 31% in October 2016 (Figure 1). Since April 2016, we identified in total 2,439 patients receiving first prescription of EtnBS by a rheumatologist. Of these, 977 (40.1%) were naïve to biologic, 1,179 (48.3%) had prior treatment with EtnI, 107 (4.4%) with adalimumab, 176 (7.2%) with other biologics. Among the patients who changed to EtnBS from prior EtnI, the 7% switched back to EtnI after an average time of 43 days. Similarly, of those who were on previous adalimumab treatment, 6% switched back to adalimumab, after an average, 57 days.

**Conclusions:** Many patients changed from EtnI to its biosimilar treatment since its launch in Sweden. However, this study showed that 7% of these patients switched back to their original treatment after short time. Despite the change from a brand biologic to the biosimilar is very likely made for economic reasons, the reasons for switching back to the innovator are not clear and may imply patients’ preference or biologic to the biosimilar is very likely made for economic reasons, the reasons for switching back to the innovator are not clear and may imply patients’ preference or clinical reasons. Interestingly, the same pattern is observed for patients changing from adalimumab to EtnBS. Long-term studies are required to confirm these early observations and investigate the reasons for switching back.

**Disclosure of Interest:** R. Alten Grant/research support from: The study was sponsored by Pfizer, P. Neregård Employee of: Pfizer, H. Jones Employee of: Pfizer, E. Singh Employee of: Pfizer, C. Curiale Employee of: Pfizer, T. Meng Employee of: Pfizer, L. Luchesse Grant/research support from: The study was sponsored by Pfizer, C. Miglio Grant/research support from: The study was sponsored by Pfizer, J. Young Grant/research support from: The study was sponsored by Pfizer, G. J. Bergman Grant/research support from: The study was sponsored by Pfizer. 

**DOI:** 10.1136/annrheumdis-2017-eular.3585

**SAT0162**  SWITCHING FROM ETANECETP TO CHS-0214: A ONE YEAR, RANDOMIZED, DOUBLE-BLIND STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. O’Dell1, A. Kivitz2, T. Takeuchi3, Y. Tanaka4, I. Louw5, T. Tiabut6, A. Molto 1, V. Abitbol2, A. Salcion 1, L. Gutermann 3, O. Conort 3

**Background:** The increasing availability of biologic treatments over the past 10 years has revolutionized the management of chronic inflammatory autoimmune diseases such as rheumatic diseases. In April 2016, the first etanercept biosimilar (EtnBS) was launched in Sweden, which may represent a cheaper option to its innovator adalimumab (EtnI) against anti-TNF and other biologic agents. In this study, we evaluate early observations and investigate the reasons for switching back.

**Objective:** The objective of this study was to describe the position of etanercept innovator (EtnI) within the Swedish biologic market for rheumatic diseases, before and after the launch of its biosimilar. The study also provides early real-world data on the market penetration of EtnBS by evaluating switching dynamics to and from this drug since the date of launch.

**Methods:** The overall biologic market share across all type of rheumatic diseases was monthly tracked over the last year of available data in the Swedish Prescription Registry (100% coverage). The proportion of patients receiving a rheumatologists prescription for any biologic in each month, from November 2015 to October 2016 was recorded. In addition, switching dynamics of patients initiating EtnBS treatment between April 2016 and October 2016 were studied. The proportion of patients receiving no biologic treatment (naive) and of those on treatment with EtnI, adalimumab and other biologic agents in the 12 months prior to initiate EtnBS treatment was reported. Furthermore, patients who switched from EtnBS back to EtnI or adalimumab and the mean time to this second switch were also evaluated.

**Conclusions:** Many patients changed from EtnI to its biosimilar treatment since its launch in Sweden. However, this study showed that 7% of these patients switched back to their original treatment after short time. Despite the change from a brand biologic to the biosimilar is very likely made for economic reasons, the reasons for switching back to the innovator are not clear and may imply patients’ preference or clinical reasons. Interestingly, the same pattern is observed for patients changing from adalimumab to EtnBS. Long-term studies are required to confirm these early observations and investigate the reasons for switching back.

**Disclosure of Interest:** R. Alten Grant/research support from: The study was sponsored by Pfizer, P. Neregård Employee of: Pfizer, H. Jones Employee of: Pfizer, E. Singh Employee of: Pfizer, C. Curiale Employee of: Pfizer, T. Meng Employee of: Pfizer, L. Luchesse Grant/research support from: The study was sponsored by Pfizer, C. Miglio Grant/research support from: The study was sponsored by Pfizer, J. Young Grant/research support from: The study was sponsored by Pfizer, G. J. Bergman Grant/research support from: The study was sponsored by Pfizer.

**DOI:** 10.1136/annrheumdis-2017-eular.2480

**SAT0163**  SYSTEMATIC SWITCH FROM INNOVATOR INFlixIMAB TO BIOSIMILAR INFlixIMAB IN INFLAMMATORY RHEUMATIC DISEASES IN DAILY CLINICAL PRACTICE: THE EXPERIENCE OF COCHIN HOSPITAL, PARIS, FRANCE

J. Avaua 1, A. Motol1, V. Abitbol 2, A. Salcion 1, L. Gutermann 3, O. Conort 3, C. Le Jeunne 4, C. Goulvestre 3, S. Chaussade 2, A. Kahan 1

**Background:** Biologics of originator biologic therapeutics are going to change the management of chronic inflammatory autoimmune diseases such as rheumatic diseases. In April 2016, the first etanercept biosimilar (EtnBS) was launched in Sweden, which may represent a cheaper option to its innovator etanercept (EtnI) against anti-TNF and other biologic agents. In this study, we evaluate early observations and investigate the reasons for switching back.

**Objective:** The objective of this study was to describe the position of etanercept innovator (EtnI) within the Swedish biologic market for rheumatic diseases, before and after the launch of its biosimilar. The study also provides early real-world data on the market penetration of EtnBS by evaluating switching dynamics to and from this drug since the date of launch.

**Methods:** The overall biologic market share across all type of rheumatic diseases was monthly tracked over the last year of available data in the Swedish Prescription Registry (100% coverage). The proportion of patients receiving a rheumatologists prescription for any biologic in each month, from November 2015 to October 2016 was recorded. In addition, switching dynamics of patients initiating EtnBS treatment between April 2016 and October 2016 were studied. The proportion of patients receiving no biologic treatment (naive) and of those on treatment with EtnI, adalimumab and other biologic agents in the 12 months prior to initiate EtnBS treatment was reported. Furthermore, patients who switched from EtnBS back to EtnI or adalimumab and the mean time to this second switch were also evaluated.

**Conclusions:** Many patients changed from EtnI to its biosimilar treatment since its launch in Sweden. However, this study showed that 7% of these patients switched back to their original treatment after short time. Despite the change from a brand biologic to the biosimilar is very likely made for economic reasons, the reasons for switching back to the innovator are not clear and may imply patients’ preference or clinical reasons. Interestingly, the same pattern is observed for patients changing from adalimumab to EtnBS. Long-term studies are required to confirm these early observations and investigate the reasons for switching back.

**Disclosure of Interest:** R. Alten Grant/research support from: The study was sponsored by Pfizer, P. Neregård Employee of: Pfizer, H. Jones Employee of: Pfizer, E. Singh Employee of: Pfizer, C. Curiale Employee of: Pfizer, T. Meng Employee of: Pfizer, L. Luchesse Grant/research support from: The study was sponsored by Pfizer, C. Miglio Grant/research support from: The study was sponsored by Pfizer, J. Young Grant/research support from: The study was sponsored by Pfizer, G. J. Bergman Grant/research support from: The study was sponsored by Pfizer.

**DOI:** 10.1136/annrheumdis-2017-eular.3585
SAT0164 ASSOCIATION BETWEEN FLARE AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

J.S. Smolen 1, H. Jones 2, E. Mahgoub 2, R. Pedersen 2, L. Marshall 2, 1Medical University of Vienna, Vienna, Austria; 2Pfizer, Collegeville, United States

Background: Biologic therapy has improved RA management, enabling some patients to achieve remission. Many clinicians decrease the biologic dose for patients in low disease activity (LDA) or remission. However, it is unclear which patients may flare and if flare contributes to radiographic progression.

Objectives: To assess whether patients who flared had a higher incidence of radiographic progression, and to compare patients with and without flares.

Methods: PRESERVE (ClinicalTrials.gov: NCT00565409) was a 2-period trial in patients with moderate RA despite MTX. Period 1 was open-label, single treatment induction with etanercept (ETN) 50mg+MTX weekly (QW) for 36 wks. Patients in LDA or remission (disease activity score for 28 joints [DAS28] ≤3.2) during wks 12 to 36 were randomized to Period 2, the randomized, double-blind phase, to evaluate maintenance of LDA/remission. Patients were randomized to ETN 50mg+MTX QW, ETN 25mg+MTX QW, or placebo+MTX QW to wk 88. This post hoc analysis evaluated flare and radiographic progression at wk 88. Flare was defined as 2 ways: 1) loss of LDA with/without DAS28 change of 0.6; and 2) relapse (DAS28-5.1 or DAS28-3.2 at ≥2 time points). Radiographic progression was evaluated according to 4 levels of stringency: 1) minimally clinically important difference (modified total Sharp score [mTSS] change ≥0.5); 2) smallest detectable difference (mTSS change ≥2.3); 3) mTSS change ≥0.5; and 4) mTSS change >0. Baseline [BL] characteristics were compared for patients with vs without flare defined as loss of LDA and DAS28 change of 0.6. Analysis of covariance and chi-square test compared continuous and categorical outcomes, respectively.

Results: Age, race, BMI, and disease duration did not differ significantly for flare vs non-flare, total N=531. BL DAS28 was higher for flare vs non-flare (p=0.289 and p=0.271, respectively).

Flare defined as loss of LDA and DAS28 change of 0.6

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Flare Patients</th>
<th>Non-flare Patients</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>mTSS ≥0</td>
<td>at wk21 (15.9)</td>
<td>31/260 (11.9)</td>
<td>0.2109</td>
</tr>
<tr>
<td>mTSS ≥0.5</td>
<td>38/214 (17.8)</td>
<td>24/260 (9.2)</td>
<td>0.1045</td>
</tr>
<tr>
<td>mTSS ≥2</td>
<td>20/271 (7.4)</td>
<td>10/260 (3.8)</td>
<td>0.0914</td>
</tr>
<tr>
<td>mTSS ≥0.5</td>
<td>9/271 (3.3)</td>
<td>2/260 (0.8)</td>
<td>0.0633</td>
</tr>
</tbody>
</table>

Flare defined as loss of DAS28 change ≥0.6

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Flare Patients</th>
<th>Non-flare Patients</th>
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<td>mTSS ≥0.5</td>
<td>9/271 (3.3)</td>
<td>2/260 (0.8)</td>
<td>0.0633</td>
</tr>
</tbody>
</table>

Flare defined as relapse

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Flare Patients</th>
<th>Non-flare Patients</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>mTSS ≥0.5</td>
<td>35/181 (19.3)</td>
<td>39/350 (11.1)</td>
<td>0.0119</td>
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<td>mTSS ≥0.5</td>
<td>31/181 (17.1)</td>
<td>31/350 (8.9)</td>
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<tr>
<td>mTSS ≥2</td>
<td>19/181 (10.5)</td>
<td>11/350 (3.1)</td>
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<td>mTSS ≥0.5</td>
<td>9/181 (5.0)</td>
<td>2/260 (0.7)</td>
<td>0.0015</td>
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</table>

1Fisher's exact test. Overall treatment group. Values are n/N.

Disclosure of Interest: None declared, H. Jones: None declared, M.-J. Brabant: None declared, E. Singh: None declared, J. Woolcott: None declared. Disclosure of Interest: None declared, H. Jones: None declared.

SAT0165 REAL-WORLD UTILIZATION OF CONCOMITANT MEDICATIONS IN PATIENTS INITIATING ETANERCEPT: A RETROSPECTIVE COHORT STUDY OF CANADIAN CLAIMS-LEVEL DATA

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Background: Methotrexate (MTX) and prednisone (pred) are immune suppressants frequently used to treat immune-mediated inflammatory diseases (IMIDs). Etanercept is a soluble TNF receptor (humanized protein) indicated for the treatment of IMIDs, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and arthritis associated with ulcerative colitis (UC). Limited information exists on how MTX or pred use changes in patients who initiate etanercept in real-world settings.

Objectives: To evaluate whether initiation of etanercept impacts use of co-therapy with MTX or pred in Canadian patients with IMIDs.

Methods: A retrospective cohort study was conducted using claims-level data from QuintilesIMS Private Drug Plan database, Ontario Public Drug Plan database, and Quebec Public Drug Plan database. Bio-naive patients initiating etanercept between 07/2013 and 06/2015, were identified and their claims made for MTX or pred were analyzed. Patients' utilization of MTX or pred was calculated as average weekly dose in mg, and then compared in the 6-months pre versus 12-months post initiation of etanercept using a paired t-test. Differences in the presence of concomitant medications pre and post- etanercept were also examined using a paired t-test.

Results: The study captured 3,745 etanercept patients (61% female, 77% aged between 18 and 65, 84% rheumatic diseases, and 15% PsO) across Canada in the selection period. Of selected patients, 33% used MTX (n=1,244) and 14% (n=523) used pred pre and post initiation of etanercept. In concomitant MTX patients, the average weekly dose dispensed was 25.0mg in the 6 months prior to initiation of etanercept, and 25.0mg in the 12 months following the first claim of etanercept (p=0.4793). In concomitant prednisone patients, the average weekly dose dispensed reduced from 123mg pre- etanercept to 108mg post- etanercept initiation (p=0.2316). 19% of patients stopped MTX (n=287) use post-etanercept initiation, compared to 36% who stopped pred use (n=289).

Conclusions: In this real-world setting, approximately 1/3 of patients stopped or reduced co-therapy of MTX, and 1/3 of patients stopped or reduced co-therapy of pred following initiation of etanercept; however, those patients who remained on co-therapy showed non-significant changes in their average consumption. Further research is needed to understand the impact on overall patient outcomes and safety.


SAT0166 MARKERS OF RESPONSE TO INFlixIMAB IN RHEUMATOID ARTHRITIS – THE PLACE OF ANTI-NUCLEAR ANTIBODY AND NUCLEASE SERUM ACTIVITY

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Background: It is important to study new potential markers of response to treatment in rheumatoid arthritis (RA), because up to 40% patients don't achieve...
remission even using biological therapy. DNase activity of the blood serum and antinuclear antibody may be useful in this context. Changes of serum DNase activity in the RA treatment by biological agents previously have been not investigated.

**Objectives:** The aim of this work is to study the dynamics clinical and laboratory parameters of DNAse serum activity in RA patients treated by infliximab (INF) and assess the prognostic potential of them in prediction of response to INF.

**Methods:** 24 RA patients were involved in the study. All patients fulfilled the EULAR/ACR 2010 RA criteria. 22/24 patients received 6 infusions of INF at a dose of 3 mg/kg according to standard protocol: at 0h, 2h, 6h and then every 8 weeks. 2/24 patient received 4 infusions of INF. All patients received synthetic DMARDs therapy by metotrexate (10–17.5 mg weekly), 18/24 patients received glucocorticoids (methylprednisolone 4–8 mg daily) and non-steroidal anti-inflammatory drugs. Prior to treatment by INF patients did not receive any biological agents. All patients had high disease activity before INF treatment (DAS28≥5.1).

ANA determination was performed by indirect immunofluorescence on Hep-2 cells using digital system AKLIDES. ANA was measured in serum samples before 1st INF administration, at 22–30 weeks after the 1st INF administration. To determine the DNase activity of serum the method of rivanol clot was used. DNase activity was measured in serum samples before 1st INF administration, 6 weeks after the 1st INF administration, at 30 week of treatment.

**Results:** At week 30, ACR70 improvement reached 5/22 of the patients, ACR50 - 9/22 of the patients, ACR20 - 14/22 of the patients. At 30 weeks of treatment INF 2/22 of patients achieved remission (SDAI<3.3), 10/22 - a low disease activity (3.3–SDAI<11). 13/24 patients were ANA-positive before INF treatment, 12/22 - after 24 weeks of treatment.

Levels of serum DNase activity did not differ before and during the INF treatment (p>0.05). For assessment prognostic value of laboratory signs in INF response prediction logistic regression was used. Prognostic model, which included changes in ANA (ΔANA) and DNase serum activity level (ΔDNAse) to INF was applied. Anti-CCP- and RF-negativity was better (p=0.02) (area under ROC-curve =1,0; 95% CI 0,844–1,00 p=0,0001) than the model, which included only anti-CCP- and RF-negativity (area under ROC-curve =0,795; 95% CI 0,597–0,924, p=0,014).

**Conclusions:** The study confirmed the efficacy of RA treatment by INF for anti-CCP- and RF negative patients. DNAse serum activity and ANA may be used as additional prognostic biomarker of INF response. For the assessment DNase activity as marker of response to therapy is needed further investigations with more number of patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6941

**SAT0167**

**CAN INFlixIMAB EFFICACY BE PREDICTED BASED ON BLOOD CONCENTRATION AT THE FOURTH DOSE?**

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**Background:** Biological drugs exhibit excellent efficacy and continuity in the treatment of rheumatoid arthritis (RA) and play an important role in RA treatment. Blood concentration is an important factor in the efficacy of biological drugs, particularly antibody drugs. Infliximab (IFX) is an antibody drug against TNF-α and is required to reach a blood concentration of ≥1 μg/mL to be effective.

**Objectives:** To investigate whether clinical efficacy can be predicted based on blood concentrations at the fourth dose of IFX in patients with RA.

**Methods:** This study included 56 patients with RA who were treated with IFX. Patients included 13 men and 43 women aged from 26 to 81 years (mean: 56.3±14.7 years). The IFX concentration was measured immediately before administering the fourth IFX dose (8 weeks after administering the third dose). We then investigated the relationship between subsequent IFX efficacy and IFX concentration immediately before the fourth dose of IFX in these patients with RA. Concentrations were measured in stored frozen serum by using the ELISA method.

**Results:** The IFX concentration immediately before the fourth dose was ≥1 μg/mL in 32 patients (57.1 μg/mL group) and <1 μg/mL in 24 patients (1.1 μg/mL group). At the fourth dose, IFX was effective in 30 patients (93.8%) in the ≥1 μg/mL group, at a mean concentration of 5.18 μg/mL, while the mean concentration was 5.69 μg/mL for the remaining 2 non-responders. IFX was also effective in 21 patients (87.5%) in the <1 μg/mL group but did not elicit any response in the other 3 patients. At this point, all 5 non-responders patients were primary non-responders, 41.2% were in the ≥1 μg/mL group and 41.2% were in the <1 μg/mL group. Based on the data, we observed no relationship between efficacy and IFX concentration. After 1 year of IFX treatment, 36 of the 56 patients were responsive and 20 were non-responders. In the 2 groups, 26 responsive patients (63.9%) and 9 non-responders (45.0%) had an IFX concentration of ≥1 μg/mL immediately before the fourth dose.

**Conclusions:** At the fourth dose, many of the patients with an IFX concentration of <1 μg/mL were also responsive to the treatment, so future efficacy was difficult to predict based on IFX concentration. In other words, during clinical evaluation, measurement of IFX concentrations is not necessary in responsive patients. However, IFX concentrations should be measured in non-responsive patients or patients with a diminished response. If the concentration is <1 μg/mL, IFX efficacy should be restored by increasing the dose or shortening the administration interval.

**Disclosure of Treatment:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6072

**SAT0168**

**DISCONTINUATION OF FIRST BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS: MAIN CAUSES AND CORRELATION BETWEEN SECONDARY INEFFICACY AND DEVELOPMENT OF IMMUNOGENICITY**

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**Background:** Biologic therapy has been a major change in Rheumatoid Arthritis (RA) prognosis, but around 40% of patients (pts) fail to respond. Part of this treatment failure can be explained by the development of anti-drug antibodies (ADA), but the ADA-associated secondary inefficacies rate is currently unclear.

**Objectives:** To assess in our RA cohort treated with Adalimumab (Ada), Infliximab (Ixfx), etanercept (Entn), certolizumab (Czp), tocilizumab (Tcz) and Abatacept (Abt) as 1st biologic agent, the frequency of drug suspension as well as the main causes for discontinuation and the secondary inefficacy rate associated with the development of immunogenicity.

**Methods:** From the RA cohort that initiated their 1st biologic agent at Hospital La Paz between 2005 and 2016, only those who had suspended their drugs were included, and causes for suspension were collected. Clinical activity was measured by DAS28 and Delta-DAS28 at 6 months of treatment to classify discontinuation by primary or secondary inefficacy. Drug levels (DL) and/or ADA were also measured by ELISA at 6 months since initiating the biologic agent in 43 pts and at drug discontinuation in 59 pts. Primary inefficacy was defined as DAS28≥3.2 and delta-DAS28 <1.2 at 6 months with DL present. Secondary inefficacy was defined as DAS28≥3.2 plus delta-DAS28 <1.2 at 6 months with ADA+. Delta-DAS28≥1.2 or Delta-DAS28 <3.2 at 6 months with subsequent loss of efficacy. Statistical analysis was performed using SPSS version 20.0.

**Results:** From the 246 pts who started their first biologic therapy, 144 (58%) pts who had definitively discontinued were included. [Ixf (n 35, 24%), Ada (n 40, 28%), Entn (n 30, 21%), Czp (n 23, 16%), Tcz (n 10, 7%) y Abt (n 6, 4%)]. 116 (80.6%) were women. The mean age was 56.3±14.7 years. From the global cohort, 18 (12.5%) drop out of the treatment due to primary inefficacy, 41 (28.5%) to secondary inefficacy, 57 (39.6%) to adverse effects (AE), 11 (7.6%) to remission and 17 (11.8%) to other causes (surgery, pregnancy, etc.). 12.5% pts who discontinued due to AE or other causes had also a primary or secondary inefficacy; by including those pts in these last causes for suspension, a total of 20 pts (14%) failed due to primary inefficacy and 57 pts (39.6%) to secondary inefficacy. The most frequent AEs were: infections (35%), cutaneous AEs (psoriasis, rash, etc. (10.5%), infusions reactions (9%) and neoplasia (9%). Of the 59 pts who had DL/ADA measured at drug discontinuation, 42.4% were ADA+. Within the group that failed due to secondary inefficacy and had DL/ADA determined, 50% were ADA+; nevertheless this rate was smaller in suspensions due to other causes. Likewise, in the ADA+ pts, 73% suspended due to secondary inefficacy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6072
discontinuation. These data suggest that the development of ADA is a frequent cause of secondary inefficacy in our RA pts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6371

**SAT0169** MAINTENANCE AND IMPROVEMENT IN CLINICAL EFFICACY BETWEEN WEEK 12 AND 24 IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB4 OR REFERENCE ETANERCEPT

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**Background:** SB4 is approved by the European Commission as a biosimilar of the reference etanercept (ETN).

**Objectives:** To evaluate the maintenance and improvement in clinical efficacy between week 12 and 24 in patients with rheumatoid arthritis (RA) treated with SB4 or ETN from a post-hoc analysis of phase III trials.

**Methods:** Patients with RA were randomised to receive 50 mg/week of either SB4 or ETN with background methotrexate. American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) responses were compared at week 12 and week 24. At week 12, patients w 24 available-case subset results were categorised as ACR responders or ACR non-responders and EULAR responders (patients with moderate or good EULAR response) or EULAR non-responders. The same was assessed for week 24 and patients with missing data at week 24 were regarded as non-responders.

**Results:** A total of 551 patients (283 patients from SB4 and 268 patients from ETN) completed 24 weeks of the study. In both treatment groups, efficacy was well maintained between week 12 and week 24. Among patients who were ACR20, 50, or 70 responders at week 12, 90.8% vs. 91.4%, 80.5% vs. 80.6%, and 74.6% vs. 77.5% of patients from SB4 and ETN, respectively, maintained their responses at week 24. Likewise, EULAR response was maintained by 93.1% vs. 92.6% of patients who had a good or moderate response at week 12. (Table). The improvement in ACR responses between week 12 and 24 was comparable between SB4 and ETN group (Table). In SB4 and ETN, respectively, 42.1% vs. 50.5% of 12-week ACR20 non-responders became ACR20 responders at week 24. Similarly, 20.9% vs. 21.9% of 12-week ACR50 non-responders became ACR50 responders and 13.0% vs. 11.4% of 12-week ACR70 non-responders became ACR70 responders. The improvement in EULAR responses was also comparable between SB4 and ETN. 43.2% vs. 52.2% of 12-week EULAR non-responders in SB4 and ETN, respectively, became EULAR responders at week 24.

**Conclusions:** Efficacy of SB4 and ETN was well maintained and the maintenance rate was comparable between week 12 and week 24. In addition, a similar and considerable proportion of patients in SB4 and ETN who did not achieve a clinical response at week 12 reached clinical response at week 24. These results suggest that etanercept non-responders at week 12 may benefit from continuing treatment up to 24 weeks.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3584

**SAT0170** B-CELL PHENOTYPE AND IGD-CD27- MEMORY B CELLS ARE AFFECTED BY TNF-INHIBITORS AND TOCILIZUMAB TREATMENT IN RHEUMATOID ARTHRITIS

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**Background:** The use of TNF-inhibitors and/or the IL-6 receptor antagonist, tocilizumab, in rheumatoid arthritis (RA) have pleiotropic effects that also involve circulating B-cells.

**Objectives:** The main goal of this study was to assess the effect of TNF-inhibitors and tocilizumab on B-cell phenotype and gene expression in RA.

**Methods:** Blood samples were collected from untreated early RA (ERA) patients (<1 year of disease duration), established RA patients under methotrexate treatment, established RA patients before and after treatment with TNF-inhibitors and tocilizumab, and healthy donors. B-cell subpopulations were characterized by flow cytometry and B-cell gene expression was analyzed by real-time PCR on isolated B-cells. Serum levels of BAFF, CXCL13 and sCD23 were determined by ELISA.

**Results:** The frequency of total CD19+ B-cells in circulation was similar between controls and all RA groups, irrespective of treatment, but double negative (DN) IgD-CD27- memory B-cells were significantly increased in ERA and established RA when compared to controls. Treatment with TNF-inhibitors and tocilizumab restored the frequency of IgD-CD27- B-cells to normal levels, but did not affect other B-cell subpopulations. TACI, CD95, CD5, HLA-DR and TLR9 expression on B-cells significantly increased after treatment with either TNF-inhibitors and/or tocilizumab, but no significant changes were observed in BAFF-R, BCMA, CD69, CD86, CXCR5, CD25, CD38 and IgM expression on B-cells when comparing baseline with post-treatment follow-ups. Alterations in B-cell gene expression of BAFF-R, TACI, TLR9, FcγRIB, BCL-2, BLMIP-1 and p2M were found in ERA and established RA patients, but no significant differences were observed after TNF-inhibitors and tocilizumab treatment when comparing baseline and follow-ups. Serum levels of CXCL13, sCD23 and BAFF were not significantly affected by treatment with TNF-inhibitors and tocilizumab.

**Conclusions:** In RA, treatment with either TNF-inhibitors or tocilizumab affects B-cell phenotype and the frequency of memory B-cell subpopulations in peripheral blood, particularly DN (IgD-CD27-) B-cells, but not B-cell gene expression or serum levels of CXCL13, sCD23 and BAFF, when comparing baseline with post-treatment follow up. Overall, our results suggest that TNF-inhibitors and tocilizumab inhibit B-cell trafficking towards inflammatory sites, thus supporting active B-cell recirculation from tissues through blood and lymphatic systems.

Disclosure of Interest: None declared


**SAT0171** ABP 501 BIOSIMILAR TO ADALUMAB: FINAL SAFETY, IMMUNOGENICITY, AND EFFICACY RESULTS FROM AN OPEN-LABEL EXTENSION STUDY

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**Background:** ABP 501 has been approved by the US FDA as the first biosimilar to the fully human recombinant monoclonal antibody, adalimumab. Totality of evidence to date suggests that ABP 501 is highly similar to adalimumab. Subjects receiving either ABP 501 or adalimumab in the active-controlled, comparative, pivotal phase 3 study in rheumatoid arthritis (parent study) continued on this open-label extension (OLE) study if they had completed the final week 26 visit of that study.

**Objectives:** To describe the safety, immunogenicity, and efficacy outcomes of ABP 501 in the OLE study.

**Methods:** Subjects who completed the parent study were screened and were included if they met the eligibility requirements. All subjects included in the OLE were treated with ABP 501 40 mg subcutaneously every other week for 70 weeks and the follow-up safety assessment at week 72 (or early termination). Data were summarized descriptively and no inferential analyses were performed.

**Results:** Of the 467 subjects enrolled in the OLE study, 466 were treated with ABP 501. Of these, 237 transitioned from the adalimumab arm of the parent study; 412/467 completed the study. Demographics and disease characteristics were balanced between subjects who transitioned from adalimumab and those who continued on ABP 501 from the parent study. Overall, the incidence of treatment-emergent adverse events (TEAEs) was 63.7% (297/466) and that of grade ≥3 TEAEs was 9.0% (42/466); incidence of TEAEs leading to discontinuation of investigational product was 3.6% (17/466). TEAEs with incidence ≥5% were nasopharyngitis (9.2%), upper respiratory tract infection (8.6%), bronchitis (8.4%), rheumatoid arthritis (6.2%), hypertension (4.7%), and pharyngitis (4.1%). The incidence of serious adverse events was 9.9% (46/466). Most common
SAT0172 ECONOMIC OUTCOMES, TREATMENT PATTERNS, AND ADVERSE EVENTS AND REACTIONS FOR PATIENTS PRESCRIBED INFLIXIMAB OR CT-P13 IN THE TURKISH POPULATION

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Background: CT-P13, a biosimilar drug product to infliximab, was approved and marketed in July 2014 in Turkey. There is little information on the costs, treatment discontinuation and adverse events and reactions between patients who switched from infliximab to CT-P13 and patients who continued infliximab.

Objectives: The study objective was to evaluate health care costs, treatment discontinuation, and adverse events and reactions between patients who switched from infliximab to CT-P13 and patients who continued infliximab in the Turkish population.

Methods: Adult patients with ≥1 claim for infliximab or CT-P13 were identified in a Turkish healthcare administrative database representing 80% of the Turkish population during the identification period (16 July 2014–31 Aug 2015). Patients were required to continuously use infliximab for ≥6 months with no hospitalizations. Eligible patients either continued on infliximab (index date: date of first infliximab prescription), or switched from infliximab to CT-P13 (index date: switch date). Patients were excluded if they had ≥1 condition with an indication for infliximab during the baseline period. Patients who switched to CT-P13 were 1:1 matched to patients who continued infliximab based on the length of infliximab use prior to the index date. Demographics and clinical characteristics were measured 12 months pre-index date. Generalized linear models were used to compare adjusted health care costs, continued use was used to evaluate the adjusted risk of discontinuation, and Poisson regression was used to evaluate the adjusted risk of adverse events and reactions.

Results: The study included 1,524 patients, of whom 1,388 were continuous infliximab users and 136 switched to CT-P13. Ankylosing spondylitis and rheumatoid arthritis were the most common conditions indicated for infliximab and CT-P13; however, patients were much less likely to be switched to CT-P13 for other conditions. After adjusting for demographics and clinical characteristics, patients who switched to CT-P13 had higher outpatient ([Turkish lira] TL 289 vs TL 181; p<0.001), inpatient (TL 64 vs TL 29; p=0.313), and pharmacy costs (TL 1,473 vs TL 1,329; p=0.371), which resulted in significantly higher total health care costs (TL 2,209 vs TL 1,640; p=0.046) compared to patients who continued infliximab. Additionally, patients who switched to CT-P13 were more likely to discontinue infliximab users and 13% of patients compared to those who continued infliximab. Of patients who discontinued CT-P13, 79% switched back to infliximab. After adjusting for baseline characteristics, patients who switched to CT-P13 were significantly more likely to discontinue treatment compared to those who continued infliximab (HR=5.53; 95% CI: 4.01–7.63). There was no difference in the incident rate ratio (IRR) between the cohorts for adverse events (IRR=0.67; 95% CI: 0.19–2.30) and reactions (IRR=0.84; 95% CI: 0.55–1.27).

Conclusions: Patients who switched to CT-P13 had significantly higher health care costs and were more likely to discontinue treatment compared to those who continued infliximab. However, there was no difference in the rate of adverse events and reactions.


DOI: 10.1136/annrheumdis-2017-eular.2833

SAT0173 SWITCHING FROM REFERENCE PRODUCT ETANERCEPT TO THE BIOSIMILAR SB4 IN A REAL-LIFE SETTING: FOLLOW-UP OF 147 PATIENTS

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Background: The etanercept biosimilar SB4 was introduced in Sweden in early 2016. SB4 has been shown in a randomized controlled trial to be equivalent to its etanercept reference product (ERP) in terms of efficacy and safety in subjects with active rheumatoid arthritis (RA) (1). In light of this, and the fact that biosimilars offer considerable cost savings, all patients being treated with ERP at our clinic were switched to treatment with SB4 in April 2016.

Objectives: To describe the clinical experiences of switching patients on treatment with ERP to SB4 at our clinic.

Methods: All patients using ERP 50 mg at our clinic were identified using the Swedish Rheumatology Quality Register (SRQ). The patients were issued prescriptions for SB4 50 mg and were sent a letter encouraging them to switch to SB4 when they ran out of ERP. The process of switching was started 21st. However, the actual date of starting treatment with SB4 might have been 0–90 days from April 20th for individual patients, as prescriptions are written in 3 month increments.

Patients were followed up clinically and in the SRQ as planned at the last visit before switching.

Results: A total of 147 RA patients and 136 psoriatic arthritis (PsA) patients from the last visit preceding the switch and the last visit after the switch registered up to January 2017 were collected from the SRQ. The paired T-test was used to compare mean DAS28 before and after switching.

At the end of January 2017, 126 patients (86%) were still on SB4. Since the switch, 9 patients have requested to be switched back to ERP, 2 made the request before initiating treatment with SB4. No objective evidence for lack of efficacy was seen in these 9 patients. Seven patients have stopped treatment with SB4 because of inactive disease. Five patients have been switched to a non-etanercept biologic because of lack of efficacy; these patients also had lack of efficacy when on ERP.

The 76 RA patients had a mean disease duration of 17 years and had been on ERP for a mean duration of 4.7 years. As of January 2017, 60 of the RA patients had been on a follow-up visit and 54 of these had available DAS28 data from both the last visit before and after switching. For the RA patients DAS28 was 2.80 before and 2.79 after switching. p=0.960. Complete DAS28 data was available for 23 of the 28 PsA patients, mean DAS28 was 2.54 before switching and 2.06 after, p<0.161. The mean duration since switching at follow-up was 22 weeks for the RA and PsA patients.

Conclusions: Switching from the etanercept reference product to the biosimilar SB4 was acceptable to most of our patients. Low mean disease activity has been maintained in the RA and PsA group after the switch.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4391

SAT0174 USE OF A 8-WEEK OBSERVATIONAL PERIOD FOR PREDICTING REMISSION AND LOW DISEASE ACTIVITY AT 52 WEEKS IN RA PATIENTS TREATED WITH CERTOLIZUMAB PEGOL – A MULTICENTER STUDY

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Background: Certolizumab pegol (CZP) is a polyethylene glycol (PEGylated Fc-fn new anti-TNFα agent. However few data still reported clinical efficacy of CZP treatment in the routine setting.

Objectives: This study aimed to provide clinical evidence of an adequate observational period for predicting remission and low disease activity (LDA) achievement at 52 weeks in RA patients treated with Certolizumab pegol (CZP).

Methods: Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed CZP from Tsurumi Biomail Communications Registry (TBCR) between May 2013 and October 2015 were enrolled. The final study cohort of 98 Japanese RA patients. We reviewed the methods about the improvement of DAS28-ESR and SDAI which was an index of disease activity of RA using Wilcoxon signed-rank test and the rate of remission and LDA patients at
from IFX to CT-P13 (Switchers cohort; SC) during the identification period; had
continuous medical/pharmacy benefit enrollment ≥120 days after the index date (date of switch for SC and a random IFX prescription
for CC); had a prescription claim for IFX within 16 weeks of the index date
and 12 months after the index date (date of switch for SC and a random IFX prescription
date for CC); had a prescription claim for CT-P13 following availability of CT-P13
(120 days after the index date for SC, and a random IFX prescription date for CC).

Conclusions: This study shows switching from IFX to CT-P13 was infrequent. However, in those switching to CT-P13, a high percentage (82%) of CT-P13
discontinuation was observed and the majority returned to IFX. Further studies
are needed to understand the reasons for these observations.

Disclosure of Interest: Y. Yazici Grant/research support from: Janssen Scientific
Affairs, LLC, L. Xie Consultant for: Janssen Scientific Affairs, LLC, A. Ogborna
Consultant for: Janssen Scientific Affairs, LLC, D. Parenti Employee of: Janssen
Scientific Affairs, LLC, K. Goyal Employee of: Janssen Scientific Affairs, LLC, A. Teeple
Employee of: Janssen Scientific Affairs, LLC, L. Ellis Employee of: Janssen
Scientific Affairs, LLC, I. Simsek Grant/research support from: Janssen Scientific

SAT0176 PATTERNS OF BIOLOGIC DMARD MONOTHERAPY IN A LARGE NATIONWIDE RHEUMATOID ARTHRITIS COHORT: DATA FROM 1036 PATIENTS


Rheumatoid arthritis - other biologic treatment

SAT0175 A DESCRIPTIVE ANALYSIS OF REAL-WORLD TREATMENT PATTERNS IN A TURKISH RHEUMATOLOGY POPULATION


1New York University Hospital for Joint Diseases, New York; 2STATinMED Research Inc, Ann Arbor; 3Janssen Scientific Affairs, LLC, Horsham, United States; 4Guven Hospital, Ankara, Turkey

Objectives: This study examined treatment patterns in a rheumatology patient (pt)
population initially prescribed innovator infliximab (IFX) that either switched to
biosimilar infliximab (CT-P13) or continued on IFX following availability of CT-P13
in the Turkish healthcare system.

Methods: Adult pts with ≥1 diagnosis code (ICD-10-CM M05.X; M06.X) for
rheumatoid arthritis (RA) and a prescription for IFX were identified in a national
Turkish health care database during the study period (01DEC2010-01DEC2015).

Eligible pts were those who continued on IFX (Continuers cohort; CC) or switched

to another biologic with 94% of these returning to IFX.

Conclusions: The new TNF-antagonist therapy of CZP was effective early and
rapidly in patients with active Japanese RA. This study suggested that eight
weeks is an adequate optimal period to judge whether the achieved remission or
not at Week 52.

Disclosure of Interest: Y. Kanayama: None declared, A. Kaneko Speakers bureau:
Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, Chugai Pharma, Abbott,
Bristol-Myers Squibb, UCBS, Janssen, and Pfizer, N. Takahashi Speakers bureau:

SAT0176 PATTERNS OF BIOLOGIC DMARD MONOTHERAPY IN A LARGE NATIONWIDE RHEUMATOID ARTHRITIS COHORT: DATA FROM 1036 PATIENTS


Rheumatoid arthritis - other biologic treatment
Background: There are limited literature data regarding the characteristics of rheumatoid arthritis (RA) patients treated with biologic DMARD (bDMARD) monotherapy.

Objectives: To evaluate the disease and treatment characteristics of RA patients treated with bDMARD monotherapy.

Methods: Multicenter, cross-sectional RA epidemiological study in Greece (06/2015–05/2016, ERE RA Study Group). Demographics, disease characteristics, treatment and co-morbidity data were collected via a web-based platform.

Results: 1036 RA patients treated with bDMARDs were identified during the one year recruitment period (female: 82%, mean age: 61.5±13 years, mean disease duration: 12.5±8.9 years, mean DAS28-ESR: 3.4±5.3). 26% (n=273) were receiving bDMARDs as monotherapy and 8% (n=23) of them had never tried conventional synthetic DMARDs (csDMARDs) before; The latter group (n=23) compared to the csDMARD-exposed (92%, n=250) group, had more often co-morbidities (cardiovascular disease (22% vs. 8%, p=0.029), chronic hepatitis (13% vs. 3%, p<0.001), hypertension (57% vs. 38%, p=0.008), COPD (13% vs. 4.4%, p=0.07)) or were active smokers (41% vs. 14%, p<0.001). csDMARD discontinuation was mainly due to adverse events (AEs) (58%) followed by inadequate response (IR) (44%). Compared to the cs- and b-DMARD combination therapy group, monotherapy treated patients were more frequently seropositive (64% vs. 57%, p<0.005), had lower DAS28-ESR (3.2 vs. 3.5, p=0.009) and were more likely to have discontinued csDMARDs for AEs (58% vs. 21%, p<0.001) or IR (44% vs. 27%, p=0.001). Tocilizumab (22.3% vs. 12.7%, p<0.001) and rituximab (19.8% vs. 13.5%, p<0.03) were utilized more often, whereas adalimumab less often (8.8% vs. 14.8%, p=0.012) as monotherapy compared to as part of combination therapy.

Conclusions: In our large RA cohort, one out of four bDMARD treated patients, were receiving bDMARDs as monotherapy. Co-morbidities rather than RA characteristics influence the initial decision for bDMARD monotherapy whereas among those starting combination cs- and b-DMARD therapy, the majority discontinue csDMARDs due to AEs.

Acknowledgements: Grant support from the Hellenic Rheumatology Society and Professional Association of Rheumatologists.


SAT0177 SAFETY EVENTS ARE SIMILAR WITH ABATACEPT VS PLACEBO TREATMENT IN RA: RESULTS FROM INTEGRATED DATA ANALYSIS FROM NINE CLINICAL TRIALS

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Background: Abatacept is a selective co-stimulation modulator that consists of the extracellular domain of human cytotoxic T lymphocyte-associated antigen-4 linked to the Fc portion of human immunoglobulin G1 and is approved initially for the treatment of RA in 2005. The integrated safety database for abatacept in adult RA comprises data from short- and long-term periods of 16 open-label and double-blind RA clinical trials, and combines studies of both IV and SC abatacept involving 7044 total patients. Of these, data from the 9 double-blind, placebo-controlled studies involving 4138 total patients were included in this analysis. The most recent overall safety analysis was performed in 2012 and reported IV and SC results separately.

Objectives: To provide an update of the overall abatacept safety profile based on data analysis from both IV and SC trials.

Methods: This evaluation included all patients with RA enrolled in 9 key double-blind, placebo-controlled clinical trials of IV and/or SC abatacept. The safety analysis includes all serious adverse events (SAEs), as well as AEs of interest including infections, malignancies and autoimmune diseases.

Results: In total, 2653 patients were exposed to abatacept and 1485 received placebo. During the double-blind, controlled period, the mean (SD) duration of exposure was 10.3 (3.5) months for the placebo group and 10.8 (3.3) months for the abatacept group for a total exposure of 2357 and 1254 patient years, respectively (Table 1). The proportion of patients as well as incidence rates for serious adverse events (SAEs), malignancies and infections were similar in both groups. Table 2 compares AEs and infections in the abatacept and placebo treatment groups.

Conclusion: In a large RA clinical trial database, safety events including deaths, serious infections, opportunistic infections, malignancies and autoimmune diseases occurred at similar frequencies and rates in the abatacept and placebo treatment groups.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4252

THE ASP358ALA VARIANT IN THE IL6R GENE IS SIGNIFICANTLY ASSOCIATED WITH DIFFERENCES IN SOLUBLE IL-6R LEVELS BUT NOT WITH DIFFERENCES IN SARILUMAB RESPONSE IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: Sarilumab is a human mAb that blocks IL-6 from binding to both membrane-bound and soluble IL-6Rs (sIL-6R). A missense variant in the IL6R gene, Asp358Ala (rs2228145), falls within a proteolytic cleavage site and individuals with an alanine at this position have increased sIL-6R in circulation.1 In addition, this variant has been associated with several diseases including RA.2

Objectives: To determine the impact of the Asp358Ala variant on sIL-6R concentrations and response of RA patients to sarilumab.

Methods: DNA was collected from patients enrolled in the MOBILITY study (NCT01061736) that evaluated the efficacy and safety of sarilumab + methotrexate (MTX) in RA patients with inadequate response to MTX. The pharmacogenetic analysis was conducted on 599 Caucasian patients (396 sarilumab 150 or 200 mg q2w + MTX, 203 placebo + MTX).

Results: Concentrations of sIL-6R were strongly associated with the Asp358Ala genotypes at baseline (p=4.2 x 10⁻⁴). The difference in sIL-6R concentrations between genotype groups continued to increase in sarilumab-treated patients through the end of treatment, particularly for the CC genotype (Figure; p=7.8 x 10⁻⁷). There was a modest association for change in sIL-6R in placebo + MTX–treated patients (p=0.0052). Variation in Asp358Ala was not associated with sarilumab efficacy, including mTSS at week 52 and ACR scores (Table).

Conclusions: The Asp358Ala variant in the IL6R gene is significantly associated with differences in sIL-6R levels at baseline and after sarilumab treatment. The differences across genotypes may be due to increases in sIL-6R production. Importantly, this variant was not associated with differences in sarilumab treatment response. These data suggest that the sarilumab doses used for this clinical study saturate both the membrane and soluble forms of IL-6R and effectively block IL-6 signaling. Sarilumab provides therapeutic benefit for RA patients irrespective of their Asp358Ala genotype status.

References:

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.


DOI: 10.1136/annrheumdis-2017-eular.4983

Efficacy and Safety of Sarilumab 200 mg q2w Administered as Combination Therapy or Monotherapy in Different Patient Populations with Active RA

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Background: Sarilumab, a human mAb blocking the IL-6Rα, was evaluated in 3 pivotal clinical trials.

Objectives: To assess efficacy and safety of sarilumab 200 mg q2w + csDMARDs or as monotherapy (MONARCH) in adults with active RA and inadequate response or intolerance to MTX (MOBILITY/MONARCH) or TNFi (TARGET).

Methods: MOBILITY (NCT01061736) was a 52-wk study; TARGET (NCT01709578) and MONARCH (NCT02332590) were 24-wk studies. Patients were randomized to placebo (Pbo) or SC sarilumab 150 or 200 mg q2w + MTX (MOBILITY) or csDMARDs (TARGET), MONARCH patients were randomized to SC monotherapy with adalimumab 40 mg q2w or sarilumab 200 mg q2w. Efficacy endpoints assessed in all 3 studies will be presented.

Results: Within studies, baseline demographic and disease characteristics were similar among treatment groups. Sarilumab 200 mg q2w improved ACR responses, HAQ-DI, DAS28-CRP, and CDAI (Table). Treatment response with sarilumab + csDMARDs was similar in MTX-IR and TNF-IR patients and with sarilumab monotherapy. Incidence of TEAEs and SAEs with sarilumab was more frequent vs Pbo (MOBILITY, TARGET) and similar to adalimumab (MONARCH). The most common TEAEs included infections, neutropenia, and injection site reactions and occurred more often with sarilumab vs Pbo (MOBILITY, TARGET). In MONARCH, rates of infection were similar with sarilumab and adalimumab.

Conclusions: The Asp358Ala variant in the IL6R gene is significantly associated with differences in sIL-6R levels at baseline and after sarilumab treatment. The differences across genotypes may be due to increases in sIL-6R production. Importantly, this variant was not associated with differences in sarilumab treatment response. These data suggest that the sarilumab doses used for this clinical study saturate both the membrane and soluble forms of IL-6R and effectively block IL-6 signaling. Sarilumab provides therapeutic benefit for RA patients irrespective of their Asp358Ala genotype status.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4983
although neutropenia was more frequent with sarilumab. Safety of sarilumab was generally comparable in monotherapy and combination studies; monotherapy was associated with fewer ALT elevations >3×ULN compared with combination therapy: MONARCH, 3%; MOBILITY, 8%; TARGET, 4%.

Conclusions: Sarilumab 200 mg q2w + csDMARDs significantly reduced disease activity compared with placebo in a similar extent regardless of population (MTX-IR or TNF-IR) and as monotherapy. Safety profile of sarilumab was generally comparable across all 3 trials, with monotherapy resulting in fewer ALT elevations.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial assistance was provided by MedThink Scientific Communications. The study was funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Disclosure of Interest: M. Genovese Grant/research support from: Roche, Sanofi, GlaxoSmithKline, R-Pharma, Rhei, and Bristol-Myers Squibb;
Consultant for: Roche, Sanofi, GlaxoSmithKline, R-Pharma, Rhei, and Bristol-Myers Squibb.
R. Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Jansen, Eli Lilly, Merck, Pfizer, Roche, Sanofi, and UCB, Consultant for: AbbVie, Akros, Amgen, AstraZeneca, Bristol-Myers Squibb, Jansen, Eli Lilly, Pfizer, Roche, and UCB, H. van Hoogstraten Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Employee of: Regeneron Pharmaceuticals, Inc, S. Jayawardena Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, G. Burnmester Grant/research support from: AbbVie, Bristol-Myers Squibb, MedImmune, Medtronic, Merck, Pfizer, Roche, and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2017-eular.1275

SAT0181 | LOW DOSE INTERLEUKIN-2 COMBINED WITH TOCILIZUMAB SELECTIVELY INCREASES REGULATORY T CELLS HELPING REFRACTORY RHEUMATOID ARTHRITIS PATIENTS ACHIEVE REMISSION MORE RAPIDLY
Z. Sheng-Xiao1, M. Xiao-Wen2, L. Xiao-Qing3, M. Miao1, W. Xiao-Yan1, R. Hong-Zhong4, W. Caogong, L. Xiao-Feng1. 1. The Second Hospital of Shanxi Medical University, Taiyuan, China

Background: Rheumatoid arthritis (RA) is a prevalent chronic autoimmune inflammatory disease. Its pathogenesis is closely associated with a failure of endogenous immune tolerance that caused by the imbalance of pro-inflammatory T helper 17 (Th17) cells and anti-inflammatory regulatory T (Treg) cells. Low-dose Interleukin-2 (IL-2) has been showed to induce both Th17 and Treg cells expansion and activation while IL-6 antagonist Tocilizumab suppresses the differentiation of Th17, which is expected to control the development of RA.

Objectives: To study the influence of the combination of IL-2 and Tocilizumab on T cells subgroups and their clinical efficacy and safety on refractory RA.

Methods: Total 50 RA patients with low Treg cells, who had been treated with glucocorticoids and DMARDs for over 6 months, were divided into three groups randomly. Patients in non-IL-2 group (n=15) were still given conventional glucocorticoids and DMARDs. Patients in IL-2 group (n=26) were not only given those treatments, but injected subcutaneously human IL-2 (aldesleukin) at 50 WIU per day for 5 days course. Patients in IL-2 and Tocilizumab group (n=9) were not only received the treatment like IL-2 group, but also treated with Tocilizumab at the dosage of 160mg during the day 1 and day 3. The demographic features, clinical manifestations and laboratory indicators were compared before and after the treatment.

Results: There was no difference among all groups in gender, age and course of the disease (p>0.05). The ratios of Th1/Th2 and Th17/Treg were significantly associated with a failure of endogenous immune tolerance that caused by the imbalance of pro-inflammatory Th1 helper 17 (Th17) cells and anti-inflammatory regulatory T (Treg) cells. Low-dose Interleukin-2 (IL-2) has been showed to induce both Th17 and Treg cells expansion and activation while IL-6 antagonist Tocilizumab suppresses the differentiation of Th17, which is expected to control the development of RA.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2351

SAT0182 | SIRUKUMAB LEADS TO SIGNIFICANT AND CLINICALLY MEANINGFUL IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE THAT MEET OR EXCEED NORMATIVE VALUES IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACtory TO TNF INHIBITORS IN POST-HOC ANALYSES OF A PHASE 3 TRIAL
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Background: Patients (pts) with rheumatoid arthritis (RA) experience reduced health-related quality of life (HRQoL). Sarilumab (SIR) is an anti-interleukin-6 (IL-6) monoclonal antibody.

Objectives: These post hoc analyses evaluated improvements over time in HRQoL relative to an age/gender-matched normative population in RA pts with inadequate responses to tumor necrosis factor inhibitors (TNF-IR) from the phase 3 SIRROUND-T trial.

Methods: 878 pts received SIR 50mg every 4 weeks (q4w), SIR 100mg every 2 weeks (q2w), or placebo (pbo) q2w. Health-related physical/emotional well-being were measured at baseline (BL) and Wk 24 by the 36-item Short Form Questionnaire (SF-36), fatigue by Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (FACIT-F), and physical function by Health Assessment Questionnaire-Disability Index (HAQ-DI).

Results: SF-36 physical and mental component summary (PCS and MCS) mean scores at BL for pbo, SIR 50mg q2w, and 100mg q2w indicated substantial impairment (PCS: 33.2, 31.8, and 32.4; MCS: 41.9, 41.2, and 42.1). Significantly greater improvements from BL were reported at Wk 24 with SIR 50mg q4w and 100mg q2w vs pbo in PCS (4.8 and 5.1 vs 1.7) and MCS (3.4 and 4.0 vs 1.1) mean scores (all P<0.001) exceeding the minimum clinically important difference (MCID) of 2.5. Significantly greater least squares mean changes in the 8 SF-36 domain raw scores were reported with both doses of SIR vs pbo at Wk 24: all were >MCID of 5.0 (Table; Figure). More pts receiving SIR 50mg q4w or 100mg q2w reported SF-36 domain scores >normative values (ranges: 11–34% and 13–42%) vs pbo (range: 6–29%). For pbo, SIR 50mg q4w, and SIR 100mg q2w, BL FACIT-F scores were 26.0, 24.2, and 25.2; clinically meaningful improvements >MCID (4 points) were reported by 54.3 and 51.4% of pts receiving SIR 50mg q4w and 100mg q2w vs 33.7% with pbo (P<0.001). Numerically greater percentages of pts reported scores >normative values with both doses of SIR vs pbo (27 and 28% vs 16%). BL HAQ-DI scores were 1.57, 1.65, and 1.61 with pbo, SIR 50mg q4w, and 100mg q2w, and 100mg q2w. Clinically meaningful improvements (change of <0.22) were reported by significantly higher proportions of pts receiving SIR 50mg q4w (52.2%) or 100mg q4w (54.8%) vs pbo (37.4%, P<0.001). Numerically more pts reported HAQ-DI scores >normative values with SIR 50mg q4w and 100mg q2w vs pbo (13 and 16% vs 9%).

Table 1. Improvements in SF-36 Domain Scores at Wk 24 (all P<0.001)

<table>
<thead>
<tr>
<th>Domain</th>
<th>LSM change SIR 50mg q4w</th>
<th>LSM change SIR 100mg q2w</th>
<th>LSM change pbo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical function</td>
<td>9.38</td>
<td>10.75</td>
<td>5.47</td>
</tr>
<tr>
<td>Role-physical</td>
<td>12.85</td>
<td>13.52</td>
<td>5.03</td>
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<td>Bodily pain</td>
<td>17.66</td>
<td>17.51</td>
<td>7.46</td>
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<tr>
<td>General health</td>
<td>6.81</td>
<td>7.76</td>
<td>1.57</td>
</tr>
<tr>
<td>Vitality</td>
<td>10.10</td>
<td>9.68</td>
<td>4.14</td>
</tr>
<tr>
<td>Social function</td>
<td>12.40</td>
<td>11.75</td>
<td>3.68</td>
</tr>
<tr>
<td>Role-emotional</td>
<td>9.29</td>
<td>9.85</td>
<td>0.42</td>
</tr>
<tr>
<td>Mental health</td>
<td>6.73</td>
<td>7.96</td>
<td>2.10</td>
</tr>
</tbody>
</table>

LSM, least squares mean.

Conclusions: In TNF-IR RA pts, SIR treatment resulted in greater and clinically meaningful improvements in HRQoL vs pbo that met or exceeded population normative values, with similar results for SIR 50mg q4w and 100mg q2w.

Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, Biogenidec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK,
SAT0183 CLINICAL REMISSION IN SUBJECTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE OR OTHER SYNTHEtic DMARDs: A REAL-WORLD CLINICAL TRIAL (TOSPACE)

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DOI: 10.1136/annrheumdis-2017-eular.3904

Background: Subcutaneous tocilizumab (TCZ-SC) has demonstrated non-inferiority to TCZ-IV and superiority to placebo

Objectives: The primary objective of this study was to assess the 24-week efficacy and safety of subcutaneous (SC) tocilizumab (TCZ) 162 mg weekly (qw) or every 2 weeks (q2w) as monotherapy or in combination with methotrexate (MTX) or other synthetic (s) DMARDs in patients with active rheumatoid arthritis (RA) in the real world setting

Methods: This multinational (Spain, Ireland, Portugal), multicenter, phase IIIb study. Subjects ≥18 years of age with active RA (DAS 28-ESR < 3.2) who have had inadequate response or intolerance to sDMARDs or to a first anti-TNF drug. The study comprised a phase 1 with open-label design in which patients received TCZ-SC 162 mg qw (+/- oral/SC MTX or other sDMARDs) for 24-weeks and the main outcome was the percentage of patients achieving sustained clinical remission (DAS 28-ESR <2.6) at Week 20 and Week 24 (primary outcome of the study); and a phase 2 where patients achieving sustained clinical remission during the phase 1 were randomized to receive TCZ-SC 162 mg qw or TCZ-SC 162 mg q2w (+/- oral/SC MTX or other sDMARDs) for an additional 24 weeks; the main outcome of the phase 2 was the percentage of patients who maintained the remission at week 48 (i.e. DAS 28-ESR <2.6)

Results: 401 patients were included in the phase 1, 74 patients received TCZ-SC monotherapy and 327 patients received TCZ-SC in combination with oral/SC MTX or other sDMARDs. Sustained clinical remission rates were comparable between the mono- and combination-therapy groups at 24 week (48.4% vs. 52.9%, p=0.523). Of the 179 patients who achieved sustained clinical remission during the phase 1, 89 were randomly assigned to receive TCZ-SC 162 mg qw and 90 to receive TCZ-SC 162 mg q2w. At the end of phase 2, the percentage of patients who maintained the remission at week 48 was 91.5% with TCZ-SC qw and 73.9% with TCZ-SC q2w (p=0.002). Main efficacy outcomes for both phases of the study are presented in the table. Rates of serious adverse events (AEs) and rates of AEs leading to drug discontinuation were similar in patients treated with mono or combination therapy, and in patients treated with TCZ-SC qw or TCZ-SC q2w.

Conclusions: In the real-world setting, treatment with TCZ-SC 162 mg qw weekly in patients with active RA is associated with rate of sustained clinical remission of approximately 50% regardless it is administered as monotherapy or in combination with a sDMARD. The proportion of patients who remained in clinical remission at week 48 was significantly higher with TCZ-SC qw than with TCZ-SC q2w. The safety profile of TCZ-SC was consistent with previous studies of TCZ-SC and TCZ-IV

Disclosure of Interest: R. Sanmartín Grant/research support from: Roche, E. Martín Molá Grant/research support from: Roche, J. Fonseca Grant/research support from: Roche, D. Veale Grant/research support from: Roche, A. Escudero Grant/research support from: Roche, C. González Grant/research support from: Roche

DOI: 10.1136/annrheumdis-2017-eular.4518
SAT0185  BIO-HOLIDAY THERAPY WITH A TIGHT CONTROL STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS WITH CLINICAL DISEASE ACTIVITY INDEX REMISSION ENABLES MAINTENANCE OF BONE METABOLISM STATUS

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Background: The cost of Bio therapy has become a major problem in health economics and is unaffordable for some patients. Thus, it is important to consider whether we should discontinue or extend the interval of Bio. At EULAR 2016, we reported that, if disease activity (DA), radiographic progression, and biochemical function via Bio-holiday therapy in rheumatoid arthritis (RA) patients with clinical disease activity index (CDAI) remission under a tight control strategy is possible. Osteoporosis is another issue for RA patients. RA patients generally develop osteoporosis more frequently than healthy individuals because of increased bone resorption and inhibited bone formation.

Methods: To investigate bone metabolism markers and bone mass index of RA patients with CDAI remission who underwent Bio-holiday therapy. Methods: Sixty-four RA patients with CDAI remission were included and were classified into two groups. Bio-holiday group (group H) comprised 34 patients (golimumab (GLM) and tocilizumab (TCZ), 18 and 16 patients, respectively) and in which patients were taken off Bio if they achieved CDAI remission. Patients were classified into 3 groups: 1) those who achieved CDAI remission maintained their therapy because of adverse events. Besides one patient who dropped out because of RA flare-up, no patients in either group discontinued their therapy because of financial constraints in the in the groups H and C, respectively. One patient in each group dropped out because of RA flare-up. No patients in either group discontinued their therapy because of adverse events. Besides one patient who dropped out because of RA flare-up, all remaining patients in the group H were able to achieve CDAI remission without delay. There were no statistical differences in the change in bone metabolism makers [urine type I collagen cross-linked N-telopeptide (NTX), serum tartrate-resistant acid phosphatase 5b (TRACP5b), serum bone-specific alkaline phosphatase (BAP), and serum osteocalcin (OC)] and bone mineral density (BMD) of lumbar spine (L-spine) and femoral neck (FN) between both groups for 2 years.

Results: The mean withdrawal periods were 12.1 and 8.8 months with GLM and TCZ, respectively. Three and four patients dropped out because of financial constraints in the in the groups H and C, respectively. One patient in each group dropped out because of RA flare-up. No patients in either group discontinued their therapy because of adverse events. Besides one patient who dropped out because of RA flare-up, all remaining patients in the group H were able to achieve CDAI remission without delay. There were no statistical differences in the change in bone metabolism makers [urine type I collagen cross-linked N-telopeptide (NTX), serum tartrate-resistant acid phosphatase 5b (TRACP5b), serum bone-specific alkaline phosphatase (BAP), and serum osteocalcin (OC)] and bone mineral density (BMD) of lumbar spine (L-spine) and femoral neck (FN) between both groups for 2 years.

Conclusions: We conclude that maintaining disease activity bone metabolism status via Bio-holiday therapy for RA patients with CDAI remission under a tight control strategy is possible. Given that the flare-up rate in RA patients with deep remission is not high, it is not difficult to resume Bio therapy and gain CDAI remission. Furthermore, this treatment is financially durable. Therefore, we recommend Bio-holiday therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2088

SAT0186  EFFECTS OF DENOSUMAB, A SUBCUTANEOUS RANK INHIBITOR, ON THE PROGRESSION OF STRUCTURAL DAMAGE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH csDMARD: RESULTS FROM THE 12-MONTH DOUBLE BLIND PHASE 3, DESIRABLE STUDY

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Background: Denosumab is a fully human monoclonal antibody (IgG2 subclass) that inhibits bone resorption and inhibiting RANKL, a key mediator of osteoclast formation, function, and survival.

Methods: Denosumab (60 mg every 6 months (Q6M)) was compared with placebo (PBO) in a 12-month, randomized, double-blind, placebo-controlled, parallel-group study in RA patients receiving csDMARD treatment. Subjects fulfilling the 1987 ACR criteria or 2010 ACR-EULAR criteria were randomized (1:1:1) to denosumab 60 mg Q6M, denosumab 60 mg Q3M, or placebo. The primary endpoint is the change in mTSS between baseline and 12 months in the value of patients modified total Sharp score (mTSS). Radiographs of hands and feet at baseline, 6 months and 12 months were scored with blinded time order by 2 readers independently. Average score of the 2 readers was used for the analysis. Comparisons of each denosumab group with placebo for the change from baseline were performed using van Elteren stratified rank test adjusting for baseline glucocorticoid use. Missing scores were imputed using linear extrapolation/interpolation.

Results: Among 679 patients randomized, 667 (placebo, n=223; Q6M, n=222; Q3M, n=222) received at least one dose of study drug, and 60 (placebo n=15; Q6M, n=23; Q3M, n=22) were withdrawn during the study. Demographic and baseline characteristics were similar across the groups (Table 1). Mean change from baseline in mTSS and erosion score (ES) at 12 months was significantly lower with both denosumab 60 mg Q6M and Q3M compared with placebo, with no obvious evidence of an effect on joint space narrowing (JSN) score for denosumab (Table 2).

Consistently, the percent of nonprogressors (ie, mTSS change ≤0.5) at 12 months was significantly greater with denosumab 60 mg Q6M (75.6%, p=0.010) and Q3M (78.1%, p=0.001) compared with placebo (64.2%). Incidence of adverse events (AEs), serious AEs, and AEs leading to discontinuation of study drug were similar across treatment groups. No events of osteonecrosis of the jaw or atypical femoral fracture were observed.

Table 1. Baseline demographics and characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>Q6M</th>
<th>Q3M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>593 (86)</td>
<td>197 (77.4)</td>
<td>252 (77.3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.0 (11.7)</td>
<td>60.5 (12.3)</td>
<td>61.2 (12.0)</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>2.1 ± 1.3</td>
<td>2.2 ± 1.3</td>
<td>2.2 ± 1.3</td>
</tr>
<tr>
<td>Rheumatoid factor positive</td>
<td>137 (48.2)</td>
<td>140 (46.5)</td>
<td>128 (38.4)</td>
</tr>
<tr>
<td>MTX use</td>
<td>190 (77.1)</td>
<td>176 (78.1)</td>
<td>189 (58.3)</td>
</tr>
<tr>
<td>Glucocorticoid use</td>
<td>60 (21.7)</td>
<td>73 (33.6)</td>
<td>68 (31.1)</td>
</tr>
<tr>
<td>DAS28-4CRP</td>
<td>3.4 ± 1.0</td>
<td>3.6 ± 1.1</td>
<td>3.6 ± 1.0</td>
</tr>
<tr>
<td>mTSS</td>
<td>13.1 ± 21.4</td>
<td>15.9 ± 22.2</td>
<td>15.2 ± 19.0</td>
</tr>
</tbody>
</table>

Data presented are Mean ± SD or n (%)

Table 2. Change from baseline in mTSS, ES and JSN at 12 months

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>Q6M</th>
<th>Q3M</th>
</tr>
</thead>
<tbody>
<tr>
<td>mTSS</td>
<td>1.40 ± 3.76</td>
<td>0.98 ± 3.77 (p = 0.004)</td>
<td>0.72 ± 3.32 (p = 0.034)</td>
</tr>
<tr>
<td>Erosion score</td>
<td>0.96 ± 2.48</td>
<td>0.51 ± 2.10 (p = 0.013)</td>
<td>0.22 ± 0.95 (p &lt; 0.001)</td>
</tr>
<tr>
<td>JSN score</td>
<td>0.51 ± 1.72</td>
<td>0.48 ± 2.08 (p = 0.287)</td>
<td>0.50 ± 1.76 (p = 0.632)</td>
</tr>
</tbody>
</table>

Data presented are Mean ± SD

Conclusions: Denosumab inhibited the progression of joint destruction significantly more than placebo and was generally well tolerated in Japanese patients with RA on csDMARDs. Denosumab has potential Utility as a new therapeutic option to inhibit structural progression for patients with RA.


DOI: 10.1136/annrheumdis-2017-eular.1208

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SAFETY, PHARMACOKINETICS AND EFFICACY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN A FIRST-IN-PATIENT PHASE 1/2 STUDY IN RHEUMATOID ARTHRITIS; ADDITIONAL DATA OF 400 MG COHORT


Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. Accumulating evidence is telling that FKN–CX3CR1 axis plays a pivotal role in leukocyte/lymphocyte accumulation in inflamed tissues in RA1. Last year, we presented an interim report (up to 200 mg cohort) of Phase 1/2 study [1].

Objectives: To evaluate safety, pharmacokinetics and efficacy of E6011 with the dosage up to 400 mg in a Phase 1/2, open-label, multiple ascending dose study in RA patients (n=18) (NCT02196558).

Methods: Active RA patients with inadequate response (IR) to MTX or TNF inhibitors (TNFi) were received 7 consecutive doses (subcutaneous) of E6011 at week 0, 1, 2 and thereafter every 2 weeks up to week 10. The safety, pharmacokinetics and efficacy up to week 12 were evaluated.

Results: Twelve, 15 and 10 subjects were enrolled in the cohort of 100, 200 and 400 mg dosage, respectively, in total 37 subjects received repeated subcutaneous (SC) administrations of E6011. As a result, repeated dose of E6011 was found safe and well tolerated. The incidence of adverse event (AE), treatment-related AE and serious AE were 56.8%, 29.7% and 5.4%, respectively. AEs occurring in ≥2 subjects were nasopharyngitis, injection site erythema, headache and oropharyngeal pain, among which there were no severe AEs, serious infections and deaths. No significant differences were observed in the incidence or severity of AEs across the cohorts.

After starting multiple SC injection of E6011, serum E6011 concentration reached steady-state at week 2, and its level was maintained up to week 12 in all cohorts. Clinical outcome was also available in the study in which response rates of ACR20, 50 and 70 at week 12 were evaluated. The percentage of patients categorized “good response” with the EULAR response criteria at week 12 (NRI) were 16.7% in 100 mg cohort, 20% in 200 mg cohort and 40% in 400 mg cohort.

Conclusions: E6011 was safe and well tolerated, and the study demonstrated a promising efficacy of E6011 in active RA patients with MTX- or TNFi-IR. The results obtained suggest that a novel approach to target FKN/CX3CR1 interaction will be clinically beneficial for RA, and support to conduct phase 2 clinical trials in which the efficacy and safety should be confirmed in a placebo controlled double-blind manner.

References:

SAT0188 FIRST-LINE TREATMENT PATTERNS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY POSITIVE VersUS NEGATIVE

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Background: Patients with RA who are at a higher risk for progressive and destructive arthritis could be identified using anti-cyclic citrullinated peptide antibodies (anti-CCP) levels. Treatment guidelines recommend the use of non-biologic DMARDs as initial treatment in RA; but, if warranted, biologic (b)DMARDs could be considered in early treatment of RA. Real-world data describing treatment patterns based on anti-CCP designations are limited.

Objectives: This study evaluated treatment patterns of patients with RA who are anti-CCP positive (+) or negative (−).

Methods: This retrospective study was based on electronic medical record (EMR) data with a supplemental chart review from a large integrated delivery system. Patients newly diagnosed with RA (International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis code 714.0) were identified between 1 January 2009 and 31 December 2014. The first RA diagnosis date was designated as the index date. Patients were required to have 12 months of continuous activity in the EMR (6 months pre- and 6 months post-index). Based on the baseline anti-CCP test results, patients were categorized as anti-CCP+ (>7.0 U) or anti-CCP− (<7.0 U). First-line therapy (time to treatment initiation, treatment change, treatment change, treatment changes and response to treatment) was evaluated in the post-index period. Response to treatment was determined based on physicians’ notes.

Results: Overall, 217 anti-CCP+ and 191 anti-CCP− patients with RA were included in this study. A higher proportion of anti-CCP+ (153, 70.5%) than anti-CCP− patients (44, 23.0%; p=0.0001) initiated treatment, generally within 1 month after diagnosis (anti-CCP+, mean [SD]: 31.1 [42.1] days and anti-CCP−, 28.1 [37.4] days; p=0.6538). MTX was most commonly used as first-line therapy. More anti-CCP+ than anti-CCP− patients received MTX (73.2 vs 56.8%; p=0.0374), while more anti-CCP– than anti-CCP+ patients received hydroxychloroquine (48 vs 13.1%; p=0.0037). Only three anti-CCP+ and no anti-CCP− patients were treated with a bDMARD. Response to treatment was similar between the cohorts (p=0.2444); 22.9% of anti-CCP+ and 18.2% of anti-CCP− patients had a complete response to the first-line therapy, and 33.3% of anti-CCP+ and 25.0% of anti-CCP− patients had a partial response to the first-line therapy. Treatment change, however, significantly differed between the two cohorts (p=0.0058); 11.1 and 9.1% of patients discontinued, 9.8 and 9.1% of patients switched, and 3.9 and 9.1% of patients augmented in the anti-CCP+ and anti-CCP− cohorts, respectively. Treatment changes occurred approximately 3 months after diagnosis (anti-CCP+, 82.0 [49.7] days and anti-CCP−, 83.8 [52.7] days; p=0.9178).

Conclusions: After diagnosis of RA, patients who are anti-CCP+ were more likely to start therapy, indicating that physicians were more aggressive in treating this cohort. Patients were treated according to guidelines with non-biologic DMARDs, predominantly MTX. Patterns of treatment change differed between the cohorts; however, treatment response was similar with a complete response rate of 20%.

SAT0189 | FACTORS INFLUENCING THE PRESCRIPTION OF TOCILIZUMAB ALONE OR IN COMBINATION WITH DMARDs IN RHEUMATOID ARTHRITIS PATIENTS IN A REAL LIFE SETTING. POOLING ANALYSIS OF 3 OBSERVATIONAL STUDIES

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Background: Tocilizumab (TCZ) as monotherapy (Mono) is nowadays a standard treatment in rheumatoid arthritis (RA) for patients in whom methotrexate (MTX) is inappropriate.

Objectives: To describe factors influencing the use of TCZ in Mono or in combination with DMARDs (Combo) in real-life practice in RA patients (pts).

Methods: Analysis: pooled data of 3 prospective, multicentre, observational studies (PEPS n=610, Spare-1 n=307, Act-solo n=577). Patients: RA pts requiring TCZ treatment according to their physician. Treatment: TCZ as prescribed in real life. Endpoint: Evaluation of factors influencing the use of TCZ in Mono or in Combo. Results: The baseline characteristics and the different mechanisms of clinical and antidestructive effects of anti-B-cell therapies are often discussed. The aim of this study is to assess clinical and antidestructive effect of Rituximab (RTX) in patients with rheumatoid arthritis (RA). Objectives: to assess clinical and antidestructive effect of Rituximab (RTX) in patients with rheumatoid arthritis (RA). Methods: 108 patients (pts) with RA, most of them were middle-age women with high disease activity (mean DAS28 6.1±1.04, RF-positive 77%, ACCP-positive 83%) treated with RTX (1000 mgx2 or 500 mgx2). Clinical effect was evaluated by EULAR criteria; radiological progression by SLE data. Results: 104 patients were treated by RTX (500 x2 or 1000 x2), had good response: after 48 week of treatment clinical improvement was achieved in 65% pts, good and moderate response by EULAR criteria in 23% and 42% pts accordingly. Noteworthy, after 12 months of treatment RTX radiological progression was absent in 50% pts with high disease activity.

Conclusions: RTX treatment slowed joint damage without clinical improvement. Clinical and antidestructive results did not always coincide which suggests different mechanisms of clinical and antidestructive effects of anti-B-cell therapy.
Germansprachspraxis, Magdeburg; 8 Rheumatologie, Chugai Pharma Europe Ltd., Frankfurt; 9 Rheumatologie, Roche Pharma AG, Grenzach-Wyhlen; 10 Rheumatologie/Immunologie der Medizinischen Klinik und Poliklinik II, Universitätsklinikum Wuerzburg, Wuerzburg; 11 Rheumapraxis, Osnabrueck, Germany

Background: According to WHO definition approximately 15% of all patients with rheumatoid arthritis (RA) suffer from anaemia (hemoglobin <13 g/dl for men and <12 g/dl for women). Interleukin 6 (IL-6) takes an active part in the pathogenesis of this inflammatory anaemia.

Objectives: The 6th interim analysis of the non-interventional ICHIBAN study (NCT01194401) evaluated the occurrence of inflammatory anaemia, characterized the patient population with anaemia, and observed the response during intravenous Tocilizumab therapy (TCZ i.v.). Patients were subgrouped according to their anemic/non-anemic status at baseline.

Methods: Since 2010 the ICHIBAN study collects clinical data of the routine use of TCZ i.v. in RA patients. The observation period for each patient is up to two years. At the due date of the current interim analysis (Dec 10, 2015) 2999 patients were enrolled. 902 patients have completed the maximal 104 weeks observation period (Group W104).

Results: At baseline, the proportion of patients with anaemia (acc. to WHO definition) was 21.4% (men) and 22.0% (women) in the group W104. On comparison, RA patients with anaemia showed, amongst others, increased inflammation parameters, a higher disease activity and higher rates of comorbidities. Already after 4 weeks with TCZ i.v. the proportion of patients with anaemia improved to 12.1% (men) and 12.7% (women). After 104 weeks therapy the proportion of patients with anaemia reduced further to 7.4% (men) and 8.4% (women). The relevant response parameters and laboratory values are shown in Table 1.

Conclusion: Despite the higher disease activity at baseline for anaemic patients, the benefit was comparable for patients with and without anaemia. DAS28-ESR values decreased on average by 2.9 (women) and 3.1 (men) in RA patients with anaemia and by 2.7 (women) and 2.8 (men) in RA patients without, resulting in similar disease scores at the end of the observational period.

The effectiveness of TCZ i.v. was also confirmed by patient reported outcomes (PROs) via visual analogue scales (VAS). In particular, a reduction of the intensity of pain (<50%) and a reduction of fatigue (<38%) was observed (Table 1).

Table 1. Treatment response to TCZ in anaemic patients (at baseline)

<table>
<thead>
<tr>
<th>Gene</th>
<th>% Anemia</th>
<th>Week 0 (Baseline)</th>
<th>Last visit with TCZ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>male</td>
<td>female</td>
<td>male</td>
</tr>
<tr>
<td>Thrombomodulin</td>
<td>21.4%</td>
<td>22.0%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Hemoglobin [g/dl]</td>
<td>12.2</td>
<td>13.8</td>
<td>12.2</td>
</tr>
<tr>
<td>Median [G, Q3]</td>
<td>13.1</td>
<td>12.7</td>
<td>12.9</td>
</tr>
<tr>
<td>Erythrocytes [10^12]/l</td>
<td>4.5</td>
<td>4.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Median [G, Q3]</td>
<td>4.1</td>
<td>4.2</td>
<td>4.2</td>
</tr>
<tr>
<td>CRP [mg/l]</td>
<td>42.1</td>
<td>7.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Median [G, Q3]</td>
<td>30.6</td>
<td>3.1</td>
<td>3.1</td>
</tr>
<tr>
<td>ESR [mm/h]</td>
<td>40.5</td>
<td>4.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Median [G, Q3]</td>
<td>42.6</td>
<td>4.0</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Conclusions: At start of therapy, approximately one out of five patients documented in ICHIBAN showed anaemia according to the WHO definition. During TCZ i.v. therapy a noticeable decrease in the rate of anaemia and improved hemoglobin values were observed. These effects can already been seen after four weeks of treatment and continue up to the end of this study (i.e. 2 years). Despite the higher burden of disease at baseline in RA patients with anaemia, TCZ i.v. therapy resulted in good clinical response rates and PROs.

Acknowledgements: We would like to thank all patients, their families, the investigators and the nurses who participated in this trial. This research was funded by Roche Pharma AG, Germany, and Chugai Pharma Europe Ltd., Germany. Support for third-party writing assistance for this abstract presentation.
SIRUKUMAB INTEGRATED SAFETY IN RHEUMATOID ARTHRITIS PATIENTS: ANALYSIS OF THE SIRROUND PHASE 3 DATA

D. Aletaha 1, C. Thorne 2, M. Schiff 3, M. Harigai 4, R. Rao 5, N. Goldstein 6, B. Cheng 6, C. Cohen 1, B. Hsu 6, K. Brown 1, 1Medical University of Vienna, Vienna, Austria; 2University of Toronto and Southlake Regional Health Centre, Newmarket, ON, Canada; 3University of Colorado School of Medicine, Denver, CO, United States; 4Tokyo Women’s Medical University, Tokyo, Japan; 5GSK Medicines Research Centre, Hertfordshire, United Kingdom; 6Janssen Research & Development, LLC, Spring House, PA; 7GlaxoSmithKline, Collegeville, PA, United States

Background: Sirukumab (SIR), a human monoclonal antibody that selectively binds the IL-6 cytokine, is in development for the treatment of rheumatoid arthritis (RA). Efficacy of SIR was shown in several phase 3 trials in RA patients (pts; SIRROUND program).

Objectives: To analyze safety data from completed/ongoing studies in the SIRROUND program.

Methods: Safety comparisons included SIR 50mg q4w and 100mg q2w doses vs placebo (pbo) in the pbo-controlled period (Wk 0–18) of 2 phase 3 studies. A long-term comparison of the safety of SIR 50mg q4w and 100mg q2w for the entire program was also performed.

Results: In phase 3 studies, 2026 pts received SIR for up to 3.4y (median duration, 1.46y). During Wk 0–18, there were more adverse events (AEs), AEs leading to discontinuation, and serious AEs (SAEs) with SIR vs pbo, with cumulative rates of SAEs remaining constant over time (Table). In general, no dose effect with SIR was observed in the 18-wk or long-term analysis. Mortality rates were similar across treatment groups through 18 wks and remained stable in long-term analysis. Serious infections were more frequent in SIR-treated pts vs pbo during Wk 0–18, with similar rates through long-term analysis. Rates of gastrointestinal (GI) perforations and malignancies were low and similar across groups during the 18-wk and long-term analysis; major adverse cardiovascular event (MACE) rates were similar through 18 wks and numerically higher with SIR 50mg q4w vs 100mg q2w in long-term analysis.

Conclusions: SIR is well tolerated in pts with moderately to severely active RA. Overall, no dose relationship was observed between SIR 50mg q4w and 100mg q2w for types or frequencies of AEs.

D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, C. Thorne Grant/research support from: AbbVie, Boehringer, Speakers bureau: AbbVie, Celgene, Chugai, Euroimmun, MSD, Pfizer, UCB, H. Kellner; None declared, P. Kästner; None declared, C. Volberg; None declared, V. Brauneuwel; None declared, I. Schwarze; None declared, M. Aringer: None declared, M. Sieburg; None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., Zweigniederlassung Deutschland, J. Flacke Employee of: Roche Pharma AG, Germany, H.-P. Tony Consultant for: Roche Pharma, AbbVie, BMS, Chugai, Janssen, Novartis, Pfizer, Sanofi, Lilly, MSD, Astra-Zeneca, G. Fliedner: None declared


SAT0195 RITUXIMAB SHOWS BETTER SUSTAINABILITY THAN TNF INHIBITORS WHEN USED FOLLOWING INITIAL BIOLOGIC DMARD FAILURE IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF REAL-WORLD OBSERVATIONS FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

D. Chouquette 1, L. Bessette 2, B. Harauzi 1, F. Massicotte 1, J.-P. Pelletier 5, J.-P. Raynauld 1, M.-A. Rémillard 1, D. Sauvageau 1, É. Villeneuve 1, 1 – Table 1. Treatment-emergent AEs in Phase 3 Studies

<table>
<thead>
<tr>
<th>Wk 0–18</th>
<th>Long-term analysis (Wk 0-safety cutoff)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE, n (%)</td>
<td>AE, n (%)</td>
</tr>
<tr>
<td>Pbo (N=850)</td>
<td>SIR 50mg q4w (N=848)</td>
</tr>
<tr>
<td>AEs, n (%)</td>
<td>444 (52.2)</td>
</tr>
<tr>
<td>AEs leading to discontinuation, n (%)</td>
<td>22 (2.6)</td>
</tr>
<tr>
<td>SAEs, n (%)</td>
<td>27 (3.2)</td>
</tr>
<tr>
<td>Serious infection, n (%)</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Incidence</td>
<td>2.40 (1.97–4.95)</td>
</tr>
<tr>
<td>GI perforation, n (%)</td>
<td>0</td>
</tr>
<tr>
<td>Incidence*</td>
<td>0 (0.01–0.19)</td>
</tr>
<tr>
<td>Malignancy, n (%)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.68 (0.08–2.47)</td>
</tr>
<tr>
<td>Incidence</td>
<td>0 (0.01–1.91)</td>
</tr>
</tbody>
</table>

*Incidence per 100 pt-years (95% CI).

Abstract SAT0196 – Table 1. First bDMARD history and Retention Characteristics of Second bDMARD used

<table>
<thead>
<tr>
<th>First bDMARD Failed</th>
<th>Second bDMARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFi</td>
<td>Rituximab</td>
</tr>
<tr>
<td>Failure type</td>
<td>All</td>
</tr>
<tr>
<td>Primary</td>
<td>Secondary</td>
</tr>
<tr>
<td>6 Months</td>
<td>120 (75.4%)</td>
</tr>
<tr>
<td>Other mode of action</td>
<td>72 (81.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>147 (75.8%)</td>
</tr>
</tbody>
</table>

Second bDMARD Retention Probability at:

<table>
<thead>
<tr>
<th>Time</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months</td>
<td>64.68% (3.45%)</td>
</tr>
<tr>
<td>12 Months</td>
<td>50.54% (3.61%)</td>
</tr>
<tr>
<td>24 Months</td>
<td>39.77% (4.97%)</td>
</tr>
<tr>
<td>60 Months</td>
<td>22.26% (3.53%)</td>
</tr>
<tr>
<td>96 Months</td>
<td>13.22% (3.62%)</td>
</tr>
</tbody>
</table>

Biology Retention Time (years)

| Mean, mean (SE) | 2.71 (0.25) |
| Lower Quartile, (95% CI) | 0.36 (0.28–0.44) |
| Median, (85% CI) | 1.08 (0.71–1.60) |
| Upper Quartile, (95% CI) | 4.26 (3.53–6.64) |

DOI: 10.1136/annrheumdis-2017-eular.5767

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was provided by Roche and Chugai and performed by Ecron Acunova GmbH, Germany.

Disclosure of Interest: C. Specker Grant/research support from: Chugai, DRFZ, Consultant for: Abbvie, Janssen, Chugai, MSD, Novartis, UCB, Lilly, Boehringer. Speakers bureau: Abbvie, Celgene, Chugai, Euroimmun, MSD, Pfizer, UCB, H. Kellner; None declared, P. Kästner; None declared, C. Volberg; None declared, V. Brauneuwel: None declared, I. Schwarze: None declared, M. Aringer: None declared, M. Sieburg: None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., Zweigniederlassung Deutschland, J. Flacke Employee of: Roche Pharma AG, Germany, H.-P. Tony Consultant for: Roche Pharma, AbbVie, BMS, Chugai, Janssen, Novartis, Pfizer, Sanofi, Lilly, MSD, Astra-Zeneca, G. Fliedner: None declared

but recent registry data point to better responses and retention if a drug with a different mode of action is prescribed.

**Objectives:** Assess the long-term retention of rituximab (RTX) and TNFi following first biologic (b)DMARD inadequate response in RHUMADATA® registry patients (pts) with RA.

**Methods:** Data from RHUMADATA® pts with RA prescribed either RTX or TNFi as the second bDMARD after 1 January 2006 were analysed. Pts were followed until treatment discontinuation or 9 January 2017 cut-off. Pt characteristics were compared using descriptive statistics, bDMARD discontinuation rates using Kaplan-Meier methods, and proportional hazard models were used to identify predictors of treatment discontinuation.

**Results:** Data for 53 and 194 pts prescribed RTX or a TNFi, respectively, as second-line treatment were extracted. No clinically significant differences in baseline characteristics were noted between treatment groups. Most pts were women (74.9%), average age (SD) was 45.2 (12.9) years at diagnosis and disease duration 10.5 (8.7) years. Most pts were stopping an anti-TNF agent: 100% of those who were switched to RTX and 83% of those who were prescribed a second anti-TNF. Overall, 77.3% of pts stopped their first bDMARD after >6 months of treatment (secondary failure). Significant differences in retention between RTX and TNFi groups (log-rank p< 0.001) were observed (Table, Figure). Results remained unchanged for pts treated with TNFi only in first line, and primary/secondary failure of the first bDMARD did not affect sustainability of the second agent. Lack of efficacy (54.4%) and AE’s (16.5%) were the most commonly cited reasons for treatment discontinuation.

**Conclusions:** Rituximab has better sustainability over a second line TNFi in RA patients having failed one prior bDMARD.

**Disclosure of Interest:** D. Choquette Grant/research support from: Roche, Consultant for: Roche, L. Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, B. Harouci Grant/research support from: BMS, Janssen, Roche, Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, Speakers bureau: Pfizer, UCB, F. Massicot: None declared, J.-P. Pelletier: None declared, J.-P. Raynaud Speakers bureau: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, Sanofi, UCB, M.-A. Rémillard: None declared, D. Sauvageau: None declared, A. Turcotte Consultant for: Abbgen, AbbVie, BMS, Celgene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, E. Villeneuve Consultant for: Celgene, Celzima, Pfizer, Speakers bureau: AbbVie, Roche, BMS, L. Coupal: None declared.

DOI: 10.1136/annrheumdis-2017-eular.1752

**SAT0197**

TREATMENT OUTCOMES WITH ANTI-TNF AND NON-ANTI-TNF DISEASE-MODIFYING THERAPY BY BASELINE BODY MASS INDEX

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**Background:** Recent studies have indicated that being overweight or obese could reduce the effect of anti-TNF treatment in patients (pts) with RA. 1-3 Other data show that certain biologic (b)DMARDs, such as abatacept, work independently of BMI. 4 Additional data on the role of BMI on treatment outcomes in clinical practice settings is required to inform clinical practice.

**Objectives:** To evaluate the impact of BMI on outcomes of disease activity in pts with RA treated with TNF and non-TNF agents (conventional or other bDMARDs).

**Methods:** Pts enrolled in a tertiary care RA registry, established in 2003, were analysed. The registry mostly comprises pts with established RA who were evaluated semi-annually for multiple clinical patient-reported outcomes and resource utilization parameters, and annually for composite disease activity measures such as DAS28 (CRP), CDAI and SDAI. The current analysis is based on pts enrolled in the RA registry with BMI values at time of enrolment. Pts were classified into groups based on BMI: normal (BMI < 25 kg/m²), overweight (BMI ≥ 25 to <30 kg/m²) and obese (BMI ≥30 kg/m²). Outcomes evaluated included change from baseline in DAS28 (CRP), CDAI, SDAI and joint counts at 12 months.

**Conclusions:** Retreatment with rituximab infusions was not associated with a higher rate of SIEs in this study. Patients who experienced an SIE had a higher prevalence of risk factors for infections.

**References:**


**Acknowledgements:** This study is sponsored by Corrona, LLC. Corrona, LLC has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.
from treatment exposure. Treatments were categorized into TNF and non-TNF, which included conventional DMARDs and other non-TNF biologics. Multivariate linear regression analyses were used to evaluate impact of BMI on treatment outcomes controlling for baseline covariates of age, sex, disease duration, comorbidities, baseline disease activity and serostatus. Separate models were run for the TNF and non-TNF groups.

**Results:** A total of 997 (78%) pts in the registry had baseline BMI values and were included in the analysis. Around 37% (n=371) had TNF exposure and were included in the TNF cohort; the remainder (63%; n=626) were included in the non-TNF cohort. Proportions of pts in the normal, overweight and obese groups for the TNF cohort were 45.5% (n=168), 27.5% (n=102) and 27.0% (n=100), respectively. For the non-TNF cohort, these were 41.7% (n=261), 33.1% (n=207) and 25.2% (n=158), respectively. In both cohorts, pts with normal BMIs were younger vs the overweight and obese BMI groups. However, obese BMI pts had higher disease activity measures at baseline (mean [SD] CDAI: 22.6 [17.8] for TNF and 24.9 [17.3] for non-TNF) vs the normal BMI pts (17.5 [15.9] for TNF and 20.5 [15.0] for non-TNF). Adjusted mean change from baseline in disease activity in the TNF cohort was significantly reduced across all disease activity measures for the normal BMI group (p < 0.05), but not for the overweight and obese groups (Fig). There were significant reductions in disease activity measures for all BMI groups (all p < 0.05) in the non-TNF cohort (Fig).

**Conclusions:** Independent of BMI, non-anti-TNF therapy demonstrated similar outcomes in pts with RA. However, obese and overweight pts with RA (vs normal weight) had less improvement in disease activity (as measured by DAS28 [CRP]) with anti-TNF therapy.

**References:**


**SAT0198**

TOCLIZUMAB FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS: DISCONTINUATION DUE TO INEFFICACY AND TOXICITY – EXPERIENCE FROM A LARGE TEACHING HOSPITAL

E. Byrne, P. Mark, S. Khalid, K.-P. Kuet, R. Kilding, K. Graves, J. Maxwell, M. Akil. Rheumatology, Sheffield Teaching Hospitals, Sheffield, United Kingdom

**Background:** Tocilizumab (TCZ) is a humanised anti interleukin-6 receptor antibody licensed for use for the treatment of moderate to severe Rheumatoid Arthritis (RA) as monotherapy or in combination with methotrexate (MTX).

**Objectives:** To describe the use of TCZ for RA in a large UK teaching centre and examine reasons for treatment discontinuation.

**Methods:** A retrospective case note review of all adult patients receiving TCZ either alone or in combination with DMARDs, for the treatment of RA between April 2009 and January 2017 in Sheffield, UK.

**Results:** 132 patients received TCZ for RA. 71% were female. 61% were CCP positive. Mean disease duration was 15.6 years (range 1.5–43). 46 (34.6%) received TCZ as monotherapy. 55 (42.1%) in combination with MTX and 31 (23.3%) other DMARDs. 23% of patients received concomitant oral prednisolone.

**Discussion:** Median duration of TCZ treatment was 27 months across the whole cohort, and 19 months in those who discontinued treatment.

**Conclusions:** Our real world data on the use of TCZ in the treatment of adult patients with RA is consistent with clinical trial data for efficacy and safety and is similar to other biological drugs used in the treatment of RA. We have seen a relatively low rate of withdrawal due to primary and secondary treatment failure.

**Disclosure of Interest:** None declared DOI: 10.1136/annrheumdis-2017-eular.5105

**SAT0199**

SUBCUTANEOUS TOCLIZUMAB MONOTHERAPY OR COMBINED WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: TOZURA, A POOLED ANALYSIS OF PHASE IV STUDIES IN 22 COUNTRIES

E. Choy1, R. Caporali2, R. Xavier3, B. Fautrel4, R. Sanmarti5, C. Bernasconi6, A. Peth-Piringer7, 1Cardiff University, Cardiff, United Kingdom; 2University of Pavia, Pavia, Italy; 3Universidade Federal do Rio Grande do Sul Porto Alegre, Rio Grande do Sul, Brazil; 4Pierre and Marie Curie University, Paris, France; 5Universitat de Barcelona, Barcelona, Spain; 6F. Hoffmann-La Roche AG, Basel, Switzerland

**Background:** Tocilizumab administered subcutaneously (TCZ-SC) has been approved for the treatment of rheumatoid arthritis (RA) both as mono- and combination therapy.

**Objectives:** To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as monotherapy or in combination with conventional synthetic DMARDs (csDMARDs) over 24 weeks in adult patients (pts) with moderate to severe RA.

**Methods:** TOZURA is a multinational, open-label, single-arm umbrella program comprising 7 single-country and 4 regional multicountry protocols (total 22 countries). Pts enrolled were inadequate responders to DMARD, and previous biologic DMARDs were allowed in 8 of 11 protocols. Pts received TCZ-SC 162 mg qw for 24 weeks administered at the investigator’s discretion as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (CS), ≤10 mg/day prednisone or equivalent, were allowed. Efficacy and safety were evaluated at weeks 1, 2, 4 and every 4 weeks for 24 weeks (plus 4 weeks for safety). Propensity score-based matching was used for between-group tests.

**Results:** Of 1804 pts treated, 353 (19.6%) received monotherapy (mono) and 1451 (80.4%) combination therapy (combo). 349 pts (19.3%) received a prior biologic DMARD. Background characteristics: 81.6% female; mean age, 54.1

**Table 1. Proportion of Patients Continuing TCZ and Treatment Duration According to Previous Biologic Treatment**

<table>
<thead>
<tr>
<th></th>
<th>Discontinued</th>
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<tbody>
<tr>
<td>Previous Biologics Received</td>
<td>N (%)</td>
<td>Treatment Duration (Mths)*</td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td>0</td>
<td>3 (17%)</td>
<td>46</td>
</tr>
<tr>
<td>1</td>
<td>15 (83%)</td>
<td>27</td>
</tr>
<tr>
<td>2 or more</td>
<td>31 (66%)</td>
<td>24 (51%)</td>
</tr>
<tr>
<td></td>
<td>24 (51%)</td>
<td>26 (58)</td>
</tr>
<tr>
<td></td>
<td>26 (25%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27 (25%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 (40%)</td>
<td></td>
</tr>
</tbody>
</table>

*To date.

**Conclusions:** Our real world data on the use of TCZ in the treatment of adult patients with RA is consistent with clinical trial data for efficacy and safety and is similar to other biological drugs used in the treatment of RA. We have seen a relatively low rate of withdrawal due to primary and secondary treatment failure.

**Disclosure of Interest:** None declared DOI: 10.1136/annrheumdis-2017-eular.5105
years; mean RA duration, 7.7 years; and 82.7% seropositive—similar between treatment groups. Baseline CS was less frequent in the mono vs combo group (41.1% vs 51.2%); however, the mean prednisone equivalent daily dose was similar (6.6 vs 6.5 mg/day, respectively). Pts who continued TCZ to week 24 based on Kaplan-Meier estimates (95% CI) were 79.3% (74.7%–83.2%) for mono and 84.3% (80.9%–87.3%) for combo. DAS28 scores decreased comparably from baseline to week 24 in both groups (mean change: mono −3.40 and combo −3.46), with no significant difference between groups (P = 0.61). Results were similar for the Clinical Disease Activity Index (CDAI, mean change by week 24: −23.5 and −23.8, with no significant difference between groups; P = 0.42). The proportion of pts who achieved DAS28 or CDAI-based remission, low disease activity or ACR20/50/70/90 responses was similar between groups (Figure 1). In all, 18.2% of pts withdrew; 6.4% did so for safety reasons (mono 9.1%, combo 5.8%), AE rates were similar between groups (Table). Serious AE (SAE) rates were 21.0/100 PY (mono: 22.8/100 PY, combo: 12.8/100 PY). Serious infection and infestation rates were 3.6/100 PY (mono: 4.0/100 PY, combo: 3.5/100 PY) — similar between groups. Six deaths occurred (0.64/100 PY, 1 in the monotherapy group (0.57/100 PY) and 5 in the combination (0.65/100 PY) group.

**Figure 1: DAS28 and CDAI Disease Activity and ACR Responses**

<table>
<thead>
<tr>
<th>Disease Activity at Week 24</th>
<th>ACR20 Responses at Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DAS28</strong></td>
<td><strong>ACR20</strong></td>
</tr>
<tr>
<td>High disease activity</td>
<td>No remission</td>
</tr>
<tr>
<td>Low disease activity</td>
<td>Remission</td>
</tr>
<tr>
<td>No disease activity</td>
<td>No remission</td>
</tr>
</tbody>
</table>

**Table: Summary of Relevant Adverse Events**

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Total Population</th>
<th>Total Monotherapy</th>
<th>Total Combination Therapy</th>
<th>Total Population</th>
<th>Total Monotherapy</th>
<th>Total Combination Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>1006</td>
<td>1006</td>
<td>1006</td>
<td>1006</td>
<td>1006</td>
<td>1006</td>
</tr>
<tr>
<td>AE, adverse events, SAE, serious adverse events, PV, patient-year.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** TCZ-SC demonstrated convincing and comparable efficacy as mono- and combination therapy in pts with RA as was previously observed with TCZ-IV. The safety profile of TCZ-SC is consistent with the known safety profile of TCZ as monotherapy and in combination with csDMARDs.

**Disclosure of Interest:** Funded by F. Hoffmann-La Roche, Ltd.

**SATO2000**

**BIOLOGIC THERAPY RETENTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ACCORDING TO THE MOSCOW ARTHRITIS REGISTRY (MAR)**

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**Background:** The use of biologics significantly improved the results of the therapy of RA pts who did not respond to the target disease activity level on traditional DMARDs treatment. However the biologic therapy is in many cases withdrawn due to inefficacy or side effects (rarely because of sustained remission). Retention on treatment is a good integral index of efficacy and safety of biologics used in the real clinical practice.

**Objectives:** To assess the treatment survival of various biologics in RA pts in the real clinical practice.

**Methods:** Patients from MAR with RA receiving biologics were enrolled. Cases with missed results were excluded. A Cox proportional hazards regression model was used to determine predictors of the patient discontinuation risk. Comparison of biologics retention rates for different biologics was performed by means of Kaplan-Meier survival curves. Bonferroni adjustment was applied because of multiplicity of comparisons.

**Results:** 306 RA pts (mean age 54.5 years, mean age of disease onset 39.6 years; 86.2% women, 18.1% smokers, RF-positive 83.7%) were included in the study and 394 treatment courses (263 retrospective and 131 prospective) were analyzed. It was shown that significant independent predictors of discontinuation risk were: the biologic drug, the sequence number of the biologic drug in the patient and the age of RA onset. Risk of withdrawal was minimal by the use of the first biologic and increased by administration of the next ones. It also increased in pts with late onset of RA. Mass body index, age of the patient and the dose of methotrexate did not show significant correlations. Abatacept (ABA) demonstrated significant superior efficacy over adalimumab (ADA) (p < 0.001), infliximab (INF) (p < 0.001), rituximab (RTM) (p = 0.004) and etanercept (ETA) (p = 0.003) when they was used as the first biologic drug. The treatment survival of tocilizumab was significantly higher compared to INF (p = 0.02). As a second-line biological therapy ADA was maintained significantly longer than the INF (p = 0.048).

**Conclusions:** Results of the real clinical practice trial showed the significant differences in the retention rates of some biologics. It is reasonable to take these differences into consideration by the planning of the biologic treatment of RA pts.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3657

**SATO2001**

**ABATACEPT BUT NOT TNF INHIBITORS BLOCK AUTOANTIBODY-MEDIATED CYTOKINE PRODUCTION BY MONOCYTES**

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1University of Erlangen-Nuremberg, Erlangen, Germany; 2University of Chengdu, Chengdu, China; 3Universidade de São Paulo, São Paulo, Brazil; 4Oncology, Inc., Mainz, Germany

**Background:** The anti-inflammatory effect of abatacept (CTLA4-Ig) is most pronounced in patients with high-titer autoantibodies (including anti-citrullinated protein antibodies, ACPA, and rheumatoid factor, RF) even exceeding the effect of TNF inhibitors (TNFi)1. Considering that autoantibodies trigger inflammatory cytokine production by monocytes2 and that abatacept binds to monocytes influencing their functional state3 we hypothesized that abatacept, in contrast to TNFi, may effectively inhibit the production of several different cytokines by ACPA-or RF-challenged monocytes.

**Objectives:** (i) To test whether abatacept inhibits the production of TNFα, IL-1b, IL-6 and IL-8 by monocytes exposed to ACPA or RF; (ii) to compare these effects of abatacept with those of TNFi and (iii) to investigate whether the effect of abatacept on cytokine production is based on IDO induction in monocytes.

**Methods:** CD14+ monocytes were isolated from peripheral blood and stimulated with MCSF for 24 hours before exposing them to random IgG alone (negative control), 10mg/mL purified anti-citrullinated vimentin antibodies (ACPA), 10mg/mL of TNF inhibitors (TNFi) with or without IDO inhibitor 1-MT. Supernatants were analyzed for four key pro-inflammatory cytokines TNFα, IL-1b, IL-6 and IL-8 by cytokine array (R&D Systems, MN). Results of the real clinical practice trial show the significant differences in the retention rates of some biologics. It is reasonable to take these differences into consideration by the planning of the biologic treatment of RA pts.

**Conclusions:** Results, of the real clinical practice trial show the significant differences in the retention rates of some biologics. It is reasonable to take these differences into consideration by the planning of the biologic treatment of RA pts.
effectors cytokines are inhibited simultaneously may explain the strong anti-inflammatory effect of abatacept in RA patients with high-titer ACPA and RF.

References:


Acknowledgements: This project was supported by an unrestricted research grant from BMS and the IMI project BTCure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4363

SAT0202 EFFICACY AND SAFETY OF SARILUMAB MONOTHERAPY VERSUS ADAлимABUM MONOTHERAPY IN PATIENTS WITH ACTIVE RHUMATOID ARTHRITIS IN THE PHASE 3 MONARCH STUDY, INCLUDING SUBPOPULATIONS


Conclusions: Sarilumab monotherapy demonstrated superiority to adalimumab monotherapy in the ITT population in change from baseline in DAS28-ESR. The extent of treatment effect with sarilumab vs adalimumab was generally consistent across subpopulations. Overall incidences of AEs and serious AEs and rates of infection and serious infection were similar between groups.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Medical writing support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.


DOI: 10.1136/annrheumdis-2017-eular.4540

SAT0203 SIGNIFICANCE OF EXTENSION OF TOCILIZUMAB INFUSION INTERVALS FROM 4 WEEKS TO 6 WEEKS IN RA PATIENTS WHO HAD SHOWN GOOD RESPONSE TO 4 WEEK INTERVALS

H. Uda1, K. Shigematsu2, O. Saiki3, Rheumatology; 2Orthopedics, Higashiosaka City Medical Center, Higashiosaka; 3Internal Medicine, Shiraiishi Hospital, Imabari, Japan

Background: A period of 4 weeks (w) has been recommended as tocilizumab (TCZ, 8mg/kg) infusions. However, we found that 5 or 6w intervals were also effective in more than 90% of RA patients with low disease activity (LDA) at 4w intervals (1).

Objectives: We conducted the study to investigate the significance of extension of intervals from 4w to 6w. We compared, in the same patients, the clinical features such as diseases activity, major and minor side reactions between at 4w and 6w. Moreover, we also considered the mechanisms.

Methods: This was a retrospective observational study. Among RA patients who had shown LDA with TCZ infusions at 4w intervals, the patients who could extend the intervals from 4w to 6w with LDA for more than 2 years without changing the doses of oral medicines were enrolled. In the same patients, we compared the events of serious and common side reactions between at 4w and 6w intervals. We examined the course of the levels of total cholesterol (TCHO), triglyceride (TG), and platelet (PLT) counts. We also examined the levels of serum trough TCZ and IL-6.

Results: Among 120 patients who maintained LDA at 4w intervals, more than 60% of patients maintained LDA at 6w intervals. When we compared the disease activity of 6w-responders between at 4w and 6w-intervals, all parameters reflecting the disease activities such as CRP and DAS28CRP score at 6w intervals were elevated significantly, but were still within LDA. At 4w intervals, serious adverse events were occurred as much as 11 cases during 2 years. At 6w intervals, however, they were decreased to 3 cases only in the same period. The common adverse reactions such as general fatigue, nausea, and dizziness occurred frequently at 4w intervals in most of the patients. At 6w intervals, these common adverse reactions were decreased significantly. At 4w intervals, the levels of TCHO and TG were elevated significantly. At 5w and 6w intervals, however, they were decreased accordingly. At 6w intervals, they were within normal limits. In most of patients, the levels of PLT counts were decreased significantly at 4w intervals. At 5w and 6w intervals, however, they were increased gradually. When TCZ were infused at 4w intervals, the serum trough TCZ levels were around 10 µg/mL. In contrast, they became undetectable when extended to 5w, and it is obvious that the trough TCZ levels of 6w were lower than 5w. The levels of IL-6 were significantly high at 4w-intervals, but the levels of IL-6 were decreased to less than 10 pg/mL at 5w-intervals.

Conclusions: The present study provide evidence that more than half of RA patients who showed good response at 4w could extend response to TCZ infusions at 6w intervals. Overall, the extension of intervals from 4w to 6w, major and minor side reactions were reduced significantly, and the levels of TCHO and PLT were also normalized with sustaining LDA, suggesting that the dose of TCZ (8mg/kg) at 4w intervals might be excessive in some patients. Taken together, we should be careful for deciding the intervals of TCZ infusion for each patient.

References:
[1] Saiki O, Uda H. Successful extension of tocilizumab infusion intervals from 4 weeks to 6 or 5 weeks in 90% of RA patients with good response to 4 weeks intervals, Clin Exp Rheumatol (2017 in press).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3602

Conclusions: Sarilumab monotherapy demonstrated superiority to adalimumab monotherapy in the ITT population in change from baseline in DAS28-ESR. The extent of treatment effect with sarilumab vs adalimumab was generally consistent across subpopulations. Overall incidences of AEs and serious AEs and rates of infection and serious infection were similar between groups.
ABATACEPT SURVIVAL IN RHEUMATOID ARTHRITIS: PATIENTS AT 2 YEARS IS 59%: ITS USE AS A 2ND LINE BIOLOGIC AGENT AND LOWER BASELINE HAQ PREDICT BETTER SURVIVAL IN CLINICAL PRACTICE: A PROSPECTIVE, OBSERVATIONAL SINGLE CENTER STUDY

I.D. Flouri1, 2, A. Repa1, N. Argoustidi1, N. Kougas1, A. Fanourakis1, I. Papapoliopoulos1, G. Adamichou1, P. Kypionidou1, E. Kampouraki1, M. Terizaki1, D.T. Bourmpas2, G. Bertisias1, P. Sidipoulos1, I.D. Flouri1, Rheumatology, Clinical Immunology and Allergy, Faculty of Medicine-University of Crete, Heraklion-Crete; 4th Internal Medicine Department, Attikon University Hospital, Athens, Greece

Background: Long-term prospective observational studies are complementary to controlled clinical trials to explore effectiveness and safety of biological therapies in real practice.

Objectives: To study abatacept survival, reasons of discontinuation and clinical responses in everyday clinical practice of patients with rheumatoid arthritis (RA).

Methods: Prospective, observational single center study at the Rheumatology Clinic, University Hospital of Heraklion, Crete. At baseline, patient demographics, co-morbidities and disease characteristics are being recorded, while during follow-up, discontinuations, disease activity and adverse events are collected. For this analysis, all patients who received Abatacept intravenously from 6/2007 till 6/2016 were included. Kaplan-Meier curves and Cox regression analysis were used to determine drug survival and predictors thereof. Linear regression was used to compare DAS difference at 12 months between different lines of bDMARD therapy.

Results: A total of 224 patients (women: 87%, seropositive: 34%) were included. Median (IQR) age was 63 (56–70) years, disease duration 7.4 (4–13.4) years and baseline DAS28 5.9 (5.2–6.5). Abatacept was the 1st bDMARD in 59 (26%) patients, 2nd in 71 (32%) and ≥3rd in 94 (42%) patients. During follow-up (total: 508 patient-years, median (IQR): 1.7 (0.7–3.3) years), 54% patients discontinued therapy (87% for treatment failure, 10% for adverse events). Two-year treatment persistence was 59%. In multivariable regression analysis, predictors of longer Abatacept survival were younger baseline HAQ [HR (95% CI) for unit increase ≥0.29 (1.5–3.48), p < 0.001], longer disease duration [HR (95% CI) for >8 vs ≤8 years=0.51 (0.30–0.88), p=0.016], Abatacept as 2nd vs 1st or ≥3rd bDMARD [HR=0.50 (0.30–0.81), p=0.022] and a more recent year of therapy start [HR=0.39 (0.16–0.95), p=0.035].

DAS28-3.2 and remission at 6 (12) months were achieved by 12% (18%) and 5% (7%) of patients respectively. DAS28 difference at 12 months was greater in patients who received Abatacept as the ≥2nd than those on ≥3rd bDMARD (p=0.009). A total of 312 adverse events were registered, of which 65 were serious (SAE). Incidence of total (serious) adverse events was 61 (13)/100 patients/year. SAE included 5 cases of cancer, 10 cardiovascular events and 24 infections, mainly of the respiratory tract.

Conclusions: In the present study, Abatacept survival at 2 years was 59%. The majority of patients discontinued therapy due to inadequate response. Use as a 2nd line biologic agent and lower baseline HAQ predicted better survival. Improvement in DAS was higher when Abatacept was used as the ≥2nd bDMARD. Rates of remission or low disease activity in clinical practice are rather low, while the safety profile was excellent.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4348

RETENTION OF TOCILIZUMAB AS MONOTHERAPY VERSUS TNF INHIBITORS WITH CONVENTIONAL SYNTHETIC DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS: A STUDY FROM THE TOCERRA COLLABORATION

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Background: Tocilizumab (TCZ) as monotherapy has been shown to be more efficacious than the TNF inhibitor (TNFi) adalimumab as monotherapy in patients with rheumatoid arthritis (RA). However, effectiveness data comparing TCZ as monotherapy versus TNFi in combination with csDMARDs is limited.

Objectives: To examine retention of TCZ administered alone (TCZ mono) versus TNFi in combination with csDMARDs (TNFi-combo) in patients with RA who had an inadequate response to ≥1 TNFi (TNFi-IR).

Methods: Patients with RA who were TNFi-IR and treated with TCZ mono or TNFi combo with baseline (BL) data, not immediately lost to follow-up and started treatment after TCZ was available across 9 European registries in TOCERRA from 2009 to 2016 were included. The hazard for TCZ discontinuation was modeled using a country-stratified Cox proportional hazards model, adjusting for

patients were as follows: female gender 86%, mean age 52±13 years, median disease duration 10 (IQR 11) years, Rheumatoid Factor positive 94%, Anti-Cyclic Citrullinated Peptide Antibodies 89%, and erosive phenotype 35%. At baseline, mean DAS28 and RAPID3 were 5.4±1.3 and 16.6±6.8, respectively. SC abatacept monotherapy was reported in 27%. Demographics and disease characteristics were similar in all groups, except for baseline DAS28 and RAPID3 in switch group (p=0.0001). According to the Mantel-Haenszel test (Fig.1), there were no significant differences between survival curves (p=0.158). Forty-three patients (33%) discontinued treatment. The most frequent reasons for drug suspension were loss of efficacy in 25%, insurance-related problems (i.e., access to medication/specialist) and adverse drug reactions in 16%. Other causes include lack of efficacy, surgeries (i.e., arthritic replacement), patient preference, and pregnancy.

Conclusions: Our results disclose a similar drug survival of SC abatacept regardless of treatment background. Patients switching from IV to SC formulation of abatacept had lower activity and functional impairment at baseline, and survival tends to be higher through follow-up. The insurance-related limitations is a reality in Latin American countries, and could have a negative impact on survival time of several drugs.

References:
[4] Acknowledgements: The authors are grateful to all the members of the Center of Dermatology and Rheumatology (FUNINDERMA) for their contribution to this work.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4348

RETENTION OF TOCILIZUMAB AS MONOTHERAPY VERSUS TNF INHIBITORS WITH CONVENTIONAL SYNTHETIC DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS: A STUDY FROM THE TOCERRA COLLABORATION

K. Lauper1, 2, D.C. Nordström3, K. Pavelka4, V. Hernandez5, M.J. Santos6, Z. Rotar2, F. Iannone1, C. Codreanu2, G. Lukina2, L.L. Gale5, K. Sarsour1, A. Petheos-Schramm1, D.S. Couvoisier1, C. Gabay1, 2, Univ Hosp of Geneva, Geneva; 2SCOM Registry, Zurich, Switzerland; 3ROB-FIN Helsinki Univ Central Hosp, Helsinki, Finland; 4Charles Univ, Prague, Czech Republic; 5Rheumatology Department, Hospital Clinic Barcelona, Barcelona, Spain; 6Rheumatology Unit, Hospital Garcia de Orta, Almada, Portugal; 7BioRx.si, Univ Med Center, Ljubljana, Slovenia; 8GISEA Univ Hosp of Bari, Bari, Italy; 9Univ of Medicine and Pharmacy, Bucharest, Romania; 10ARBITER, Inst of Rheumatology, Moscow, Russian Federation; 11Genentech, South San Francisco, CA, United States; 12F. Hoffmann-La Roche, Basel, Switzerland

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Methods: Patients with RA who were TNFi-IR and treated with TCZ mono or TNFi combo with baseline (BL) data, not immediately lost to follow-up and started treatment after TCZ was available across 9 European registries in TOCERRA from 2009 to 2016 were included. The hazard for TCZ discontinuation was modeled using a country-stratified Cox proportional hazards model, adjusting for
age, gender, disease duration, seropositivity, HAQ and CDAI at BL, number of previous csDMARD and biological DMARD (bDMARD), glucocorticoid and calendar year of treatment initiation. Missing data on covariates were imputed using multiple imputation with chained equations. Results: A total of 4748 patients were eligible, including 585 who received TCZ mono and 4163 who received TNFi combo. Patients who received TCZ mono were older with a longer disease duration, more previous bDMARDS and less glucocorticoids at baseline (Table 1) compared with patients who received TNFi combo. The crude median retention for TCZ mono was 1.82 years (95% CI: 1.59–2.09) and 1.54 years (95% CI: 1.43–1.64) for TNFi combo. (P<0.65). Causes of discontinuation differed between TCZ mono and TNFi combo (P<0.001): TCZ mono stopped more frequently for ineffectiveness (25.7% vs. 13.8%) and TNFi combo stopped more frequently for safety issues (18.3% vs. 12.8%). In a country-stratified, covariate-adjusted analysis, we found that hazards of discontinuation were significantly lower among those who received TCZ mono vs. TNFi combo (HR: 0.71, P<0.001). More previous treatment with bDMARDS and a greater HAQ and CDAI at BL were significantly associated with greater risk of discontinuation.

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>TCZ mono (N = 585)</th>
<th>TNFi combo (N = 4163)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, median [IQR]</td>
<td>57.8 [44.2-65.5]</td>
<td>54.3 [44.2-65.7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender, N (%)</td>
<td>485 (82.9%)</td>
<td>333 (80.0%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Disease duration, yr, median [IQR]</td>
<td>9.7 [4.5-16.7]</td>
<td>7.8 [3.1-14.3]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Seropositivity (RF and/or ACPA), N (%)</td>
<td>445 (76.3%)</td>
<td>323 (78.1%)</td>
<td>0.17</td>
</tr>
<tr>
<td>N previous bDMARDS, N (%)</td>
<td>1</td>
<td>2</td>
<td>2-3</td>
</tr>
<tr>
<td>1</td>
<td>250 (42.7%)</td>
<td>2882 (69.2%)</td>
<td>1526 (36.2%)</td>
</tr>
<tr>
<td>2</td>
<td>206 (35.2%)</td>
<td>129 (21.2%)</td>
<td>112 (26.6%)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>191 (33.0%)</td>
<td>2487 (59.8%)</td>
<td>4103 (9.8%)</td>
</tr>
<tr>
<td>Cooccurrent csDMARD, N (%)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>MTX</td>
<td>--</td>
<td>1766 (42.4%)</td>
<td>219 (30.1%)</td>
</tr>
<tr>
<td>MTX + other</td>
<td>--</td>
<td>1106 (26.5%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CDAI, mean (SD)</td>
<td>23.2 (16.1)</td>
<td>21.9 (14.7)</td>
<td>0.25</td>
</tr>
<tr>
<td>HAQ, mean (SD)</td>
<td>1.4 (0.7)</td>
<td>1.1 (0.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: In routine care across 9 European countries, TCZ mono retention is better than TNFi combo in patients with RA who were TNFi-IR.

Acknowledgements: Funding by F. Hoffmann-La Roche/Genentech.

Disclosure of Interest: K. Lauper: None declared, D. Nordström Grant/research support from: AbbVie, BMS, MSD, Roche, UCB and Pfizer, K. Pavelka Grant/research support from: AbbVie, Roche, Medis, MSD and Pfizer, Consultant for: AbbVie, Roche, Amgen, MSD, BMS, UCB and Egis, V. Hernandez: None declared, M. J. Santos: None declared, Z. Rotar: None declared, F. Iannone: None declared, C. Codreanu: None declared.

Conflict of Interest: None declared.

Acknowledgements: This study is the first to assess the effects of biological RA therapies as compared to synthetic DMARD ones. It highlights the protective effect of both biological and non-biological DMARD on bone loss during the first two years of treatment with no significant difference between them. Our results suggest that the effects of RA treatments depend on the inflammatory and disease activity which must be monitored clearly. Tocilizumab seems to be more effective than the other biological therapies, but further studies are necessary to confirm or infirm this tendency.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6503

SAT0208 CYCLING VERSUS SWAPPING IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH AN INADEQUATE RESPONSE TO AT LEAST ONE TUMOR NECROSIS FACTOR ALPHA INHIBITOR: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: In patients with rheumatoid arthritis (RA) who do not respond or lose response, opinions are divided on whether it is better to try an alternative TNFi (cycling) or switch to a therapy with a different mode of action (swapping).

Objectives: To compare the efficacy and safety of the cycling versus the swapping strategies.

Methods: We searched 4 electronic databases, sources of gray literature, and bibliographic references of relevant articles for observational studies evaluating the efficacy and safety of targeted therapies in adult RA patients who failed to respond to at least one TNFi. Studies were excluded if they were single-arm or had insufficient data to evaluate the outcomes of interest. Two independent reviewers selected studies, extracted data and evaluated study quality using the Newcastle-Ottawa Scale (NOS). Our primary outcome measure was change in Disease Activity Score 28 joints (DAS28). We also evaluated the modified American College of Rheumatology 20%, 50% and 70% response criteria (mACR20, mACR50, mACR70) with the majority response criteria (mACR which excludes acute phase reactants) and total serious adverse events. All analyses were based on the random-effects model.

Results: Of 33,716 citations, 24 observational studies (n=10,074 patients) representing 14 countries, met the inclusion criteria. Eight were conference abstracts. Most publications (13 of 24) were based on registries. Most studies had a NOS score equal to or greater than 7 (out of 9) with comparability being the weakest domain. The mean age of patients was 48.7–62.8 years, the majority were females (78%) with a disease duration of 6–17.3 years and a baseline disability score 0–2.0. Sixteen studies compared TNFi swapping directly with TNFi cycling while 13 were suitable for analysis. Most compared TNFi to rituximab (10 of 13) with two studies investigating tocilizumab or abatacept and one comparing non-TNFi as a group. Other comparisons reported were: (i) cycling vs. switching for well disease modifying anti-rheumatic drugs (cDMARDs) vs. cDMARDs, (ii) cycling vs. another cycling alternative, (iii) swapping vs. another swapping alternative, (iv) swapping monotherapy vs. swapping combined with cDMARDs, and (v) combination of TNFi and non-TNFi vs. TNFi alone. At 12 and 24 weeks, DAS28 score improved significantly in those swapping compared to those cycling (mean difference (MD) 0.89, 95% confidence interval (CI) 0.03 to 1.74 and MD 0.34 95% CI: 0.2, 0.48; respectively). Similar results were observed for the mACR50 favoring the swapping strategy at 24 weeks (OR =1.45 95% CI: 1.06, 1.98). At 52 weeks no difference was observed. No statistically significant differences were observed across groups in the odds of achieving DAS28 remission, mACR20 or mACR70, or experiencing a serious adverse event.

Conclusions: Current evidence from observational studies shows greater improvements with the swapping strategy compared with the cycling strategy in terms of efficacy for RA patients failing their first TNFi. No differences were observed when those failing their second TNFi were compared. Clinical trials were not available for anakinra, certolizumab pegol, golimumab, or tocilizumab.

Acknowledgements: Funding for this project was provided by the Rheumatology Research Foundation Investigator Award.

Disclosure of Interest: None declared.
**SAT0209** OBSERVATIONAL STUDY ON THE EFFECTS OF IL-6 INHIBITOR THERAPY ON MYOSTATIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid cachexia (RC), a phenotype of increased adiposity, reduced lean mass and insulin resistance can occur in rheumatoid arthritis (RA). It is most prevalent in those with high disease activity and is associated with increased cardiovascular morbidity and mortality. Tocilizumab (TCZ), a monoclonal anti-IL-6 antibody, successfully reduces disease activity in RA. It has also been associated with improved insulin sensitivity, increased lean mass and hyperlipidaemia. The serum concentration of myostatin, a myokine released by skeletal muscle, is increased in most disease states associated with cachexia. Moreover, its knockdown and inhibition increase lean mass. However, its role in RA has not been fully elucidated.

**Objectives:** To investigate the effect of tocilizumab treatment on serum myostatin in patients with RA.

**Methods:** 19 patients with RA (16 female, 3 male) mean age 49.6yrs, mean DAS28 6.1, median disease duration 10yrs (range 0 to 30), mean BMI 27.4, received 13 IV infusions of TCZ 8mg/kg every four weeks as part of a 52 week, single-centre, open-label study (ACT-NEUT [1]). 8 had previously been exposed to a biological agent, 4 were on regular steroids, and all patients received concurrent methotrexate. Serum myostatin was measured at 0, 1, 3 and 6months of treatment using ELISA, BMI, serum lipid profile, CRP, ESR and DAS28 were measured at each visit (0, 1, 3 and 6months). Data were analysed using STATA 14. Change between 0, 3 and 6months was analysed using Wilcoxon signed rank test. Statistical significance was confirmed using mixed model analysis adjusting for BMI, age and gender.

**Results:** DAS28, CRP and ESR all significantly decreased with TCZ treatment. A significant increase in BMI (25.5 (IQR 21.6–31.7) vs 26.0 (IQR 21.4–32.5) p=0.028) was seen with TCZ. Baseline serum myostatin concentrations were negatively correlated with baseline DAS28 (r2=0.39 p=0.038). Treatment with tocilizumab was seen with TCZ. Baseline serum myostatin concentrations were negatively correlated with baseline BMI, age and gender. Linear regression with adjustment for age, BMI and gender assessed correlation at baseline.

**Conclusions:** There was a global improvement of DAS28 in a cohort of RA patients receiving biological therapy followed and treated under recommendations of T2T approach demonstrating that with the strategies mentioned above it is possible to obtain a good control of the activity of the disease.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5579

**SAT0210** IMPROVEMENT OF DISEASE ACTIVITY IN A 5-YEAR COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS RECEIVING BIOLOGICAL THERAPY

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**Background:** Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA), this strategy has become recognized as a standard of good practice embodying the principle that rapid attainment of remission, or low disease activity, can halt joint damage and maintain good quality of life. However, there is no direct comparison between biologicals in cohorts of patients with long-standing RA using T2T approach in real-life settings, which could have implications in treatment decisions and health economics.

**Objectives:** The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 5 year period in patients with biological therapy in a large cohort of patients from a Colombian specialized in RA center with multidisciplinary approach.

**Methods:** A descriptive dynamic cohort study was performed. Records of patients using biological DMARD treatment (Anti-TNF and others) from specialized in RA centre were reviewed; those patients were followed-up under T2T strategy. Clinical follow-up was according to DAS28 as follows: every 3–5 weeks (DAS28 ≥ 3.1), every 7–9 weeks (DAS28 ≥ 3.1 and ≤ 5.1), and every 11–13 weeks (DAS28 ≤ 3.1). Therapy had to be adjusted with DAS28 ≥ 3.2 unless patient’s conditions don’t permit it. We divided patients in three groups: low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients. Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson’s statistics.

**Results:** During 60 month period we included 695 patients with biological therapy, 85% were female and 15% male. Mean age was 58 years ± 11. At beginning mean DAS28 was 4.1±1.1 and 20% of patients were in SDA, and 55% in MDA. At the end of 5 year period mean DAS28 was 3.2±0.89 and only 7% of patients were in SDA and 33% in MDA. The median was analyzed using t-Student assuming normality for DAS28 distribution. It showed statistical significant improvement (p<0.00).

**Conclusions:** We have demonstrated a significant correlation between myostatin and DAS28 and a significant change in myostatin with tocilizumab treatment. It is possible that IL-6 blockade results in a rise in myostatin. This might attenuate any improvement in muscle wasting. Future studies should measure body composition and muscle function to help understand the changes we have observed.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5831

**SAT0211** REAL WORLD DATA OF RITUXIMAB EFFECTIVENESS IN RHEUMATOID ARTHRITIS: DIFFERENCES BETWEEN BIOLOGIC-NAIVE PATIENTS AND PREVIOUSLY EXPOSED TO BIOLOGICS


**Background:** Rituximab is only approved for rheumatoid arthritis (RA) treatment in patients with an incomplete response or intolerance to others DMARDs, including TNF alfa inhibitors. It represents a significant advance in RA biologics arsenal due to its safety and efficacy profiles.

**Objectives:** To evaluate the effectiveness of rituximab in RA patients and to compare the response between first-line rituximab patients and those previously exposed to other biologics.

**Methods:** An observational retrospective study was conducted, including all the consecutive patients with diagnosis of RA under rituximab, followed at our Rheumatology department until December 2016. Demographic and clinical data were obtained by consulting the national database (Reuma.pt). DAS28 variations and EULAR response were measured at 6, 12 and 18 months. Parametric and non parametric tests were used for statistics (SPSS 20.0).

**Results:** We included 63 RA patients (81% of women), with a mean (SD) age of 61 (10) years and a mean disease duration of 19 (10) years; 86% rheumatoid factor positive and 87% anti- citrullinated peptide antibody (ACPA) positive. Bone erosions and extra-articular manifestations were present in 85,7% and 58,7% of the patients, respectively. At baseline, the mean DAS28 was 5.79 (65% and 29% of patients with severe and moderate disease activity, respectively, and 6% in clinical remission). Thirty patients were treated with rituximab as first-line therapy and 33 patients were previously exposed to other biologics. Combination therapy
with methotrexate (MTX) was observed in 48% and with other classic DMARDs in 30%, while 22.3% received rituximab monotherapy. First-line rituximab option was justified by lung involvement in 21%, past malignancy in 13%, recurrent infections in 5%, congestive cardiac failure in 3%, vascular involvement in 3% and untreated latent tuberculosis in 3%. In the group previously exposed to biologics, 13% switched therapy due to ineffectiveness and 87% due to adverse events. No significant differences were found among the 2 groups in terms of age, gender, comorbid use of MTX and baseline DAS28. The group previously exposed to biologics had a longer disease duration (mean 23 vs 15 years, p<0.001) and fewer patients with ACPA seropositivity (79% vs 97%, p=0.035). There was a significant reduction of DAS28 at 6, 12 and 18 months (p<0.001 for all). Fifty six percent of the patients achieved a EULAR response at 6 months, 46% at 12 months and 59% at 18 months. DAS28 variation at 6 months differed significantly between groups, with a better clinical response in naive biological patients comparing to their previously exposed to biologics (mean ± SD 1.17 ± 0.67 vs 3.47 ± 0.20, p=0.038). There were no differences in terms of DAS28 variation at 12 and 18 months (p=0.642 and p=0.135, respectively) and in EULAR responses at 6, 12 and 18 months between the groups (p=0.289, p=0.523 and p=1.000, respectively).

Conclusions: Our study confirms the effectiveness of rituximab in RA patients and suggests a higher magnitude of response in naive biological patients at 6 months of RTX therapy. These findings put in perspective an extension of rituximab as a first-line biologic for RA treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4494
CHARACTERISTICS OF PATIENTS WITH ANKYLOSING Spondylitis, RHEUMATOID and PSORIATIC ARTHRITIS IN TREATMENT WITH BIOLOGIC AGENTS IN VERONA’S COHORT: RESULTS FROM VENETO’S REGION BIOLOGICS REGISTRY

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Background: Since 2013, in Verona’s Region, data registration is mandatory for all patients affected by Rheumatoid arthritis (RA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS) in treatment with biologic agents. The biologic DMARDs currently marketed in Italy are: anti-TNF (originator and biosimilar infliximab, etanercept, adalimumab, certolizumab and golimumab), anti-IL6 (tocilizumab), anti-CD20 (rituximab), CTLA4-4 like (abatacept) and anti-IL12/23 (ustekinumab).

Objectives: The aim of this study was first to describe the characteristics of patients treated with RA, PA, AS under biologics and then, to extract and analyze real-life data regarding rheumatic treatments in Verona’s cohort.

Methods: The study has been carried out on behalf of Regione del Veneto, Giunta regionale -Ricerca Sanitaria Finalizzata-Venezia-Italy. Data used for analysis were recorded in the Veneto Region Biologics Registry (VRBR). VRBR provides the core variables such as onset and type of disease, anthropometric characteristics (age, sex, body weight, height) are registered at the beginning. Furthermore, prior and concomitant rheumatic treatment (conventional and biologic DMARDs, corticosteroids, NSAIDs), disease activity indicators (DAS 28-PCR, ASDAS-PCR, pain-NRS), prognostic factors (positivity for rheumatoid factor and/or anti-citrulline antibodies in AR, presence of radiological erosions) were assembled at baseline, every 6 months and at the time of biologic’s switch or swap.

Results: A total of 983 patients under biologics were examined; 543 (55.2%) with RA, 272 (27.2%) with PsA, 108 (11.0%) with AS, and 58 (5.9%) with AS between these. 27%), 27.2% of patients were naïve to biologics, 128 with AR, 84 with AP, 50 with SA. Mean duration of disease was of 15.3, 10.7 and 12.6 years respectively for RA, PA and AS. Radiological erosions were present in 73% of RA-patients and the percentage was higher in those with positivity for rheumatoid factor and/ or anti-CCP antibodies (84.4% versus 56.2%). More than half of the patients in this cohort were treated at least with one biologic agent; anti-TNFs were the main biologic used (RA:54.8%, PA:92.7%, AS: 100%) followed by Abatacept (25.4%), tocilizumab (12.3%) and rituximab (5.9%) in patients with RA. Methotrexate (MTX) was the prevalent associated c-DMARDs (41.8% in RA and 34.2% in PA) with mean dose of 11.9 mg/week in RA and 12.1 mg/week in PA. The optimal dose of methotrexate was not achieved prevalently because of drug intolerance.

Conclusions: In our database, 70% of RA patients received ABA were biologic naive. Remission or low disease activity was achieved approximately 50% of patients in first follow-up visit with an average of 4.5 months after beginning of the treatment. Functional improvement was observed in two thirds of patients.
EARLY PATIENT-REPORTED OUTCOMES AND CLINICAL OUTCOMES WITH ABT-494 IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WHO ARE INADEQUATE RESPONDERS TO METHOTREXATE OR TUMOR NECROSIS FACTOR INHIBITORS: POST-HOC ANALYSIS OF PHASE 2 RANDOMIZED CONTROLLED TRIALS

V. Strand1, N. Tundia2, I.H. Song2, S. Meerwein2, J. Lin2, N. Chen2, A. Friedman2, *1Stanford University, Palo Alto; AbbVie Inc., North Chicago, United States

Background: Janus kinase (JAK) inhibitors are being evaluated for treatment of active rheumatoid arthritis (RA). Understanding their onset of action on patient reported outcomes (PROs) and clinical endpoints in RA patients (pts) is limited.

Objectives: To assess onset of benefit with ABT-494, a selective JAK1 inhibitor vs placebo (PBO) in RA pts with active disease ≥3 months in 2 randomized controlled trials (RCTs) evaluating safety and efficacy of ABT-494. MTX-IR and MTX-NAI (NCT01960855) to tumor necrosis factor inhibitors (TNF-IR).

Methods: Data were pooled separately for each RCT in pts who received 6mg or 12mg bid ABT-494 or PBO. Analyses included cumulative assessment of PROs such as patient global assessment of disease activity (PIGA), pain Visual Analogue Scale (VAS) and Health Assessment Questionnaire Disability Index (HAQ-DI) in terms of Routine Assessment of Patient Index Data 3 (RAPID3) scores, and clinical outcomes such as DAS28 (CRP) and CDAI. To assess onset and maintenance of effect, the number of pts whose improvements met or exceeded minimal important differences (MID) RAPID3: reduction ≥3.6; DAS28: reduction ≥1.2; CDAI: reduction ≥11.0 and were calculated at weeks 2 and 12.

Results: In M13–537 (N=150 pts) and M13–550 (N=166 pts) RCTs, significantly more pts in ABT-494 12mg groups reported improvements ≥MID in RAPID3 vs PBO at Wk 2: 68% vs 30% and 73% vs 38%, respectively (Table). In M13–537, significantly more pts receiving ABT-494 6mg bid vs PBO (54% vs 30%) had improvements ≥MID in RAPID3. These responses were sustained throughout both trials in pts receiving 12mg ABT-494 (M13–537: 80%; M13–550: 71%). Significantly higher MID and maintained changes ≥MID in DAS28 were seen both in RCTs and in CDAI in M13–550. Based on KM analyses, in M13–537, estimated mean time to achievement of RAPID3 MID was shorter for both ABT-494 doses vs PBO (12mg: 3.9±0.5 weeks; 6mg: 3.9±0.4 weeks; PBO 6.0±0.6 weeks). Similarly, estimated mean time to these responses was shorter with both ABT-494 doses vs PBO (12mg: 3.6±0.4 weeks; 6mg: 4.9±0.6 weeks; PBO 6.0±0.6 weeks) in M13–550, although it was underestimated due to censoring.

Table. Number of patients reporting clinically meaningful improvements over study period.

<table>
<thead>
<tr>
<th></th>
<th>ABT-494 6mg N=50</th>
<th>ABT-494 12mg N=50</th>
<th>PBO N=55</th>
<th>ABT-494 6mg N=55</th>
<th>ABT-494 12mg N=55</th>
<th>PBO N=55</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPID3 MID</td>
<td>Week 2 68%</td>
<td>63%</td>
<td>25%</td>
<td>40%</td>
<td>37%</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td>Week 12 75%</td>
<td>69%</td>
<td>38%</td>
<td>54%</td>
<td>51%</td>
<td>33%</td>
</tr>
<tr>
<td>DAS28 ≥3.6</td>
<td>Week 2 71%</td>
<td>64%</td>
<td>39%</td>
<td>46%</td>
<td>44%</td>
<td>32%</td>
</tr>
<tr>
<td></td>
<td>Week 12 79%</td>
<td>73%</td>
<td>41%</td>
<td>60%</td>
<td>58%</td>
<td>43%</td>
</tr>
<tr>
<td>CDAI ≥11.0</td>
<td>Week 2 73%</td>
<td>67%</td>
<td>38%</td>
<td>50%</td>
<td>47%</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>Week 12 81%</td>
<td>77%</td>
<td>45%</td>
<td>63%</td>
<td>60%</td>
<td>45%</td>
</tr>
</tbody>
</table>

Conclusions: Patients treated with ABT-494 showed fast clinically meaningful improvements in patient reported disease activity, pain, physical function cumulatively assessed as RAPID3, as well as clinical outcomes DAS28 and CDAI, as early as week 2 and sustained through week 12 in both MTX-IR and TNF-IR populations.

Disclosure of Interest: Joann Hettasch, Fishawack Group, Conshohocken, PA was provided by AbbVie. AbbVie participates in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content.


SAT0218 EFFECT OF TOCILIZUMAB IN DMARD-NAÏVE EARLY RHEUMATOID ARTHRITIS PATIENTS ON HEALTH-RELATED QUALITY OF LIFE: RESULTS OF THE U-ACT-EARLY TRIAL

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Background: Tocilizumab (TCZ), a humanized interleukin-6 receptor inhibitor, has been shown effective in suppressing symptoms of rheumatoid arthritis (RA). In U-Act-Early, a significantly greater proportion of patients with early RA who initiated TCZ (84%) or TCZ plus MTX therapy (86%) achieved sustained remission (Disease Activity Score assessing 28 joints (DAS28) <2.6 with <2 swollen joints for ≥24 weeks), when compared to those initiating MTX (44%)[1].

Objectives: To determine the effect of treat-to-target TCZ therapy, with or without MTX, on health-related quality of life (HRQoL) in disease modifying anti-rheumatic drugs (DMARD)-naive patients with early RA.

Methods: Patients (n=317) were randomized to initiate TCZ, TCZ+MTX or MTX therapy and treated according to a step-up strategy. TCZ was given (8 mg/kg) every 4 weeks and MTX (oral) was started at 10 mg/week and increased with steps of 5 mg steps 4 weekly up to 30 mg/week (or maximum tolerable dose) until remission. If after 20 weeks remission was not achieved, hydroxychloroquine was added and discontinued 12 weeks thereafter if the target still was not achieved. Patients who originally initiated monotherapy then switched to TCZ+MTX therapy and those already on this combination therapy switched to a tumour necrosis factor inhibitor. To evaluate the effect of TCZ on HRQoL, we used the 36-item Short-Form (SF-36), which can be summarized into a physical (PCS) and mental (MCS) component score. HRQoL was measured at baseline and after 12, 24, 52, and 104 weeks. A linear mixed effect model with a random intercept was used to evaluate differences between treatment strategies over time with visit (time), strategy, baseline SF-36 score, baseline DAS28 level (i.e., DAS28 <5.1 or ≥5.1) and centre as fixed effects. The proportions of patients exceeding the minimum clinically important differences (MCID, ≥2.5-point increase from baseline) were tested for significance using the two-sided Pearson’s chi-squared test.

Results: In the SF-36 PCS in patients initiating treatment with TCZ (TCZ vs MTX: p=0.041, TCZ+MTX vs MTX; p<0.011, Fig. 1). For the SF-36 MCS, no significant differences over time were noted between the treatment arms (p=0.11). A significantly higher proportion of patients initiating treatment with TCZ (76%; p=0.016, 89%; p=0.009) or TCZ-MTX (73%; p=0.049, 89%; p=0.027) achieved MCID in the SF-36 PCS at week 12 and week 52, when compared to those initiating treatment with MTX (59% and 73%, respectively). Although the proportions of patients achieving MCID in the SF-36 MCS were numerically higher in the TCZ arms, no significant differences were found (p=0.06).

Conclusions: Initiation of TCZ, with or without MTX, at start of therapy resulted in statistically significant and clinically relevant improvements in the SF-36 PCS when compared to initiation of MTX alone and may be considered as a valuable treatment strategy in DMARD-naive patients with early RA.

References:

Disclosure of Interest: X. Teitgema: None declared, J. Jacobs: None declared, P. Welsing: None declared, A. Pethö-Schramm Employee of: Employee of F.Hoffmann-La Roche, M. Born Employee of: Roche Nederland B.V., J. van Laar Consultant for: Received fees from MSD, Pfizer, Roche, Eli Lilly and BMS, F. Laeberle: None declared, J. Bijlsma Grant/research support from: Received research grants (to his department) and consultancy fees from AbbVie, BMS, Crescendo, MSD, Mundipharma, Pfizer, Roche, Sun and UCB.

SAT0219  Efficacy and Safety of Atacicept in Patients with High Disease Activity in a 24-Week, Randomized, Placebo-Controlled, Phase IIb Study (ADDRESS II)

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Background: Atacicept targets B-cell stimulating factors BlyS and APRIL, and has shown evidence of clinical response in SLE.

Objectives: Exploration of atacicept efficacy and safety in a pre-defined subpopulation of SLE patients with high disease activity (HDA, SLEDAI-2K ≥10 at Screening) in the phase IIb ADDRESS II study (NCT01972588).

Methods: Autoantibody positive patients on standard of care therapy were randomized 1:1:1 to double-blind weekly SC injections of atacicept 75 or 150 mg or placebo (PBO) for 24 weeks. Analyses of the HDA subpopulation are now reported.

Results: 52% of the ITT population had HDA (n=158: 52 PBO; 55 atacicept 75 mg; 51 atacicept 150 mg). 92% were female, 67% were white, and baseline characteristics were balanced between groups. At week 24 (Table 1; Figure 1), the proportion of SLE Responder Index (SRI)-4 (p<0.05) and SRI-6 (p<0.005) responses was greater with atacicept 150 mg vs PBO. BICLA response rate was higher with both doses (p<0.05). More patients achieved SLEDAI-2K ≤2 with atacicept 150 mg vs PBO (p<0.01). Time to severe/flare was significantly reduced at both atacicept doses vs PBO (p<0.05). Patients in the quartile with the largest decline in serum IgG had the highest SRI-6 response rates (Table 2). Treatment-emergent adverse event (TEAE) rates were similar between groups (PBO 71.2%; 75 mg 78.2%; 150 mg 74.5%). Serious/severe infections were not increased with atacicept 150 mg (PBO 9.6%; 75 mg 10.9%; 150 mg 0%). There were no patient deaths.

Conclusions: In SLE patients with HDA, Atacicept 150 mg demonstrated significant clinical responses in a pre-defined subset of patients with acceptable safety.

Acknowledgements: The study was sponsored by EMD Serono Research & Development Institute Inc., USA (a business of Merck KGaA, Germany). Medical writing support was provided by Bioscript Science, UK, and funded by Merck KGaA, Germany.

Disclosure of Interest: J. Merrill Consultant for: received consulting fees from Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen, D. Wallace Consultant for: received consulting fees from EMD Serono, A. Kao Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, P. Fraser Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, D. Isenberg Consultant for: received consulting fees from EMD Serono


Table 1. Disease activity endpoints at week 24

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Atacicept 75 mg</th>
<th>Atacicept 150 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRI-4 response, n (%)</td>
<td>22 (42.3)</td>
<td>32 (58.2)</td>
<td>32 (62.7)*</td>
</tr>
<tr>
<td>BICLA response a, n (%)</td>
<td>15 (28.8)</td>
<td>23 (41.8)</td>
<td>28 (54.9)*</td>
</tr>
<tr>
<td>SLEDAI-2K ≤2, n (%)</td>
<td>14 (29.2)</td>
<td>26 (50.0)*</td>
<td>26 (49.0)*</td>
</tr>
<tr>
<td>Clinical SLEDAI-2K ≤2, n (%)</td>
<td>15 (28.9)</td>
<td>24 (43.6)</td>
<td>25 (49.0)*</td>
</tr>
<tr>
<td>Severe flare by SFI, n (%)</td>
<td>13 (25.0)</td>
<td>5 (9.1)</td>
<td>3 (5.9)</td>
</tr>
<tr>
<td>Time to severe flare by SFI, HR (95% CI)</td>
<td>0.33 (0.12, 0.94)*</td>
<td>0.19 (0.05, 0.68)*</td>
<td></td>
</tr>
<tr>
<td>Severe flare by BILAG A, n (%)</td>
<td>12 (23.1)</td>
<td>1 (1.8)</td>
<td>4 (7.8)</td>
</tr>
<tr>
<td>Time to severe flare by BILAG A, HR (95% CI)</td>
<td>0.08 (0.01, 0.59)*</td>
<td>0.32 (0.10, 0.99)*</td>
<td></td>
</tr>
<tr>
<td>Moderate/severe flare by BILAG A/2B, n (%)</td>
<td>13 (25.0)</td>
<td>5 (9.1)</td>
<td>5 (9.8)</td>
</tr>
<tr>
<td>Time to moderate/severe flare by BILAG A/2B, HR (95% CI)</td>
<td>0.33 (0.12, 0.95)*</td>
<td>0.34 (0.12, 0.95)*</td>
<td></td>
</tr>
<tr>
<td>Any flare by BILAG A/B, n (%)</td>
<td>31 (59.6)</td>
<td>23 (41.8)</td>
<td>17 (33.3)</td>
</tr>
<tr>
<td>Time to any flare by BILAG A/B, HR (95% CI)</td>
<td>0.67 (0.38, 1.17)</td>
<td>0.47 (0.26, 0.86)*</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05; † p<0.01; *excluding anti-dsDNA and complement parameters; HR, hazard ratio, SRI, SLE responder index; *patients with baseline data used for % calculation.

Table 2. Serum IgG reduction by quartile and SRI-6 response at week 24

<table>
<thead>
<tr>
<th>IgG reduction (by quartile), g/L</th>
<th>Placebo</th>
<th>Atacicept 75 mg</th>
<th>Atacicept 150 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (0–2.97)</td>
<td>38.1</td>
<td>30.8</td>
<td>53.8</td>
</tr>
<tr>
<td>Q2 (2.98–4.30)</td>
<td>38.1</td>
<td>30.8</td>
<td>53.8</td>
</tr>
<tr>
<td>Q3 (4.31–5.56)</td>
<td>5.57</td>
<td>14.73</td>
<td></td>
</tr>
<tr>
<td>Q4 (5.57–14.73)</td>
<td>5.33</td>
<td>5.33</td>
<td>5.33</td>
</tr>
</tbody>
</table>

SRI-6 response rate (%) | Referent | -7.3 | 15.7 | 25.5

SRI, SLE Responder Index.
SAT0221

SIX-MONTH PROTEINURIA MEASUREMENT PREDICTS RENAL RESPONSE AT 18 MONTHS IN LUPUS NEPHRITIS: ANALYSIS OF TWO PHASE III RANDOMIZED CLINICAL TRIALS

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Background: Early identification of patients with lupus nephritis (LN) likely to achieve complete renal response (CRR) may expedite the evaluation of new therapies and guide clinical care. Prior analyses have shown that early improvement in proteinuria is associated with subsequent renal response. Several ongoing LN trials including NOBILITY, an assessment of the efficacy of the anti-CD20 monoclonal antibody obinutuzumab in combination with standard of care immunosuppression, will evaluate proteinuric response at 6 months as a key secondary endpoint. Whether short-term response accurately predicts future CRR, however, is uncertain.

Objectives: To assess the predictive value of early measurements of the level of proteinuria and to identify proteinuria cutoffs that best identify patients who will achieve CRR at 18 months.

Methods: LUNAR and BIIB059 were multicenter, double-blinded studies that in total randomized 522 patients with ISN/RPS class III or class IV LN to blinded investigational infusions or placebo in combination with standard of care immunosuppression. 4, 5 CRR was assessed at 18 months and defined for this analysis as achievement of urine protein to creatinine ratio (UPCR) <0.5 with normal serum creatinine that was not increased from baseline by >25%. Bootstrapping was used to generate nonparametric receiver operating characteristic (ROC) curves and estimate area under the curve (AUC). The Youden index was used to identify UPCR cutoff values that best identify patients who will achieve CRR at 18 months.

Results: ROC curves were constructed for proteinuric measurements at baseline and 3, 6, 9, and 12 months after randomization (Figure 1). AUC increased from baseline to month 3 (0.64 vs. 0.80, P <0.001) and from month 3 to month 6 (0.80 vs. 0.84, P =0.01) but did not increase beyond month 6 (P >0.05 for each pairwise comparison). Achievement of 6-month UPCR <1 was 83.8% sensitive and 71.0% specific for CRR at 18 months and had PPV and NPV of 64.9% and 87.2%, respectively. Evaluation of lower 6-month UPCR cutoff values yielded improvements in specificity and PPV but marked decreases in sensitivity and NPV. In multivariate analysis, the addition of 6-month serum creatinine and percent change in UPCR from baseline did not result in meaningful increases in AUC compared with 6-month proteinuria measurement alone.

Figure: Receiver operating characteristic curves for CRR at 18 months

Conclusions: Level of proteinuria at 6 months alone was predictive of CRR at 18 months in aggregated data from two phase III LN clinical trials. After 6 months of treatment, UPCR <1 had high sensitivity and NPV for CRR at 18 months. This cutoff might be used to prospectively identify patients who are unlikely to achieve complete response within 18 months on the initial therapy for LN. The impact of these findings on guiding treatment decisions outside the setting of randomized clinical trials requires further investigation.

References:
2. Dall’Era Arthritis Rheumatol 2015.
5. M. Kurtinecz 1, Y. Asukai2, 3


DOI: 10.1136/annrheumdis-2017-eular.3833

SAT0222

BIIB059, A MONOClonAL ANTIBODY TARGETING BDCA2, SHOWS EVIDENCE OF BIOLOGICAL ACTIVITY AND EARLY CLINICAL PROOF OF CONCEPT IN SUBJECTS WITH ACTIVE CUTANEOUS LE

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Background: Type I interferons (IFN-I) are central to the pathogenesis of systemic lupus erythematosus (SLE). BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon engagement, inhibits the production of IFN-I and other inflammatory mediators. Targeting BDCA2, therefore, represents an attractive therapeutic strategy for inhibiting pDC-driven inflammation that is such a key feature of SLE pathogenesis. BIIB059, an investigational anti-BDCA2 humanized monoclonal antibody has been shown to engage BDCA2, and this interaction leads to BDCA2 internalization and the consequent in vitro inhibition of TLR-induced IFN-I production by pDCs (Pellerin 2015).

Objectives: This first-in-patient study aimed to assess safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) effects and clinical activity of BIIB059 in adult SLE patients with active cutaneous lupus (CLE) following administration of a single BIIB059 dose.

Methods: A Phase 1b randomized, double-blinded, placebo controlled, multicenter clinical trial was conducted in 12 adult SLE subjects (meeting 1997 ACR criteria) with active cutaneous manifestations (including acnè sub-acute and/or chronic cutaneous forms of cutaneous lupus erythematosus (CLE)). Subjects received a single IV administration of either BIIB059 20mg/kg (n=8) or placebo (n=4). A panel of IFN-responsive genes (IRG) was assessed from whole blood by qPCR at baseline and several post-dose time points. Skin biopsies from active lesions were obtained and evaluated at baseline and week 4 for IFN-regulated proteins, including MxA and IFITM3 using quantitative immunohistochemistry.CLE disease activity was assessed using the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), and safety data, including adverse events (AEs) and laboratory tests, were also evaluated. The incidence of AEs was similar between BIIB059- and placebo-treated SLE subjects, and most AEs were mild or moderate in severity.

Conclusions: A single dose of BIIB059 resulted in inhibition of the IRG in peripheral blood and MxA and IFITM3 expression in lesional skin of SLE subjects, consistent with BIIB059’s proposed mechanism of action. The clinical and biomarker data together confirm the role of human pDCs in the pathogenesis of SLE, and support further development of BIIB059 in SLE.


DOI: 10.1136/annrheumdis-2017-eular.5414

SAT0223

INDIRECT COMPARATIVE CLINICAL EFFECTIVENESS OF INTRAVENOUS AND SUBCUTANEOUS FORMULATIONS OF BELUMUMAB FOR THE TREATMENT OF ADULT PATIENTS WITH ACTIVE, AUTOANTIBODY-POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS WITH HIGH DISEASE ACTIVITY

D. Parks 1, S. Ramsgooderan 1, M. Kurtinecz 1, Y. Asukai 2, R. Alfonso-Cristancho 3, 5, GSK, Collegeville, United States; 4GSK, Uxbridge, United Kingdom

Background: The efficacy of belimumab (BEL) vs placebo (PBO), in adult

References:
[5] M. Kurtinecz 1, Y. Asukai2, 3

Disclosure of Interest: M. Cascino Employee of: Roche/Genentech, T. Schindler Employee of: Roche/Genentech, L. Gomez Mendez Grant/research support from: Roche/Genentech, P. Brunetta Employee of: Roche/Genentech, L. Dragoni Employee of: Roche/Genentech, M. Dall’Era: None declared, J. Garg Employee of: Roche/Genentech

DOI: 10.1136/annrheumdis-2017-eular.5414
patients with active, autoimmunocomplex-positive systemic lupus erythematosus (SLE) who are receiving standard SLE therapy has been demonstrated. To date, no direct comparison of intravenous (IV) BEL vs subcutaneous (SC) BEL has been performed, hence the importance of an indirect treatment comparison (ITC).

**Objectives:** To indirectly compare the clinical effectiveness of BEL IV and SC formulations in patients with SLE high disease activity (HDA) via an ITC.

**Methods:**
Three BEL IV Phase III randomised controlled trials (RCTs; HDA/BLISS-52, 327/577; HDA/BLISS-76, 265/548; HDA/North East Asia study [BEL113750], 427/677) and one BEL SC RCT (HDA/BEL112341; 356/836) were compared via a Bayesian ITC (BEL207255). We evaluated the relative efficacy of the formulations in patients meeting three measures of HDA at baseline: 1; BLISS-52 and BLISS-76, CR < 0.9 g/L or C4 < 0.16 g/L; BEL112341 and BEL113750, C3 <0.9 g/L or C4 < 0.10 g/L; and 2; anti-dsDNA positive [≥30 IU/ml] or 3; Safety of Estrogen in Lupus Erythematosus National Assessment-SLE Disease Activity Index [SELENA-SLEDAI] scores ≥10). Analyses were conducted in patients meeting Criteria 1; low C3/C4 and anti-dsDNA; and Criteria 2; low C3/C4 and high anti-dsDNA or SELENA-SLEDAI ≥10 or low C3/C4. The primary endpoint was SLE Responder Index (SRI) response (≥4-point reduction in SELENA-SLEDAI, no worsening in Physician’s Global Assessment, no new 1A/2B British Isles Lupus Assessment Group domain scores) at Week 52. Secondary endpoints included ≥4-point reduction in SELENA-SLEDAI and SLE Flare Index rate. Safety endpoints were not assessed.

**Results:** Baseline characteristics were relatively similar between RCTs and a fixed effects model binomial distribution with logit link was used for all efficacy endpoints (Table). In this indirect comparison, no differences were identified between BEL IV and BEL SC for the efficacy endpoints.

**Conclusions:** In this indirect comparison, BEL IV and BEL SC were similar for SRI response; ≥4-point reduction in SELENA-SLEDAI, or rate of severe flare at Week 52 in patients with SLE. Outcomes were consistent irrespective of the criteria applied.

**Acknowledgements:** Study funded by GSK. Katie White, PhD, Fishawack Indicia Ltd, UK, provided editorial assistance funded by GSK.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4701

**SAT0224**

THE ROLE OF INTENSIVE IMMUNOSUPPRESSIVE THERAPY IN THE MANAGEMENT OF SLE-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: A SINGLE-CENTER COHORT STUDY

Q. Wang, J. Zhao, J. Qian, Z. Tian, M. Li, X. Zeng.1 Rheumatology; 2Internal Medicine; 3Cardiology, Peking Union Medical College Hospital, Beijing, China

**Background:** Autoimmune and inflammatory mechanisms could play a significant role in the pathogenesis of pulmonary arterial hypertension (PAH), especially in patients with systemic lupus erythematosus (SLE). The effect of immunosuppressive therapy in the treatment of SLE-associated PAH (SLE-PAH) has not been fully investigated in a large cohort previously.

**Objectives:** We aimed to review the clinical outcomes in patients with SLE-PAH cohort treated with intensive immunosuppressive therapy with or without PAH-targeted therapy.

**Methods:** In this single-center cohort study, 126 patients with SLE-PAH were consecutively enrolled between May 2006 through December 2015. All patients were performed right heart catheterization to confirm the diagnosis of PAH, and all received intensive immunosuppressive therapy including combination of high-dose glucocorticosteroids and immunosuppressants, such as cyclophosphamide, mycophenolate and calcineurin inhibitors. Baseline demographics, clinical features, laboratory findings, hemodynamic measurements and treatment were analyzed.

- Kaplan-Meier curves and Cox proportional hazards regression analysis were performed, hence the importance of an indirect treatment comparison (ITC).
- **Patients** included**: Patients with SLE-PAH cohort treated with intensive immunosuppressive therapy with or without PAH-targeted therapy.

**Conclusions:** Intensive immunosuppressive therapy markedly improved the long-term outcomes of SLE patients with PAH, especially in the early stage of PAH.

References:

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5954

**SAT0225**

CEREBLON MODULATOR CC-220 DECREASES NAÏVE AND MEMORY B CELLS AND PLASMACYTOID DENDRITIC CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS: EXPOSURE-RESPONSE RESULTS FROM A PHASE 2A PROOF OF CONCEPT STUDY

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**Background:** CC-220 is a cereblon E3 ligase modulatory compound currently in development for the treatment of Systemic Lupus Erythematosus as well as other autoimmune conditions and multiple myeloma. As a high affinity ligand for cereblon, CC-220 administration results in significant reductions in ikaros (IKZF1) and aixol (IKZF3), transcription factors which are genetically linked to SLE risk, are over expressed in the peripheral blood of SLE patients compared to healthy controls.

**Objectives:** To describe the pharmacokinetics (PK), pharmacodynamics (PD), and the PK-PD relationship of CC-220 in subjects with SLE.

**Methods:** CC-220-SLE-001 is a randomized, double-blind, placebo-controlled,


SAT0226 | A FIRST-IN-HUMAN STUDY OF BMS-986165, A SELECTIVE, POTENT, ALLOSTERIC SMALL MOLECULE INHIBITOR OF TYROSINE KINASE 2

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Background: Tyrosine kinase 2 (Tyk2) is a member of the JAK family that phosphorylates STAT proteins downstream of the IL-12, IL-23 and the Type I interferon pathways and thus is a highly promising therapeutic target for SLE. CC-220 in patients with SLE. Forty-two (42) adult SLE subjects fulfilling SLE ACR phase 2a dose escalation study to investigate the safety, PK, PD, and efficacy of BMS-986165, a novel inhibitor of Tyk2.

Methods: We report the first evidence of safety, pharmacokinetics (PK), target engagement (TE), and pharmacodynamic activity (PD) of BMS-986165, a novel inhibitor of Tyk2.

Results: BMS-986165 was safe and overall well-tolerated. There were no serious adverse events and the frequency of non-serious adverse events were similar between cohorts, with moderate accumulation in the non-alternating dose cohort. CC-220 significantly reduced total CD20+ B cells by as much as 91.2%, switched memory B cells by as much as 81.4%, BAFFR+ B cells by as much as 67.5%, and plasmacytoid dendritic cells (pDCs) by as much as 86.5% (Day 85 median percent change from baseline). Whereas reductions in B cells were observed, CD4+ as well as CD8+ T cells increased, and the rise in T cells paralleled the drop in plasma. In plasma, we preferentially observed decreased B cells, pDCs and neutrophils with increased exposure to CC-220.

Conclusions: It was determined that 0.3 mg QD to 0.6/0.3 mg alternating QD reduced concentrations of B cells and pDCs while avoiding neutropenia. These findings, in combination with the PK, safety, and exploratory efficacy data, support continued development of CC-220 in SLE.
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Saturday, 17 June 2017

larger when derived from commercial claims ($21,600–55,400) than from public
payers (Medicare and Medicaid, $16,000–23,000).
Conclusions: Our ﬁndings suggest that patients with SLE, especially those with
moderate or severe disease, use considerably more health care services and
incur greater direct and indirect costs relative to those with mild disease. Thus,
SLE remains a signiﬁcant driver of health care resource utilization and costs.
Disclosure of Interest: E. Hammond Employee of: AstraZeneca, I. Murimi: None
declared, D. Lin: None declared, H. Kan Shareholder of: GSK, J. Tierce: None
declared, X. Wang Employee of: AstraZeneca, H. Nab Employee of: AstraZeneca,
B. Desta Employee of: AstraZeneca, G. C. Alexander: None declared
DOI: 10.1136/annrheumdis-2017-eular.5224

SAT0228

APOPTOTIC EFFECT OF BLYS ON ENDOTHELIAL CELLS AND
ENDOTHELIAL PROGENITOR CELLS IS MEDIATED BY BLYS
RECEPTROS AND IS REVERTED BY BELIMUMAB

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Background: Circulating endothelial progenitor cells (EPCs) are surrogate
markers of endothelial function. Several studies demonstrated a reduction and
functional impairment of EPCs in patients with Systemic Lupus Erythematosus
(SLE), partially accounting for endothelial dysfunction. In murine models of
atherosclerosis, treatment with a B Lymphocyte Stimulator (BLyS) inhibitor slowed
the progression and reduced the size of atherosclerotic plaque. Belimumab (BLM)
is a human anti-BLyS monoclonal antibody approved for the treatment of SLE.
Objectives: We aimed at evaluating the effect of BLyS inhibition on EPCs and
endothelial cells both ex vivo – in SLE patients receiving BLM– and in vitro.
Moreover we investigated the expression of receptors for BLyS on EPC and
mature endothelial cell surface.
Methods: We enrolled consecutive patients with SLE who were due to start BLM,
without known cardiovascular disease and age and sex-matched healthy subjects.
Peripheral blood mononuclear cells (PBMC) were isolated by Ficoll densitygradient centrifugation. Cells were incubated with anti-CD34 and anti-VEGFR2/KDR monoclonal antibodies; acquisition was performed by ﬂow cytometry:
EPCs were deﬁned as CD34/KDR double-positive cells. Recovered EPC isolated
from healthy donors’ PBMC were plated on dishes coated with human ﬁbronectin.
Apoptosis was investigated after 6, 12 and 24 hours of incubation with BLyS
at different concentrations – 5, 20 and 100 ng/ml – and re-evaluated after 6
hours of co-incubation with BLM at 173 and 300 μg/ml. The same experiments
were repeated with the human endothelial cell line EA.hy926. Finally, EPCs and
EA.hy926 were incubated with monoclonal antibodies anti-B Activating FactorReceptor (BAFF-R), B-cell maturation antigen (BCMA) and transmembrane
activator and calcium modulator and cyclophilin ligand (CAML) interactor (TACI)
and analysed by ﬂow cytometry; the results were expressed as mean ﬂuorescence
intensity (MFI).
Results: We treated with BLM 10 female patients (mean age 45.6±10.2 yrs,
mean disease duration 17.8±10.8 yrs) with active disease (mean baseline SLEDAI
8.4±2.6). Number of EPCs was signiﬁcantly lower in SLE patients than in NHS
(p=0.005). After 4 weeks of BLM, mean EPC number increased from 0.013±0.016
to 0.021±0.016 (p=0.012 vs baseline; p=n.s. vs NHS). At week 12, EPC number
did not signiﬁcantly differ compared to week 4 nor to baseline.
In vitro studies demonstrated that 20 ng/ml of BLyS induced apoptosis of EPC
after 6 hours of incubation; this effect was reverted by the addiction of BLM.
Similarly, after 6 hours of incubation with 20 ng/ml of BLyS we detected an
increase in EA.hy926 apoptosis that was reverted by co-incubation BLM. Both
EPCs and EA.hy926 expressed on their surface BAFF-R (MFI =3.8 and 1.5,
respectively) and BCMA (MFI =1.25 and 1.15, respectively); EPCs also expressed
TACI (MFI =1.4).
Conclusions: The results of this study demonstrated that the reduction of EPCs
number detected in SLE patients was restored by BLM. In vitro results support
a direct pro-apoptotic effect of BLyS that was reverted by the addition of BLM
both in EPCs and EA.hy926 culture. The apoptotic effect of BLyS seems to be
mediated by the three receptors (BAFF-R, BCMA and TACI) that are expressed
on EPCs and mature endothelial cells surface.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6174

SAT0229

THE USE OF ANTIMALARIAL DRUGS DURING PREGNANCY
CAN PREVENT THE DEVELOPMENT OF PREECLAMPSIA IN
WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The antimalarial drugs decrease the risk of lupus activity during
gestation, but the beneﬁcial effect on other maternal-fetal complications is
controversial.
Objectives: To analyze the beneﬁcial effect of antimalarial drugs on maternal-fetal
complications in pregnant women with systemic lupus erythematosus (SLE).

Methods: A prospective cohort of pregnant women with SLE (ACR 1997) from
January 2009 to June 2015 was studied. The patients were assessed every
4 to 6 weeks and postpartum both, by a rheumatologist and a gynecologist.
Clinical, biochemical, and immunological characteristics, along with maternal and
fetal complications were registered. For analysis, the patients were allocated to
one of two groups: pregnancies exposed to antimalarial drugs in comparison
to those not exposed. A logistic regression analysis including variables such as
smoking, obesity, infections, ﬁrst pregnancy, age, SLE ﬂare, drugs (prednisone,
antimalarials, aspirin, and azathioprine), anti-DNA antibodies, anticardiolipin
antibodies, and antiphospholipid syndrome was performed.
Results: We studied 197 lupus pregnancies, 154 expose to antimalarial drugs
and 47 unexposed. We found no differences between groups in age, years of
evolution of SLE, ﬁrst pregnancy, childhood-onset SLE, lupus nephritis, and use
of prednisone, aspirin and azathioprine. The rate of most maternal and fetal
complications was also similar in both groups (Table). A lower incidence of
preeclampsia was observed in patients exposed to antimalarial drugs compared
to those not exposed (9% vs 23%, p=0.01). Additionally, 2 maternal deaths
in patients not exposed to antimalarial drugs. The logistic regression analysis
showed that the use of antimalarial drugs during pregnancy is a protective factor
for the development of preeclampsia (RR 0.1, 95% CI 0.05–0.58, p=0.004); on
the other hand, active SLE before pregnancy (RR 4.8, 95% CI 1.3–17.8, p=0.01)
and lupus nephritis (RR 2.9, 95% CI 0.9–8.8, p=0.05) were associated factors
with the development of preeclampsia.
Table 1. Maternal and fetal outcomes
Maternal complications
Preeclampsia
PROM
Cesarean section
Maternal death
SLE ﬂare
Renal ﬂare
Infection
Fetal complications a
Live births a
Prematurity a
Miscarriage a
Stillbirth a
Weeks’ gestation c
Birth weight (g) c
Apgar score 1 c
Apgar score 2 c

Antimalarial drugs (n=154)

No antimalarial drugs (n=43)

P value

74 (48.0)
14 (9.0)
15 (9.7)
99 (64.2)
0 (0)
60 (38.9)
23 (14.9)
21 (13.6)
71 (46.1)
137 (88.9)
40 (25.9)
13 (8.4)
4 (2.5)
35.1±5.9
2,534±651
7.4±1.6
8.6±1.4

18 (41.8)
10 (23.2)
1 (2.3)
29 (67.4)
2 (4.6)
8 (18.6)
5 (11.6)
5 (11.6)
22 (51.1)
38 (88.3)
13 (30.2)
5 (11.6)
0 (0)
35.0±6.3
2,444±827
7.2±1.6
8.3±1.3

0.47
0.01
0.12
0.53
0.007
0.01
0.58
0.73
0.56 b
0.98 b
0.58 b
0.52 b
0.28 b
0.89 d
0.5 d
0.41 d
0.37 d

a
Results expressed in mean (SD). b Student’s t-test. c Results expressed in numbers and percentages. d Chi-square test.

Conclusions: Our study suggests that the use of antimalarial drugs during
pregnancy can prevent the development of preeclampsia in women with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6035

SAT0230

NEW ORAL ANICOAGULANTS IN PATIENTS WITH
ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is an acquired thrombophilia
characterized by reccurent venous and arterial thrombosis, obstetric pathology
(fetal loss), and synthesis of antiphospholipid antibodies. Warfarin is a “golden”
standard of APS therapy. However it has number of disadvantages. Dabigatran
etexilate is a direct thrombin inhibitor and its main differences from warfarin are
ﬁxed dose, no need of regular INR monitoring,less elimination half-life.
Objectives: To evaluate efﬁcacy and safety of dabigatran etexilate in patients
with APS.
Methods: 38 patients (pts) (F:26, M:12) with primary and secondary APS,
37,2±9,9 years old. 24 pts with primary APS, 14 pts with secondary APS: 13 had
systemic lupus erythematosus (SLE) + APS, 1 rheumathoid arthritis (RA) + APS.
The diagnosis of APS was established due to international APS criteria (Sydney),
SLE – SLICC 2012, RA - ACR/EULAR 2010. The majority number of pts (n=28)
received warfarin, others – sulodexide (n=1), low molecular heparin (n=1), had no
anticoagulant therapy (n=3), 5 pts received dabigatran etexilate before inclusion
to trial. The control of coagulogram was done 3 times: before inclusion to trial,
in 24 weeks and in 48 weeks after inclusion. Trial assays were performed in
the laboratory in V.A. Nasonova Research Institute of Rheumatology, Moscow,
Russian Federation. APPT and thrombin time tests were done with the automated
coagulometer Coalysys Plus C (Behnk Electronic, Germany); thrombin time test
was done with STA-thrombin reagent (Diagnostica Stago, France), APPT with
STA-Cephascreen reagent (Diagnostica Stago, France). Lupus anticoagulant was
assessed by the dilute Russell’s viper venom time, using Siemens Healthcare
(Germany) LA1 (screening) and LA2 (conﬁrmation). IgG or IgM antibodies
against cardiolipin and β2 glycoprotein I (β2GPI) were measured with automated
enzyme-immunoassay analyzer Alegria with Anti-Cardiolipin IgG/IgM and Antibeta-2-Glycoprotein I IgG/IgM reagents (Orgentec Diagnostika GmbH, Germany).


Triple positivity was defined as positive antibodies against cardiolipin and j2GPI and a positive test for lupus anticoagulant.

Results: 32 pts had high or medium level of aPL (cardiolipin antibodies IgG,IgM, anti-j2GPI antibodies IgG,IgM). 6 had low or normal level of aPL. 12 pts were triple positive. APPT and thrombin time before inclusion to trial were 30.2 [28.5;33.5] and 16.1 [14.9;17.0], on 24 week after dabigatran etexilate start 51.0 [40.6;57.0] and 163.5 [108;240.0] and on 48 week 58.7 [45.6;63.2] and 194.1 [152;265.5] respectively. 1 patient was excluded due to non-compliance. During follow-up period from 1.5 to 12 (10.6;3.2) months 7 pts (22.6%, 20.7 per 100 patient-years) experienced recurrent thrombosis including superficial vein thrombosis (n=3, 6.5, 5.9 per 100 patient-years), thrombosis of paraneoplastic veins (n=1, 3.2%, 2.9 per 100 patient-years), acute cerebrovascular disorders (n=4; 12.9%, 11.8 per 100 patient-years). All pts with recurrent thrombosis had high or medium level of aPL; 2/7 were triple positive, both had acute cerebrovascular disorders. 5 pts (16.1%, 14.8 per 100 patient-years) experienced bleeding; 2 hemorrhoidal bleedings, 1 uterine bleeding, 2 nasal bleedings. There was no case of severe bleeding.

Conclusions: Dabigitran etexilate could be used in patients with APS in the case of warfarin non-effectiveness. These findings need to be confirmed in larger studies.

Disclose of Interest: None declared


SAT0232 B-CELL SUBPOPULATION DYNAMICS IN SLE PATIENTS FOLLOWING RITUXIMAB THERAPY


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Objectives: To study B-cell subpopulation dynamics in SLE patients following Rituximab (RTX) therapy.

Methods: The study included 31 SLE pts (3m/28f) with high (SLEDAI≥20–28 pts.) and moderate (SLEDAI<20–10–3 pts.) disease activity; out of them 12 pts with SLE nephritis, 5 pts with neuropsychiatric and 8 with vasculitis. RTX was administered to pts who failed to respond to glucocorticoids (GCs) and cytostatics (CTs). B-cells subpopulations were assessed before RTX administration (Mo0), and at Mo3 and Mo6 of RTX therapy, RTX was administered at 500 to 2000 mg doses depending on disease activity. The absolute counts of CD19+ B-cells, the total population of memory B-cells (CD19+CD27+), “preswitch” (CD19+IgD-CD27+) and “postswitch” (CD19+IgD-CD27+) memory B-cells, “naïve” (CD19+IgD-CD27-), plasma cells (CD19+CD38+) and double negative B-cells (CD19+CD27-IgD-) were measured. 3 cell subsets were analyzed with multicolor flow cytometry using a panel of monoclonal antibodies to B-lymphocytes’ surface membrane markers.

Results: Following initiation of RTX SLE clinical and lab activity indices decreased in all 31 pts by Mo3 and Mo6 of follow up (SLEDAI-2K Mo0–Mo3 12.18; Mo3–Mo6 6.4; Mo6–Mo24 2.4, as well as absolute count CD19+ B-cell population (Mo0–Mo6 0.1,19x10^9 [0.05;0.26], Mo3–Mo6 0.1x10^9 [0.003;0.005], Mo6–Mo24 0.004x10^9 [0.002;0.005]). B-cell repopulation by Mo6 in 15 out of 31 pts without signs of relapse and 4 pts with earlier relapse SLE was dependent on “naïve” B-cells (Mo 0.005x10^9 [0.0026;0.005] vs Mo 0.003x10^9 [0.0023;0.003]), double negative (Mo 0.001x10^9 [0.0002;0.002] vs Me 0.0035x10^9 [0.0018;0.005]), “postswitch” memory B-cells (Me 0.0006x10^9 [0.00007;0.0001] vs Me 0.0023x10^9 [0.0005;0.003]).

Conclusions: Decrease in clinical and lab SLE activity was documented in all 31 pts by Mo3 after one course of RTX therapy. In 4 pts with earlier relapse SLE at Mo3 B-cell was found repopulation and significant increase “naïve” B-cells, double negative, “postswitch” and “preswitch” memory B-cells compared with the group without relapse.

Disclose of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8174
immune complexes (IC), and autoantibodies are supposed to participate in IC formation. Thus, the fraction of autoantibodies participating in IC formation merits a diagnosis as a diagnostic and/or prognostic marker. We have developed a technique to quantify autoantibody content in IC (Sohrabian et al. Ann Rheum Dis 2015;74(Suppl 1):A74).

Objectives: To elaborate on the quantification of autoantibodies in IC as a measure of disease activity and prognosis for response in belimumab-treated SLE patients.

Methods: Fifty-five SLE cases classified according to the ACR criteria were treated with belimumab and followed for one year. High disease activity was defined as SLE Disease Activity Index 2000 (SLEDAI-2K) ≥10, or as low levels of complements C3 and/or C4. Treatment regimens were recorded using the SLE Responder Index (SRI), or as a value of modified SLEDAI-2K with suppression of autoantibody and complement data (clinical remission). Low disease activity was also recorded as Lupus Low Disease Activity State (LLDAS).

Results: Data were recorded at 3, 6, and 12 months. IC were purified from sera by binding to C1q-coated beads, and thereafter eluted. Autoantibody levels were determined in unmodified serum and in solubilised IC with addressable laser bead immunoassay (FIDIS Connective, TheraDiag, Paris) for autoantibodies against dsDNA, histones, ribosomal P antigen, proliferating cell nuclear antigen (PCNA), SSA/Ro60, SSA/Ro66, SSB, Sm, U1RNP, and the Sm/RNP complex.

Autoantibody levels in serum and in IC were compared with Mann-Whitney’s U test between patients with high and low disease activity at baseline and between patients with and without treatment response during the follow-up period.

Results: Antibodies against dsDNA, SSA/Ro60 and Sm/RNP were found in 65%, 54% and 43%, other antibodies with lower percentages. Low complement levels were associated with high serum anti-dsDNA (p=0.003) and anti-ribosomal P antibody (p=0.008) levels, whereas high SLEDAI-2K associated with high anti-dsDNA (p=0.02) and anti-SM/RNP (p=0.047) levels. Serum levels of antibodies against SSA/Ro60, SSA/Ro66, SSB and SSA/Ro66 were lower in patients attaining LLDAS after 6 months (p=0.02, 0.051 [trend] and 0.04, respectively); these associations were stronger for corresponding IC fractions (p=0.01, 0.005, and 0.02, respectively). Baseline levels of anti-dsDNA and anti-histones in IC associated with clinical remission ever during the follow-up period (p=0.003 and p=0.05). Low levels of anti-Sm and anti-Sm/RNP in serum but not in IC associated with clinical remission at month 6 (p=0.02 and 0.04 respectively), and for Sm/RNP also at month 3 (p=0.04).

Serum levels of all antibodies except SSA/Ro52 declined during the first 6 months, most prominently for dsDNA, histones ribosomal P, PCNA and Sm/RNP (p<0.0001 for all). Levels of antibodies in IC declined only for dsDNA (p=0.048).

Conclusions: Autoantibodies in serum and in IC show different associations to disease activity and to treatment response. High baseline anti-dsDNA levels in IC were most strongly associated with clinical remission, and decreased during belimumab treatment. Belimumab effect might primarily relate to autoantibodies in IC.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5054

SAT0235  BII059, A MONOCLONAL ANTIBODY TARGETING BDCA2 SHOWS SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS IN HEALTHY VOLUNTEER SUBJECTS

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Background: Type I interferons (IFN-I) are central to the pathogenesis of systemic lupus erythematosus (SLE). BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon engagement, inhibits the production of IFN-I and other inflammatory cytokines. Targeting BDCA2 therefore represents an attractive therapeutic strategy for inhibiting pDC-derived IFN-I and may be an effective therapy for the treatment of SLE. BII059, an investigational anti-BDCA2 humanized monoclonal antibody, has been shown to engage BDCA2, and this interaction leads to BDCA2 internalization and the consequent in vitro inhibition of TLR-induced IFN-I by pDCs (Pellerin 2015).

Objectives: This study is a first-in-human study that aimed to assess safety, tolerability, PK and PD of BII059 in HV subjects following administration of single ascending doses of BII059.

Methods: A randomized, double-blind, placebo controlled, single ascending dose-escalation was conducted in adult HV. Subjects received a single administration of either BII059 or placebo. BII059 was administered IV at 0.05, 0.3, 1, 3, 10 or 20mg/kg or SC at 50mg at ratio of 2:1:3. Blood samples were obtained before and after dose administration up to week 16. Target modulation of BDCA2 and serum BDCA2 concentration were measured using flow cytometry, and an enzyme-linked immunosorbent assay (ELISA), respectively, and anti-drug antibodies (ADA) were measured using a bridging ELISA.

Results: 54 HV (38 BII059; 16 placebo) were assigned to cohort 1–7. BII059 demonstrated non-linear PK consistent with target mediated drug disposition. Bioavailability of SC administration was ~50%. Treatment with BII059 led to rapid and complete down-modulation of BDCA2 on the surface of pDCs at all doses levels. Time to reappearance of BDCA2 on pDC surface correlated with circulating levels of BII059, establishing an in vivo pharmacokinetic/pharmacodynamics (PK/PD) relationship. Single dose administration of BII059 was well tolerated across all dose levels. All AEs were mild to moderate in severity with no serious AEs. There were no clinically significant changes in laboratory assessments, physical examinations, or electrocardiogram (ECG) values. Anti-drug antibodies were detected at low levels in a small number of BII059-treated subjects. Responses were largely transient and demonstrated no impact on BII059 exposure or association with any safety event.

Conclusions: The first-in-human study in HV demonstrated acceptable safety/tolerability and PK profile in healthy subjects and supports further multiple-dose studies with BII059. BII059 treatment showed dose dependent target engagement and internalization of BDCA2 establishing a PK/PD correlation in vivo on circulating pDCs. These data support further evaluation of clinical efficacy and safety of BII059 as a potential novel therapy in SLE patients.

Acknowledgements: None declared

DOI: 10.1136/annrheumdis-2017-eular.6109

SAT0234  PROSPECTIVE SINGLE CENTRE STUDY OF EFFECTIVENESS OF UPFRONT RITUXIMAB AND MYCOPHENOLENATE WITH MINIMUM STEROID IN SLE

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Background: Treatment options for SLE have significant morbidity and mortality. Side effects from corticosteroid usage limit patient adherence and treatment efficacy. B cell depletion appears to target a critical pathophysiological pathway in SLE. Trials with rituximab have shown mixed results. Rituximab study demonstrated efficacy and steroid sparing action of rituximab and mycophenolate (1).

Objectives: We aim to analyse our experience of using rituximab and mycophenolate upfront on presentation with minimum oral steroids.

Methods: 19 patients with SLE, seen between Jan 2015 to march 2016, were included in the study. All patients completed 6 months of follow-up. Patients were treated with 2 doses of rituximab (1 g) and mycophenolate (500 mg) on days 1 and 15, and maintenance treatment of mycophenolate mofetil (2000mg) and low dose prednisolone (<7.5 mg) which was tapered off.

Results: 10 were females and 2 males. Mean age of the patients was 24.5. 9 had lupus nephritis, 1 mesentric vasculitis, 1 CNS vasculitis and 1 severe cutaneous vasculitis with pancytopenia. Average SLEDAI improved from 14 to 4. 6/9 LN attained complete renal remission and 2 partial remission, one patient died due to infection and renal disease 15 days after infusion. 2 vasculitis and one NPSLE patient improved completely. Two patients had infection requiring hospitalization with in 6 weeks of infusion and one patient had severe bradycardia during the infusion and received only one rituximab. Steroid was stopped by 6 months in 6 patients and in the dose was below 5 mg in rest.

Conclusions: Early Rituximab and mycophenolate is an effective option for treating severe lupus and has steroid sparing property.

References:

Disclosure of Interest: None declared
SAFETY AND DISEASE ACTIVITY CHANGES IN AN EXTENSION OF A PHASE IIb STUDY OF ATACICEPT IN PATIENTS WITH SLE (ADDRESS II)

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DOI: 10.1136/annrheumdis-2017-eular.3665

Methods: Atacicept was given as weekly subcutaneous injection to completers of ADDRESS II on average for an additional ≥ 24 weeks (i.e. ≥ 48 weeks total from Day 1 of ADDRESS II). Patients already receiving atacicept continued on the same dose (75 mg or 150 mg); those receiving placebo (PBO) switched to atacicept 150 mg (PBO/150 mg).

Conclusions: This extension study of ADDRESS II evaluated safety and disease activity in patients with SLE given continued atacicept treatment to week 48 (NCT01972568).

BONE MARROW AS A TARGET ORGAN OF SYSTEMIC LUPUS ERYTHEMATOSUS: ANALYSIS OF CASES WITH AUTOIMMUNE MYELOFIBROSIS

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Background: Cytopenia in the course of systemic lupus erythematosus (SLE) may be due to multiple factors. One of these factors can be SLE-associated autoimmune myelofibrosis (AIMF). However, the frequency of SLE-associated AIMF is unknown as well as the role of clinical and laboratory parameters in the development of AIMF is not clear.

Objectives: Our aim was to identify the frequency of SLE-associated AIMF and compared SLE-associated AIMF group with non-AIMF group in terms of clinical findings and morphological properties of the bone marrow (BM) in cytopenic SLE patients.

Methods: We retrospectively analyzed 224 SLE patients’ files who met 1997 revised Classification criteria for SLE. BM aspirates and trephine biopsies were re-examined. Patients were divided into two groups according to whether they had cytophoblastic crisis or not. In the BM aspirate, the presence of dysplasia, and lymphoid infiltration were recorded.

Results: 45 (20%) of 224 SLE patients were found to experience BM biopsy due to cytopenia. Four patients were excluded from analyses (2 drug-induced cytopenia, 1 lymphoma, 1 insufficient BM biopsy samples). While AIMF was detected in 29 (70.7%) of the 41 patients, 12 patients did not have AIMF. All patients with AIMF had reticulin fibrosis, 2 patients (6.9%) had also collagen fibrosis. Between the AIMF and non-AIMF groups, Concor differences were identified in terms of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), SLEDAI, BM cellularity, or BM dysplastic changes (p<0.989, p=0.387, p=0.788, p=0.672, and p=0.494, respectively). In the AIMF group, 27 patients responded to immunosuppressive therapy and corticosteroids, but 2 patients were unresponsive. The response time was longer for the AIMF group compared to the non-AIMF group (3.3±3.1 months vs 1.7±1.2 months, p=0.091). Correlation analysis revealed that higher the grade of BM fibrosis, longer the response time (r=0.471, p=0.002).

Conclusions: AIMF may be underestimated in SLE patients. AIMF as an additional factor for cytopenia in SLE patients may lead to delayed response to appropriate therapy, which was dependent on the presence of high grade fibrosis.

Acknowledgements: None declared

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4330

GLUCOCORTICOID WITHDRAWAL IN AN INCEPTION COHORT OF LUPUS NEPHRITIS PATIENTS

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Background: Few studies have addressed glucocorticoid (GC) withdrawal in lupus nephritis (LN). Yet, this remains a pivotal issue due to GC-induced side effects on the one hand, and to the risk of relapse on the other hand.

Objectives: We reviewed the data of the Louvain Lupus Nephritis Inception Cohort (LOULLINIC) i.e. to determine the percentage of patients able to permanently or transiently stop GC; ii): to compare their baseline and follow-up characteristics to patients who never stopped; and iii): to assess the consequences of GC withdrawal.

Methods: Ninety patients with new-onset biopsy-proven LN were included. All were under the care of the same senior physician (FAH) during follow-up. Clinical, pathological and biological data were extracted from our data base. The SLICC/ACR-DI was assessed at last visit. Unpaired t-tests, Mann-Whitney tests and ANOVA were used, as appropriate.

Results: Out of 90 patients with incident LN, 43 (48%) ever stopped GC (group P), of which 32 permanently (group DP). Median time to stop GC was 37 months. 47 patients (52%) never stopped GC (group N). At baseline, serum creatinine, uP/C ratio, ISN/RPS classes, activity and chronicity indices did not differ between groups, nor did the mean initial dose of methylprednisolone (MP) (N: 28 mg/d; E: 32 mg/d; P: 31 mg/d), the use of IV MP pulses (82
and 77% in N and E groups, respectively) and of IV cyclophosphamide (61 and 77%, respectively).

During the first year, mean (SD) u/pC decreased statistically more in group E compared to group N (p=0.028 by ANOVA), with striking differences at month 3 (N: 1.73±1.87; E: 0.96±1.34; p<0.038 by unpaired t-test). This difference at month 3 was also observed in P patients (0.85±0.76; p=0.02 by unpaired t-test).

Interestingly, the median MP dose at month 3 was statistically higher in group E (19.8±3) compared to group N (15±3) (p=0.005 by unpaired t-test).

At last follow-up, serum creatinine was statistically lower in E and P patients compared to N patients. Eight of the 11 patients from the T group suffered from a renal relapse (100% of the rest of patients, after a median time of 30 months). Importantly, SLICC/ACR-DI was significantly lower in E and P patients, compared to N patients (p=0.0068 and 0.0027, respectively).

Conclusions: In half of LN patients, complete GC withdrawal is achievable and in one-third it can be maintained long-term. As expected, patients able to stop GC display less damage at last follow-up. Patients who were able to stop GC decreased their proteinuria much more promptly during the first year of treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3132

SAT0239  | LATE-ONSET NEUTROPENIA FOLLOWING RITUXIMAB TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS – A ROLE OF THE BAFF/APRIL PATHWAY

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Background: Rituximab-mediated late-onset neutropenia (LON) has been studied in various diseases, but data from systemic lupus erythematosus (SLE) are limited.

Objectives: To study the prevalence and contributing factors for LON following treatment with rituximab in patients with SLE, including B cell related cytokines and growth factors of the myeloid lineage.

Methods: Patients from the Karolinska SLE cohort treated with rituximab (n=107) were enrolled in this observational study. Rituximab was given according to the lymphoma course (weekly for four weeks), the arthritis course (at week 0 and 2), or as a single infusion, with or without concomitant pulses of cyclophosphamide. LON was defined as an absolute neutrophil count <1500 cells/μL, occurring four weeks to two years after initiation of rituximab treatment, provided that other apparent causes were excluded. Neutropenia occurring later than two years after treatment initiation but during sustained B cell depletion were also considered LON.

Blisibimod was well-tolerated. The most common adverse events were upper respiratory tract infection (10.6% vs 14.3% on placebo), urinary tract infection (6.9% vs 10.7%), injection site erythema (7.8% vs 2.0%), injection site reaction (7.3% vs 2.6%), and diarrhea (7.3% vs 2.6%).

SAT0240  | PHASE 3 TRIAL RESULTS WITH BLISIBIMOD, A SELECTIVE INHIBITOR OF B-CELL ACTIVATING FACTOR, IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Targeted, biologic inhibitors of B-cell Activating Factor (BAFF) have been evaluated in Phase 3 trials in over 5000 patients with SLE. Post hoc analyses of these studies identify lower placebo response and greater treatment effect using more stringent endpoints in patients entering with higher disease activity, greater corticosteroid doses, and/or anti-double-stranded DNA (dsDNA) and low complement C3 or C4.

Objectives: The Phase 3 CHABILIS-SCL-01 trial evaluated blisibimod, an inhibitor of B-cell activating factor (BAFF), in a "responder population" identified from prior studies with this drug class.

Methods: 442 SLE patients with anti-nuclear antibodies or anti-dsDNA, SELENA-SLEDAI score ≤10 on standard of care medications were randomized to receive weekly subcutaneous blisibimod (200 mg) or placebo. Corticosteroid taper was encouraged from Week 8 with the goal to reach <7.5 mg prednisone/day.

Conclusions: With a deliberate focus on a "responder population" for whom lower placebo responses were observed in previous trials, much higher placebo response rates were observed in the CHABILIS-SCL-01 trial. Modest benefits of blisibimod were observed on serological effects and corticosteroid tapering.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2400

SAT0241  | EARLY RESPONSE TO BELIMUMAB IN SLE-RELATED JOINT INVOLVEMENT EVALUATED BY ULTRASOUND GRADIENT ASSESSMENT

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Background: Belimumab (BLM), a fully human monoclonal antibody directed against B lymphocyte stimulator (BllyS), is currently the only biological drug...
approved for the treatment of active Systemic Lupus erythematosus (SLE) patients not responding to standard of care. Data from RCTs and observational studies have demonstrated its efficacy, especially in patients with joint involvement. Focusing on this specific manifestation, the response has been also demonstrated by using Disease Activity Score on 28 joints (DAS28) (1). No data are available about the response to BLM in terms of synovitis, assessed by ultrasound (US).

Objectives: In the present 6-months longitudinal study, we evaluated the response to BLM in SLE patients treated for joint involvement, by using clinimetric indices and US assessment.

Methods: SLE patients starting BLM in the period between August 2013 and December 2016 were prospectively examined. The present analysis was restricted to patients requiring BLM for joint involvement. A complete physical examination and US assessment were performed at baseline (T0) and after 3 (T3) and 6 months (T6). At each time, we assessed the global disease activity by Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) and the joint involvement activity by DAS28. US evaluation of 12 joints (I-V metacarpophalangeal, I-V proximal interphalangeal, wrist and knee bilateral) was performed to identify inflammatory features (synovial effusion and hypertrophy, power Doppler) according to the OMERAQI definitions. These elementary lesions were scored according to a semi-quantitative scale (0=absent, 1=mild, 2=moderate and 3=severe) and a total score, corresponding to the patient’s inflammatory status (0–216) was obtained by their sum.

Results: Moving from 35 SLE patients starting BLM, 14 (14 female; mean age±SD 48.6±18.6 years; mean disease duration±SD 255.4±124.2 months) were treated for prevalent joint involvement. At baseline, the mean DAS28±SD was 4.5±1.1 and the mean SLEDAI-2K±SD was 6.1±1.5 and the mean daily prednisone±SD was 7.8±3.5 mg. After 3 months of treatment we observed a significant reduction in mean DAS28 (3.1±0.6 vs 4.5±1.1, P=0.007) and in mean SLEDAI-2K (3.5±2.1 vs 6.1±1.5, P=0.003) compared to baseline. The mean daily prednisone significantly decreased at T6 (4.7±1.4 vs 7.8±3.5 mg, P=0.03) while the rest of the therapy remained stable for 6 months. Of note, the mean total US score significantly decreased at T3 compared to T0 (13.7±24.4 vs 22.2±22.6, P=0.001). This result was maintained in 12 patients (85.7%) after 6 months with a statistically significant difference compared to T0 (7.9±6.6 vs 22.2±22.6, P=0.003) (Figure 1).

Conclusions: The results of the present study demonstrated the efficacy of BLM in SLE-related joint involvement, evaluated by SLEDAI-2K and DAS28, confirming previous data reported in the scientific literature. For the first time, we demonstrated an improvement to BLM as proved by the reduction of the total US synovitis score after 3 months, reflecting the improvement of the joint inflammatory status.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4238
result may be limited by small sample size. In type I IFNGS test—high pts, a log-linear logistic model was used to describe the treatment effect of aniflurab. PT dropouts were more likely in nonresponders. Clinical simulations demonstrated dosages <300 mg would result in inadequate PK exposure and suboptimal efficacy in some pts with SLE. In contrast, simulations indicated minimal efficacy improvement for dosages >300 mg, consistent with the Phase IIb MUSE study outcomes.

Conclusions: Based on E—R analyses and overall risk assessment, a 300 mg Q4W, intravenous dosage regimen is recommended for pivotal aniflurab studies in pts with SLE.

References:

Acknowledgements: Funded by Medimmune. Medical writing support: R. Plant, QW. Commentary, funded by Medimmune.


DOI: 10.1136/annrheumdis-2017-eular.3517

SAT0244 | A LONG-TERM FOLLOW-UP STUDY OF ALLOGENIC MESENCHYAL STEM CELLS TRANSPLANTATION IN PATIENTS WITH DRUG-RESISTANT SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Allogenic mesenchymal stem cells (MSC) transplantation showed therapeutic effect in active and refractory systemic lupus erythematosus (SLE).

Objectives: To determine the long-term safety and efficacy of allogenic MSC transplantation (allo-MSC) in severe SLE patients refractory to previous therapies.

Methods: All consecutive SLE patients who received at least one allo-MSCST were analyzed. SLEDAI score of more than or equal to 8 or with at least one BILAG grade A or at least two BILAG grade B manifestations. All the patients were refractory to corticosteroid and/or immunosuppressive drugs treatment. Allogenic bone marrow and/or umbilical cord derived MSCs were infused intravenously, with one million cells per kilogram of bodyweight for each infusion. The primary end point was 5-year overall survival. Secondary end points included complete clinical remission, partial clinical remission and relapse.

Results: Eighty-one patients were enrolled and underwent allo-MSCST. Thirteen patients died within 5 years post-MSCST and the 5-year overall survival rate was 84% (68/81). At 5-year follow-up, 22 patients (22/68, 32%) were in complete clinical remission and another 6 patients (6/68, 9%) were in partial clinical remission, and the 5-year disease remission rate was 41% (28/68). In total, 37 patients had achieved clinical remission (27 in complete remission and 10 in partial remission) at the 5 years visit and then 9 patients subsequently relapsed. The 5-year overall rate of relapse was 24% (9/37). SLEDAI scores, levels of serum albumin and complement C3, peripheral white blood cell and platelet numbers, as well as proteinuria levels continued to improve during the follow-up.

Conclusions: Allogenic MSCST is safe and resulted in long-term clinical remission in severe and drug-resistant SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2656

SAT0246 | EXPLORE STUDY: RITUXIMAB USE IN SYSTEMIC LUPUS ERYTHEMATOSUS, A NEW LOOK ON OLD DATA
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Background: Even if randomized trials EXPLORER and LUNAR failed to prove the superiority of rituximab versus placebo in patients with systemic lupus erythematosus, several encouraging indications as refractory lupus nephritis and new clinical trials renewed interest for this molecule.

We hypothesized that SLE response criteria used in EXPLORER were not sensible enough to show rituximab efficacy and that new response criteria could show a significant difference.

Objectives: Our objective was to reanalyze EXPLORER trial’s raw data using the newly described SLE response criteria.

Methods: We proceeded to a pre-specified re-analyze of EXPLORER trial’s raw data. The patients included in EXPLORER study had active SLE disease defined by a British Isles Lupus Assessment Group (BILAG) score A or 2 BILAG B despite immunosuppressive regimen. Renal and neurological SLE were excluded.

Patients were randomized through a 2/1 ratio to receive either two 1gr rituximab infusions (day 0 and 15) repeated at month 6 or a placebo. Standard SLE treatment and other immunosuppressant were continued. Patients received in a stratified manner prednisone ranging from 0.5 to 1.0 mg/kg depending on disease severity at inclusion. The original efficacy criterion was a composite clinical score using BILAG at week 52.

In our new analysis, rituximab efficacy was assessed at week 52 using 4 criteria: SRI-4 (Systemic lupus erythematosus Responder Index) with and without a concomitant oral prednisone (OP) tapering objective of -10mg at month 6 (SRI-4 with and without OP tapering), Lupus Low Disease Activity Score (LLDAS) and BILAG-based Combined Lupus Assessment (BICLA).

Results: Data from all 257 patients were available. There was 234 women (91%) with a mean age of 40.3 years among which 177 (69%) received hydroxychloroquine.

At week 52, SRI-4 response rate was 27.2% in the rituximab group vs 22.7% in the placebo group (p=0.43); SRI-4 with OP tapering was 16% in the rituximab group vs 13.6% in the placebo group (p=0.62); LLDAS was 16% in the rituximab group vs 12.5% in the placebo group (p=0.46) and BICLA was 15.4% in the rituximab group vs 15.9% in the placebo group (p=0.91).

Subgroup analyses demonstrated a trend for better efficacy of rituximab compared to placebo in the subgroup of patients co-treated with methotrexate: SRI-4 of 30.6% in the rituximab group vs 12% in the placebo group (p=0.08). This trend was not found in the subgroup co-treated with azathioprine: SRI-4 of 26.7% in the rituximab group vs 30.6% in the placebo group (p=0.68), nor in the subgroup co-treated with mycophenolic acid: SRI-4 of 23.1% in the rituximab group vs 21.6% in the placebo group (p=0.86). In the subgroup of patients with a BILAG A/B in hematological system or vasculitis at baseline, there was a significantly higher SRI-4 response rate with rituximab: 28.6% vs 5.3% in the hematological group (n=61, p=0.047) and 39.3% vs 0% in the vasculitis group (n=38, p=0.037).

Cumulative dose of steroids at week 52 were not statistically different: 423mg in the rituximab group vs 4390mg in the placebo group (p=0.65).

Conclusions: Our study confirms the results from the original EXPLORER study. These results might be partly related to the study’s design, notably the high daily oral prednisone used. Our work suggests efficacy in subgroups with vasculitis and hematological involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2661

SAT0245 | SERUM IFN GAMA MAY PREDICT THERAPEUTIC EFFECT OF MESENCHYAL STEM CELLS TRANSPLANTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS
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Background: Umbilical cord (UC) derived mesenchymal stem cells (MSCs) show immunoregulatory properties on various immune cells and display clinical effect on lots of autoimmune disease like systemic lupus erythematosus (SLE).

Objectives: The aim of this study is to investigate the effect of SLE environment on UC MSCs and to observe the possible serum biomarker to predict the therapeutic effect.

Methods: UC MSCs were co-cultured with peripheral blood mononuclear cells (PBMC) from active lupus patients at a ratio of 1:4. The proliferation, apoptosis and surface markers of UC MSCs were observed. UC MSCs functional molecules were assessed by real-time PCR and the signaling pathways were analyzed by western blot. Different recombinant cytokines were used to stimulate UC MSCs and the functional factors were determined by real-time PCR. In the last, twenty-six patients with SLE, refractory to conventional therapies, were given UC MSCs transplantation. The clinical effect was followed-up for one year to classify responder and non-responder groups, and baseline serum cytokines were analyzed by ELISA.

Results: The co-culture of lupus patients PBMC had no effect on UC MSCs surface markers and apoptosis, but promoted MSCs proliferation. Lupus PBMC were more prone to stimulate UC MSCs to secret VEGF as well as CXCL-12, compared to PBMC from normal controls. Furthermore, lupus PBMC activated Akt, ikB and Stat5 signaling pathways in UC MSCs but did not affect Erk1/2 and Smad3 pathways. When stimulated by different cytokines, we found that interferon-γ (IFN-γ) was still the most important cytokine to induce IDO1 as well as IDO2 productions in UC MSCs: both had dose-dependent manners. Moreover, our clinical study showed that baseline higher levels IFN-γ might predict a good response to MSCs transplantation in active lupus patients.

Conclusions: Baseline IFN-γ levels may predict clinical response to MSCs therapy for active lupus patients, which will help us to choose appropriate patient for clinical transplantation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1785
**SAT0247 Efficacy and Safety of Modified-Release Prednisone in Managing Moderate Activity Systemic Lupus Erythematosus During Pregnancy: An Implemented Case-Control Study**

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**Background:** Systemic lupus erythematosus (SLE) primarily affects women of childbearing age. Despite the overall favorable outcome, pregnancy represents a challenge for both patients and clinicians. Since the complications rate is linked to the baseline disease activity, the achievement of remission is recommended before pregnancy. Prednisone represents a cornerstone in SLE management and is safely used, at low doses (< 7.5 mg daily), during pregnancy. Modified-release prednisone (MRP) optimize corticosteroid treatment strategy in rheumatic diseases, thanks to its capability of respect the physiological cortisol circadian secretion. MRP has been approved from FDA in SLE treatment, but no data are available regarding its administration during pregnancy.

**Objectives:** We aimed to investigate whether this drug is safe and effective as the immediate release prednisone (IRP) in SLE pregnant patients.

**Methods:** We retrospectively evaluated 9 female patients, fulfilling the ACR criteria for SLE, consulting our Centers in a 4-years observational range. All of them, thanks to a stable disease (not requiring treatment regimen modifications during 12 months), experienced a successful pregnancy during the observation. All the cases were taking low-dose MRP (5 to 7.5 mg/daily) as a baseline treatment, from at least 6 months. They were matched to 9 controls, defined as SLE patients with the same age and duration of disease, taking the same prednisone dose from at least 6 months, in the IR formulation. Overall pregnancy outcome features: SLE disease activity (calculated at least once during pregnancy, SLEPDAI) and at baseline/post-partum (SLEDAI) score; patient’s global assessment (VAS) at baseline, during pregnancy and in postpartum (mm); need of treatment changes at baseline/post-partum (SLEDAI) score; patient’s global assessment (VAS) at baseline, during pregnancy and in postpartum (mm); need of treatment changes (add-on strategy), the observed rates involved 1/9 (MRP) and 5/9 (IR) (p<0.05). Patients VAS (MRP vs. IR) was 0.001). Results

**Results:** Mean MRP age group was 26±7; disease duration, 4±8 years; IR one, respectively, 28±6 and 3±9 (both, p=ns). SLEDAI at baseline was 1±0.1 among MRP and 1±0.3 among IR women; SLEPDAI, 1±0.9 and 2±0.2 (both, p=ns). No major perinatal complications were detected. Preterm births, cesarean section rates, newborns weight and APGAR scores did not differ between the two subpopulations (all, p=ns). SLEDAI assessed at postpartum was 2±0.6 in MRP subjects and 3±0.4 in IR (p=0.05). Patients VAS (MRP vs IR) was 3±0.4 and 2±09 at baseline (p=ns); 2±0.6 and 4±0.7 during pregnancy (p<0.05) and 3±0.3 and 4±0.9 at postpartum (p<0.05). Regarding treatment regimen changes (add-on strategy), the observed rates involved 1/9 (MRP) and 5/9 (IR) women during the observational gap (pregnancy+postpartum) (p=0.001). Results

**Conclusion:** Activity (SLEDAI) score was significantly higher at postpartum and treatment had to be increased in IR patients, in comparison to the MRP, to manage SLE. VAS, conversely, was significantly higher among IR, both during pregnancy and postpartum. No major perinatal side effects were observed during the study; minor and expected complications rates did not differ between the two subpopulations. Despite the limited number of subjects, MRP treatment seems to be as safe, but more effective, in comparison to the standard IR one, during pregnancy of SLE-affected women.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3135

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**SAT0248 Baseline Clas-Damage Is a Major Predictor of Skin Response to Belimumab in a Multicentric Cohort of SLE Patients**

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**Background:** Belimumab is used to treat several systemic lupus erythematosus (SLE) manifestations and predictors of response are advisable in clinical practice.

**Objectives:** To explore the effects of belimumab treatment on skin involvement in SLE patients in a real-life setting.

**Methods:** SLE patients treated with belimumab (10 mg/kg day 0, 14, 28 and then every 28 days), as add-on therapy in 11 Italian cohorts were prospectively followed-up for 24 months. Skin involvement was measured by the CLASIa score (Cutaneous Cutaneous LE Disease Area and Severity Index Activity) at baseline and every six months until month 24. Damage was measured by CLASI-Damage (CLASId); Response was defined as CLASId <2 at measured timepoints.

**Results:** The following variables were tested to determine baseline predictors of response at 12, 18 and 24 months: age, disease duration, cumulative prednisone dose; SLE activity index 2000 (SLEDAI-2K); prednisone dose >7.5 mg/day, baseline CLASId and CLASId, concomitant immunosuppressants (yes/no) and number of previous immunosuppressants. Statistical analysis was performed with SPSS 22.0 software.

**Results:** 188 patients were studied, among whom 48 (25.5%) had skin involvement as the leading feature for belimumab therapy. Mean follow-up period was 17.5±10.96 months. Thirty-eight patients completed a 6-month follow-up; 27 completed a 12-month follow-up; 19 completed a 18-month follow-up and 15 completed a 24-month follow-up. None of the patients discontinued due to adverse events (7/14, 50%), lack of efficacy (4/14, 28.5%) or other causes (3/14, 21.4%). CLASId, daily prednisone dosage and SLEDAI-2K significantly decreased during the follow-up (p<0.001). CLASId was achieved by 25 (38%) patients (65.7%) at 6 months, 19/27 (70%) at 12 months, 11/19 (58%) at 18 months and 10/15 (67%) at 24 months. A lower baseline CLASId was associated with CLASIa response at 18 and 24 months (responders vs. non-responders: 3.4±2.4 vs. 9.5±5.6; 3.5±2.5 vs. 11.2±6.5; p<0.005 for both), while a lower baseline CLASId was associated with CLASIa response at each timepoint (responders vs. non-responders: at 12 months 0.3±0.9 vs. 2.4±2.6; at 18 months 0.3±0.8 vs. 2.5±2.9; at 24 months 0.6±0.8 vs. 3.25±2.7; p=0.01 for all). Multivariate analysis was only performed at 12 months due to low patient number at 24 months. CLASId was the only independent negative predictor of response (OR 0.52, p=0.05). Notably, CLASId remained stable during the follow-up.

**Conclusions:** Belimumab use in cutaneous involvement is associated with reduced activity in skin lesions and hindrance of skin damage. Early use of belimumab before damage is established is likely to be associated with a better outcome.

**Acknowledgements:** Dr. Margherita Zen, Dr. Maddalena Larosa, Dr. Francesca Ometto, Dr. Mara Felicetti for helping in data collection and statistical analysis

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6461

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**SAT0249 Safety, Pharmacokinetics, Pharmacodynamics and Inhibition of T-Cell Dependent Antibody Response (TDAR) With MEDI4920, a Novel Engineered CD40 Ligand (CD40L) Antagonist: Results of a First-Time-in-Human Study**

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**Background:** The CD40/CD40L pathway is involved in the T-cell-dependent activation of B cells, which subsequently produce autoantibodies and inflammatory mediators that contribute to autoimmune disease pathology. MEDI4920 is an engineered fusion protein and antagonist of CD40L that lacks the fragment crystallisable (Fc) domain thought to be involved in thromboembolic events (TEs) and neutralizes the FcγR-dependent co-stimulatory activity of Fc fusion products. MEDI4920 has demonstrated a favorable tolerability profile in healthy volunteers. We report the results of a first-time-in-human study evaluating the safety, tolerability, pharmacokinetics (PK), and antibody responses to MEDI4920 in healthy adult male subjects.

**Objectives:** The primary objective of this Phase I, randomised, double-blind, placebo-controlled, single-ascending dose study was to evaluate the safety and tolerability of MEDI4920 in healthy subjects. Secondary objectives were to characterize T-cell dependent antibody response (TDAR) to keyhole limpet hemocyanin (KLH) neoantigen, pharmacokinetics (PK), and anti-drug antibodies (ADAs) to MEDI4920.

**Methods:** Fifty-six healthy adult male subjects, aged 19–49 years, received a single intravenous dose of either MEDI4920 (3, 10, 30, 100, 300, 1000 or 3000 mg) or placebo. TDAR inhibition was analysed by measuring serum concentrations of ADAs to MEDI4920.
IgG and IgM antibodies to KLH over time. A dose—response model was generated for TDAR inhibition. Blood samples were collected to evaluate PK, total soluble CD40L (sCD40L) and ADA concentrations.

Results: No deaths, TEs, severe or serious hypersensitivity reactions or infections or infusion-related reactions were observed in the study. One serious adverse event (fractured tibia) was reported in the placebo arm. MEDI4920 showed inhibition of the TDAR IgG response after the second administration of KLH on Day 15 at higher doses (≥300 mg; Figure 1A). An E\textsubscript{max} model adequately characterised the TDAR dose—response at Day 43 (p<0.001; ED\textsubscript{50}=491 mg), with the 3000 mg dose showing 86% inhibition of the TDAR (95% CI: 68–94%; Figure 1B). MEDI4920 exhibited linear PK. MEDI4920 produced a dose-dependent increase in total sCD40L concentrations. A high ADA incidence (90%) was observed in dose cohorts <100 mg; however, ADA incidence (29%) and ADA titres decreased with ≥300 mg doses of MEDI4920. ADA-high subjects had reduced MEDI4920 and total sCD40L concentrations compared with ADA-negative subjects or those with low ADA titres. ADA incidence did not correlate with any clinical events.

Conclusions: MEDI4920 demonstrated an acceptable safety and tolerability profile, and dose-dependent inhibition of TDAR. The dose-dependent increase in total sCD40L concentrations indicates binding of MEDI4920 to sCD40L and target engagement. The decreases in ADA incidence and ADA titres correlate with increasing MEDI4920 dose, consistent with the immunosuppressive mechanism of action of this molecule. These results support further exploration of MEDI4920 administration in subjects with autoimmune diseases where the CD40/CD40L pathway is activated.

Acknowledgements: Funded by MedImmune. Medical writing support: D. Trivedi, MedImmune LLC, Gaithersburg, MD, USA. Technical editing support: R. Plant, QXV Comms, an Ashfield company, which was funded by MedImmune.


DOI: 10.1136/annrheumdis-2017-eular.3468

SAT0250 BODY MASS INDEX IS INVERSELY ASSOCIATED WITH RESPONSE TO RITUXIMAB IN LUPUS NEPHRITIS: ANALYSIS OF THE LUNAR TRIAL

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Background: Increased body mass index (BMI) has been associated with poor functional capacity and systemic inflammation in lupus, 1 alterations in rituximab (RTX) pharmacokinetics, 2 and failure to achieve trial endpoints among patients treated with RTX for ANCA-associated vasculitis. 3 Although RTX is not approved for the treatment of lupus nephritis (LN), current EULAR/ERA-EDTA guidelines include RTX for use in refractory cases. 4 The effect of BMI on outcomes of patients treated with RTX for LN is unknown.

Objectives: To assess the association between pre-treatment BMI and renal response using data from the LUNAR trial.

Methods: LUNAR randomized 144 patients with ISN/RPS class III or IV LN to RTX (2 doses of 1000 mg at baseline and month 6) or placebo in combination with mycophenolate and a steroid taper. 5 BMI was measured at the screening visit. Complete renal response (CRR) was defined as achievement of UPCR <0.5, normal serum creatinine not increased from baseline by >15%, and inactive urinary sediment at week 52. Alternative definitions of response and achievement of CRR at week 78 were also considered. Logistic regression was used to model interactions and to calculate odds ratios (OR) and 95% CI. Peripheral CD19+ B cell measurements were examined.

Results: We identified qualitative interactions between BMI and treatment for CRR and alternative response measures. In unadjusted analysis, each 5 kg/m\textsuperscript{2} increase in pre-treatment BMI was associated with OR =0.47 (95% CI 0.24–0.92) in the RTX group and OR =1.44 (95% CI 0.93–2.23) in the placebo group for achievement of CRR (P value for interaction =0.006). The results of analysis adjusted for baseline UPCR and serum creatinine are presented in the Table. A sensitivity analysis identified consistent associations between BMI and response in the RTX group only. Among patients in the RTX group, increased BMI was associated with increased time to peripheral CD19+ B cell measurements observed differences in response are mediated by differences in the timing and/or degree of B cell depletion. These findings warrant additional analyses to better understand the relationships between patient characteristics, pharmacokinetics, B cell depletion, and treatment response in the LN population.

References:
SAT0251 | PREDICTING AND MANAGING PRIMARY AND SECONDARY NON-RESPONSE TO RITUXIMAB USING B-CELL BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Rituximab (RTX) is the most commonly used biologic for the treatment of SLE. However, there is no currently acceptable predictors of response, which is of particular importance in this heterogeneous disease with other biologics being restricted to certain subgroups.

Objectives: To assess factors associated with primary and secondary non-response to RTX in SLE in order to develop more targeted and effective B-cell therapy.

Methods: A prospective observational study was conducted in 125 SLE patients treated with RTX in Leeds for over 12 years. A major clinical response was defined as improvement of all active BILAG-2004 domains to grade C/better and no A/B flare. Partial responders were defined by 1 persistent BILAG B. B-cell subsets were measured using highly sensitive flow cytometry. Predictors of response were analysed using logistic regression analysis.

Results: 117 patients had evaluable data. In cycle 1 (C1), 96/117 (82%) achieved BILAG response [major=50%-partial=32%]. In MVA, younger age & B-cell depletion at 6 weeks increased the odds of major response (Table 1). Complete depletion was predicted by normal complement & lower pre-RTX plasmablasts. 77 (with data on 72) C1 responders were retreated on clinical relapse. Of these, 61/72 (85%) responded in C2. Of 11 C2 non-responders, 9 met secondary non-depletion non response (2NDNR) criteria, as defined by infusion reaction & defective depletion (incidence=12%) and tested positive for anti-RTX antibodies. Lack of concomitant immunosuppressant & higher pre-RTX plasmablasts predicted 2NDNR.

Conclusions: B-cell subsets should be monitored in the routine care of SLE patients receiving RTX and should aim to achieve complete depletion. About 1 in 8 SLE patients lose depletion on repeat cycles and this is associated with anti-RTX antibodies. Intensive RTX treatment regimens in those predicted not to completely deplete, or alternatively use of humanised anti-CD20mAbs are likely to increase clinical response rates to B-cell depleting agents.

Acknowledgements: This research was funded/supported by NIHR (DRF–2014–07–155) and (CS-2013–13–032). The views expressed are those of the author(s) & not necessarily those of the NHS, NIHR or the Dept of Health

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6943

SAT0252 | THE NUMBER OF TREG CELLS IN PERIPHERAL BLOOD IN PSS PATIENTS IS DECREASED AND LOW DOSE IL-2 CAN PROMOTE ITS PROLIFERATION

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Background: PSS is a kind of autoimmune disease without clear pathogenesis. Treg cell plays an important role in autoimmune disease. However, opinions about change of amount of Treg cells in peripheral blood in autoimmune disease are various. Besides, the researches mainly focus on RA and SLE but not PSS.

Objectives: To explore the change of the number of Th17 and Treg (CD4+CD25+Fopx3+T cells) cells in peripheral blood in PSS and the effects of low dose IL-2 therapy on the balance of Treg and Th17 cells.

Methods: One hundred and ninety two PSS patients in our department, and 30 healthy controls were put in the research. The amount of Th17 cells and Treg cells were calculated by flow cytometry. Eighty eight in 192 were given low-dose IL-2 (50 WIU/day for 5 days) by hypodermic injection combined with standard therapy which includes glucocorticoid, immune-suppressants, biological agents or combination of them, while others (12 in 69) were given standard therapy only. The amount of these cells were calculated again after therapy.

Results: There was significant decrease in the absolute number of Treg cells and significant increase of the ratio of Th17/Treg in PSS patients when compared with healthy controls. There was no significant difference in absolute number of Th17 cells between PSS patients and healthy controls. Further, the number of Treg cells were negatively relative to ESSDAI. Traditional DMARDs had no obvious impact on Treg and Th17 cells. The amount of Treg cells significantly increased after the treatment of IL-2 by 1 week. But there was no significant improvement in clinical manifestations in the short time when comparing combinational treatment of IL-2 and classical drugs with classical therapy. No obvious adverse reactions were observed.

Table 1. Absolute number and percentage of CD4+T subsets in peripheral blood in PSS patients and Healthy controls.

<table>
<thead>
<tr>
<th>Study Participants</th>
<th>Health</th>
<th>PSS</th>
<th>Untreated PSS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Th17</strong></td>
<td><strong>Th17%</strong></td>
<td><strong>Treg%</strong></td>
<td><strong>Treg</strong></td>
</tr>
<tr>
<td>Major (n=58)</td>
<td>6.44 (5.10, 8.55)</td>
<td>0.96 (0.67, 1.33)</td>
<td>4.80 (4.19, 6.37)</td>
</tr>
<tr>
<td>Partial (n=59)</td>
<td>7.09 (4.05, 11.48)</td>
<td>1.26 (0.77, 1.95)</td>
<td>4.64 (3.10, 6.44)</td>
</tr>
<tr>
<td>Non/Partial (n=117)</td>
<td>6.08 (4.30, 12.60)</td>
<td>1.26 (0.86, 1.92)</td>
<td>4.70 (3.52, 6.91)</td>
</tr>
</tbody>
</table>

Conclusions: The number of CD4+CD25+Fopx3+T cells in peripheral blood was decreased obviously and was inversely related to ESSDAI. While there was no significant difference of Th17 cells between PSS patients and healthy controls. And there was no correlation between the number of Th17 cells and ESSDAI. So the imbalance of Th17/Treg is due to the decrease of Treg cells not increase of Th17 cell which indicates that the pathogenesis of PSS maybe mainly because of shortage of autoimmune tolerance. Low dose IL-2 therapy can effectively promote proliferation of Treg cells by which low dose IL-2 may induce and restore autoimmune tolerance to benefit disease control.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6366
SAT0253  Efficacy and Safety of Leflunomide Therapy in Lupus Nephritis: A Meta-Analysis

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Objectives: To evaluate the efficacy and safety of leflunomide in treating lupus nephritis (LN).

Methods: According to the requirements of meta-analysis, a literature search about efficacy and safety of leflunomide therapy in LN was performed among Cochrane clinical controlled trials database, PubMed, BMJ-Clinical Evidence, CNKI, VIP and Wanfang data from the establishment of the database till December 2010. All included RCTs were graded in term of randomization, allocation concealment and blinding and non-RCTs were graded in term of grouping method, blinding, withdrawal and loss of follow-up, baseline comparability, diagnostic criteria and bias control. RevMan 5.0 software was used for meta-analysis.

Results: A total of 682 literatures were included. Five RCTs and 2 non-RCTs were enrolled for meta-analysis. Leflunomide group was treated with leflunomide and glucocorticoid, while control group was given cyclophosphamide and glucocorticoid or placebo. The 24 h urine protein, SCR and SLEDAI scores of leflunomide group were significantly lower than that of cyclophosphamide group. There was no significant difference in C3, positive rate of anti-ds DNA between leflunomide group and cyclophosphamide group. There was no significant difference in infection, herpes zoster, interstitial lung disease, hypertension or cardiovascular disease between the two groups.

Conclusions: Based on the current evidence, the efficacy and safety of leflunomide for treatment of LN are close to cyclophosphamide. Further evidence from RCT studies is needed to elucidate the efficacy and safety of leflunomide for LN.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2051

SAT0254  Safety, Tolerability, and Pharmacokinetics of Subcutaneous and Intravenous Anifrolumab in Healthy Volunteers

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Background: Anifrolumab is a fully human anti–interferon-α receptor monoclonal antibody in Phase III development for systemic lupus erythematosus (SLE). In Phase IIb trials, intravenous (IV) anifrolumab (300 mg every 4 weeks) significantly decreased SLE disease activity with safety and tolerability comparable to placebo.

Objectives: The primary objective of this Phase I, double-blind, randomized, controlled study (NCT02601625) was to characterize the pharmacokinetics (PK), safety, and tolerability of anifrolumab administered subcutaneously (SC) and intravenously to healthy volunteers.

Methods: Thirty male and female adults were assigned to three sequential treatment cohorts of equal size (anifrolumab 300 mg SC injection; anifrolumab 300 mg IV; anifrolumab 600 mg SC by infusion). Individuals were randomized within each cohort to receive a single dose of either anifrolumab (n=6/cohort) or placebo (PBO) (n=4/cohort). Serial blood samples were collected up to Day 85. Serum anifrolumab concentrations were analyzed with a validated assay. PK parameters were estimated by noncompartmental analysis. Immunogenicity of anifrolumab was assessed by measuring serum anti-drug antibodies (ADAs).

Results: Anifrolumab serum concentration-time profiles and primary PK parameters in healthy volunteers are presented in the figure and table, respectively. Anifrolumab serum concentrations were below the limit of detection in all individuals by 85 days post dose. Maximum serum concentrations in the SC cohorts occurred after 4 to 7 days. Exposure to SC anifrolumab increased approximately dose proportionally from 300 mg to 600 mg based on AUC. At the 300 mg dose, anifrolumab SC administration reached approximately 86% of the IV administration exposure. SC administration of anifrolumab 300 mg and PBO elicited minimal injection-site reactions. Transient injection-site induration followed by 12 weeks of observational follow-up and/or long-term extension. Stable doses of corticosteroids (<10 mg prednisone or equivalent daily), non-steroidal anti-inflammatory drugs, and antimalarials were permitted. Safety assessments included clinical evaluation of adverse events (AEs), laboratory parameters, electrocardiograms, physical examinations, and overall tolerability. Exploratory efficacy assessments included hSS, Cutaneous Lupus Area and Severity Index (CLASI) skin scores, Physician Global Assessment (PGA), swollen joint counts (SJC), and tender joint counts (TJC).

Conclusions: Exposure of anifrolumab 300 mg SC was approximately 86% of IV administration, with single SC administrations of anifrolumab being generally well-tolerated in healthy volunteers.

References:


SAT0255  A Randomized, Placebo-Controlled, Double-Blind, Ascending-Dose, Safety Study of CC-220 in Subjects with Systemic Lupus Erythematosus

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Background: CC-220 is a CUL4CRBN E3 ubiquitin ligase modulator that binds to cereblon and leads to potent and deep reduction of the transcription factors Ikaros (IKZF1) and Aiolos (IKZF3), which are overexpressed in the peripheral blood of Systemic Lupus Erythematosus (SLE) subjects. This study evaluated the safety, and tolerability of CC-220 in subjects in SLE. Exploratory efficacy assessments were included.

Methods: Subjects with history of SLE ≥6 months and a baseline of hybrid SLENA-SLEDAI (hSS) score ≥4 were randomized to 1 of 4 escalating doses of CC-220 or matching placebo (PBO). The 4 active treatments were CC-220 0.3 mg QOD, 0.3 mg QD, 0.3 mg alternating with 0.6 mg QD, and 0.6 mg QD; subjects were randomized 4:1 active to PBO in each group for 12 weeks of treatment, followed by 12 weeks of observational follow-up and/or long-term extension. Stable doses of corticosteroids (<10 mg prednisone or equivalent daily), non-steroidal anti-inflammatory drugs, and antimalarials were permitted. Safety assessments included clinical evaluation of adverse events (AEs), laboratory parameters, electrocardiograms, physical examinations, and overall tolerability. Exploratory efficacy assessments included hSS, Cutaneous Lupus Area and Severity Index (CLASI) skin scores, Physician Global Assessment (PGA), swollen joint counts (SJC), and tender joint counts (TJC).

Results: A total of 42 adult subjects were randomized; 39 subjects were female (93%); Mean age was 47.2 years; 64% were White and 31% were Black or African-American. Mean SLE duration was 9.4 years, with a mean baseline hSS score of 6.6, CLASI activity score of 9.8, and PGA score of 1.3. Seventy-nine percent of subjects completed the study; 9 of 42 subjects discontinued, of which 6 subjects discontinued due to an adverse event (AE): 1 in the placebo group and 5 in the 2 highest CC-220 groups combined. No discontinuations were due to lack of efficacy. Four subjects had serious AEs (highest CC-220 doses: n=2 [pneumonia]; PBO: n=2). Three subjects had neutropenia (grade 3: n=2; grade 1: n=1); 2 subjects in the highest CC-220 dose group had dermatitis, and 1 subject in the 0.3 mg QD and 1 in the 0.6 mg QD dose groups had urticaria. Mean reductions in the CLASI activity score at day 85 ranged from 4.3 to 7.8 in the CC-220 treatment groups compared to an increase of 0.4 in the placebo group.

Conclusions: CC-220 was generally well tolerated in this SLE population over 12 weeks of treatment, with neutropenia and dermatitis observed at the highest doses studied. Treatment with CC-220 resulted in a trend toward greater improvement in five of six individuals in the anifrolumab 600-mg group and two of four in the PBO group. Transient, mild to moderate injection-site induration and pruritus occurred simultaneously in two of six individuals in the anifrolumab 600-mg group, but not those in the PBO group. Adverse events were reported by 50% (n=9) of anifrolumab-treated and 33% (n=4) of PBO-treated individuals. No serious adverse events were observed. ADAs were detected in only one individual in the anifrolumab 300-mg IV group at the Day-85 assessment.

Anifrolumab Serum Concentration-Time Profiles

Conclusions: Exposure of anifrolumab 300 mg SC was approximately 86% of IV administration, with single SC administrations of anifrolumab being generally well-tolerated in healthy volunteers.

Conclusions: Exposure of anifrolumab 300 mg SC was approximately 86% of IV administration, with single SC administrations of anifrolumab being generally well-tolerated in healthy volunteers.

References:


in multiple measures of SLE disease activity compared with PBO. These results support further development of CC-220 in SLE patient population.

**Disclosure of Interest:** V. Werth Grant/research support from: Celgene Corporation, Consultant for: Celgene Corporation, R. Furie Consultant for: Celgene Corporation, S. Korish Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, M. Delev Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, A. Azaryan Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, P. Schafer Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, D. Hough Shareholder of: Celgene Corporation, Employee of: Celgene Corporation

**DOI:** 10.1136/annrheumdis-2017-eular.3546


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6547

**SAT0256**

**MULTI-TARGET THERAPY WITH MIZORIBINE, TACROLIMUS, AND PREDNISOLONE IN LUPUS NEPHRITIS: ANALYSIS OF 47 CASES**

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**Immune-rheumatology center, St.luke hospital, Tokyo, Japan**

**Background:** Mizoribine (MIZB), an inosine monophosphate dehydrogenase inhibitor, is an effective glucocorticoid-sparing agent for gromerulonephritis and variety of rheumatic diseases. However, its clinical usefulness as multi-target therapy in patients of lupus nephritis has been unclear.

**Objectives:** To evaluate efficacy of multi-target therapy with MIZB, tacrolimus (TAC) and prednisolone (PSL) for lupus nephritis.

**Methods:** We extracted all the cases with lupus nephritis treated with PSL, MIZB and TAC during period from 2008/1 to 2016/10. A retrospective medical chart review was performed to collect following data: baseline patient characteristics, dose of PSL, serum creatinine, urine protein, compliment, anti-DNA ab, remission rates, and safety profiles. We define complete remission as urine protein <0.5 g/gCr and normal serum creatinine, partial remission as urine protein decreasing more than 50% of baseline, and -3g/day of proteinuria and creatinine not increasing within 15%. Patients' records were followed from the beginning of multi-target treatment to 12 months after.

**Results:** 43 cases (female: n=37; male: n=6; mean age: 37.4 years old) were included for analysis. Of 30 cases who underwent renal biopsy, 10 cases were classified as class IV nephritis, and 7 cases were classified as class III nephritis. Mean urine protein (g/gCr) at baseline, at 3 months, and at 6 months were 1.9, 0.4, and 0, respectively. Mean dose of steroid was 32.8 mg/day at baseline, 9.8 mg/day at 3 months, and 8.7 mg/day at 6 month. 79.1% of the patients achieved complete remission at 3 months, and the remission rate was more than 80% at 6 months and later. As for adverse events, 14 cases had some infection, 3 out of 14 needed antibiotics treatment. Four cases had renal impairment after starting TAC, all of them recovered after stopping or decreasing dose of TAC.

**Conclusions:** Multi-target therapy with MIZB, TAC and PSL showed good remission rate, and few severe adverse events. We need the further evaluation of long-term efficacy of the therapy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3374

**SAT0258**

**SYNERGIC B-CELL IMMUNOMODULATION WITH RITUXIMAB AND BELIMUMAB IS CLINICALLY EFFECTIVE IN SEVERE AND REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS – THE SYNOBIOE PROOF-OF-CONCEPT STUDY**

K. Krajii1, S. W. Kamerling1, E. de Rooij1, P. L. van Dalea2, I. Bajema3, O. W. van Tongt1, T. J. Dijkhuizen1, C. W. van Kooij1, Y. K. Teng1, V. Nephrology, LUMC, Leiden; 2Immunology, Erasmus MC, Rotterdam; 3Pathology, Rheumatology, LUMC, Leiden, Netherlands

**Background:** The pathogenesis of systemic lupus erythematosus (SLE) is characterized by B-cell hyperactivity leading to autoreactive plasma cells (PCs) that produce pathogenic autoantibodies and contribute to onset and maintenance of SLE. Therefore, novel treatment strategies in SLE are aimed at targeting autoreactive PCs. Rituximab (RTX) is used as off-label treatment in SLE and depletes CD20+ B-cells effectively, but is unable to deplete CD20- PCs. Belimumab (BLM), an anti-BAFF (B-cell activating factor) antibody, demonstrated efficacy in SLE as add-on therapy and resulted in reduction of B-cells and PCs.

**Objectives:** Because RTX+BLM has potential to target autoreactive PCs, we designed an open-label, proof-of-concept study to assess the clinical efficacy and safety of RTX+BLM in severe, refractory SLE patients.

**Methods:** A phase 2 proof-of-concept study, the SynBioSe study, was set up to treat severe, serologically active and refractory SLE patients with RTX following BLM treatment. The following endpoints were assessed at 24 weeks: a) clinical efficacy by SLEDAI; b) immunological effects on B-cells and PCs by high sensitivity flow cytometry, immunoglobulins and autoantibody levels, and c) safety parameters.

**Results:** The study included 11 severe, refractory SLE patients of which 10 had lupus nephritis and 1 patient had neuropsychiatric lupus with a median SLEDAI of 18 (range 8–29). Treatment with RTX+BLM led to clinically significant improvement to a median SLEDAI score of 2 [0–13] (p=0.002). Low disease activity (SLEDAI <4) was achieved in 80%. Clinical response was achieved while tapering steroids from a median dose of 60 [60–70] mg to 7.5 mg [0–12.5] and concomitant mycophenolate (MMF) was tapered to zero in all patients. With respect to safety, 23 adverse events (AEs) were reported of which none were serious AEs, 8 mild infections and 2 hypogammaglobulinemia. Complement usage was restored in all patients with a median increase in C3 of 33% [range 0–100%] at 12 weeks. At 12 weeks, RTX+BLM led to reduction of anti-dsDNA antibodies, from median 120 IU/ml [18–505] to 35 IU/ml [10–374] (p=0.012). CD19+ B-cells were depleted throughout the complete follow up from median 206106 cells/L [range 210105–511105] at screening to 5x104 [0–24x104] at 24 weeks, p=0.004, including transitional B-cells (from median 1.3x104 cells/L [1.1–3x104] at screening to 9.85 [0–3.4x104] at 24 weeks, p<NS). Importantly, total immunoglobulin levels only declined temporarily. The latter was further corroborated by transient reductions in CD3-CD38brCD27brCD20- PCs from median 1.6x105 cells/L [5.6x105–1.1x106] to 1.5x105 cells/L [5.3x105–3.1x105] at 12 weeks (p=NS). At 24 weeks, these PCs were restored to baseline levels (1.4x105 cells/L [9.2x104–3x105]).

**Conclusions:** This is the first study to demonstrate that RTX+BLM effectively reduced disease activity in severe, refractory SLE without raising major safety issues, while reducing other immunosuppressant drugs. Autoreactive PCs were specifically targeted by RTX+BLM. Therefore, combination therapy of RTX+BLM is a promising strategy in severe SLE.

**Trial registration:**ClinicalTrials.gov NCT02284984

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2364
HIGH PLASMA CONCENTRATION OF MYCOPHENOLATE ACID IN EARLY PHASE OF INDUCTION THERAPY PREDICTS GOODrenal function in LN class III-IV

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Background: Mycophenolate mofetil (MMF) is recommended as initial induction treatment for most cases of lupus nephritis (LN) class III-IV. Although the association between area under the concentration-versus-time curve (AUC) of mycophenolic acid (MPA) and therapeutic efficacy has been well shown in renal transplantation, it has been poorly investigated in LN. Furthermore, MMF interacts with multiple factors and its concentration may be decreased by high renal transplantation, it has been poorly investigated in LN. Furthermore, MMF treatment for most cases of lupus nephritis (LN) class III-IV. Although the background of LN class III-IV.

Methods: We prospectively enrolled patients with biopsy proven LN class III or IV who hospitalized from Apr to Oct 2016. As induction therapy, PSL was started at dose of 1mg/kg/day and tapered to 10mg/day by 12 weeks. Fixed dose of MMF at 2mg/kg/day was continuously introduced. We evaluated the association between AUC of MPA at different phases of induction treatment, early and middle, and prospectively investigated which concentration predicted future renal response in LN class III-IV.

Objectives: To investigate the relationship between the plasma concentration of MPA in early or middle phase of induction therapy and future renal response.

Methods: We prospectively enrolled patients with biopsy proven LN class III or IV who hospitalized from Apr to Oct 2016. As induction therapy, PSL was started at dose of 1mg/kg/day and tapered to 10mg/day by 12 weeks. Fixed dose of MMF at 2mg/kg/day was continuously introduced. We evaluated the association between AUC of MPA at different phases of induction treatment, early and middle, and prospectively investigated which concentration predicted future renal response in LN class III-IV.

Results: We enrolled 35 patients. AUC of MPA in early phase was correlated (R²=0.54, P<0.001) with CRI at week 12. The AUC of MPA in middle phase was not correlated (R²=0.17, P=0.7), but that of the early phase tended to correlate with CRI at week 12 (R²=0.43, P=0.02).

Conclusions: High AUC of MPA at the early phase of induction therapy might predict renal response.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4622

SAT0260 OROVAN FUNCTION PRESERVATION WITH GONADOTROPIN-RELEASING HORMONE ANALOGUES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH CYCLOPHOSPHAMIDE

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Background: The fertility in childbearing Systemic Lupus Erythematosus (SLE) patients can be impaired due to several conditions. In particular, treatment with alkylating agents, as cyclophosphamide (CYC), could determine menstrual irregularities and premature ovarian failure (POF). Gonadotropin-releasing hormone analogues (GnRH-a) is one of the preventive strategy suggested by the recently published EULAR recommendations (1). They are characterized by good safety profile and effectiveness in reducing POF rate in patients with malignancies and autoimmune diseases. So far, only few studies have been published focusing on the use of GnRH-a to prevent POF in SLE patients receiving CYC treatment.

Objectives: In the present case-control study, we aimed at evaluating the efficacy of GnRH-a on the ovarian function preservation in SLE patients treated with CYC.

Methods: We enrolled consecutive SLE patients, fulfilled the 1997 ACR revised criteria treated with CYC in the period between 2005 and 2012, receiving GnRH-a (GnRH-a-). As control, SLE patients treated with CYC not receiving GnRH-a (GnRH-a-) were assessed. Clinical and laboratory data were collected in a standardized, computerized and electronically filled form. Ovarian function was assessed by the evaluation of FSH and estradiol level (E2). GnRH-a (triptorelin 3.75 mg/monthly intramuscularly) was prescribed. SLE patients treated with CYC were followed after the treatment every six months during the first year and then annually.

Results: Thirty-three SLE patients treated by CYC were evaluated in the present analysis. 75.7% of patients were treated for lupus nephritis. Among [FC1] those, 18 (52.9%) were LN (class III-IV) for more than 6 years, mean age of 36.2±12.4 years; and 15 GnRH-a- (mean±SD age 31±0.10±5.6 years) and 15 GnRH-a+ (mean±SD age 31±0.10±5.6 years; mean±SD disease duration 6.3±7.7 years). The mean±SD SLEDAI-2K score in GnRH-a- patients was 10.1±3.7, in GnRH-a+ patients 8.3±3.3 (P=NS). Moreover, no differences were identified concerning the duration of CYC treatment (GnRH-a+: 6.1±2.6 months versus GnRH-a+: 6.1±2.6 months, P=NS) and follow-up (GnRH-a+: 8.1±1.2 years versus GnRH-a+: 9.3±7.2 years, P=NS). The prevalence of POF was significantly higher in GnRH-a- (5 patients, 33.3%) in comparison with GnRH-a+ (2 patients, 11.1%, P=0.0002). A significantly higher mean age at the time of CYC treatment was observed in GnRH-a+ (27.5±8 months, P=0.0002) than in GnRH-a- (21.7±5 months, P=0.0002). The prevalence of POF was significantly higher in GnRH-a- (5 patients, 33.3%) in comparison with GnRH-a+ (2 patients, 11.1%, P=0.0002). A significantly higher mean age at the time of CYC treatment was observed in GnRH-a+ (27.5±8 months, P=0.0002) than in GnRH-a- (21.7±5 months, P=0.0002). The prevalence of POF was significantly higher in GnRH-a- (5 patients, 33.3%) in comparison with GnRH-a+ (2 patients, 11.1%, P=0.0002). A significantly higher mean age at the time of CYC treatment was observed in GnRH-a+ (27.5±8 months, P=0.0002) than in GnRH-a- (21.7±5 months, P=0.0002). The prevalence of POF was significantly higher in GnRH-a- (5 patients, 33.3%) in comparison with GnRH-a+ (2 patients, 11.1%, P=0.0002). A significantly higher mean age at the time of CYC treatment was observed in GnRH-a+ (27.5±8 months, P=0.0002) than in GnRH-a- (21.7±5 months, P=0.0002).

Conclusions: The results of the present study showed the protective role of GnRH-a for the preservation of ovarian function in SLE patients treated by CYC. Furthermore, the age resulted the only risk factor associated with POF development.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6381
BCL2-ASSOCIATED ATHANOGENE 3 PROTEIN IS ASSOCIATED WITH B-CELL HYPERACTIVITY INCLUDING LYMPHOMA IN PRIMARY SJÖGREN’S SYNDROME

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Background: Bcl2-associated athanogene 3 (BAG-3) is a co-chaperone protein that interacts with the ATPase domain on heat-shock protein 70. BAG-3 is involved in several biologic processes including apoptosis, cytoskeleton organization and autophagy and, therefore, it has been extensively investigated in the field of tumorigenesis (1). In particular, BAG-3 expression is constitutive in human primary tumors including leukemias and lymphomas and it is induced in different normal cell types, including leukocytes, by a variety of stimuli. BAG-3 is able to induce and maintain cell proliferation, resistance to therapy and cell motility, namely metastatization. On this basis, a role of BAG-3 in chronic inflammatory diseases may be postulated, but data on this topic are not available.

Objectives: The purpose of our study was to investigate the expression of BAG-3 in primary Sjögren’s syndrome (pSS) and the relationship with clinical and serological features.

Methods: BAG-3 concentration was assessed in the serum of 103 patients with pSS according to the 2002 American-European classification criteria and in 40 sex and age matched healthy donors (HD). Clinical and serological records were collected and statistical analysis was performed with SPSS 21.0.

Results: Twenty-six pSS patients were positive for BAG-3 (BAG-3+), with serum levels ranging from 32.1 to 950 pg/ml. When setting the cut off value according to the highest value found in HD (300 pg/ml), we identified 13 pSS patients displaying a peculiar clinical serological phenotype. In detail, in this subgroup of pSS patients the prevalence of purpura, low C4, both anti-RO and anti-La autoantibodies, rheumatoid factor and lymphoma was higher, when compared to pSS patients with BAG-3 levels <300 pg/ml or BAG-3- (all p<0.05). Furthermore, they displayed less frequently sicca symptoms such as xerostomia and xerophtalmia (both p<0.05). Binary logistic regression analysis revealed that pSS patients with BAG-3 levels >300 pg/ml had on odds ratio (OR) of 12 (95% CI 1.9–86, p=0.009) for lymphoma and this association was independent of the presence of purpura, a well known marker of lymphoma in pSS. When including low complement, another feature associated with lymphoma, in the multivariable analysis, both low C4 and BAG-3 levels >300 pg/ml resulted independently associated to lymphoma (OR=24 and 12.4 respectively).

Conclusions: Our study assessed for the first time serum BAG-3 levels in a large cohort of pSS patients. The results showed that the highest levels of BAG-3 identify a peculiar clinical and serological pSS phenotype, as consequence of a B-cell hyperactivity. Since it is known that BAG-3 is an anti-apoptotic protein involved in B-cell proliferation and activity, as well as in oligoclonal and monoclonal expansion in pSS.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3857

NEOPLASIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SPAIN: RELESSER REGISTRY DATA


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Background: There is limited evidence on the risk of neoplasia in autoimmune diseases such as systemic lupus erythematosus.

Objectives: The objective of this study is to analyze the incidence of cancer in the Spanish population with SLE and the factors associated in its development: RelesSER Registry Data.

Methods: We calculated the incidence density of malignant neoplasms, the standardized incidence ratio and the average time to develop the first neoplasm after diagnosis of SLE in patients of the SLE registry of the Spanish Rheumatology Society (RelesSER) fulfilling ACF97 criteria. We carried out a bivariate analysis of the associated factors to neoplasms and multivariate by logistic regression.

Results: A total of 3607 patients (90.4% female) were included. We registered 140 neoplasms in women (4.3%) and 14 in men (4%) (p<0.821). Incidence density 7.3/1000 patient-years (95% CI:4.85–10.98) (7.39 in patient-years women and 6.93 in men) without significant differences. After stratification by gender and age, cancer appeared in 3.2% of the women aged under 45 versus 3.8% of the men; 4.1% of women aged 45–65 years versus 5.9% of men and a 5.3% of women 65 and older versus 2.5% of men the same age. The standardized incidence ratio (SIR) was 2.16; 1.51 in men and 2.38 in women, highest for women under 65 years old. The SIR for >65 years was 0.96; 0.59 in men and 1.55 in women.

The average time until de development of the first malignant neoplasm was 10 years (RI:5.75–17.00), being lower in women (9.5 [RI: 5.00–17.00]) than in men [12.5 (8.75–17.5)] and in patients under 45 years versus over 45 years [8.0 (RI: 5.00–16.00)].

Malignant neoplasms were the cause of death in 10% of the patients (15/154), predominantly hematological and breast cancers, both at 19% followed by lung cancer in 14.3%.

Factors associated to malignant neoplasms in the bivariate analysis are shown in (table 1). No immunosuppressive therapy was associated with the development of neoplasms. In the multivariable model, adjusted for age and time of disease duration, age was the only significant variable (OR:1.030; 95% CI: 1.003–1.059; p<0.029) with a trend for ACE inhibitors use (OR:1.866; 95% CI: 0.808–4.306; p=0.144), SLEDAI (last visit) (OR: 0.904; 95% CI: 0.806–1.015; p=0.089), SLICC/ACR DI (without neoplasias) (OR: 1.160; 95% CI: 0.961–1.401; p=0.123), and duration of the disease in months (OR: 1.003; 95% CI: 1.000–1.006; p=0.068).

Conclusions: The incidence of neoplasia in Spanish women with SLE is higher than expected for age and gender. Malignant neoplasms were the cause of death in 10% of the patients, predominating hematological and breast cancers followed by lung cancer.

Acknowledgments: The RelesSER registry has been supported by the FIS (ISCIII) - European Regional Development Fund (FEDER), fellowship P11/02857. It has also been partially funded by: GSK, UCB, Roche and Novartis.

Disclosure of Interest: None declared


VALVULOPATHY AND PULMONARY HYPERTENSION IN A SERIES OF PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME


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Objectives: To evaluate the prevalence of cardiac valvular involvement and the risk of pulmonary arterial hypertension (PAH) associated with antiphospholipid syndrome (APS) in a series of patients fulfilling ACR1997 criteria.
pulmonary arterial hypertension (PAH) and predictive risk factors in a cohort of patients with antiphospholipid antibodies.

Methods: We included 232 patients from our cohort who underwent an echocardiogram. A total of 84 (36%) patients with primary antiphospholipid syndrome (PFS), 47 (20%) with APS secondary to systemic lupus erythematosus (SLE), 47 (20%) patients with antiphospholipid antibodies 23%) with SLE without AAF. The determinations of AAF and lupus anticoagulant were performed according to the indications of the international thrombosis society. Statistical analysis was performed with SPSS 18; using the Chi square test and the Fisher exact test.

Results: In patients with AAF, the echocardiogram was pathological in 88 patients (52%) (p=0.023). Valvular affection was evidenced in 64 (38%) (p=0.005) and PAH in 16 (p ns). Seventeen patients (35%), SAF (48), SAFS (26), AIF (14) and 9 patients in the non-AAF group (12%) presented with valvular affection (p=0.002). PAH presented 19 patients, 9 with SAFP (47%), 6 in the SAFS group (32%), 1 in the silent AAF group (5%) and 3 in the non-AAF group (16%) (p=). Both PAH and valvular involvement were asymptomatic in most cases, although two patients required valvular replacement. The most frequently affected valve in all groups was mitral valve (84%), except in patients with PAH where the most prevalent valvular pathology was tricuspid insufficiency. Patients with valvulopathy and APS had a higher prevalence of total thrombosis than SLE without valvulopathy (p=0.05). Patients with valvulopathy also significantly increased stroke and thrombocytopenia (p=0.04).

Conclusions: Subclinical valvular involvement is very common in patients with AAF. Every patient with AAA should be given an echocardiogram in the initial protocol of their study in order to rule out both significant valvulopathy and PAH that can modify the patient's condition.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2548

SAT0265 | CLINICAL CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN AN EGYPTIAN POPULATION: A RETROSPECTIVE COHORT

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with a myriad of manifestations, that could vary among different ethnic and racial groups.

Objectives: To study the prevalence of various manifestations of SLE in an Egyptian population.

Methods: Information in this study was derived from the medical records of SLE patients who followed up in a private clinic in Cairo from January 1980 to June 2015.

Results: This descriptive retrospective case series included 1109 juvenile (19.4%) and adult (80.6%) patients, of which 114 (10.3%) were males and 995 were females (89.7%). Age of onset showed a mean of 26±11.19 years, and the mean of disease duration was 48.78±58.46 months (median: 26 years). The most common manifestations were synovitis (76.7%), malar rash (48.5%), leukopenia (45.7%), and photosensitivity (45.6%). At least one of the antiphospholipid antibodies was present in 41.8% of the patients tested for APL (636 patients). However thrombocytopenic manifestations and/or recurrent fetal loss occurred in 11.5% of the patients. Neuropsychiatric manifestations were evident only in 6.4% of the patients, with seizures as the most common neuropsychiatric manifestation, present in 4% of the patients. 33.1% of the patients had nephritis, which followed the onset of the disease by a mean duration of 20±21.3 months (median=12 months). There were gender differences in the disease characteristics. Cutaneous vasculitis, nephritis, retinopathy, and pleuritis (ISEDAI) were statistically higher in males (p=0.04), p=0.001, and p=0.041 respectively). Whereas, synovitis, and alopecia were statistically higher in females (p=0.012 and p=0.006 respectively). Patients with juvenile onset had a statistically higher frequency of nephritis (p=0.01), seizures (p=0.012) haemolytic anemia (p=0.001), and hypocomplementinemia (p=0.02).

Conclusions: Synovitis and malar rash were the most common manifestations in our study. Secondary antiphospholipid was present in 11.5% of the patients. Male patients and juvenile patients showed a tendency towards a more severe disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2151

SAT0266 | EFFECT OF THE METABOLIC SYNDROME ON ORGAN DAMAGE AND MORTALITY IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL ANALYSIS

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Objectives: To study the relationship between serum 25-hydroxyvitamin D3 levels and flares of systemic lupus erythematosus (SLE) in a longitudinal cohort of Chinese patients.

Methods: Patients who fulfilled ≥4 of the ACR criteria for SLE were recruited from our rheumatology out-patient clinics in November 2011. Blood was taken at 10 AM and was assayed for the serum levels of 25-hydroxyvitamin D3 by liquid chromatography tandem mass spectrometry (LC-MS/MS) in our laboratory, using an assay with a coefficient of variation < 5%. Patients were followed longitudinally every 2–4 months for serial assessment of disease activity by SELENA-SLEDAI and the occurrence of mild/moderate or severe SLE flares (by SELENA flare instrument). Comparison was made among these groups in the baseline and mean sumrated SLEDAI over time (area under the curve), and the annual incidence of mild/moderate and severe flares by the one-way ANOVA test.

Results: 276 SLE patients were studied (94% women; age 41.0±13.8 years; SLE duration 9.3±7.2 years). The mean follow-up time of the patients since accrual at their last clinic visits (0.7±0.7 vs 0.26±0.6; p=0.001). The annual incidence of mild/moderate and severe flares by the one-way ANOVA test. Comparison was made among these groups in the baseline and mean sumrated SLEDAI over time (area under the curve), and the annual incidence of mild/moderate and severe flares by the one-way ANOVA test.

Conclusions: In this 5-year longitudinal study, the MetS was significantly associated with need for organ damage, vascular events and mortality in patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3939

SAT0267 | SERUM 25-HYDROXYVITAMIN D3 LEVELS AND FLARES OF SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL COHORT ANALYSIS

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Objectives: To study the relationship between serum 25-hydroxyvitamin D3 levels and flares of systemic lupus erythematosus (SLE) in a longitudinal cohort of Chinese patients.

Methods: Patients who fulfilled ≥4 of the ACR criteria for SLE were recruited from our rheumatology out-patient clinics in November 2011. Blood was taken at 10 AM and was assayed for the serum levels of 25-hydroxyvitamin D3 by liquid chromatography tandem mass spectrometry (LC-MS/MS) in our laboratory, using an assay with a coefficient of variation < 5%. Patients were followed longitudinally every 2–4 months for serial assessment of disease activity by SELENA-SLEDAI and the occurrence of mild/moderate or severe SLE flares (by SELENA flare instrument). Comparison was made among these groups in the baseline and mean sumrated SLEDAI over time (area under the curve), and the annual incidence of mild/moderate and severe flares by the one-way ANOVA test.

Results: 276 SLE patients were studied (94% women; age 41.0±13.8 years; SLE duration 9.3±7.2 years). The mean follow-up time of the patients since accrual at their last clinic visits (0.7±0.7 vs 0.26±0.6; p=0.001). The annual incidence of mild/moderate and severe flares by the one-way ANOVA test. Comparison was made among these groups in the baseline and mean sumrated SLEDAI over time (area under the curve), and the annual incidence of mild/moderate and severe flares by the one-way ANOVA test.

Conclusions: In this 5-year longitudinal study, the MetS was significantly associated with need for organ damage, vascular events and mortality in patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2548
but non-significant trend of higher annual rates of mild/moderate and severe flares over time was also observed in patients with vitamin D deficiency. At the last visit, 27 (10%) patients had new damage scores; 5 patients had new vascular events; and 4 patients had new onset diabetes mellitus. There were no significant differences among the three groups of patients with regard to the incidence of new damage or vascular events over time.

Conclusions: Vitamin D insufficiency and deficiency were frequent in our cohort of SLE patients. Patients with vitamin D deficiency were associated with higher baseline and mean disease activity scores, as well as a trend of more severe lupus flares over time.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3945

SAT0268 CLINICAL PRESENTATION OF NASAL INVOLVEMENT IN PRIMARY SJÖGREN’S SYNDROME: A MULTIDISCIPLINARY TEAM APPROACH TO A NEGLECTED AND DISABLING CONDITION

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Background: Dry nose is reported quite frequently by patients affected by primary Sjögren’s syndrome (pSS) in daily practice. However, a clear definition of nasal involvement in pSS is not available.

Objectives: a) to explore clinical presentation of nasal involvement in pSS analyzing key symptoms, objective findings at the inspection of the external and inner nose and nasal cytology b) to investigate any associations/correlation between nasal involvement and other clinical-serological disease manifestations c) to assess the overall impact of nasal involvement on patients reported outcomes (PROs).

Methods: Consecutive pSS patients (AECG 2002) were seen by a team of ENT specialists and through patient interview. SGUS of the parotid and submandibular glands were performed. Nasal symptoms were recorded using a self-reported questionnaire and through patient interview. Additional clinical information was obtained from the medical records review.

Results: Forty-six pSS patients were included in the study [M:F =45:1; median age 55 (33–79) years]. Nasal symptoms were more frequently present in patients with RS and AR. The SNOT22 scores were more frequently positive in patients with RS and AR. Nasal cytology evaluation, all the patients underwent a complete ENT evaluation. Nasal symptoms were recorded using a self-reported questionnaire and through patient interview. Additional clinical information was obtained from the medical records review.

Conclusions: Dry nose is reported quite frequently by patients affected by primary Sjögren’s syndrome (pSS) in daily practice. However, a clear definition of nasal involvement in pSS is not available.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6368

SAT0270 ULTRASONOGRAPHY OF MAJOR SALIVARY GLANDS IN JUVENILE SJÖGREN’S SYNDROME – PRELIMINARY FINDINGS IN A MULTI-CENTER STUDY

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Background: Juvenile Sjögren’s syndrome (JS) is a rare, poorly defined and possibly underdiagnosed condition. There is little information on the use of major salivary gland ultrasonography (SGUS) in this patient-group.

Objectives: To characterize symptoms and clinical findings of JS and to investigate SGUS as a diagnostic tool.

Methods: Sixty-four patients were recruited from Brazil (n=40), Norway (n=11), the Netherlands (n=8) and Spain (n=5). All patients had disease onset at the age of 18 or younger. Clinical examination and sialometry was performed in 60/64 patients. Additional clinical information was obtained from the medical records and through patient interview. SGUS of the parotid and submandibular glands was performed in all patients using linear high-frequency transducers (6–15 MHz), by an expert in SGUS. Glanderal homogeneity and presence of hypoechogenic areas were evaluated and glands characterized as normal or SS-like.

Results: The female:male ratio was 6:1. Mean age at diagnosis was 12.1 years (range 4–18), with first symptoms occurring at 10.3 years (range 1–17). Time from onset of symptoms until diagnosis was 1.6 years (range 2–8 years). Subjective oral and ocular symptoms were reported in 70% and 64% patients, respectively. Reduced secretion of tears was detected in 41% patients, and hyposalivation was recorded in 31% patients. Minor salivary gland lip biopsy had been performed and focus score determined in 34 patients; 28 biopsies (82%) had focus score ≥ 1. Serologically, 92% were positive for ANA, 73% were anti-Ro/SSA+, 38% were anti-La/SSB+, and 41% were RF+. Salivary gland enlargement had been experienced by 53% of the patients; one patient had also experienced lacrimal gland enlargement. Systemic manifestations at some time-point, was registered in 66% of the patients. Systemic treatment at inclusion was registered in 67% of the patients; previous systemic treatment was registered in 83%. Diagnostic criteria for primary Sjögren’s syndrome (pSS) was fulfilled by 54/64 patients (53%) and 39/64 patients (61%),

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4349

RDW LEVELS ARE ASSOCIATED WITH DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic Lupus Erythematosus (SLE) patients show higher Red blood cells Distribution Width (RDW) regardless of anaemia status. RDW has been proposed to provide evidence of subclinical iron deficiency. Increased RDW is associated with increased damage accrual.

Objectives: To determine whether RDW levels in SLE patients are associated with damage accrual.

Methods: This cross-sectional study was conducted in 276 SLE patients, 257 females and 19 males. Evaluations included interview, medical records review, physical examination and laboratory tests. Disease activity was measured with the SLEDAI. Damage accrual was ascertained with the SLICC/ACR damage index (SDI). Univariable and multivariable Poison regression models were performed to determine associations of RDW levels with damage accrual. RDW levels were stratified by tertiles of RDW. The multivariable model was adjusted for variables known to be associated with this outcome (age at diagnosis, gender, socioeconomic status, ethnicity, tobacco use, disease duration, SLEDAI, anemia, antimalarials and immunosuppressive drugs use, average daily dose and time of exposure to prednisone (PNDI)).

Results: The patients mean (SD) age at diagnosis was 34.38 (13.33) years; nearly all patients were mestizo. Disease duration was 7.04 (6.16) years. The SLEDAI was 5.24 (4.67) and the SDI 0.92 (1.28). The average daily dose of PNDI was 6.39 (6.07) mg/d and the time of exposure to PNDI was 85.89 (59.59) years. RDW levels were 14.57 (1.52)% Hemoglobin levels were 12.4 (1.7) g/dl. We divided the RDW levels into tertiles with cut points in 13.8 and 14.0; the highest tertiles were associated with disease damage; with a Rate Ratio (RR) 1.57 (1.07–2.28; p: 0.020 for the highest tertile, and 1.67 (1.52–4.02; p: 0.007) for the medium tertile.

Conclusions: Higher RDW levels are associated with damage accrual in SLE patients independent of other well-known risk factors for such occurrence.

References:
AECG criteria and ACR/EULAR criteria, respectively. SGUS revealed SS-like changes in 37/64 patients (59%); interestingly, SS-like findings were observed in 22/23 patients in the European cohort, compared to 15/40 patients in the Brazilian cohort.

Conclusions: Common symptoms and findings in SS include dry mouth, systemic manifestations and salivary gland enlargement, followed by reduced tear secretion and hyposalivation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5804

SAT0271 | IS THERE A NEED TO INCLUDE SEROLOGICAL PATTERN TO PREDICT DAMAGE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: DIAPS APPLICATION

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease defined as the presence of antiphospholipid antibodies (aPL), at least a clinical thrombotic event and is associated with an important risk of organ damage. The new index proposed, Damage Index in patients with Thrombotic Antiphospholipid Syndrome (DIAPS) may be an useful tool to estimate cumulative damage in patients with primary and secondary APS. It includes 38 clinical items expanded in order to show the complexity of clinical manifestations in APS patients.

Objectives: The aim of this study is to analyze the serological pattern as potential predictive factor for an increased DIAPS.

Methods: All consecutive patients known with APS according to the Sapporo and/or Sydney classification criteria were included in our monocentric cohort. Data on medical history, clinical manifestations, aPL profile and medication were collected. DIAPS score was used to measure damage in each patient. The relation between DIAPS and positive aPL and DIAPS score was analysed.

Results: Seventy six patients with APS were included: 11 patients with primary APS, 65 patients with secondary APS. Their mean disease duration was 9.59±3.39years. The most frequent clinical manifestation from DIAPS was the peripheral vascular (deep vein thrombosis, intermittent claudication, tissue loss, venous varus insufficiency) found in 61.8% of patients, followed by hypertension; fasting glucose >5.6mmol/L or treatment for hyperglycaemia. 289 patients included were 87% female; 51% Caucasian, 29% Asian, and 12% African American; median follow-up was 10.0 (4.6 -15.0) years. Time-adjusted-mean SLEDAI (AMS) over the study period was 3.67. 81% (211) patients received GC (time-adjusted mean 4.25mg prednisolone) and AMS was significantly higher in GC-exposed patients (4.19 ± 1.97 [EMI], p<0.01). MetS criteria were met by 49 (17%) of patients (Table I). Hyperglycemia and hypertension were significantly more frequent in GC-treated patients, but the prevalence of obesity and other MetS domains, or MetS overall, were not. There were significantly more patients with MetS score ≥0 in the GC-exposed subset (43/78 vs 76/211, p<0.01).

The prevalence of obesity of 17% is lower than in the general population. There was no significant change in BMI across the period of observation and surprisingly, no association between GC exposure and change in BMI.

Conclusions: The prevalence of MetS in SLE was lower than previously reported in other, smaller, lupus cohorts. This study suggests GC exposure was associated with hyperglycemia and hypertension in SLE. Potential negative effects of active disease on MetS domains require further investigation.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6764

SAT0273 | FACTORS RELATED TO ALEXITHYMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Several evidences described a considerable prevalence of alexithymia among patients with chronic diseases, such as systemic autoimmune diseases. In patients affected by Systemic Lupus Erythematosus (SLE), alexithymia seems to be related to mood disorders and personality traits. The association between alexithymia and quality of life was also found.

Objectives: In this study we evaluated alexithymia in relation to HR-Qol (Health related Quality of Life) and to factor associated to HR-Qol, such as mood disorders, fatigue, work activity and physical activity.

Methods: We consecutively enrolled SLE patients and healthy controls in a cross sectional study with a retrospective design. We used the Toronto Alexithymia Scale 20 (TAS-20). AHF-Qol was expressed by MOS-SF-36. Mood disorders was assessed by BDI and HAM-H. Fatigue was assessed by Work Productivity and Activity Impairment (WPAI). Cognitive impairment was defined according to MOCA screening test.

Results: Fifty-two SLE patients and 50 age-matched healthy subjects were enrolled in the study. Mean TAS-20 score was significantly higher in SLE compared to controls (p<0.01). Alexithymic patients presented increased values of BDI score and HAM-H score (p<0.05) and reduced Facit-Fatigue score (p<0.05). We found increased values of Work missed due to health reasons (p<0.05) and activity impairment score (p<0.05) in patients with SLE compared to controls. No differences were found between SLE and controls in mood disorders, fatigue, physical activity and sleep quality.

Conclusion: This study indicated that alexithymia is strongly associated with HR-Qol, such as mood disorders, fatigue, work ability, sleep quality and physical activity.
predictors of TAS-20 values were to be fibromyalgic and to have mild-to-severe depression according to BDI. In multiple logistic regression, alexithymia was significantly associated to BDI score (OR 1.2, 95% CI 1.0–1.4) and inversely associated to cognitive impairment (OR 0.91, 95% CI 0.02–0.8).

Conclusions: SLE patients frequently present alexithymic tract. Alexithymia status seems correlated to be disease stage, to disease course (activity and damage) and to SLE therapy, nor to HR-QoL expressed by SF-36. Nevertheless, alexithymia could be tightly related to QoL-associated factors as depression and fibromyalgia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5679

SAT0274 UNRINARY VITAMIN D-BINDING PROTEIN AS A BIOMARKER FOR LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is a major complication of systemic lupus erythematosus (SLE). However, conventional biomarkers for assessing renal disease activity are imperfect in predicting clinical outcomes associated with LN.

Objectives: The aim of this study is to identify urinary protein biomarkers that reliably reflect the disease activity or predict clinical outcomes.

Methods: A quantitative proteomic analysis using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS), was performed to identify protein biomarker candidates that can differentiate between SLE patients with and without LN. Selected biomarker candidates were further verified using urine samples from a larger cohort of SLE patients (n=121) by enzyme-linked immunosorbent assay (ELISA) to investigate their predictive values for LN activity measure. Furthermore, association between urinary level of selected panel of potential biomarkers and prognosis of LN was assessed with a 4-year follow-up study of renal outcomes.

Results: From proteomic assay, vitamin D binding protein (VDBP), transthyretin (TH), retinol binding protein 4 (RBP4) and progestin D synthase (PTGDS) were selected as candidates for quantification. These proteins were significantly elevated in SLE patients with LN, especially in patients with active LN (n=21). Among them, VDBP well correlated with severity of proteinuria (rho =0.661, P<0.001) and renal SLE disease activity index (renal SLEDAI) (rho =0.520, P<0.001). In the 4-year follow-up, VDBP was a significant risk factor (hazard ratio 9.627, 95% CI 1.698 to 54.571, P=0.011) for the development of proteinic flare (random urine protein/creatinine ratio >1.0) in SLE patients without proteinuria (random urine protein/creatinine ratio <0.5) (n=100) after adjustments of multiple flares.

Conclusions: Urinary VDBP correlated with proteinuria and renal SLEDAI, and predicted the development of proteinuria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4356

SAT0275 COMPARISON OF CLINICAL AND SEROLOGICAL DIFFERENCES ACCORDING TO THE AUTOANTIBODY CLUSTER IN WOMEN WITH SYSTEMIC LUPUS ERTHEMATOSUS: RESULTS FROM THE KOREAN LUPUS NETWORK (KORNET) REGISTRY

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Objectives: Individual autoantibodies are associated with the clinical features in patients with systemic lupus erythematosus (SLE). However, few studies have investigated differences in disease presentation based on autoantibody profiles in Korean SLE patients. This study evaluated autoantibody clusters and investigated differences in disease presentation based on autoantibody profiles in Korean SLE patients.

Methods: A quantitative proteomic analysis using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS), was performed to identify protein biomarker candidates that can differentiate between SLE patients with and without LN. Selected biomarker candidates were further verified using urine samples from a larger cohort of SLE patients (n=121) by enzyme-linked immunosorbent assay (ELISA) to investigate their predictive values for LN activity measure. Furthermore, association between urinary level of selected panel of potential biomarkers and prognosis of LN was assessed with a 4-year follow-up study of renal outcomes.

Results: From proteomic assay, vitamin D binding protein (VDBP), transthyretin (TH), retinol binding protein 4 (RBPA) and progestin D synthase (PTGDS) were selected as candidates for quantification. These proteins were significantly elevated in SLE patients with LN, especially in patients with active LN (n=21). Among them, VDBP well correlated with severity of proteinuria (rho =0.661, P<0.001) and renal SLE disease activity index (renal SLEDAI) (rho =0.520, P<0.001). In the 4-year follow-up, VDBP was a significant risk factor (hazard ratio 9.627, 95% CI 1.698 to 54.571, P=0.011) for the development of proteinic flare (random urine protein/creatinine ratio >1.0) in SLE patients without proteinuria (random urine protein/creatinine ratio <0.5) (n=100) after adjustments of multiple flares.

Conclusions: Urinary VDBP correlated with proteinuria and renal SLEDAI, and predicted the development of proteinuria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4356

SAT0277 EYE TOXICITY IN PATIENTS WITH SYSTEMIC LUPUS ERTHEMATOSUS TREATED WITH ANTIMALARIALS IN DOMINICAN REPUBLIC

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Background: Antimalarials are derivatives of quinine indicated in the treatment of autoimmune inflammatory diseases. The mechanism of antimalarial toxicity is unclear. It is hypothesized that toxicity is a result of drug binding to retinal pigments, damaging photoreceptors resulting in vision loss. Early retinal toxicity is asymptomatic with subtle alterations in foveal pigmentation generally not evident at routine ophthalmologic examination, progressively producing classic “bull’s-eye” maculopathy, manifested as a decrease in central, color and night vision, and central scotoma. To prevent the sequelae of antimalarial use, sensitive tools are used to detect toxic maculopathy such as: campimetry, optical coherence tomography (OCT) and eye fundus.

Objectives: To evaluate ocular toxicity in patients with systemic lupus erythematosus treated with antimalarials.

Methods: Multicenter cross-sectional study, two rheumatology departments clinical records were analyzed from January 2016 to January 2017, with diagnosis of systemic lupus erythematosus according to ACR 1997 criteria, with >4 years using antimalarial drugs. 298 patients were identified, 93 of them fulfilled inclusion criteria, and were evaluated by two retinologists performing OCT on each patient. Accumulated antimalarial doses were calculated and all variables were analyzed with SPSS software V.22.

Results: 97.8% were females, the mean age was 37±13 years, 78.5% of the patients used 4mg/kg of chloroquine (CQ) versus 21.5% took 6mg/kg of hydroxychloroquine (HCQ), the mean use duration was 5.1±2 years, 19.4% of patients had retinal pigment epithelium (RPE) changes suggesting maculopathy, of which, 15% used CQ versus 4.35% with HCQ, 54.50% using CQ had a cumulative dose of 365 grams, 10.50% with HCQ had cumulative doses of 292 grams, and the mean for the cumulative dose of both antimalarials was 485 grams.

Conclusions: Previous studies have shown that the antimalarial toxicity rate are between 7.5% - 13.1%, in our population we observed that our patients had a higher toxicity rate associated with the use of CQ compared to HCQ, and no association was found relevant with other variables. We understand that both, patients and physicians who manage this drug, should be educated about the need to maintain an adequate ophthalmologic control, due to the progressive toxic damage from 1 to 3 years of drug use, and the discontinuation of treatment is necessary to carry out prospective studies with a greater number of patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4142

SAT0278 COGNITIVE DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERTHEMATOSUS IN DOMINICAN REPUBLIC

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Background: Cognitive dysfunction (CD) is a deficit of cognitive faculties including attention, memory, language, executive function and visuospatial processing. CD is the most frequent neuropsychiatric manifestation of SLE (55–80%) 1 and this is 3 times higher in patients with Systemic Lupus Erythematosus (SLE) than in healthy subjects. 2 This is not routinely evaluated because it requires a lot of time. Brief and simple questionnaires are needed to identify CD. A study carried out by D’Amico et al. evaluated 21 SLE patients and all of them had CD.3 Pedraza et al. analyzed the MMSE score and Montreal Cognitiv
Assessment (MOCA) and concluded that MOCA performs much better than MMSE for cognitive impairment correct diagnosis.

**Objectives:** To determine the prevalence of CD in SLE patients and compare MMSE and MOCA diagnostic effectiveness.

**Methods:** All patients with at least 18 years old that met ACR/EULAR 2012 SLE classification criteria were included. Patients with associated comorbidity; not SLE related, that could alter cognitive functions, were excluded. 55 patients that fulfilled the inclusion criteria were admitted to Hospital Doctorc Padre Billini’s rheumatology department from March to April 2016. After obtaining written consent, the psychology department applied both tests, MMSE and MOCA. A standardized form registered demographic variables. Data was analyzed using Microsoft Excel 2013.

**Results:** 94.5% of the patients were women, 53% were between 31–45 years old, 52.7% were mulatto ethnic, 34.5% had at least a high school degree, 27.2% were diagnosed 1 year before enrollment, 60% had a low activity score using SLEDAI (≤4). hypertension was the most common comorbidity with a 38.1%, 90.9% were taking corticoids, 80% were on antimalarial drugs (6 abandoned treatment, 2 by eye involvement, 1 allergic reaction, 2 were diagnosed with SLE the interview day), the most frequent neuropsychiatric symptom ever presented was convulsion (7.2%). Using MMSE 25.4% of the patients showed CD, however after adjusting the results according to the educational level, the percentage increased to 41.8%. MOCA classified that 67.2% of the patients had CD, of which 13 patients were MMSS positive, and finally, 22 classified after the score adjustment.

**Conclusions:** MOCA is more effective than MMSE to detect CD. Nonetheless the MMSE SE should be considered as an option for patients with low levels of education.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4279

**SAT0279**

**INCREASED FREQUENCY OF NAILFOLD VIDEOCAPILLAROSCOPY ABNORMALITIES IN PRIMARY ANTIPHOSPHOLIPID (PAPS) PATIENTS**

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**Background:** Primary antiphospholipid syndrome (PAPS) is characterized by venous and arterial thrombosis, obstetric morbidity and the presence of antiphospholipid antibodies. Nailfold videocapillaroscopy is considered a tool of choice in the identification of cutaneous microangiopathy, a specific feature of this disease.

**Objectives:** To evaluate findings on nailfold videocapillaroscopy in patients with PAPS and their association with clinical and serological features.

**Methods:** We prospectively included 26 PAPS patients according to the modified SLEDAI 2012 criteria and the Alarcón-Segovia criteria for haemato logic antiphospholipid syndrome, who regularly attend a tertiary referral center in Mexico City, and who fulfilled the ACR/EULAR 2012 SLE classification criteria. A complete clinical, demographic, and serological investigation was performed. Nailfold videocapillaroscopy was performed using the Optilia 200x (Optilia Ltd, Berlin, Germany) at the baseline. Capillary morphology was evaluated by a rheumatologist certified by the EULAR Working Group on Optical Imaging and identified five categories of abnormalities: dilated capillaries, capillary haemorrhages, capillary rarefactions, microaneurysms and abnormal patterns, according to the 2015 Cutolo technique.

**Results:** Data were analyzed using statistical software. The proportions of abnormalities in the capillaries of PAPS patients were significantly higher compared to controls group (p<0.05) with a higher frequency of dilated capillaries (23% vs 7%), capillary haemorrhages (11% vs 5%), capillary rarefactions (27% vs 12%) and abnormal patterns (27% vs 7%). A sub-analysis of patients with high titers of anti-Ro52KDa antibodies showed a frequency of abnormalities similar to the group overall.

**Conclusions:** These findings suggest that scalaring and microvascular involvement is more frequent in PAPS patients. The coexistence of hypertension or other comorbidities may contribute to the development of capillary abnormalities in PAPS patients.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5663

**SAT0278**

**ANTI-RO52 KDA AND ANTI-RO60 KDA ANALYSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TO DETECT ANTI-RO FALSE-NEGATIVES**


**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by immune system disruption with autoantibodies production. One of theeregulated autoantibodies is the specific to the Ro antigen, a ribonucleoprotein associated to a small RNA, constituted by the 52KDa and 60 KDa polypeptides, whose epitopes are mainly conformational. The routine detection method for anti-Ro is an enzyme immunoassay, however, is possible to obtain false-negatives for anti-Ro and this could be avoided by analyzing both subunits. These cases with high levels of anti-Ro52KDa and anti-Ro60KDa levels have been measured by colorimetric methods. Biostatistical analysis was performed with R 3.3.2.

**Objectives:** To identify false-negatives for anti-Ro by analyzing both 52KDa and 60 KDa subunits separately, as well as to characterize if there are clinical or molecular differences in this subgroup of patients compared to anti-Ro negative cases.

**Methods:** A cross-sectional, observational study of patients diagnosed of SLE according to SLICC 2012 criteria was performed. In these patients a complete blood-test was made, and clinical data by personal interview was collected. INFA. Anti-Ro, Anti-Ro52KDa and anti-Ro60KDa levels were measured by colorimetric methods. Biostatistical analysis was performed with R 3.3.2.

**Results:** We selected 69 SLE patients with negative results for anti-Ro (2.34±4.17 U/mL) out of 142 total SLE patients. A total of 51 patients were negative for both anti-Ro subunits and 18 cases presented positive results (up to 20 pg/mL) for at least one of them. The subgroup of patients that exhibit simultaneously high levels of anti-Ro52KDa and anti-Ro60KDa have higher clinical activity compared to negative anti-Ro cases (75% of active patients against 41.2% in anti-Ro negative patients). However, no differences in the accumulated damage evaluated by SLICC score between negative anti-Ro cases and patients with at least one positive subunit were observed. We analyzed serum levels of INF1A cytokine in the four groups of patients, and anti-Ro and subunits negative cases showed significant lower INF1A levels than the other patients (8.26±14.87 pg/mL and 26.62±40.71 pg/mL respectively; P=0.04). In addition, patients with high levels of anti-Ro52KDa subunit are those with the highest INF1A levels (anti-Ro S2+/anti-Ro06- 23.5±47.6pg/mL of INF1A; Anti-Ro S2+/anti-Ro60+ 36.4±37.9pg/mL of INF1A).

**Conclusions:** In our anti-Ro seronegative patients, a 26% of false-negative cases were detected. These cases with high levels of almost one anti-Ro subunit showed significantly higher levels of INF1A in contrast to negative cases, supporting the fact that they are indeed a different group from the negative cases. Moreover, the high INF1A levels could be the reason of the observed differences in the clinical activity measured by SLEDAI score in both groups.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5758

**SAT0280**

**A TEN-YEAR SURVIVAL ANALYSIS OF FILIPINO PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT THE NATIONAL KIDNEY AND TRANSPLANT INSTITUTE (PHILIPPINES)**

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**Background:** Systemic lupus erythematosus (SLE) is increasingly being diagnosed in our country. Despite the increasing number of patients, there are no studies describing their clinical profile at the time of diagnosis at the National Kidney and Transplant Institute (NKTI). This study aims to describe patients’ initial clinical presentations, outcomes, and their survival rate within ten years.

**Objectives:** To determine survival rate and presenting characteristics of Filipino patients first diagnosed with SLE at the National Kidney and Transplant Institute (NKTI)

**Methods:** This is a retrospective cohort study using chart review of patients first diagnosed with SLE in 2004 followed up in the next ten years.
Results: Eighty-five patients were first diagnosed with SLE wherein their average age was 28.10 years old ± 12.03, 34.12% had hypertension, and 74.12% with renal involvement. The patients’ cumulative 10-year survival was 75% with average survival time of 9.84 years. Moreover, biopsy- proven lupus nephritis had significantly longer survival time (mean=10.57 years, p=0.006) while those with joint and cardopulmonary manifestion had shorter survival (mean=0.71 years, p=0.030) as well as those on hemodialysis (mean=8.82 years, p=0.040). Lastly, eleven patients (12.94%) expired during the study period with active diseases and infections as the common causes of mortality.

Conclusions: Although renal involvement was the most common initial manifestation, it did not correlated with disease activity indices, such as DAS28.

Disclosure of Interest: None declared

SAT0281 JOINT ACTIVITY INDICES CORRELATES WITH ULTRASONOGRAPHIC SCORE IN SLE PATIENTS WITH MUSCULO-SKELETAL INVOLVEMENT

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Background: Joint involvement represents one of the most frequent manifestations in Systemic Lupus Erythematosus (SLE) patients (incidence 69–95%), with different degrees of severity. Currently, there are no validated indices to evaluate joint involvement in SLE. Musculo-skeletal ultrasonography (US) has been widely applied in patients affected by different arthropathies. US-detected synovitis reflects the inflammatory state at the joint level, as demonstrated by the correlation with histological modifications. Furthermore, US-synovitis significantly correlates with disease activity indices, such as DAS28.

Objectives: In the present study, we aimed assessing a correlation between the composite indices DAS28 (Disease Activity Score 28), CDAI (Clinical Disease Activity Index), SDAI (Simplified Disease Activity Index), STR (Swollen to Tender Ratio) and the US-detected synovitis in a cohort of SLE patients with joint involvement.

Methods: One hundred seven patients (M/F 7/100, mean age ±SD 48.4±13.6 years, mean disease duration ±SD 156.0±129.6 months) with at least one tender joint were enrolled. We registred the number of swollen and tender joint count (0–28) and the patient’s/physician’s disease activity on visual analogue scale (0–100). DAS28-ESR, CDAI, SDAI and STR were calculated. The US evaluation of 12 joints (I-V metacarpophalangeal, I-V proximal interphalangeal, wrist and knee bilateral) was performed to identify inflammatory features (synovial effusion, synovial hypertrophy and power Doppler) according with OMERACT definitions. These elementary lesions were scored according to a semi-quantitative scale (0 = absent, 1 = mild, 2 = moderate and 3 = severe). The sum of the semi-quantitative scores allows obtaining a total score of the patient’s inflammatory state (0–216).

Results: As reported in Figure 1, by using the Spearman analysis, a positive correlation between US-score and SDAI (r=0.33, P=0.02), CDAI (r=0.29, P=0.03) and STR (r=0.42, P=0.0005) was identified. In particular, SLE patients with high disease activity according with STR value (≥1) showed a higher US score (16.3±19.3) in comparison with moderate (7.7±4.5, P=NS) or low disease activity (7.1±7.9, P=0.02). Moreover, US score resulted significantly lower in patients with DAS28 remission compared to those with an active disease (4.5±4.4 versus 7.05±5.1, P=0.03; Mann-Whitney test).

Conclusions: We analyzed a large SLE cohort with articular involvement identifying a significant correlation between US scoreand the composite indices CDAI, SDAI and STR. Furthermore, US-score may be able to discriminate DAS28-remission patients. Taken together, these results suggest the ability of composite indices in detecting the joint activity in SLE patients and the possibility to use them in clinical practice to assess this frequent and potentially disabling manifestation.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5231

SAT0282 AUTOIMMUNITY AND PREGNANCY: EVIDENCE FROM AN OBSERVATIONAL STUDY

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Background: Obstetrical APS is defined by positive aPLs and a history of one or more unexplained deaths of morphologically normal fetus at or beyond the 10th week of gestation (WG) or one or more consecutive spontaneous abortions before the 10th WG. Also one or more premature birth before 34 WG because of eclampsia, severe pre-eclampsia, or recognized features of placental insufficiency represent one of the diagnostic criteria (1). Infertility is defined as the inability of a couple practicing frequent intercourse and not using contraception to conceive a child after 12 months. Autoimmune diseases are not included among major causes of infertility, despite defective embryonic implantation could be considered an aspect of recurrent fetal losses in patients with positive antiphospholipid antibodies, due to their capabilities to reduce trophoblast proliferation and growth (2).

Objectives: The aim of our study was to evaluate the prevalence of aPLs and pregnancy outcome in a population of women undergoing in vitro fertilization.

Methods: from December 2012 to December 2016, we selected 75 consecutive patients undergoing in vitro fertilization and evidence positive autoantibodies. Each of them was evaluated for genetic, anatomic, hormonal and infective causes of infertility. Moreover antinuclear antibodies (ANA), anticardiolipin antibodies (aCL), anti-β2-glycoprotein I (β2GPI), lupus anticoagulant (LA) and extractable nuclear antigens (ENA) profile were assessed.

Results: patients mean age was 41.38±4.87 years, ranging from 31 to 53 years. Prevalence of aPLs in our population was 68%. All women showed at least twice positive aPLs. aCL IgM and LA were the main antibody populations observed. ANA were positive in 50% of women, whereas SSA or SSB were positive in 4.17%. In 22.9% of patients a systemic autoimmune disease was newly diagnosed, mainly systemic lupus erythematosus. All patients with history of recurrent miscarriages and positive aPLs were treated with subcutaneous low weight heparin plus daily oral acetylsalicylic acid (ASA 100 mg) (3). Full term pregnancy was obtained in 45.8% of patients.

Conclusions: Prevalence of aPLs in the general population is 1–5%, whereas in our selected series positive aPLs were detected in 68% of the patients, suggesting that prevalence of aPLs may be increased in infertile patients (4). Moreover, a systemic autoimmune disease was newly diagnosed in 22.9% of patients suggesting that paucisymptomatic disease can be underestimated. Finally we would suggest that treating autoimmune co-morbidities ameliorates implantation rates in women undergoing in vitro fertilization (5).

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6425
OBJECTIVES: Aim of the study was to assess the prevalence of anti-carbamylated vimentin in a cohort of SLE patients and to evaluate the possible associations with clinical and histological features of the disease.

Methods: Patients with SLE classified according to 1987 ACR criteria were enrolled. Clinical, serological and histological data were collected. Sera obtained from each patient were tested for anti-carbamylated vimentin by a home-made enzyme-linked immunosorbent assay. Data were analyzed using the mean ± standard deviation or median (interquartile range) when appropriate. To investigate difference in anti-carbamylated vimentin prevalence and anti-carbamylated vimentin serum levels Mann-Whitney and Chi square test were applied. P value <0.05 was considered statistically significant.

Results: We enrolled 109 SLE patients (102F:7M, mean age 39.4±12.6 years, mean disease duration 10.5±9.5 years, mean SLEDAI 2K 5±5.5).

Overall, 30 out of 109 patients (27.5%) were positive for anti-carbamylated vimentin. According to the clinical features, the prevalence of anti-carbamylated vimentin was significantly higher in patients with lupus nephritis (18/44) compared to those without renal involvement (12/66) (41.8% vs 18.2%, p=0.006; moreover, anti-carbamylated vimentin serum levels were significantly higher in patients with lupus nephritis (2561 (1783) OD) compared to those without [1970 (1123) OD; p=0.0178].

We didn’t find any difference in prevalence or titre of anti-carbamylated vimentin according to sex, age, disease duration, cumulative damage or the presence of anti-double-stranded DNA antibodies.

Conclusions: Higher prevalence and serum levels of anti-carbamylated vimentin in patients with lupus nephritis compared to those without renal involvement may suggest a role of the immune response in patients with glomerulonephritis and suggest their possible role as a biomarker of kidney involvement in SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5819

SAT0284 ASSOCIATION OF PATHOGENIC AND REGULATORY B-CELL SUBSETS WITH CLINICAL AND HISTOLOGICAL FEATURES IN PRIMARY SJÖGREN’S SYNDROME

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Background: Several data pointed out that B-cells play a central role in the development, maintenance and progression of primary Sjögren’s syndrome (pSS). B-lymphocyte hyperactivity, salivary gland (SG) infiltration, and the development of B-cell follicles containing germinal center (GC)-like structures, represent hallmark of the disease. On this basis, B-cell depletion therapy with anti-CD20 monoclonal antibodies is widely accepted; however, the percentage of IL-10-producing B-cells was higher in patients with GC (p=0.02) compared to those without GC. Although we observed a reduction of all B-cell subsets in pSS patients with ESSDAI≥5 compared to patients with ESSDAI<5 (p=0.02), we didn’t find any difference in prevalence or titre of anti-carbamylated vimentin antibodies in patients with rheumatoid arthritis.

Carbamylation is a non-enzymatic post-translational modification consisting in the addition of a cyanate group on lysine and arginine residues; since carbamylation has not been yet evaluated.

We demonstrated for the first time that a subset of circulating mature B-cells, Bm2’, also called GC founders, is strongly associated with higher disease activity and with the presence of SG-GC. Moreover, a higher ESSDAI in a subset of patients with higher IL-10-producing B-cells is associated with systemic lupus erythematosus (SLE). Pathogenic B-cell hyperactivity is a hallmark of pSS, however B-cells are also a source of inhibitory cytokines such as IL-10 and TGF-beta and the increase of IL-10 producing B cells that we observed in active pSS patients may suggest an ongoing compensatory mechanism to counteract chronic inflammation. Therefore, the design of novel B cell targeted therapies should ensure that only pathogenic B cells are depleted and regulatory B cell subsets are not hampered while, ideally, potentiated.


Disclosure of Interest: None declared


SAT0285 THE PHYSICAL PERFORMANCE OF SYMBIOTIC LUPUS ERYTHEMATOSUS PATIENTS WITH LOW DISEASE ACTIVITY: COULD THE CARDIOPULMONARY EXERCISE TESTING REFINE ITS ASSESSMENT?

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Background: Even during remission, the systemic lupus erythematosus (SLE) patients have reduced exercise performance and this contributes to impairment of their quality of life. Several causes as depression and deconditioning, arthrosis, anemia, cardiovascular and respiratory involvement are widely accepted; however the weight of each factor is less known in particular individuals.

Objectives: Our study aimed to assess through cardiopulmonary exercise testing (CPX) the exercise performance of a SLE cohort and to establish its main determinants.

Methods: Thirty-one SLE patients with low disease activity underwent a CPX cycle ergometer; the main metabolic parameters and standard 12-leads ECG were recorded; before exercise testing, a cardiac Doppler ultrasound was performed. The patient’s characteristics, cumulative organ damage and laboratory data were retrieved by medical chart review. The control group consisted of 25 age and sex-matched healthy, non-trained individuals.

Results: Within the study group, 28 (90.3%) were female, the mean age was 42.7±10.6 years and disease median duration 7.9 years. The aerobic performance was decreased by 16.2% (17.6 vs 21.36 ml/kg/min, p=0.022), the main disease characteristics which correlated with maximum oxygen uptake (VO2max) were anemia (p=0.035), renal involvement (p=0.05) and antiphospholipid syndrome (APS) (p=0.042) but not disease duration, cumulative organ damage and laboratory tests. The immunological tests (hypocomplementemia, anti-Ro, anti-Smith, anti-dsDNA, AAN or APL antibodies).

One quarter of patients did not reach the ventilatory anaerobic threshold (VAT, exercise intensity that is associated with VO2max). Moreover, due to musculoskeletal pain (5 patients), dyspnea (2 patients with history of pulmonary embolism) and sudden rise in blood pressure (1 patient). Among the rest of them (23 patients, 74%), the VAT was at the lower limit of normal range (41.03% vs 54.0% for controls, p=0.014) corresponding to a “training reserve” of 31%. Of particular importance from this point of view were the criteria for test termination: dyspnea in 4 patients (1 with anemia, 1 with pulmonary fibrosis and 2 by hyperventilation proved by mean VE/VO2 = 4.15, fatigue (9 patients) and arthrosis (7 patients). Notably, among patients with established diagnosis of mild pulmonary fibrosis, COPD, ischemic or valvular heart disease, not dyspnea but arthrosis or fatigue was the reason for test termination, even if the VO2max was lower than recorded in the rest of the group (15.8 vs 19.2 ml/kg/min, p=0.037).

Conclusions: The exercise aerobic capacity of SLE patients is diminished and correlates with anemia, renal involvement and with history of pulmonary embolism. Surprisingly, even in patients with mild cardiovascular or respiratory involvement, the decreasing of exercise performance is limited mainly from musculoskeletal symptoms and from deconditioning.

scientific abstracts

SAT0286 | INCIDENCE AND MORTALITY OF PRIMARY SJÖGREN’S SYNDROME: TIME TRENDS OVER A 40-YEAR PERIOD IN A POPULATION-BASED COHORT IN THE UNITED STATES

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Background: Few studies have reported the incidence of primary Sjögren’s syndrome (pSS) in well-defined populations worldwide, and none of them covered a period of time long-enough to analyze potential time trends in incidence rates. Whether pSS is associated with a higher mortality rate compared to the general population is also unclear from previously published studies.

Objectives: To estimate the incidence and mortality rates of pSS among residents of Olmsted County, Minnesota, and their evolution over time.

Methods: All medical records of patients with a diagnosis or suspicion of SS in Olmsted County, MN, from January 1, 2006 to December 31, 2015 were reviewed to identify incident cases of pSS (defined according to physician diagnosis). All patients with doubtful cases and all patients with an associated systemic autoimmune disease were excluded. These cases were combined with a previous 1976–2005 incident cohort from the same population (reference). Incidence rates were age and sex adjusted to the US white 2010 population. Survival rates were compared with the expected rates in the general population of Minnesota.

Results: With 61 incident cases of pSS diagnosed in Olmsted County in 2006–2015, the total cohort included 172 patients with incident pSS in 1976–2015. Of the 172 patients, 151 (88%) were women and 161 (94%) were white, with a mean (SD) age at diagnosis of 58.3 (16.7) years. The average age- and sex-adjusted annual incidence for 2006–2015 was 5.9 per 100,000 population (95% CI 4.4–7.4), and overall incidence for the entire period was 5.8 (95% CI 4.9–6.6) per 100,000. Incidence was 2 to 7 times higher in females compared to males in the different age classes (5.9 times higher on average), and increased progressively with age, culminating at 19.6 per 100,000 in females aged 65–74 years, with a slight decline thereafter to 15.9 per 100,000 among females aged 75 years and older. The incidence increased with calendar time over the 40-year period (p=0.005, figure). There was no apparent seasonality in the incidence of pSS, with similar number of cases diagnosed during all four seasons. There was no difference in mortality in the pSS cohort compared to expected (standardized mortality ratio 1.15, 95% CI 0.86–1.50).

Conclusions: The average annual incidence of pSS in this population based-cohort was 5.8/100,000, with a progressive increase over the 40 years of the study. Overall survival of pSS patients was not different from the general population.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6619

SAT0287 | TH1, TH2 AND TH17 LYMPHOCYTE SUBPOPULATIONS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid antibody syndrome (APS) is characterized by thrombosis at different levels and maternal fetal complications in the presence of antiphospholipid antibodies (aPL). Lymphoid subpopulations and cellular immune responses have not been fully studied.

Objectives: To analyze the lymphoid subpopulations, Th1, Th2 and Th17 immune response in patients with APS and long term evolution.

Methods: Patients with APS, > 18 years of age, of both sexes and a group of healthy blood donors matched for age and sex were included. All patients were receiving oral anticoagulants (Coumadin type). No patient had a recent episode of thrombosis or other manifestation of APS at the time of the study. Peripheral blood was obtained and lymphoid subpopulations were determined by flow cytometry in order to identify cells expressing CD4+CD25+Foxp3+ and CD8+CD25+Foxp3+. The dendriticritic cells analyzed were: Type 1: Lin-1–HLA-DR+CD11c+; Type 2: Lin-HLA-DR+CD123+; B lymphocytes with antiCD19-APC; Monocytes with anti-CD14-PE; NK: CD3-/CD16+56+ and NKT: CD3+CD16+56+. Th1 cells were identified by IFN-g positivity; Th2: positivity for IL-4+; Th17: positivity for IL-17+. Parametric statistics and Mann-Whitney U-test were used.

Results: A total of 39 patients with APS were included, age: 51±9.12±8.9, evolution time: 12.8±5.9 years and 35 healthy controls. In patients with APS there was a decrease in the total CD6 count (p<0.05) in NK (p<0.005), DC1 (p<0.005) and DC2 (p<0.0005) compared to the control group (Table 1). We found a significant decrease in Th1, Th2 and Th17 cytokines basal and after activation compared to healthy controls.

Conclusions: This study shows profound alterations in innate and adaptive immunity in patients with long-term APS, characterized by a decrease in certain lymphocyte subpopulations, with consequent functional alteration. These abnormalities can become new therapeutic targets in order to restore immune imbalance. Our findings may explain in part, the development of thrombosis and other complications, despite treatment with oral anticoagulants in APS patients with long term disease evolution.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6222

SAT0288 | QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The quality of life (QoL) in patients with SLE is deeply affected by multiple factors including psychological and physical factors, the functional status and the general perception over health.

Objectives: Evaluation of Quality of life and the perceptions over the disease in patients with SLE functional status and the general perception over health.

Methods: This is a 10 month prospective, cross-sectional study performed on 52 patients hospitalized diagnosed with SLE according to SLICC 2012 criteria. There were evaluated demographic data, organs manifestations, disease activity scores (SLEDAI, SLICC) and treatment. To evaluate the QoL several questionnaires were performed: Health Assessment Questionnaire (HAQ), EuroQol five dimensions questionnaire (EQ5d), Illness Perception Questionnaire and SF-36.

Results: All patients were women with the mean age 49 years with a mean duration of illness 136 months (14). The mean SLEDAI – 5.52 (5.37) and SLICC – 2.25 (1.71). The mean HAQ value was 0.83 (0.81). The HAQ score doesn’t correlate with SLLC (p<0.461) with SLEDAI (p=0.172), but it was correlated with the neuropsychiatric manifestations. So the psychiatric affection influences performing the usually daily activities (p<0.005).

When assessing Illness Perception Questionnaire, patients considered their life seriously affected by pain, mean value 6,3 (2,6), 72% consider the illness will be worse in the future, 58% would avoid the same situation, 72% consider the illness will be more extensive.

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present for the rest of their lives, 90% appreciate that treatment is improving the QoL mean 9.3 (1.3), 68% consider to have many severe symptoms, more than 80% patients consider themselves preoccupied for their illness, more than 70% are emotionally affected by their illness and 48% consider stress being the main determinant factor of their illness. Our patients required preoccupation to stay in bed due to the disease, 8.33% can not wash or dress themselves, 12.5% are unable to perform usual daily activities, 62% experience pain or a moderate uncomfortable state and 65% are worried and or depressed. Cardio-vascular manifestations are correlated with diminished mobility (p<0.002), leading to deficiency in self care (p<0.002)also correlated with renal (p=0.001) and psychiatric (p<0.002) manifestations. Psychiatric manifestations also affect usual daily activities (p=0.05). Age is correlated with pain and uncomfortable state (p<0.004) but the responses to this item of EQ5D are not correlated with organ affection, biological modification or disease activity scores. The presence of cutaneous manifestations is correlated with anxiety and depression (p<0.002).

Based on SF36 when calculating the mean value on each category was observed all the 8 categories affected - smallest values at physical role (37,32) and general health (34,21), less influenced part being the social function (51,32).None of this items of SF36 is correlated with SLICC or SLEDAI.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5316

SAT0289 | CARDIOVASCULAR RISK STATUS MODIFICATION IN SLE PATIENTS: MEANS OF CAROTID ULTRASOUND EXAMINATION

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Background: Systemic lupus erythematosus (SLE) is associated with a higher cardiovascular risk (CVR), at least doubled when compared with the general population, as well as an increased prevalence of atherosclerosis,which occurs prematurely and independently of traditional CVR factors. The presence of atheromatous plaques documented with carotid ultrasound (US) examination implies a change in the patient’s CVR category to “very high risk”, according to the European Guidelines on cardiovascular disease prevention in clinical practice, 2016”. General guidelines do not take into account the specific increase in CVR risk that it’s present in patients with autoimmune diseases.

Objectives: To examine if the use of carotid US leads to a more accurate CVR classification in SLE patients, and in that way to a better CVR management.

Methods: Cross-sectional study that encompassed 102 SLE patients currently being followed in our Rheumatology Department. Demographic variables, the presence of CVR factors and previous/current CV events, disease duration and dose of prednisolone were analyzed and profile was assessed using blood tests, as well as carotid intima media thickness and the presence of carotid plaques using US scan. The current CVR status was calculated using the SCORE classification (low risk <1%, moderate risk <5%, high risk <10% and very high risk >10%).

Results: 95% of our patients were women, mean age was 51.6±11.0 years, median disease duration was 16 years (IQR 9–28). 35.29% of patients presented with at least one CVR factor before the SLE diagnosis,and 61.76% at the time of the research (19.60% current smokers, 39.21% high blood pressure (HBP), 33.33% dyslipidemia, 7.84% type II diabetes. A CV event was diagnosed in 11.76% of our patients throughout their SLE disease. According to the SCORE classification, 55% of them had a low CVR (53.92%), 26 moderate CVR (25.49%), 6 high CVR (5.88%) and 15 of them very highCVR (14.70%). Carotid plaques were found in 28 patients (27.45%): 23 of them had never had a CV event (22.54%), 21.42% of them were former smokers, 4.28% had HBP, 5.77% dyslipidemia and 17.86% type II diabetes. After adjustment of the SCORE classification with the presence of carotid plaques,16.36% of patients from the “low CVR” category would be re-classified as having “very high CVR”, as well as 30.76% from the “moderate CVR” category and 50% from the “high CVR” category. Of note,8 patients within the “very high CVR” category also presented carotid plaques. Out of this patients with atheroma plaque,13 were not using statins,and in 2 of them it would have been mandatory in order to achieve the LDL <70mg/dl target. In 2 of the 15 patients that were indeed under statins this target was not achieved. In 60.71% of the patients under hypothyroidism use and 17.64% of them used steroids as a regular basis (33.33% of them within the medium range dose).

Conclusions: More than half of our SLE patients presented with at least 1 CVR factor. Around 15% of patients were categorized as ‘very high CVR” according to the SCORE classification. The presence of carotid plaque was found in 27.45% of our patients and 82% of them hadn’t suffered any CV event. The use of carotid US examination allowed us to re-classify 20 patients (19.60% in the “very high risk” category according to the SCORE classification. The need for a change in CVR management (i.e., change in statin regime)was demonstrated in 4 of this 20 “re-classified” patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5316

SAT0290 | OSTEONECROSIS IS THE MOST COMMON ORGAN DAMAGE AND IS ASSOCIATED WITH CUMULATIVE STEROID DOSAGE AS WELL AS LUPUS NEPHRITIS ETHIS ITSELF IN PATIENTS WITH SLE

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Background: In patients with SLE, musculoskeletal system is common organ system affected cumulative dosages of corticosteroids. Osteonecrosis (ON) is common in musculoskeletal damage accrual and often disabling. Steroid use has been a risk factor in the development of ON, but SLE itself has also been suggested to have a role. It is important to understand factors related to the development of ON.

Objectives: We investigated the overall profile of organ damage accrual, particularly musculoskeletal damage and focused on factors associated with ON in a single Asian cohort.

Methods: Patients with SLE who met American College of Rheumatology (ACR) criteria were enrolled and followed from 1998 to 2014 in the Hanyang BAE Lupus cohort. Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was measured annually. ON was confirmed by X-ray, bone scan or MRI. Patients with ON was compared to controls without ON from the same cohort for clinical, laboratory, and therapeutic factors. Univariate logistic regression followed by multivariate logistic regression were used to determine risk factors for ON.

Results: We recruited 1,219 SLE patients. The most common type of organ damage was musculoskeletal damage (205 patients, 16.8%). ON was the most common subtype (133 patients, 10.9%) of the musculoskeletal damage. The mean time from diagnosis of SLE to development of ON was 4.97±4.15 (0.17–20.25) years. One hundred twenty-nine patients were eligible for identifying distribution of ON. Overall, 291 joints were affected by ON and mean number of ON joint per patients with ON was 2.3±1.23 (1–9). The percentage of >2 joint involvement was 24.6%. The hip (femoral head) was the most frequently involved joint (65.6%), followed by the knee (distal femur, proximal tibia, proximal fibula, patella) (23.6%), shoulder (humeral head: 5.2%) and ankle (distal tibia, distal fibula, talus: 5.2%). In univariate analysis, age at diagnosis, follow up duration, accumulative number of ACR criteria, serositis, renal disorder & neurologic disorder (based on ACR criteria), cyclophosphamide & mycophenolate use, and cumulative steroid dosages were significantly associated with ON. In multivariate analysis, renal disorder (p=0.019), and cumulative steroid usage (p=0.0131) were significantly associated with ON.

To evaluate the effect of cumulative steroid usage on ON, age, sex and disease duration matched ON cases and controls (1:4, a total of 665 patients) were selected from the same cohort. Total cumulative steroid dosage was divided into 4 groups by grams (>0 & ≤5g, >5g & ≤10g, >10g & ≤20g, >20g). More than 10g group of cumulative steroid use was significantly associated with ON. And then we stratified 530 patients according to biopsy proven lupus nephritis (class III to V) and cumulative steroid dose (10g cut-off), and tested Chi-square test and logistic regression. ON was significantly higher in the group with lupus nephritis within >10g group of total cumulative steroid.

Table 1: Total cumulative steroid dose as risk factor for ON

<table>
<thead>
<tr>
<th>Steroid dose (g)</th>
<th>Number of ON patients</th>
<th>Total number of patients</th>
<th>ON%</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20g</td>
<td>106</td>
<td>596</td>
<td>17.8%</td>
<td>3.07 (1.9 – 4.9)</td>
</tr>
<tr>
<td>10g ≤20g</td>
<td>73</td>
<td>390</td>
<td>18.8%</td>
<td>2.57 (1.6 – 4.1)</td>
</tr>
<tr>
<td>5g ≤10g</td>
<td>73</td>
<td>377</td>
<td>19.3%</td>
<td>2.28 (1.4 – 3.6)</td>
</tr>
<tr>
<td>0g ≤5g</td>
<td>76</td>
<td>368</td>
<td>20.7%</td>
<td>1.93 (1.2 – 3.0)</td>
</tr>
<tr>
<td>&lt;0g</td>
<td>77</td>
<td>372</td>
<td>20.6%</td>
<td>1.91 (1.2 – 3.0)</td>
</tr>
</tbody>
</table>

Conclusions: ON was the most frequent damage in lupus patients. We confirmed again cumulative steroid dosage as a risk factor for the development of ON. In addition, lupus nephritis itself was suggested as an independent risk factor for ON.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5457
SAT0291  NON-REPORTING OF SYSTEMIC LUPUS ERYTHEMATOSUS IN DEATH CERTIFICATES OF LUPUS PATIENTS: ITS EXTENT AND PREDICTORS
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1 Department of Internal Medicine, Division of Clinical Immunology and Rheumatology, University Hospital Centre Zagreb; 2University of Zagreb, School of Medicine; 3Croatian Institute of Public Health, Zagreb, Croatia

Background: Systemic lupus erythematosus (SLE) is frequently not reported in death certificates of lupus patients, despite its known role as an underlying and/or immediate cause of death. Possible reasons may be insufficient access to patients’ medical records at time of death (including details on their medical history) and/or physicians’ unawareness of the contribution of SLE to death.

Objectives: We aimed to analyze the extent and predictors of non-reporting of SLE in death certificates of 90 deceased SLE patients regularly followed-up in a routine academic setting at our Department.

Methods: We retrospectively observed 90 SLE patients (68 females) deceased within the 2002-2011 period. All patients were ≥18 years of age and Croatian residents at the time of death, fulfilling >4 classification criteria of the American College of Rheumatology (ACR). We identified patients with SLE listed as a cause of death in the death certificate. An extensive set of variables was compared between patients with and without SLE reported in the certificate: demographics, ACR criteria at time of death and damage according to the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC)/ACR index and its components at the time of death. We also compared the proportion of in-hospital deaths and autopsies performed. Frequencies were compared using the χ² and Fisher’s exact test, and continuous variables using the t-test and Mann-Whitney U test.

Results: SLE was reported in death certificates of 41/90 (46%) patients. Patients with SLE not reported in their death certificates were older at death (62±14 vs. 53±15 years) and diagnosed (53±14 vs 42±18 years) and had a lower proportion of renal disorder (20/49 vs. 29/41), cardiovascular and pulmonary damage (18/49 vs. 28/41 and 7/49 vs. 13/41, respectively), and died less frequently in hospital (28/49 vs. 35/41) and due to infections (4/49 vs. 26/41) (p<0.05). Conversely, these patients had a higher frequency of malignancy as a feature of damage (17/49 vs. 6/41) and a cause of death (14/49 vs. 1/41) (p<0.05). Only patients without SLE listed in their death certificate accrued gastrointestinal damage (7/49 vs. 0/41, p=0.015), hence this type of damage could not be included in the multivariate logistic regression model. In the multivariate model, the presence of infection as a cause of death was the single variable related to (non-)reporting of SLE (OR 0.053; 95% CI 0.012-0.237) (Table 1).

Conclusions: Non-reporting of SLE in death certificates of lupus patients may be an obstacle towards assessing the true extent of SLE-related mortality, calling into question the reliability of vital statistics data extracted only from death certificates. Infections as causes of death and gastrointestinal damage may influence reporting of SLE in death certificates.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5580

SAT0292  LONG-TERM PROGNOSIS AND PREDICTING FACTORS OF CHINESE PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME
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Background: Antiphospholipid syndrome (APS) is an acquired autoimmune prothrombotic condition characterized by persistent circulating antiphospholipid antibodies (APL). The pathogenic mechanisms that lead to clinical manifestations associated with APL are only partially understood. And to date, long-term anticoagulation has been the only treatment shown to reduce vascular complications. Objectives: The aims of the present study were to assess and identify the predictive factors of long-term outcomes and mortality of antiphospholipid syndrome (APS) in Chinese patients.

Methods: Records of 160 patients with APS admitted to Peking Union Medical College Hospital in Beijing between 2005 and 2015 were investigated. Demographic characteristics, cumulative clinical and laboratory features, autoantibody profiles were retrieved from the database. Survival rates were studied by Kaplan-Meier method, and COX proportional hazard model was adopted to perform the analysis of predicting factors for mortality.

Results: The entire cohort consisted of 110 (68.8%) female and 50 (31.3%) male patients. Mean (SD) age at study entry was 36.5±14.9 years. The most prevalent thrombotic risk factors were hypertension, dyslipidemia, and smoking, present in 5-15% of the total cohort. In total, 50.6% of the patients had primary APS, 45.9% had APS associated with SLE, 2.0% APS associated with other connective tissue diseases. The most prevalent immunological features at baseline were LA (71.3%), aCL (55.0%), and j2GPI (49.4%). No significant statistical differences were found in the clinical presentation of the APS according to absence or presence of any of these antibodies. During the 10-year period, 16 (10.0%) patients (8 female and 8 male) died. The overall 1, 3, and 5-year survival rate was 92.6%, 89.1% and 87.1%, respectively. The most common causes of death were severe thrombotic events, including pulmonary embolism, strokes, and myocardial infarction (43.8% of total deaths), infections (18.8%). COX proportional hazard model show thrombocytopenia is the independent prognostic factor of mortality (HR 8.228, 95% CI 1.866-36.282).

Table 1. Baseline characteristics of APS patients

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Prevalence</th>
<th>Thrombotic event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, %</td>
<td>110 (68.8%)</td>
<td>42 (62.4%) 68 (62.4%)</td>
</tr>
<tr>
<td>Age, year, mean±SD</td>
<td>36.5±14.9</td>
<td>34.2±14.9 37.4±14.9</td>
</tr>
<tr>
<td>Thrombotic events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial thrombosis</td>
<td>59 (36.9%)</td>
<td>– 59 (54.1%)</td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>72 (45.0%)</td>
<td>– 72 (66.1%)</td>
</tr>
<tr>
<td>Coexistance of arterial and venous thrombosis</td>
<td>22 (13.8)</td>
<td>– 22 (20.2%)</td>
</tr>
<tr>
<td>Systemic autoimmune diseases</td>
<td>79 (49.4)</td>
<td>33 (64.7%) 46 (42.2%)</td>
</tr>
<tr>
<td>Thrombophoric risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>8 (5.0%)</td>
<td>2 (3.9%) 5 (5.5%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>20 (12.5%)</td>
<td>6 (11.8%) 14 (12.8%)</td>
</tr>
<tr>
<td>HTN (systolic &gt;140)</td>
<td>24 (15.0%)</td>
<td>7 (13.9%) 17 (15.6%)</td>
</tr>
<tr>
<td>APL</td>
<td>88 (55.0%)</td>
<td>32 (62.7%) 56 (51.4%)</td>
</tr>
<tr>
<td>j2GPI</td>
<td>79 (49.4%)</td>
<td>31 (60.8%) 48 (44.0%)</td>
</tr>
<tr>
<td>Lupus anticoagulants</td>
<td>114 (71.3%)</td>
<td>39 (76.5%) 75 (68.8%)</td>
</tr>
<tr>
<td>Tri-positive</td>
<td>41 (25.6%)</td>
<td>21 (41.2%) 20 (18.3%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>71 (44.4%)</td>
<td>23 (45.1%) 48 (44.0%)</td>
</tr>
<tr>
<td>Hypocomplementaemia</td>
<td>59 (36.9%)</td>
<td>25 (49.0%) 34 (31.2%)</td>
</tr>
</tbody>
</table>

Conclusions: patients with APS develop significant morbidity and mortality despite current treatment. More attention should be devoted to APS patients with thrombocytopenia.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8282

SAT0293  PNEUMOCOCCAL INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: A 5-fold increase in the risk of death is due to infection in systemic lupus erythematosus (SLE) patients when compared to age- and sex-matched controls Pneumococcal infection (PI) has been reported to be more frequent and severe in SLE

Objectives: Our study aimed to analyze the risk factors associated with the occurrence and severity of PI in SLE patients.

Methods: Medical records of all SLE patients and all patients admitted with PI in the Department of Internal Medicine (Bichat Hospital, Paris, France) from January 2005 to December 2014 were retrospectively reviewed. Clinical characteristics and APS associated with PI occurrence and severity were analyzed, both in SLE and non-SLE patients.

Results: One hundred and ninety SLE patients (42.2±14.9 years; 87.4% females) were hospitalized over a 10-year period. PI was the reason for admission in 6 (3.2%) patients, including 5 cases of invasive infection. With a follow-up of 2112.8
years for the total cohort, incidence of invasive PI in SLE was of 236/100,000 patient-years. As compared to the incidence in general French population, invasive PI was 26 times more frequent in SLE patients. PI occurred at a younger age (43.5 ± 14.9 versus 65.3 ± 18.7 years, p < 0.009) and was more severe, with a higher frequency of invasive infection (p < 0.001) and higher need for ICU admission (p < 0.05) in SLE as compared to non-SLE patients. Of note, unlike PI sites, including pneumococcal endocarditis (n=1), arthritis (n=1) and peritonitis (n=1) were observed in SLE patients only. Risk factors associated with PI in SLE patients were a serum gammaglobulin level ≤5g/L (p=0.003) and a past history of lupus nephritis (p=0.047), only. Steroids (p < 0.001) and immunosuppressive drugs (p=0.027) were associated with infection severity.

Conclusions: Pneumococcal infections occur at a younger age, are more frequent and severe in SLE patients. Hypogammaglobulinemia and lupus nephritis increased the risk for PI, whereas steroids and immunosuppressive drugs were associated with infection severity only. Our study shows that SLE patients have an increased risk for invasive PI and points to the need for vaccination against streptococcus pneumoniae in SLE.

Disclosure of Interest: None declared


SAT0294 | COMPARISON OF CLINICAL CARE BETWEEN CHINESE AND AMERICAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

J. Dong1, H. Ma1, W.N. Roberts2, L. Wang1, F. Khan3, K.A. Lyn Shue3, L. Zhao1, L. Pan1.

Background: In addition to gender and ethnicity, modifiable variables like geography, socioeconomic status, health system structure, education, and physician expertise may influence outcomes in systemic lupus erythematosus (SLE).

Objectives: To compare characteristics of and treatment options for subsets of Chinese and American patients with SLE to elucidate factors that contribute to disease activity and damage.

Methods: Chart review of 77 Chinese (Qingdao) and 48 Midwestern American (Louisville, Kentucky) patients meeting American College of Rheumatology (ACR) criteria for a diagnosis of SLE followed up for four years were analyzed retrospectively. Organ damage was assessed using the Systemic Lupus International Collaborating Clinics (SLICC)/ACR Damage Index (SDI), and disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Statistics were parametric exploratory tests of significance and multiple regression analyses in this hypothesis-generating effort.

Results: The interval between the time of onset and diagnosis was 44 months shorter in the Chinese arm (p < 0.001), and Chinese patients followed up at six times greater frequency than American patients (p < 0.001). Despite the lack of formal matching, the two cohorts featured similar disease activity according to the SLEDAI. Based on the SDI, rates of organ damage were higher in the American group. Chinese patients received more steroids, cyclophosphamide, hydroxychloroquine, intravenous immune globulin, and cyclosporine than the Louisville group, while the Louisville patients received more myophenolate mofetil and azathioprine (p < 0.001).

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Qingdao (n=77)</th>
<th>Louisville (n=48)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset age (years)</td>
<td>30.24±11.95</td>
<td>30.21±12.21</td>
<td>0.989</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>30.69±11.92</td>
<td>34.5±12.99</td>
<td>0.114</td>
</tr>
<tr>
<td>Duration between SLE onset and diagnosis (months)</td>
<td>7.94±18.46</td>
<td>52.3±89.90</td>
<td>0.001</td>
</tr>
<tr>
<td>Clinic visits per year</td>
<td>10.93±7.9</td>
<td>15.3±10.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interval between the last two times of follow up (months)</td>
<td>1.89±1.31</td>
<td>12.5±12.83</td>
<td>0.014</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>5.97±15.7</td>
<td>5.2±13.5</td>
<td>0.466</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>5.81±13.2</td>
<td>4.6±13.7</td>
<td>0.156</td>
</tr>
<tr>
<td>SDI</td>
<td>0.44±0.64</td>
<td>1.23±0.64</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Medication</th>
<th>Qingdao (n=77)</th>
<th>Louisville (n=48)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>77 (100%)</td>
<td>29 (60.4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>34 (44.1%)</td>
<td>6 (12.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>72 (92.7%)</td>
<td>32 (66.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>9 (11.6%)</td>
<td>3 (6.2%)</td>
<td>0.489</td>
</tr>
<tr>
<td>Myophenolate mofetil</td>
<td>10 (12.9%)</td>
<td>18 (37.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>2 (2.6%)</td>
<td>1 (2.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intravenous immune globulin</td>
<td>12 (15.8%)</td>
<td>1 (2.0%)</td>
<td>0.083</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>17 (22.0%)</td>
<td>12 (25.0%)</td>
<td>0.083</td>
</tr>
</tbody>
</table>

Conclusions: Our results strengthen the hypothesis that a specific autoantibody-mediated LQTS occur in SLE patients positive to anti-Ro antibodies. This interference in the ventricular repolarization appears to be associated with increased levels of antibodies against Ro52/TRIM21 antibodies, and supports the realization of an electrocardiogram as part of the routine evaluation in SLE patient with circulating anti-Ro antibodies.

Disclosure of Interest: None declared


SAT0296 | RELATIONSHIP BETWEEN DISEASE ACTIVITY INDEX SCORES AND SUBJECTIVE ASSESSMENTS IN EARLY SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives: To evaluate the disease activity in patients with early systemic lupus erythematosus (early SLE) and to compare it to patient’s and physician’s global assessment.

Methods: Cross-sectional study including 41 early SLE patients that fulfilled the classification criteria. The early disease was defined one with the duration 2 years from the diagnosis. The disease activity was assessed by SLEDAI-2K and SLAM. Global indices were anticipated by patient and physician global assessments (PGA and MDGA), rated by 0–100 numeric score. We correlated disease activity indices with global assessments by Pearson coefficient.

SAT0295 | ANTI-RO52/TRIM21 ANTIBODIES ARE ASSOCIATED WITH QT INTERVAL PROLONGATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Long QT syndrome (LQTS) is characterized by an abnormal QT corrected (QTC) interval prolongation that is associated with increased risk of sudden death. Studies have associated LQTS with several rheumatic diseases, and evidence points towards a link between the degree of systemic inflammation and the duration of QTC interval. Moreover, recent evidence suggests that anti-Ro antibodies may play a role in the QTC prolongation by mechanisms not fully understood, thus constituting a novel autoimmune-mediated LQTS.

Objectives: This study aimed to assess whether QTC interval prolongation is associated with the presence of anti-Ro antibodies in SLE, particularly with reactivities against Ro52/TRIM21 antigens.

Methods: Consecutive patients fulfilling the 1997 ACR criteria for SLE were included. Patients with history of ischemic heart disease, with implantable pacemakers, and those taking drugs that potentially could affect QT interval (except for antimalarials) were excluded. Patients underwent a resting 12-lead electrocardiogram to measure QTC interval corrected by Bazett’s formula. A QTC interval duration greater than 480 msec in women and 440 msec in men was set to be abnormal. Serum anti-Ro and anti-Ro52/TRIM21 antibody levels were measured by ELISA. Data were expressed as frequencies and means ± standard deviation, and differences were tested by Yates’O continuity corrected chi square or Mann-Whitney tests, while linear regressions were performed to assess linearity between autoantibody levels and QTC duration. The GraphPad Prism 4.02 software was used for calculations.

Results: Sixty-six patients with mean age of 39±13 years (57 female gender) were included. A QTC prolongation was found in 10 patients (15%), with mean QTC interval of 470±18 msec as compared to 414±23 sec in those with no LQTS. Main clinical and demographic characteristics were similar for both groups, except for a lesser use of antimalarials and higher serum creatinine levels in patients with LQTS. Disease activity was similar between groups. Anti-Ro antibody levels were significantly higher in patients with prolonged QTC interval (75±66 U/mL vs. 29±44 U/mL; P<0.005); similarly, anti-Ro52/TRIM21 levels were higher in those with LQTS (50±55 U/mL vs. 14±30 U/mL; P=0.01). Notably, a linear association (see the Figure) between the QTC intervals and levels of anti-Ro antibodies (r2=0.073; P=0.02) and anti-Ro52/TRIM21 antibodies (r2=0.078; P=0.02) was observed.

Conclusions: Our results strengthen the hypothesis that a specific autoantibody-mediated LQTS occur in SLE patients positive to anti-Ro antibodies. This interference in the ventricular repolarization appears to be associated with increased levels of antibodies against Ro52/TRIM21 antigens, and supports the realization of an electrocardiogram as part of the routine evaluation in SLE patient with circulating anti-Ro antibodies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5561

884 Saturday, 17 June 2017 Scientific Abstracts
Results: There were 41 SLE patients integrated in the study, female: male ratio 9.25:1, mean age (SD) 39 (12.35) years (range 20–67 years), disease duration (SD) was 9.92 (9.18) month (range 1–24). The mean disease activity by SLEDAI was 11.2±7.84 (range 2–34) and SLAM – 8.83±4.41 (range 3–22) points, both indices denoted high disease activity level. Mean PGA values were 48.93 (19.13) (range 1–80), and mean MDGA values 45 (19.04) (range 1–80). Also, PGA and MDGA didn’t correlate with SLEDAI (r=0.25, p=0.05; r=0.27, p=0.05), while a statistically significant correlation was determined with SLAM index (r=0.85, p<0.001; r=0.46, p=0.002). A subclass analysis of SLAM components showed that cortical dysfunction (depression, psychosis) and the presence of headache correlated with PGA (r=0.36, p=0.05; r=0.4, p=0.05), so we can establish that the difference in correlation between SLAM and SLEDAI with PGA and MDGA is explained by a more accurate disease assessment by SLAM, including also subjective complaints that influences the global patient’s status.

Conclusions: The use of SLAM for disease activity assessment in early SLE patients is more sensible than SLEDAI and its results correlates with PGA and MDGA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3710

SAT0297 SLE PATIENTS WITH SECONDARY SJÖGREN’S SYNDROME ARE CHARACTERIZED BY TYPICAL AUTOANTIBODIES AND A PRO-INFLAMMATORY STATE


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Background: Sjögren’s syndrome occurs in isolation (primary Sjögren’s syndrome, pSS), but it is also often secondary (sSS) to, and sometimes difficult to delineate from, other rheumatic diseases, in particular from systemic lupus erythematosus (SLE). Consequently there is a need to investigate similarities and differences between SLE patients with (SLE-sSS) and without sSS (SLE-noSS).

Objectives: To investigate the occurrence of sSS in a large cohort of SLE patients and to explore clinical and laboratory characteristics associated with SLE-sSS as compared to SLE-noSS and controls.

Methods: We included 504 consecutive SLE patients and 322 population controls, individually matched for age and gender to the first patients. All patients fulfilled the 1982 revised ACR criteria for SLE. SLE-sSS was defined according to the American-European consensus criteria (AECC). Accordingly, subjective and objective quantifications of sicca symptoms were recorded on all subjects. All underwent a thorough clinical investigation. SLE-associated autoantibodies, (ANA screening by BioPlex 2200 system, Bio-Rad) and Rheumatoid factor (RF, Phadia Immunocap 250) were determined with standardized methods for all subjects, Routine laboratory workup and a panel of cytokines (MSD 30-plex cytokine assays, performed on samples from 433 consecutive SLE patients and 319 controls) were measured on fasting blood samples.

Results: SLE-sSS, as defined by AECC, occurred in 23% of the SLE patients. Compared to SLE-noSS the SLE-sSS group was older, both at inclusion (55 vs 43yrs, p<0.0001) and at disease onset (40 vs. 32 yrs p<0.0001), and with a greater number of females (96 vs. 83%, p=0.0007), higher occurrence of leucopenia (57 vs. 45%, p=0.02) and peripheral neuropathy (15 vs 7%, p=0.01). Nephritis was less common in SLE-sSS (32 vs 43%, p=0.03). Higher levels of total IgG, positivity for anti-SSA/Ro52, anti-SSA/Ro60, anti-SSB antibodies, RF, and ANA further confirmed the SLE-sSS group. 20/30 investigated cytokines were detectable, of these 19/20 were higher in SLE than in controls. 6/20 cytokines (TNF-a, IL-6, MCP-4, MIP-1j, IL12/IL-23p40 and IP-10) were upregulated in SLE-sSS vs. SLE-noSS (see table for figures).

Conclusions: Through strictly applying the AECC criteria we report that the frequency of SLE-sSS increases with age and affects roughly 1/4 of SLE patients. Nephritis was less common while leucopenia and peripheral neuropathy were more common among SLE-sSS patients. In addition to excess of well-known SS-associated autoantibodies we report higher levels of six pro-inflammatory cytokines in SLE-sSS as compared to SLE-noSS. These findings demonstrate that, though often regarded as a milder version of SLE, patients with SLE-sSS are characterized by a state of chronic systemic inflammation.

Acknowledgements: Susanna Eketjäll at Cardiovascular and Metabolic Diseases, Innovative Medicines and Early Development Biotech Unit, AstraZeneca, Integrated Cardio Metabolic Centre (ICMC), Karolinska Institutet, Huddinge, Sweden.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5449

SAT0298 INFLUENCE OF AGE ONSET IN CLINICAL AND BIOLOGICAL SPECTRUM OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a multi systemic autoimmune disease which can affect patients at any age. Objectives: We aimed to study influence of age onset in clinical and biological spectrum of SLE. Methods: medical records of 89 patients diagnosed as SLE according to the ACR criteria of 1997, between January 2004 and December 2016, were retrospectively analyzed. Patients were divided into 3 groups according to the age of onset: Juvenile onset patients (group 1) (G1) (<16 years), Adult onset patients (group 2) (G2) (>16 and <50 years). Late onset patients (group 3) (G3) (>50 years). Clinical and biological comparative study was conducted between the 3 groups. Data were analyzed by chi-square test and potentially associated factors were tested by binary logistic regression.

Results: among the patients 11.2% are in G1, 75.3% in G2 and 13.5% in G3. Prevalence of SLE was higher in female than male (F/M=9/1) but predominance of women was lower in G1 than in G2 (F/M=10/1) compared to G2 (F/M=10/1) and G3 (F/M=11/1). Patients in G3 had more hypertenion (41.7%) compared to G2 (6%) (p=0.05) and G1 (0%) (p=0.04). Vespertilio erythema was less frequently found in G3 (33.3%) compared to G2 (64.2%) (p=0.045) and G1 (80%) (p=0.04). Anti Sm antibodies were more frequent in G1 (87.5%) compared to G2 (38.5%) (p=0.009) and G3 (18.2%) (p=0.003). Multivariate analysis showed that hypertension is significantly associated to late onset lupus (OR=29, 95% IC=[2.77 – 320], p=0.05) and anti Sm antibody is more frequent in juvenile onset patients (OR=12, 95% CI=[1.4 – 117], p=0.024).

Conclusions: according to our study, prevalence of lupus is higher in female regardless of age onset. Late onset lupus is associated to a high frequency of co morbidity while anti Sm antibody seems to be a hallmark of juvenile onset.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3003

SAT0299 ATYPICAL ANTIbODIES IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME


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Background: One of the main features of primary Sjögren’s syndrome (pSS) is...
the polyclonal activation of B cells, leading to the synthesis of a large variety of autoantibodies.

**Objectives:** The aim of this study is to describe the prevalence of atypical autoantibodies in patients with pSS from the JpSgrenSER registry.

**Methods:** JpSgrenSER is a multicenter transversal study of pSS patients fulfilling the 2010 European/American consensus criteria. Patients were included by randomization from thirty-three Rheumatology Spanish departments. Data were collected by reviewing clinical records and interviewing the patients. Informed consent was obtained and local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians, and rates. Chi-square was used to establish the statistical associations, being considered as p < 0.05 as significant.

**Results:** Four hundred and thirty-seven patients were included. Ninety-five percent of them were women. The median age of the cohort was 58 years. Thirty-six percent of patients AntiSSA+ and 21% of patients AntiScl-70+ were significantly related to the presence of antiRo, antiDNA antibodies (p = 0.001). Regarding AntiDNA+ patients, there were minimal non-significant differences in age at diagnosis and age at onset of symptoms compared to AntiDNA- patients (47 ± 0.5 years and 43.5 ± 4.6 years, respectively). The association with some systemic manifestation was only observed with joint involvement, which was significantly more frequent in AntiDNA+ patients (56.5% vs 34.2%, p < 0.003).

Regarding AntiSm+ patients, a significant negative association with AntiDNA antibodies was observed, being 70% of patients AntiDNA-; we also found a significant positive association with AntiRo and AntiLa, being 100% and 68% of patients AntiRo+ and AntiLa+ respectively. A significant negative association with lymphopenia was observed (no AntiSm+ patient had lymphopenia). AntiRNP+ patients showed a significant negative association with AntiDNA antibodies, being 80% of patients AntiDNA-, and a significant positive association with AntiRo (96% AntiRo+). A significant positive association was also observed with decreased C4 compared to AntiRNP- patients (28% vs 13.38%, p < 0.025).

Regarding patients with antiphospholipid antibodies, a significant negative association was observed with antiDNA antibodies, being 93% of patients AntiDNA-. A significant positive association with some systemic manifestation was only observed with the presence of anaemia (44% vs 17.7%). A significant positive association with decreased C3 and C4 was also observed, compared with the AntiRNP- patients (C3 20% vs 13.67% and C4 33% vs 12.67%).

**Conclusions:** More than 5% of pSS patients had antibodies characteristic of other autoimmune diseases. These atypical autoantibodies were significantly related to some pSS characteristic: antiSm, antiRNP and antiLa+, respectively. A significant negative association with lymphopenia was observed (no AntiSm+ patient had lymphopenia). AntiRNP+ patients showed a significant negative association with AntiDNA antibodies, being 80% of patients AntiDNA-, and a significant positive association with AntiRo (96% AntiRo+). A significant positive association was also observed with decreased C4 compared to AntiRNP- patients (28% vs 13.38%, p < 0.025).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2600
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Objectives: Baseline characterization of European patients diagnosed with primary Sjögren syndrome (SS) according to the 2002 AE criteria. Methods: The Big Data SS Project was founded in 2014 to take a “high-definition” picture of the main features of primary SS by merging international SS databases. International experts of the EULAR-SS Task Force were invited to participate. By January 2017, the database included 9302 consecutive patients recruited from 21 counties of the 5 continents.

Results: A total of 6866 (71%) patients were included from European countries. In comparison with non-European countries, European patients had a higher mean age (54 ± 51 yrs, p < 0.001), higher frequency of men (7% vs 5%, p=0.001), dry eyes (94% vs 88%, p < 0.001), dry mouth (94% vs 91%, p < 0.001), and lower frequency of abnormal ocular (84 vs 86%, p=0.049) and oral (75 vs 81%, p < 0.001) tests. Immunologically, European patients had a lower frequency of anti-Ro/La antibodies (69 vs 78%, p < 0.001) and a higher frequency of RF (50 vs 47%, p=0.01), low C4 (14 vs 9%, p < 0.001) and cryoglobulins (8% vs 3%, p < 0.001). Logistic regression identified as independent variables older age (OR 1.02, male gender (OR 2.62), abnormal oral tests (OR 2.26), anti-Ro/La antibodies (OR 0.69), RF (OR 1.76), low C4 (OR 1.97) and cryoglobulins (OR 3.85).

Conclusions: European patients are diagnosed at older age, are more frequently men, and presented a lower frequency of anti-Ro/La antibodies and a higher frequency of immunological markers related to mixed cryoglobulinemia.

Disclosure of Interest: None declared

SAT0303 CLINICAL DIFFERENCES BETWEEN DEFINITE AND PROBABLE ANTIPHOSPHOLIPID (APS) PATIENTS: SHOULD THEY BE TREATED THE SAME?
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Background: The management of patients with recurrent thromboses/pregnancy morbidity and transient detection of antiphospholipids antibodies (aPL) can be a medical challenge. Although these patients are commonly seen in practice, there are no specific guidelines for the treatment in this situations.

Objectives: To investigate the clinical differences between definite and probable APS patients.

Methods: We performed a cross-sectional study in a group of 90 outpatients seen in our department. Seventy-seven of them met the Sydney classification criteria for definite APS, and thirteen had thrombosis or gestational morbidity, but no definite serological criteria for the diagnosis of APS. Clinical and serological features were collected during visits and by chart review, and the two groups were compared. Transient aPL was defined as only one detection of aPL (lupus anticoagulant, anticardiolipin IgM/IgG and/or anti-beta-2-glycoprotein 1 IgM/IgG) after 2 or more assays, at least 12 weeks apart.

Results: Demographic and clinical characteristics are shown in Table 1. In a bivariate analysis, there was no difference between groups regarding the criteria and non-criteria manifestations of APS, except for the presence of livedo (<p=0.033). In a multivariate regression analysis, the model was adjusted to age, sex, and variables with p  0.10 in the bivariate analysis (age, sex, race, livedo, Raynaud’s phenomenon). No difference between groups was found after the analysis.

Conclusions: This study suggests patients with transient detection of aPL have the same clinical characteristics of patients with definite APS, including thrombotic features, pregnancy morbidity, and non-criteria manifestations. In this context, our data suggests that both groups should be treated according to the current treatment guidelines for APS.

Disclosure of Interest: None declared

SAT0304 STIMULATORY AND INHIBITORY KILLER IMMUNOGLOBULIN-LIKE RECEPTORS ON NATURAL KILLER T (NKT) CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RELATION TO DISEASE ACTIVITY
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Background: Natural killer T (NKT) cells are a unique subgroup of T cells that represents a bridge between innate and adaptive immunity. The functions of NKT-cells are regulated by the balance between activating and inhibitory Killer cell immunoglobulin-like receptors (KIRs). Systemic lupus erythematosus (SLE) patients showed aberrant expression of KIRs on NKT-cells. Whether the expression pattern of KIRs on NKT-cells is associated with disease activity in SLE is still unknown.

Objectives: Assessment of expression of stimulatory and inhibitory KIRs on NKT-cells in SLE patients and its relation to disease activity.

Methods: We recruited 40 SLE patients and 20 age and gender matched healthy controls. According to SLE disease activity index (SLEDAI), patients were divided into two groups; active SLE (n=20) and inactive SLE (n=20). SLE was active when SLEDAI was ≥4. Immuno-phenotyping by flow cytometry was done using markers for NKT-cells (CD3 and CD56), stimulatory KIRs (KIR2DL4, CD158D) and inhibitory KIRs (KIR3DL1, CD158E1). Absolute counts and percentage of NKT-cells expressing CD158D and CD158E1 together with their mean fluorescence intensity (MFI) were measured. The histogram of CD158 expression was used to assess KIRs on NKT-cells.

Flow cytometry charts of lymphocytes and NKT-cells in SLE patients (active and inactive) and controls are shown in (Figure 1).

Laboratory work included ANA, anti-dsDNA, Anti-smith, C3, C4, CRP and ESR.

Results: Mean age of patients was 29.9±10.8 years. Females constituted 95% (n=38) of patients. Mean disease duration was 4.4±4.5 years. Mean SLEDAI was 11.7±7.43.

NKT-cells absolute number (cell/mm³) was significantly decreased in SLE patients (89±135) compared to controls (287±133), (P<0.001). Likewise, the absolute number of NKT-cells (cell/mm³) was significantly lower in active SLE patients (65.2±57.8) compared to inactive ones (114.5±181.1), (P<0.001).

Table 1. Demographic and clinical characteristics (N=90)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definite APS (N=77)</th>
<th>Probable APS (N=13)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42.0±12</td>
<td>40.5±13</td>
<td>NS</td>
</tr>
<tr>
<td>Female gender</td>
<td>64 (83.1)</td>
<td>12 (92.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Caucasian</td>
<td>60 (64.9)</td>
<td>8 (61.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Time first manifestation (mo)</td>
<td>120 (33.3–50)</td>
<td>174 (81–202)</td>
<td>NS</td>
</tr>
<tr>
<td>Criteria manifestations</td>
<td>72 (93.5)</td>
<td>13 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Thrombotic</td>
<td>72 (93.5)</td>
<td>13 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Obstetric</td>
<td>28 (43.8)</td>
<td>1 (8.3)**</td>
<td>**</td>
</tr>
<tr>
<td>Non criteria</td>
<td>20 (26)</td>
<td>0 (0)</td>
<td>p=0.003</td>
</tr>
<tr>
<td>Livedo</td>
<td>11 (14.3)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Valvulopathy†††</td>
<td>7 (11.7)</td>
<td>1 (11.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>21 (27.3)</td>
<td>1 (7.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Migraine</td>
<td>36 (46.8)</td>
<td>8 (61.5)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NP=64; ††=12; †††=9, †††=9. Mo = months. CVD = cardiovascular disease. Values showed as N (%) for categorical variables, mean ± SD for normal distribution and Median (interquartile range) for asymmetric distribution.
The expression of inhibitory KIRs was significantly lower in SLE patients (2.8±2.8%) compared to controls (5.5±2.01%) (P<0.001). While, stimulatory KIRs were significantly higher in SLE patients (3.2±3.7%) than controls (1.0±0.5%) (P<0.001). Active SLE patients showed significantly increased expression of stimulatory KIRs (5.29±4.29%) than inactive patients (1.13±0.89%) (P<0.004). However, inhibitory KIRs were significantly decreased in active (1.28±1.32%) than inactive SLE patients (4.38±3.05%) (P<0.003). Expression of stimulatory KIRs correlated positively with ESR (r=0.3, P=0.04) and negatively with C4 (r=0.4, P=0.01). In contrast, inhibitory KIRs negatively correlated with ESR (r=-0.5, P=0.03) and positively with C4 (r=0.4, P=0.02). Using Receiver operating characteristic (ROC) curve analysis, expression of inhibitory KIRs on NKT-cells predicted disease activity at a cut-off value of ≤1.7% with 80% sensitivity and 80% specificity (P=0.001). While, expression of stimulatory KIRs on NKT-cells predicted active disease at a cut-off value of ≥1.4% with 80% sensitivity (P=0.001) and specificity (80%) (P=0.003).

Conclusions: SLE activity is associated with an increased expression of stimulatory KIRs as well as a decreased expression of inhibitory KIRs on NKT cells. This may play a role in the pathogenesis of flares and acceleration of disease activity in SLE and could be a therapeutic target for SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3920

SAT0306

ASSOCIATION BETWEEN QUALITY OF SLEEP, QUALITY OF LIFE AND DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) patients are known to have sleep disturbances. Quality of sleep may affect quality of life, but this association has not been systematically evaluated.

Objectives: The aim of this study was to examine the association of quality of sleep, quality of life and SLE disease activity in patients diagnosed with SLE.

Methods: 132 SLE patients with a confirmed diagnosis of SLE according to the ACR classification criteria (GCS) by hematoin eosin (HE) and/or IHC staining for follicular dendritic cells (FDC) detection is mandatory, representa-
ing a risk factor for lymphoma development. Focus score (FS) is one of the main instrument to quantify MSG impairment, nonetheless quality information regarding the type of infiltrate such as the entity, structure and localization, are lacking.

Objectives: Aim of this study is to find any association of specific histological features of MSG from patients with pSS with the principal clinical and laboratory features. Moreover, to investigate the utility of histological parameters, other than FDC or GCS, in characterizing patients.

Methods: Patients with pSS were enrolled in our SS clinic, and clinical/laboratory data (table) referring to the time of MSG biopsy, gathered on a dedicated database. MSG, removed for diagnostic purposes, were preserved as paraffin embedded tissue, then cut and sequentially stained by H&E and IHC [polyclonal rabbit anti-CD21 (FDC)]. Images were collected by Zeiss Axioscan and analysed (ZEN software) as follows: FS calculation, mean foci area, percentage of infiltration, presence of segregated foci (SF) (specifically, clear evidence of T and B cells area by CD3-CD20 double staining), GCS and lymphoepithelial lesions (LELs) detection.

Results: 53 MSG from patients with pSS were collected and analysed. Patients clinical and laboratory data are reported in table. FS positively correlated with the percentage of infiltration (p<0.001) as well as with the presence of SF (p<0.005), GCS (p<0.02) and LELs (p<0.005). Mean foci area and percentage of infiltration correlated with SF (p=0.0002 and p<0.001, respectively), GCS (p=0.0004 and p<0.001, respectively) and LELs (both p<0.001). SF correlated with GCS and LEL (p<0.001). Anti nuclear antibodies (ANA) were associated with the presence of SF (p=0.029, OR=5.7 CI=1.1–28.8) while gland swelling was associated with the presence of GCS (p=0.043, OR=1.1–15).

Conclusions: The FS was associated with the presence of GCS and LELs, as well as with more organized infiltrates characterized by segregation in T and B areas (SF), thus representing an useful tool which mirrors the risk of lymphoma. From our study, the qualitative characteristics of the biopsy, including SF, percentage of infiltration or the mean foci area, appear to be strictly linked.

Moreover, their association with the presence of GCS and LELs supports the importance to consider also these features during histological examination. The lack of correlation between histological features and specific SS phenotypes except for the relationship between glandular swelling and GCS which confirms how this clinical aspect should be considered as a risk factor for lymphoma development.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5862

SAT0307

RECURRENT RATE OF THROMBOSIS FOR PATIENTS WITH ANTI-PHOSPHOLIPID ANTIBODIES INITIALLY AND DISAPPEARED LATER AFTER THROMBOLYSIS

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Background: In case of anti-phospholipid syndrome, anticoagulants are recommended. However, there were no data about recurrence rate for thrombosis in patients with anti phospholipid antibodies (APS) initially which disappeared later.

Objectives: We compared recurrence rate of thrombosis between negative conversion group and control group.

Methods: We reviewed the medical records of patients diagnosed with thrombosis such as cerebral infarct, myocardial infarct, deep vein thrombosis, or thrombosis of other vessels at a tertiary medical center from January 2013 to March 2016. Of these, 14 patients whose APA status was converted from positive to negative after more than 12 weeks were enrolled as negative conversion group. Forty-six patients without APA were matched with the ratio of 1:3 according to age, sex, sex, thrombosis type (arterial or venous) and therapeutic agents as control group.

Results: There was no difference between negative conversion group and control group in smoking status, presence of diabetes or hypertension, duration from the thrombosis to last visits or to recurrence, the proportion of patients taking glucocorticoids. There was no difference in the overall recurrence of thrombosis between two groups (negative conversion group, 3/14 (21%) vs. control group,
Background: Sjögren syndrome (SS) is a chronic autoimmune disease characterized by a sicca syndrome and a wide spectrum of extra-glandular manifestations.

Objectives: The aim of this study was to describe clinical, biological and immunological characteristics of patients with SS and to compare them in primary and associated SS.

Methods: We conducted a monocentric, retrospective study over a period of 15 years. Patients who fulfilled the American European Consensus Group criteria for SS were included. The sex-ratio female/male was 9/1. The mean age at disease onset was 45 years (range 15–74 years) and at diagnosis was 47 years (range 20–94 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years). The aim of this study was to describe clinical, biological and immunological characteristics of patients with SS and to compare them in primary and associated SS.

Results: SS was diagnosed in 270 patients. The sex-ratio female/male was 9/1. The mean age at disease onset was 45 years (range 15–74 years) and at diagnosis was 47 years (range 20–94 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years).

Conclusions: The cumulative incidence of thrombotic events was not significantly different between SS and the control group.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7877

SAT0308 | CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL FEATURES OF SJÖGREN SYNDROME: A STUDY OF 270 TUNISIAN PATIENTS

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Background: Sjögren syndrome (SS) is a chronic autoimmune disease characterized by a sicca syndrome and a wide spectrum of extra-glandular manifestations.

Objectives: The aim of this study was to describe clinical, biological and immunological characteristics of patients with SS and to compare them in primary and associated SS.

Methods: We conducted a monocentric, retrospective study over a period of 15 years. Patients who fulfilled the American European Consensus Group criteria for SS were included. The sex-ratio female/male was 9/1. The mean age at disease onset was 45 years (range 15–74 years) and at diagnosis was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years).

Results: SS was diagnosed in 270 patients. The sex-ratio female/male was 9/1. The mean age at disease onset was 45 years (range 15–74 years) and at diagnosis was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years). Sjögren syndrome was diagnosed in 270 patients. The sex-ratio female/male was 27/3. The mean age at disease onset was 47 years (range 15–76 years) with a mean delay of 3 years (range 0–25 years).

Conclusions: The cumulative incidence of thrombotic events was not significantly different between SS and the control group.

Disclosure of Interest: None declared


SAT0309 | CAN WE FORESEE SLE IN ITP PATIENTS? TO DISTINGUISH ITP PATIENTS WITH HIGH RISK OF SLE BY A NATIONWIDE COHORT STUDY-BASED DECISION TREE

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Background: Immune thrombocytopenic purpura (ITP) is an autoimmune- mediated disease, which is occasionally the initial presentation of systemic lupus erythematosus (SLE), and thus periodical follow up has been suggested. Whereas long-term surveillance on all ITP patients would be time and cost-consuming, and thus to distinguish those with high probability of SLE development among ITP patients should be more practical.

Objectives: To distinguish ITP patients with high risk of SLE development by a decision tree model.

Methods: We enrolled ITP patients without previous SLE diagnosis from the National Health Insurance research database between 1997 and 2012 and identified those certificated with catastrophic illness of SLE during follow up, by which the diagnosis was reconfirmed by another rheumatologists. We also analyzed the symptoms and comorbidities as well as the dose of average oral steroid to derive the decision trees, which classified the ITP patients with different probability of development of SLE.

Results: A total of 10,265 ITP patients were enrolled, among whom 80 patients developed SLE while following up. The whole ITP patients were allocated to training group (7,186 patients including 57 with SLE) and testing group (3,079 patients including 23 with SLE); the former was used for derivation of the decision-tree based model and the latter for validation of the previously mentioned model, and provided high sensitivity (78.2%), specificity (99.2%) and negative prediction value (99.8%, Fig.). To reduce the complexity, we also pruned our decision tree to propose less-complicated models.

Conclusions: We derived classification decision tree suitable for various clinical scenarios of ITP patients, among whom those with high probability of development of SLE would be distinguished.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3589

SAT0310 | ULTRASONOGRAPHIC SCORING OF THE MAJOR SALIVARY GLANDS IN SJÖGREN’S SYNDROME: A COMPARATIVE STUDY WITH DISEASE ACTIVITY INDEXES

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Background: Sjögren’s syndrome (SS) is characterised by chronic autoimmune inflammation primarily affects the salivary and lacrimal glands. Recently, ultrasonography (USG) of major salivary glands (SG-USG) has been used to evaluate salivary glands in primary and secondary SS.

Objectives: We aimed to investigate the association between the ultrasonographic scores of major salivary glands and disease activity indexes in patients with primary SS.

Methods: Forty-two primary SS patients fulfilling ACR-EULAR classification criteria (2002) were included. Disease activity indexes (Sjögren’s Syndrome Patients Reported Index (ESSPRI), Visual Analogue Scale (VAS), EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI)) were recorded. Major salivary glands (bilateral parotids and submandibular glands) were scored according to two different scoring system [Hocevar A. (0–48) ve Milic VD. (0–12)].

Results: Demographics, clinical characteristics, disease activity indexes and SG-USG scores were summarised in table 1 and table 2.
Table 1. Demographics and Clinical Characteristics of SjS patients (n=42)

| Age (year) | 54±11 |
| Duration of follow-up (month) | 55±51 |
| Skin symptoms | SjS complicated |
| Arthritis | R/C |
| Parotitis | 9 (21%)
| Raynaud’s Phenomenon | 5 (12%)
| Leucocyte cholestasis | 5 (12%)
| Peripheral neuropathy | 1 (2%)
| Intestinal anastomosis | 2 (5%)
| Lymphadenopathy | 1 (2%)
| SjS disease severity | ANA 34 (81%)
| Anti-Ro/La | 19 (45%)

Table 2: Disease Activity Indexes and 7G-USG Scores of SjS Patients

<table>
<thead>
<tr>
<th>Score</th>
<th>n=42</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESSPRS-total</td>
<td>15,4±4,5</td>
</tr>
<tr>
<td>Dryness</td>
<td>5,7±2,2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5,2±2,6</td>
</tr>
<tr>
<td>Pain</td>
<td>5,4±2,6</td>
</tr>
<tr>
<td>VAS</td>
<td>55±20</td>
</tr>
<tr>
<td>ESSDI-total</td>
<td>1±1</td>
</tr>
<tr>
<td>Hovecr-USG Score</td>
<td>20±10</td>
</tr>
<tr>
<td>Mic-USG Score</td>
<td>6±3</td>
</tr>
</tbody>
</table>

Twenty-four (57%) and 25 (60%) patients had the cut-off-values of >17 (Hocevar) and ≥6 (Mic USG). The patients with the scores of >17 (Hocevar) were found to have higher scores of ESSPR total (18±5 vs 14±5; P=0.01) and higher lymph nodes and USG scores were shown to be higher in anti-Ro(+) SjS patients (25±10 vs 14±5; P<0.01) USG scores were not found to be associated with the scores of ESSDI, VAS, and ESSPR items.

**Conclusions:** The scoring system of major salivary glands was found to be related to patient reported activity in SjS. USG scores were associated with anti-Ro positivity. Evaluation of SG-USG might promote the diagnosis and follow-up of the SjS patients.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.8196

**SAT0311 PROLONGED EXPOSURE TO ANTIPHOSPHOLIPID ANTIBODIES IS ASSOCIATED WITH ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Antiphospholipid syndrome has been shown to be associated with increased cardiovascular mortality, but the role of antiphospholipid antibodies (aPL) on endothelial dysfunction remains elusive.

**Objectives:** We investigated the association between endothelial dysfunction and aPL in systemic lupus erythematosus (SLE) patients.

**Methods:** 188 SLE patients and 62 controls were enrolled. Endothelial function was measured by flow-mediated dilatation (FMD). Cardiovascular risk factors were assessed and quarter measurement of anti-cardiolipin (aCL) and anti-β2-glycoprotein I Ab were used to calculate time-integrated values throughout disease duration. Circulating endothelial progenitor cell (EPC), defined by CD34+KDR+ mononuclear cells, was quantified by flow cytometry.

**Results:** Median FMD was significantly lower in SLE patient than in controls (6.9 versus 9.3%, P<0.001). In univariate analysis, older age, hypertension, thrombocytopenia, and persistent positive lupus anticoagulant (LAC) were associated with decreased FMD in SLE patients (P<0.021, P<0.001, P<0.004, and P=0.028). Time-integrated aCL value (TI-aCL), but not a single value, was correlated with decreased FMD (P<0.001). Multivariate analysis showed that hypertension and Ti-aCL were independent factors for decreased FMD (P=0.027, P=0.008). Addition of positive LAC increased the adjusted probability of decreased FMD (P=0.023). FMD was correlated with EPC number (γ=0.342, P=0.005) and Ti-aCL was also an independent factor of reduced EPC after multiple adjustment (P=0.019). The predicted probability of endothelial dysfunction at median EPC level was higher in group with high Ti-aCL than in group with low Ti-aCL (P=0.004).

**Conclusions:** Cumulative burden of sPLA2 is closely associated with endothelial dysfunction in SLE patients, which was mediated in part by reduction of EPC.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3063

**SAT0312 MICRONRNA-125B AS A POTENTIAL FIBROTIC AND APOTOTIC REGULATOR IN SYSTEMIC SCLEROSIS**

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**Background:** MicroRNAs (miRs) are a class of small, noncoding RNAs that regulate many biological processes. Some microRNAs are involved in skin fibrosis.

**Objectives:** To analyze the differential expression, regulation and the pathophysiological role of miR-125b in systemic sclerosis (SSc).

**Methods:** For screening a low density array was run on pooled RNA from fibroblasts derived from 3 SSc patients vs. 3 healthy controls (HC). For further validation we performed qPCR on RNA derived from cultured fibroblasts, whole skin biopsies as well as on paraffin fixed dermis and epidermis. Next, fibroblasts were stimulated with pro-inflammatory and/or pro-fibrotic cytokines such as TGFBβ, IL-1β, -13, -17A, TNFa and PDDG. In order to identify downstream effects of miR-125b, knockdown with anti-miR-125b (or scrambled controls) in HC fibroblasts was performed. RNA was isolated from healthy fibroblasts (n=4) after knockdown and was proceeded to deep sequencing (Illumina HiSeq2000). Sequencing data were validated using qPCR on HC as well as SSc fibroblasts. Apoptosis was assessed by Caspase-Glo 3/7 assay and immunofluorescence of cleaved caspase 3 on cultured fibroblasts.

**Results:** Screening identified miR-125b as one of the candidate miRs differentially expressed in SSc. MiR-125b was confirmed by qPCR in primary dermal fibroblasts (SSc =11, HC =8), where it was downregulated by 47% (median expression 53%, Q1,3 33%, 70%; P<0.001). MiR-125b expression appeared to be independent from main cytokines operative in SSc. Additionally, the expression of miR-125b was assessed in skin biopsies of both SSc patients (n=4) and HC (n=5). In SSc, miR-125b was downregulated by 35% (median expression 65%, Q1,3 61%, 78%; P<0.05). To localize its expression in the skin, we separately analyzed miR-125b expression in dermis and epidermis of paraffin fixed skin. In both cases, expression of miR-125b was downregulated RNA sequencing identified >3500 differentially expressed genes with P<0.05. More than half of the differently expressed genes with at least 15% change were predicted targets of miR-125b by TargetScan and MirWalk, indicating successful functional inhibition of miR-125b. Gene ontology revealed extracellular matrix organization and apoptosis regulation as the two main clusters of differentially expressed genes. Among them, BAK1, BMF and BBC3 are participants of the BCL2 apoptosis pathway and predicted targets of miR-125b. Consistent with the sequencing results, qPCR showed that knockdown of miR-125b upregulates their target gene BCL2L1 (4x±1, 48 and 72 hours after transfection (P<0.05 for each). That was confirmed also on protein level by Western blot. Accordingly, miR-125b knockdown resulted in a higher rate of apoptosis (mean±SD: 60% ± 29%, P=0.01) compared to scrambled controls, measured by Caspase-Glo 3/7 assay. Moreover, miR-125b knockdown reduced TGFB-induced γSMA expression both on RNA and protein levels, suggesting that miR-125b might play an additional role in the cytoksete reorganization of fibroblasts during fibrosis.

**Conclusions:** MiR-125b is differentially expressed in SSc skin and primary dermal fibroblasts. MiR-125b downregulation increases apoptosis, inhibits cytoksete reorganization and therefore might become a potential anti-fibrotic therapeutic strategy.

**Disclosure of Interest:** A. Kozlova: None declared, E. Pacher: None declared, F. Renoux Grant/research support from: Swisslife, M. Rudnik: None declared, B. Maurer Shareholder of: Patent licensed: miR-29 for the treatment of systemic sclerosis, Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Pfizer, Roche, Actelion, A. Jüngel: None declared, J. Distler Shareholder of: 4D Science, Grant/research support from: Anamara, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inviventia, JB Therapeutics, Medac, Pfizer, RuiYi, UCBC, G. Kania Grant/research support from: Bayer, O. Distler Shareholder of: Patent licensed: miR-29 for the treatment of systemic sclerosis, Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inviventia, JB Therapeutics, Medac, Pfizer.

**DOI:** 10.1136/annrheumdis-2017-eular.3806

SATURDAY, 17 JUNE 2017

Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models
ROLE OF CD248 MOLECULE AS POTENTIAL REGULATOR OF TRANS-DIFFERENTIATION TOWARD MYOFIBROBLASTS OF PERIVASCULAR STROMAL CELLS IN SYSTEMIC SCLEROSIS PATIENTS


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Background: The microvascular damage is a pivotal event in the pathogenesis of Systemic Sclerosis (SSc) and, after injury, both endothelial cells (ECs) and pericytes might trans-differentiate toward myofibroblast, responsible of fibrosis. Platelet-derived growth factor B (PDGF-B) and transforming growth factor-β (TGF-β) play a key role in myofibrogenesis. PDGF-B is a potent mitogen for myofibroblastic cells, while TGF-β stimulates myofibroblast activation, including alpha smooth muscle actin (αSMA) expression. A key regulator of PDGF-B and TGF-β signaling may be the CD248, a trans-membrane receptor required for proliferation and migration of pericytes and fibroblasts. It has been showed that, in an animal model of kidney fibrosis, the genetic deletion of CD248 modulates the response of renal pericytes to injury, by reducing the differentiation of myofibroblasts. The expression of CD248 is required for TGF-β-induced αSMA expression in pericytes and CD248 enhances the PDGF pathway, mediating the proliferation and migration of pericytes and fibroblasts.

Objectives: The aim of this work was to evaluate the expression of CD248, in SSc skin biopsies and its possible role in perivascular stromal cells proliferation, responsible to myofibroblast trans-differentiation, during SSc.

Methods: After ethical approval, skin biopsies and bone marrow mesenchymal stem cells (MSCs) were collected from 20 diffuse SSc patients and 10 healthy controls (HC). CD248 expression was investigated in the skin, and in isolated MSCs treated with TGF-β or PDGF-B, by immunofluorescence, qRT-PCR and western. Furthermore, we silenced CD248 in SSc-MSCs, to confirm the role of this molecule in TGF-β- or PDGF-signaling modulation.

Results: CD248 expression in SSc skin was significantly higher when compared with HC skin. In particular, an increased expression of CD248 was found in ECs, stromal fibroblast and perivascular like stromal cells, co-expressing CD90, a marker of un-differentiated MSCs. Furthermore, in both, HC- and SSc-MSCs, TGF-β treatment induced a significant reduction of CD248 mRNA expression in parallel with a significant increase of αSMA and a decrease of proliferation (ki67), when compared with untreated-(UT-) cells. Interestingly, the ability of TGF-β to inhibit CD248 expression in HC-MSCs was significantly higher than SSc-MSCs, suggesting that local environment in SSc patients affect TGF-β ability to suppress CD248 expression in SSc-MSCs. After treatment with PDGF-B in both SSc- and HC-MSCs, CD248 expression was not affected, while significant reduction of αSMA and an increased expression of ki67 was observed compared with UT-cells. After silencing of CD248 in SSc-MSCs, both TGF-β and PDGFB signaling were inhibited.

Conclusions: CD248 over-expression may play an important role in tissue fibrosis by modulating the pericytes to myofibroblast trans-differentiation, via regulation of both PDGFB and TGF-β signaling, during SSc.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2866

IN VITRO AMELIORATE EXPERIMENTAL LUNG FIBROSIS INDUCED BY BLEOMYCIN


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Background: Systemic Sclerosis (SSc) is an autoimmune disorder frequently affected by interstitial lung disease (ILD) that significantly deteriorates long term outcomes. In previous experiments we proved that specifically engineered gold-nanoparticles (GNP) loaded with imatinib and targeted with an anti CD44 Ab (GNP-HCim) significantly inhibited proliferation and induced apoptosis of fibroblast-like cells derived from I LD-SSC patients [1]. In vitro, GNP-HCim showed higher efficacy compared to the drug alone.

Objectives: To demonstrate in vivo the efficacy of GNP-HCim in ameliorating bleomycin-induced lung fibrosis.

Methods: Eight-week-old C57BL6 male mice (n=8/group) were assigned to either: (1) controls receiving intratracheal aerosolization of saline solution and unloaded functionalised GNP (GNP-HC); (2) mice treated with intratracheal instillation of bleomycin (50 μL) on day 0 and GNP-HC; (3) mice treated with bleomycin on day 0 plus GNP-HCim; (4) mice treated with bleomycin plus intraperitoneal (i.p.) imatinib (50 mg/kg, once daily). GNP-HC or GNP-HCim were administered by intratracheal instillation on day 10–15–20–25 and 3 h before culling. All mice were sacrificed on day 28. Lung specimens were analysed by electron microscopy, immunohistochemistry and immunofluorescence (IF). Data were evaluated by 2 blind observers and analysed with GraphPrism software for statistics.

Results: The administration of imatinib i.p. or via GNP-HCim reduced pathologic changes of the lungs as evaluated by the Lung Injury score and the Ashcroft score (p<0.05 for both). Collagen quantification by Picro Sirius Red revealed a significantly reduced staining only in the GNP-HCim group (p=0.0135 vs controls). IF revealed a significant reduction in the number of CD45+ lymphocyte and myofibroblast counts when mice were implanted with GNP-HCim (14.5±2.9/50 μm² of lung), while mice injected with GNP-HC (7.6±1.7/50 μm²) were comparable to the controls (24.0±3.5/50 μm², p=0.003 and p=0.0013 respectively). IF also showed significantly reduced counts of CD45+ (15.21±1.67/50 μm² vs 29±2.247/50 μm² in controls, p=0.0006) and CD44+ cells in groups treated with GNP-HCim (18.6±1.49/sq mm) or imatinib (13.57±0.864) versus controls (28.56±2.854, p=0.0111 and p=0.0004 respectively). In imatinib i.p. and GNP-HCim-treated groups there was a significant reduction of phosphorylated c-Abl and PDGF-R, two downstream targets of imatinib, to levels comparable to group 1 controls with respect to the bleomycin group (p<0.05 for both). Finally, electron microscopy revealed accumulation of GNP-HCim and GNP in alveolar macrophages.

Conclusions: In the experimental model of bleomycin-induced lung fibrosis imatinib delivered to lungs through inhalation of anti CD44 targeted GNP was as effective as imatinib administered by i.p. route. These data favour the use of GNP-HCim as a new therapeutic approach to SSC-ILD, which might be associated to a lower toxicity and side effects of systemic treatment.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5108
PSGL-1-deficient female mice. Aged PSGL-1-/- females showed reduced flow TPV/ET ratio in the pulmonary artery and RV remodeling, indicating PAH. Moreover, pulmonary artery rings from aged PSGL-1-/- females presented increased vasoconstriction response to KCl and reduced vasodilation response to acetylcholine. Importantly, NO production by lung EC was reduced in aged PSGL-1-/- females. Expression of AT2R was reduced in lungs of PSGL-1-/- females from a young age. With ageing, the levels of angiotensin II and the percentages of IFN-γ were increased in PSGL-1-/- females.

Conclusions: Together, these studies implicate leukocyte-endothelium interactions for the maintenance of vascular homeostasis and protection against PAH in PSGL-1-deficient female mice.

References:

Acknowledgements: We want to thank Ana Vanessa Alonso and Lorena Flores from the Unit of Advanced Imaging of the CNIC for their crucial support in echocardiography performance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5014
**SAT0320** SSc-IGG EFFECTS ARE MEDIATED THROUGH DISTINCT PATHWAYS IN THP-1 CELLS

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**Background:** Peripheral blood mononuclear cells (PBMCs) are thought to play a key role in the pathogenesis and progress of systemic scleroderma (SSc) with patients displaying distinct changes in cell counts, receptor expression profile and cytokine secretion patterns. SSc-IgG with elevated anti-AT,R (angiotensin II type 1 receptor)/ET,R (endothelin-1 type 1 A receptor) - AAb (autoantibody) titers have been correlated to disease severity and progression 1. It remains poorly understood through which pathways SSc-IgG mediates its effects.

**Objectives:** In this study we sought to analyze the expression patterns of THP-1 cells (a monocytic cell line) after SSc-IgG application and their reversibility through application of numerous pharmacological inhibitors.

**Methods:** Transcription of IL-8 and CCL-18 in THP-1 cells after SSc-IgG and normal IgG stimulation was quantified by qPCR. Simulations of THP-1 cells with total IgG of phenotypically different groups of SSc patients as well as ET-1 and AT-2 were carried out. In addition, stimulation with pharmacological inhibitors was conducted in a dose-dependent manner. The results were quantified by IL-8- and CCL18-ELISA of the supernatants.

**Results:** Expression of IL-8 and CCL-18 is induced by SSc-IgG treatment in comparison to normal IgG which does not follow this trend. IL-8 secretion of THP-1 cells upon SSc-IgG stimulation is mediated through specific autoantibody effects and transduced through NF-κB, ERK-, and AP-1 pathways. CCL-18 secretion of THP-1 cells upon SSc-IgG stimulation is not mediated through aforementioned pathways.

**Conclusions:** A stable cell culture system able to reproduce previous PBMC data on IL-8 and CCL-18 induction upon SSc-IgG-treatment could be established and insight was gained regarding key pathways which are involved in the transduction leading to IL-8 secretion. The effects of specific surface receptor expression profiles on transcription remain to be elucidated.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5314

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**SAT0319** MULTIPARAMETRIC DETECTION OF AUTOANTIBODIES TO INVESTIGATE RELATIONSHIPS BETWEEN SEROLOGICAL AND CLINICAL SUBSETS OF SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Systemic sclerosis (SSc) is a largely heterogeneous autoimmune disease, with patients exhibiting an extensive range of clinical presentations and various disease course. The most widely used classification divides SSc into two major subsets diffuse cutaneous (dcSSc) and limited (lcSSc) SSc by the extent and severity of skin fibrosis. However, not all patients fit into these subsets. This has created great interest to examine disease heterogeneity at the molecular level to uncover unrecognized SSc subtypes that may differ with regard to clinical and severity of skin fibrosis. However, not all patients fit into these subsets. This has created great interest to examine disease heterogeneity at the molecular level to uncover unrecognized SSc subtypes that may differ with regard to clinical manifestations, prognosis or therapy response.

**Objectives:** In large-scale "omics"-type autoantibody (AAB) profiling studies we have recently identified novel SSc-associated autoantigens. Here, we describe the development of a 50 marker multiplexed AAB assay to facilitate the discovery and validation of AAB-based patient subgroups.

**Methods:** A Luminex bead-based AAB assay was designed by combining 8 connective tissue disease (anti-centromere, anti-Scl70, U1-snRNP, SSA, SSc, Ro52, RNP, dsDNA) and anti-functional AAB (P) antigens with 12 novel antigens (including BC022, JMJD3/KDM6B, and PPP1R12). Novel AAB targets were previously detected in SSc patients with a p-value <0.05 (Mann-Whitney-U-test) and frequency>15%. AAB reactivity was analysed in 92 SSc patients (dcSSc: n=32; lcSSc: n=50, SSc overlap: n=9). The mean modified Rodnan skin score (MRRSS), mean disease duration (month), and mean age (years) of the SSc cohort was 10.51, 162.5 and 56.94, respectively. To analyze the individual-level patient similarity of AAB reactivity, the total number of AAB reactive in each patient was calculated and referenced to the number of all available antigens in percent. Patient’s demographic and clinical data were dichotomized into patients with higher or lower than the mean value. Hierarchical cluster analysis was performed to investigate the relationship between AAB patient signatures and clinical and demographic features.

**Results:** Based on their AAB reactivity pattern, the Scs sample cohort can be decomposed into four prominent clusters and additional fine-level clusters. lcSSc patients were spread over three clusters, each with clearly distinct AAB profile. Compared to dcSSc patients, lcSSc patients were more heterogeneous in their AAB profile. The percentage of lcSSc patients in clusters 1-3 was 70%, 90% and 50%, respectively. Patients in cluster 2 had an extended AAB repertoire that is anti-centromere, KDM6B, SSA, BC022 and PPP1R12. 63% of all patients in cluster 4 were dcSSc and anti-Scl70 positive, who were most afflicted of the disease. AAB signatures of patients were mapped against dichotomized demographic and clinical features. Moving from cluster 1 to 4 the number of patients with shorter disease duration, lower age, higher mRSS and higher frequency of lung involvement increased.

**Conclusions:** The multiplexed analysis of AABs in SSc enables defining an AAB reactivity score and patient clusters. This might support to subclassify SSc beyond lcSSc and dcSSc.


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**SAT0321** MKP-1 AS A PROTECTIVE FACTOR AND NOVEL DRUG TARGET IN SCLERODERMA: MKP-1 DEFICIENT MICE DEVELOP MORE SEVERE DERMAL FIBROSIS IN A WIDELY USED EXPERIMENTAL MODEL OF SCLERODERMA

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**Background:** Scleroderma is a chronic connective tissue disease of unknown etiology. In early stages, vascular injury and inflammation lead to fibrosis, resulting in irreversible damage in various organs. Inflammation is believed to be necessary in order to activate fibroblasts to over-produce extracellular matrix components. At the present, there is no effective standard treatment to reverse or slow down the progression of scleroderma but one of the feasible approaches is to target key inflammatory pathways that are involved in the pathogenesis of the disease.

MKP-1 (Mitogen-Activated Protein Kinase Phosphatase-1) is a nuclear phosphatase present in most cell types and tissues. Studies with MKP-1 deficient mice have undoubtedly shown that MKP-1 is an important regulator of innate and adaptive immune responses to limit and suppress inflammation (1) but its role in fibrosing diseases has not been studied.

**Objectives:** In the present study, we aimed to investigate the potential protective role of MKP-1 in the pathogenesis of scleroderma by using MKP-1 deficient mice and a widely studied experimental model of scleroderma.

**Methods:** We used bleomycin-induced dermal fibrosis in the mouse as an experimental model of scleroderma (2). Wild type (WT) and MKP-1 deficient mice were injected subcutaneously with bleomycin every other day for 28 days. Dermal mortality. Epigenetic changes might play important roles in mediating chronic fibroblast activation. Trimethylation of H3 at lysine residue K27 (H3K27me3) is a repressive epigenetic mark that was recently identified as an important negative regulator of fibroblast activation [1]. Jumonji domain containing protein 3 (JMJD3) mediates H3K27me3-demethylation. JMJD3 inhibitors are being tested as a therapeutic approach in the treatment of the fibrogenic disease.
thickness and collagen accumulation were determined by histological analyses. The expression of several inflammatory and pro-fibrotic mediators were measured by quantitative RT-PCR.

Results: We found that bleomycin-induced dermal thickness and lipodystrophy were increased in MKP-1 deficient mice. Collagen accumulation in the dermis and expression of MMPs and TIMPs in the epidermis were enhanced in the skin from MKP-1 deficient mice as compared to the skin from WT animals. Affected skin from MKP-1 deficient mice presented increased expression of factors related to inflammation and fibrosis, namely IL-6, TGF-β1, fibronectin-1 and YKL-40 as well as chemokines MCP-1, MIP-1α and MIP-2.

Conclusions: This study demonstrates, for the first time, that MKP-1 deficient mice develop more severe bleomycin-induced dermal fibrosis than their WT counterparts, indicating that MKP-1 regulates the inflammatory and fibrotic processes typical for experimentally-induced scleroderma. These findings suggest that compounds which enhance expression/activity of MKP-1 have potential as novel drugs for the stage-specific modulation of the pathogenesis of scleroderma.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4816

SAT0323 ADAM-17 IS EXPRESSED IN THE INFLAMMATORY MYOPATHY, AND IS INVOLVED WITH INTERRUSSIONAL LUNG DISEASE (ILD)
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Background: A disintegrin and metalloprotease (ADAM) family is protease that is thought to have an important role in tissue destruction and inflammatory reaction. ADAMs are also involved in the amputation from the cell surface of inflammatory cytokines. ADAM-17 is one of the ADAM family, and is first described as the protease responsible for tumor necrosis factor (TNF)-α shedding. The implication of ADAM-17 substrates in immunoregulation has made this enzyme an efficient therapeutic target in the treatment of a number of pathological conditions including airway inflammation and arthritis.

Objectives: The function of ADAM-17 in myositis is unclear. Therefore, we clarify the expression of ADAM-17 in inflammatory myopathy and the role of inflammation in interstitial lung diseases (ILD).

Methods: The serum were collected from the patients who were diagnosed with inflammatory myopathy in Showa University Hospital from 2003 to 2015. Twenty-six patients were diagnosed with dermatomyositis (DM), and 10 patients were diagnosed clinically amyopathic dermatomyositis (CADM). Clinical manifestations and clinical data were also collected. The levels of ADAM-17 in the serum samples were measured using enzyme-linked immunosorbent assay (ELISA). ADAM-17 expression was determined in MVEC cocultures from DM using immunohistological staining. To determine that the role of lung fibrosis in inflammatory myopathy with ILD, we used human lung fibroblasts (HLF). ADAM-17 expression on HLF was also demonstrated by immunohistological staining. ADAM-17 expression in interleukine (IL)-6 and IL-6 receptor (IL-6R) stimulated HLF was performed by ELISA.

Results: ADAM-17 in inflammatory myopathy was significantly higher than in healthy control (n=19) (1048±312 pg/ml and 36±18 pg/ml, respectively, p<0.05). ADAM-17 in corticosteroid and/or immunosuppressant treatment patient serum was also significantly decreased compared with in pre-treatment patient serum (1465±562 pg/ml and 1069±503 pg/ml, respectively, p<0.01). In addition, ADAM-17 in inflammatory myopathy with ILD patients (n=46) was significantly higher than in non-ILD patients (n=24) (1379±454 pg/ml and 413±526 pg/ml, respectively, p<0.05), while ADAM-15 did not have the differences between ILD and non-ILD group. Finally, we found the expression of ADAM-17 in muscle biopsy tissue. Hence, ADAM-17 on HLF was expressed by immunohistochemistry. ADAM-17 in IL-6 and IL-6R stimulated HLF was significantly higher compared with non-stimulated HLF (485±6 pg/ml and 0±0 pg/ml, respectively, p<0.05).

Conclusions: ADAM-17 is expressed in inflammatory myopathies especially with ILD and expressed on HLF, suggesting that ADAM-17 may play the role in lung fibrosis. ADAM-17 may be a potential target in inflammatory myopathies with ILD.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3402

SAT0324 INCREASED FREQUENCIES OF CIRCULATING CXCL10-, CXCL8- AND CCL4-PRODUCING MONOCYTES AND SIGLEC-3-EXPRESSION MYELOID DENDRITIC CELLS IN SYSTEMIC SCLEROSIS PATIENTS
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Background: Systemic sclerosis (SSc) is an inflammatory and fibrotic disease characterized by vascular dysfunction, excessive extracellular matrix deposition and immune dysregulation. Recent observations suggest that monocytes and dendritic cells (DCs) might be involved in SSc; including cell recruitment, trafficking, activation and an enhanced pro-fibrotic phenotype. Hence these cells might be important contributors to the disease pathogenesis. However, detailed analysis of circulating monocytes and DCs in SSc in relationship to disease activity has not been performed so far.

Objectives: To investigate the ex vivo pro-inflammatory properties of classical and non-classical monocytes as well as myeloid dendritic cells (mDCs) in SSc patients in relationship to disease activity.

Methods: This study enrolled 43 SSc patients, 30 classified as limited cutaneous SSc (lcSSc) and 13 as diffuse cutaneous (dcSSc). The healthy control group (HC) included 20 age- and gender- matched individuals. The Spontaneous production of CXCL10, CCL4, CXCL4 and IL-6 was intracellularly evaluated in classical and non-classical monocyte-665b. SIGLEC-3-expressing mDCs from peripheral blood using flow cytometry. In addition, the production of these cytokines was determined upon toll like receptor 4 (TLR4) plus Interferon-γ (IFN-γ) in vitro stimulation.

Results: The frequency of non-classical monocytes spontaneously producing CXCL10 was increased in both lcSSc and dcSSc subsets of SSc patients (p<0.05) and CCL4 was augmented in the dcSSc patient subset (p<0.05). The proportion of CCL4 producing- mDCs were also elevated in dcSSc patients (p<0.01) compared to HC, but p<0.01 compared to dcSSc. Upon in vitro stimulation the frequency of non-classical monocytes expressing CXCL8 was significantly lower compared to untreated conditions (p=0.016) in both lcSSc and dcSSc patients. In nonclassical mDCs, the proportion of CCL4 producing mDCs was significantly increased in dcSSc compared to lcSSc (p<0.01). The percentage of CCL4 producing mDCs was significantly greater in the dcSSc group compared to both lcSSc and HC (p<0.01). In both SSc subsets and HC, the percentage of mDCs producing CXCL10 was significantly greater in the dcSSc group compared to both lcSSc and HC (p<0.01) and the percentage of mDCs producing CXCL8 was significantly lower in the dcSSc group compared to both lcSSc and HC (p<0.01). In SSc subsets and HC, the percentage of mDCs producing CXCL8 was significantly lower compared to untreated conditions (p<0.01). The proportion of mDCs producing CXCL10 was also significantly greater in the dcSSc group compared to untreated conditions (p<0.01).

Conclusions: The frequency of non-classical monocytes spontaneously producing CXCL10 was increased in both lcSSc and dcSSc subsets of SSc patients (p<0.05) and CCL4 was augmented in the dcSSc patient subset (p<0.05). The proportion of CCL4 producing- mDCs were also elevated in dcSSc patients (p<0.01) compared to HC, but p<0.01 compared to dcSSc. Upon in vitro stimulation the frequency of non-classical monocytes expressing CXCL8 was significantly lower compared to untreated conditions (p=0.016) in both lcSSc and dcSSc patients. In nonclassical mDCs, the proportion of CCL4 producing mDCs was significantly increased in dcSSc compared to lcSSc (p<0.01). The percentage of CCL4 producing mDCs was significantly greater in the dcSSc group compared to both lcSSc and HC (p<0.01). In both SSc subsets and HC, the percentage of mDCs producing CXCL10 was significantly greater in the dcSSc group compared to both lcSSc and HC (p<0.01) and the percentage of mDCs producing CXCL8 was significantly lower in the dcSSc group compared to both lcSSc and HC (p<0.01). In SSc subsets and HC, the percentage of mDCs producing CXCL8 was significantly lower compared to untreated conditions (p<0.01). The proportion of mDCs producing CXCL10 was also significantly greater in the dcSSc group compared to untreated conditions (p<0.01).

Acknowledgements: Thanks to Prof. Bashar Kahaleh and to Dr. Yongking Wang from University of Toledo Medical Center, Division of Rheumatology and Immunology, OH, USA, for providing SSc microvascular endothelial cells.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5173
increased in both patient groups (p<0.01) and mDCs expressing CXCL8 only in lcSSc (p<0.01). SSC patients characterized by the presence or history of lung fibrosis, displayed a higher frequency of non-classical monocytes expressing CCL4 and CXCL10 in dSSc patients as compared to those without this clinical manifestation (p<0.01 and p<0.05 respectively). Strikingly, the percentage of classical monocytes producing CXCL8 was augmented upon in vitro stimulation in lcSSc patients with lung fibrosis as compared to those without (p<0.01). No differences were found in the percentage of IL-6 producing cells.

Conclusions: These data point towards a role of activated non-classical monocytes and mDCs producing enhanced levels of proinflammatory cytokines in SSC patients with lung fibrosis.

Acknowledgements: TC is supported by a grant from the Portuguese national funding agency for science, research and technology; Fundação para a Ciência e a Tecnologia [SFRH/BD/93526/2013].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5050

SATURDAY, 17 JUNE 2017

Scleroderma, myositis and related syndromes

A. Corrado

THE ASSOCIATION OF SERUM TYPE 1 INTERFERON ACTIVITY AND AUTOANTIBODIES IN INFAMMATORY MYOSITIS

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Background: Recent reports had shown that most of clinically amyopathic dermatomyositis (CADM), which showed poor prognosis, was positive for anti-Melanoma differentiation-associated gene 5 (MDA5) antibody (Ab). It had been shown that patients not only with lupus but with dermatomyositis (DM) also showed increased type 1 interferon (IFN) signature. MIK acts as a cytosolic RNA sensor, which drives type 1 IFN production. These facts suggested that type 1 IFN might have some roles in anti-MDA5 Ab positive patients.

Objectives: We evaluated the association of serum type 1 IFN signature and autoantibodies in patients with inflammatory myositis, in particular anti-MDA5 Ab positive patients and anti-aminocytic/IFN syntheses (ARS) Ab positive patients.

Methods: Sera from 33 inflammatory myositis patients (13 DM, 10 PM and 10 CADM) were studied for type 1 IFN activity, using a functional reporter cell assay. Briefly WISH cells were incubated with serum containing media for 6 hours. Serum IFN signature scores of the incubated cells were evaluated by the summ of gene expressions of Mx1, IFIT3, IFI44L and IFI44 by real time PCR (Reference).

Anti-MDA5 Ab and Anti-ARS Ab were measured by ELISA. We divided these patients into three groups, anti-MDAS Ab positive group (MDA5 group), anti-ARS Ab positive group (ARS group) and double negative group (DN group). We included double positive patients into MDA5 group. The presence of interstitial lung disease (ILD) and the prognosis were also investigated.

Results: MDA5 group had 12 patients (8 CADM and 4 DM), ARS group had 8 patients (4 DM, 1 CADM and 3 PM), and DN group had 13 patients (5 DM, 1 CADM and 7 PM). 9 of MDA5 group, 5 of ARS group, and 1 of DN group were complicated with ILD. Serum IFN signature scores of MDA5 group were significant higher than those of ARS group and DN group (12.43 1.406, 2.407, p=0.0005).

Conclusions: We characterized two major groups in inflammatory myositis patients. ARS group was characterized by low IFN signature with the susceptibility to DM and ILD. MDA5 group was characterized by high serum IFN signature with the high susceptibility to CADM. Our results suggest that these two entities may have different onset mechanisms, leading to different outcomes.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4900

SAT0326 | NUTRITIONAL STATUS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic connective tissue disease characterized by involvement of multiple organs. Many clinical aspects, such as gastrointestinal involvement, mood disturbances, functional status, and inflammation, may lead to disease-related malnutrition [1]. The connection between inadequate nutritional status and systemic sclerosis is still not well established. It is important to identify the symptoms of malnutrition, because it is known as a predictor of poor clinical outcome [2].

Objectives: To assess nutritional status in patients with systemic sclerosis.

Methods: The study involved fifty-two patients with SSc (44 women and 8 men, mean age 54.3±11.7 year) who were diagnosed according to ACR/EULAR criteria. Inadequate nutritional status and systemic sclerosis is still not well established. It was assessed by simplified nutritional appetite questionnaire (SNAQ). In all patients hand grip strength and triceps skinfold were established. The C-reactive protein (CRP), lipid profile, and level of haemoglobin/lymphocytes were measured in serum.

Results: Inadequate nutritional status was diagnosed in 14 patients (26.9%) with SSc. According to SGA 11 (21.15%) patients had signs of mild malnutrition, while 41 (78,85%) were well-nourished. Considering BMI, 1 patient (1,92%) was underweight, 24 (46,15%) were eutrophic, 21 (40,38%) overweight and 6 (11,54%) obese. Significantly lower BMI had patients with inadequate nutritional status (23,17±4,77 vs. 25,98±3,34; p=0,009).

Conclusions: Malnutrition in systemic sclerosis is still underestimated clinical issue. This study provides useful data about nutritional status of patients with systemic sclerosis.
systemic sclerosis. Altered level of albumin and decreased appetite may lead to worsening in nutritional status. Assessment of nutritional status in this group of patients should be performed regularly, because it can be potentially modified.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5032

SAT0328 AN OPEN-LABEL STUDY OF AMBRISENTAN WITH ANTI-FIBROTIc AGENT COMBINATION THERAPY IN THE TREATMENT OF DIFFUSE SYSTEMIC SCLEROSIS
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Background: Systemic sclerosis (SSc) is marked by immune dysregulation, inappropriate fibrosis and a vasculopathy for which there is currently no universally accepted disease modifying regimen. Ambisentan, a selective type A endothelin receptor antagonist (ERA) has known benefits in the treatment of the vasculopathy and pulmonary arterial hypertension and has been postulated to have anti-fibrotic effects. The additive effect of an ERA in combination with an anti-fibrotic agent has not previously been studied in SSc.

Objectives: To determine the safety and efficacy of ambisentan in combination with an anti-fibrotic agent in diffuse systemic sclerosis (dSSc) patients.

Methods: Patients already on anti-fibrotic therapy for early dSSc with onset of skin sclerosis less than 48 months before study entry were placed on ambisentan 5mg daily for 12 months in an open-label study. Laboratory and clinical parameters to assess safety, as well as severity and progression of SSc were obtained at study entry and at 3, 6, 9, and 12 months. The primary end point of this study was the median skin score. No statistically significant change was observed in PFTs and HRCT findings. The total amount of ambisentan was maintained throughout the study.

Results: Of 15 patients who were recruited, 10 patients were on anti-fibrotic therapy at study entry. Among this group, 4 patients (30.8%) developed renal crisis (CI 95% 16.1–45.8) (December 2015). The Incidence rate was 72 patients (88% women, mean±SD age at diagnosis 48.5±16.7 years [range 15–87]) were identified, corresponding to a crude point prevalence of 13.8/10 5 (CI 95% 11–17/10 5) (December 2015). The Incidence rate was also observed to be 268 cases per 100,000/y (95% CI 250–287) (December 2015). Mortality in SSc patients remains 3.5 times higher than the general population3. We sought to generate updated data on the epidemiology and burden of SSc in the Greek population.

Objectives: To study the prevalence and incidence of SSc, describe the clinical characteristics and assess mortality and main causes of death in Crete (Greece) over a 5-year period (2010–2015).

Methods: We conducted a cohort Study in defined geographic area (6.5% of Greek population). We reviewed demographics, clinical features, autoantibodies status and the causes of death from the Scleroderma cohort followed at the Rheumatology clinic of the University Hospital, Heraklion. The cause of death was categorized as related or not to scleroderma. Incidence and prevalence were estimated including patients living permanently in Crete who fulfilled SSc 2013 criteria and HRCT findings improved in PM/DM patients with ILD without any adverse events or drug toxicity was observed.

Conclusions: After IVCYC according to the Euro-Lupus nephritis protocol PFT and HRCT findings improved in PM/DM patients with ILD without any adverse events or drug toxicity was observed. Longitudinal controlled studies are needed to confirm the safety and the efficacy of this treatment protocol.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5878

SAT0330 LOWER PREVALENCE BUT COMPARABLE CLINICAL CHARACTERISTICS AND PROGNOSIS OF SYSTEMIC SCLEROSIS IN CRETE-GREECE AS COMPARED TO OTHER EUROPEAN COUNTRIES: A SINGLE CENTER EXPERIENCE

Background: Systemic Sclerosis (SSc) is a rare, multisystemic connective tissue disease with significant morbidity. Prevalence and incidence of SSc varies worldwide (0.7–265 cases per 100,000/y1,2 and 0.06–12.2 cases per 100,000/y3,4 respectively). Mortality in SSc patients remains 3.5 times higher than the general population. We sought to generate updated data on the epidemiology and burden of SSc in the Greek population.

Objectives: To study the prevalence and incidence of SSc, describe the clinical characteristics and assess mortality and main causes of death in Crete (Greece) over a 5-year period (2010–2015).

Methods: We conducted a cohort Study in defined geographic area (6.5% of Greek population). We reviewed demographics, clinical features, autoantibodies status and the causes of death from the Scleroderma cohort followed at the Rheumatology clinic of the University Hospital, Heraklion. The cause of death was categorized as related or not to scleroderma. Incidence and prevalence were estimated including patients living permanently in Crete who fulfilled SSc 2013 ACR/EULAR Classification Criteria for Scleroderma.

Results: 72 patients (88% women, mean±SD age at diagnosis 48.5±16.7 years [range 15–87]) were identified, corresponding to a crude point prevalence of 13.8/10 5 (CI 95% 11–17/10 5) (December 2015). The Incidence rate was estimated at 0.05/10 5 per year (period 2010–2015). Diffuse SSc (dSSc) was present in 77% (CI 95% 72.2–81.8). Mortality in dSSc occurred in 19.4% (9.7% with systemic lupus erythematosus). Frequencies of anti-Scl70 and anti-centromere antibodies were 59.7% and 9.7%, respectively. Arthritis was present in 69.5%, lung involvement in 61% (9.7% pulmonary arterial hypertension [PAH]), whereas only a single patient developed renal crisis. 8.3% developed cancer. Case fatality rate during 2010–2015 was 9.7% (CI 95% 7.4–11.9) with an average (±SD) age of death at 65.2 (± 17.6) years. Mortality cases were related to SSc in 30.7%. The main cause of death was sepsis (30.8%) followed by PAH and cardiac arrest (15.4%) each. Male gender (p=0.001) and presence of PAH (p=0.001) were related to mortality. Mean disease duration until death was 5.3 years.
AMINAPHTONE INCREASES SKIN BLOOD PERFUSION AND IMPROVES CLINICAL SYMPTOMS IN PATIENTS’ WITH BOTH PRIMARY AND SECONDARY RAYNAUD’S PHENOMENON: AN OPEN SIX MONTH PILOT STUDY

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Background: Aminaphtone (1,4-Dihydroxy-3-methyl-2-naphthyl-4-aminobenzoate) is a vasoactive drug that was recently demonstrated to improve the symptoms of Raynaud’s phenomenon (RP) and to down-regulate endothelin-1 production by endothelial cells (1–3).

Objectives: To evaluate skin blood perfusion and clinical symptom changes during aminaphtone treatment in patients with both primary and secondary RP, during a six-month follow-up.

Methods: Forty-six patients with active RP were enrolled during routine clinical assessment in November 2015 (11 primary RP, mean age 49±19SD years, mean RP duration 6±3 years; 35 secondary RP to systemic sclerosis, mean age 61±17 years, mean RP duration 11±9 years), after informed consent. Aminaphtone was administered 75 mg twice daily (off label) in addition to current treatments (the patients were on a stable drug regimen for at least two months before, which remained unmodified during the follow-up). Blood perfusion was measured by Laser Speckle Contrast Analysis (LASCA) and values recorded as perfusion units (PU) (4), at the level of fingertips, periungual areas, dorsum and palm of hands, and face, at baseline (T0), after one (T1), four (T4), twelve (T12) and twenty-four weeks (T24) of treatment. Raynaud’s condition score (RCS) and both frequency and duration of Raynaud’s attacks were assessed at the same time. Forty-six patients with RP (9 primary RP and 37 secondary RP to systemic sclerosis) not treated with aminaphtone were also enrolled as a control group and evaluated at T0 and T24.

Results: A progressive statistically significant increase of blood perfusion was observed from T0 to T12 in all skin areas analyzed (median PU at T0, T1, T4, T12, T24 respectively: fingertips 55, 88, 101, 107, 98 periungual areas 44, 88, 91, 92; dorsum of hands 38, 61, 71, 75; palm of hands 56, 85, 94, 82, whole face 127, 138, 144, 159; p<0.001 for all areas). From T12 to T24 was not observed any further increase of blood perfusion. A progressive statistically significant decrease of RCS (median at T0, T1, T4, T12, T24: 7, 6, 4, 4, 4, p<0.0001) and Raynaud duration (median: 20, 20, 10, 4, 4 minutes; p<0.0001) was also recorded from T0 to T12. The results were similar in both primary and secondary RP patients (p=0.40). Aminaphtone administration had to be stopped in 2 patients due to headache, and one patient was lost during follow-up. Any statistically significant variation of blood perfusion was not observed in the control group (median PU at T0 and T24 respectively: fingertips 70, 71; periungual areas 68, 70; dorsum of hands 57, 57; palm of hands 59, 59; whole face 132, 130; p=n.s. for all areas).

Conclusions: This study demonstrates that aminaphtone treatment seems able to increase skin blood perfusion and to improve RP symptoms, even in patients affected by systemic sclerosis. These preliminary results should be further confirmed by a randomized clinical trial, also to assess the role that aminaphtone plays in the treatment/prevention of disease clinical complications.
Table 1 Comparing analysis between two patient groups (Sarcopenia/ No Sarcopenia)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sarcopenia, n = 35</th>
<th>No Sarcopenia, n = 94</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>32 (91.4%)</td>
<td>85 (90.4%)</td>
<td>0.862</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.5 ± 14.8</td>
<td>59.0 ± 13.5</td>
<td>0.838</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>8.6 ± 6.0</td>
<td>8.9 ± 6.9</td>
<td>0.832</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>20.6 ± 2.7</td>
<td>23.5 ± 5.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hand grip strength (kgf)</td>
<td>10.3 ± 6.1</td>
<td>18.7 ± 8.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Knee extension strength (kgf)</td>
<td>13.6 ± 7.2</td>
<td>22.3 ± 16.3</td>
<td>0.003</td>
</tr>
<tr>
<td>Peak flow (l/min)</td>
<td>305.8 ± 102.0</td>
<td>348.3 ± 101.9</td>
<td>0.042</td>
</tr>
<tr>
<td>SF-36* Physical Health Summary</td>
<td>40.5 ± 18.1</td>
<td>48.5 ± 19.6</td>
<td>0.043</td>
</tr>
<tr>
<td>SF-36* Physical Function</td>
<td>41.7 ± 27.1</td>
<td>54.3 ± 27.4</td>
<td>0.026</td>
</tr>
<tr>
<td>HQAO score</td>
<td>0.66 ± 0.2</td>
<td>0.64 ± 0.07</td>
<td>0.010</td>
</tr>
<tr>
<td>IPAG (level of activity)</td>
<td>5 (14.3%)</td>
<td>28 (29.8)</td>
<td>0.073</td>
</tr>
<tr>
<td>Number of medication</td>
<td>6.2 ± 3.8</td>
<td>4.8 ± 3.2</td>
<td>0.037</td>
</tr>
<tr>
<td>Number of immunosuppressive medication</td>
<td>1.4 ± 1.1</td>
<td>1.0 ± 1.0</td>
<td>0.048</td>
</tr>
</tbody>
</table>

- *statistically significant

- SSc = Systemic Sclerosis; SF-36 = Short Form 36; HQAO = Scleroderma Health Assessment Questionnaire; IPAG = International Physical Activity Questionnaire; CRP = C-reactive protein

**Disclosures:**


**Disclosure of Interest:** None declared

ARA+SSc had a significantly higher ratio compared to ARA- and ACA+ pts (mean 61.24±41.40 [45.78 – 76.70] vs. 39.62±17.99 [29.66 – 49.58] and 37.77±10.20 [32.12 – 43.42] μmol/mmol respectively, p<0.05). Kyn/Tp ratio was significantly correlated with SRC (p<0.05). We found a direct correlation with mRSS (r=0.269, p<0.05), peak mRSS (r=0.276), urate level (r=0.376), CRP (r=0.285) and ESR (r=0.301) respectively. Conversely, Neo levels, although considered significantly higher in SSc compared to HC (mean 12.63±9.30 [10.21 – 15.06] vs. 7.11±3.31 [4.74 – 9.48] mmol/L, respectively, p<0.05), were not significantly different in diffuse compared to limited SSc, but were higher in ARA+ compared to ARA- and ATA+ patients (mean 19.33±7.52 [16.43 – 22.23] vs 10.54 – 19.31 vs 10.81±4.95 [8.07 – 13.56] vs 10.02±6.63 [6.24 – 13.80] respectively, p<0.05). Neo levels significantly correlated with PAH. A direct correlation (p=0.05) was found with CRP (r=0.471) and ESR (r=0.430).

Conclusions: These data suggest that Kyn/Tp ratio and Neo levels may reflect auto-pathogenic mechanisms in SSc and be elevated in the subgroup of dCSSc that are ARA+, or those manifesting SSc manifestations highly associated with ARA+. A specific IFN-gamma signature could be thought to be responsible for the higher levels found in patients although larger studies are required.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3786

SAT0336 MALNUTRITION AND SARCOPENIA IN A LARGE COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease that may affect gastrointestinal tract, leading to malabsorption and malnutrition. Previous studies defined this complication with no widely accepted criteria. No thorough evaluations of sarcopenia are available.

Methods: 141 SSc consecutive outpatients have been enrolled. A thorough history, blood samples and body composition by densitometry were collected. Malnutrition was defined accordingly to recently published and widely accepted ESPEN criteria (1); sarcopenia was diagnosed in patients with a reduced skeletal muscle mass index (2).

Results: The table summarizes cohort's characteristics. Malnutrition was diagnosed in 9.2% (CI95%: 4.4–14.0%). Malnourished patients were more often treated with steroids (p=0.039), had worse gastrointestinal symptoms accordingly to UCLA questionnaire (p=0.007), lower physical activity accordingly to International physical activity questionnaire (p=0.029), longer disease duration (p=0.019), worse predicted DLSO/VA and FVC (p=0.006 and 0.009 respectively, p=0.013), confirmed to be worse in malnourished patients, and were associated with more frequent visceral manifestation (73% vs. 63%). Sarcopenia was diagnosed in 20.7% (CI95% 14.0–27.4%); 11/29 sarcopenic patients were also malnourished and 6/29 were cachectic (i.e. sarcopenia + systemic inflammation).

Table 1. Patients’ characteristics

<table>
<thead>
<tr>
<th>Age</th>
<th>63 (13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female)³</td>
<td>118 (44.4)</td>
</tr>
<tr>
<td>Diffuse disease subset²</td>
<td>44 (31.2)</td>
</tr>
<tr>
<td>Disease duration (year)</td>
<td>13.3(7.2)</td>
</tr>
<tr>
<td>Interstitial lung disease²</td>
<td>39 (27.7)</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension²</td>
<td>12 (8.5)</td>
</tr>
<tr>
<td>Active disease accordingly to Valentín²</td>
<td>27 (19.1)</td>
</tr>
<tr>
<td>FVC predicted (%)</td>
<td>103 (23)</td>
</tr>
<tr>
<td>DLSO/VA predicted (%)</td>
<td>75 (21)</td>
</tr>
<tr>
<td>mRSS*</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Medsgger severity score</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/h)</td>
<td>26 (16)</td>
</tr>
<tr>
<td>C-reactive protein (mg/l)²</td>
<td>3 (0)</td>
</tr>
<tr>
<td>Endotoxin receptor antagonists²</td>
<td>16 (11.3)</td>
</tr>
<tr>
<td>Procalcitonin (ng/ml)²</td>
<td>130 (82.2)</td>
</tr>
<tr>
<td>Steroids²</td>
<td>23 (16.3)</td>
</tr>
<tr>
<td>Immunosuppressive treatment³</td>
<td>35 (24.8)</td>
</tr>
</tbody>
</table>

¹Expressed as media (IQ); ²Expressed as absolute value (%).

Conclusions: Malnutrition defined with widely accepted diagnostic criteria was found to be lower than previously reported (3–7) using screening tool or non-validated criteria. Sarcopenia was found to be somewhat common, although no previous study on comparable cohorts are available. Lung involvement and dysfunction was shown to be significantly linked with nutritional status and may not be explained only by muscle weakness given the absence of correlation between muscle weakness and FVC but only with DLSO/VA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3420

SAT0337 IMPACT OF ORGAN INVOLVEMENT ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IIM) are associated with considerable morbidity, primarily related to severe muscle weakness and visceral involvement, resulting in decreased mobility and impaired quality of life. Results from the OMERACT Myositis Special Interest Group indicate that there is insufficient knowledge on patient-reported outcomes (PROs) in IIM².

Objectives: To analyse the association between organ involvement and PROs in IIM patients, taking the presence of autoantibodies into account.

Methods: Data of IIM patients, recorded in the National Database of the German collaborative arthritis centres between 2007 and 2014, were analysed. Physician-reported data on myositis disease phenotypes, organ involvement and antibody status were linked with PROs on functional status (FFBH, range 0–100, 100 indicating full capability), and numerical rating scales (0–10) for pain, fatigue, general health, physical and emotional well-being and coping. Multivariable linear regression analysis was used to investigate the impact of phenotype, organ involvement and autoantibodies on PROs, adjusted for sex, age and disease duration.

Results: A total of 142 IIM patients - 60 polymyositis (PM), 46 dermatomyositis (DM), 15 antisyntethase syndrome (ASS), 12 overlap (OL), 9 others - with mean disease duration of 7.4 years were included. 85% showed muscular, 36% skin involvement, 22% arthritis, 28% interstitial lung disease, 17% dysphagia and 9% cardiomyopathy. Visceral (lung, cardiac or gastrointestinal) manifestation was present in 46% (PM), 54% (DM), 100% (ASS), and 80% (overlap). While moderate to severe (4–10) fatigue was predominately reported in overlap (64%) and ASS (70%), pain was more frequent in overlap (55%) and emotional discomfort was reported most frequently in ASS (57%). For all PROs, worse outcomes were documented in patients with visceral manifestation. Myositis-specific autoantibodies, predominantly Anti-Jo1, were present in 63% of the patients, and were associated with more frequent visceral manifestation (73% vs. 46%), especially interstitial lung disease (50% vs. 15%), and arthritis (32% vs. 13%), but less skin involvement (49% vs. 67%), DM and PM subtypes showed almost identical coefficients for fatigue, physical well-being, general health and coping, while PM was associated with higher emotional strain. Pulmonary hypertension had a severe impact on pain, functional status and daily activities. Cardiomyopathy was associated with impaired general health, arthritis with poorer scores for coping, physical and emotional well-being.

Conclusions: IIM patients with distinct subtypes differ considerably regarding the frequency of organ involvement and self-reported dimensions of disease burden. Anti-Jo1 positivity is associated with higher visceral organ involvement and arthritic manifestations and may therefore also indicate a higher patient-reported disease burden.

References:

Acknowledgements: The database is funded by unconditional grants from the German Collaborative Arthritis Centres and from a consortium of 11 pharmaceutical companies to the German Academy for Continuing Medical Education in Rheumatology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3822

SAT0338 SURVIVAL IN A TURKISH INFLAMMATORY MYOSITIS COHORT: A SINGLE-CENTRE STUDY

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Background: Inflammatory myositis is an uncommon group of diseases that
can be associated with significant morbidity and mortality related to systemic involvement or treatment-related complications.  

**Objectives:** This study aimed to describe the clinical features and survival of patients with inflammatory myositis in our centre.  

**Methods:** We performed a single-centre, retrospective study on patients with inflammatory myositis (polymyositis [PM], dermatomyositis [DM], or Anti-Jo1 syndrome) seen from 2000 to 2014, noting their demographic data, clinical features and outcome until December 2016. The primary outcome assessed was all-cause mortality. Cumulative mortality rates were estimated using the Kaplan-Meier test; the Log Rank (Mantle-Cox) test was used to compare subgroup differences in survival.  

**Results:** Seventy-four patients (19 PM, 28 DM, 27 Anti-Jo1 syndrome) were available for the study. Median age at diagnosis was 47 years (min 17, max 75) and median follow-up time was 93 months (min 4, max 311). Sixty-one patients (82.4%) were female and 13 (17.6%) were male. Malignancy was found in 4 patients (2 invasive ductal adenocarcinoma of breast, 1 over cancer and 1 non-small cell lung cancer) and they were all female DM patients. Nineteen patients (25.7%) died at the end of the follow-up. The 19 patients with PM consisted of 15 female and 6 male, with a median age at diagnosis of 45 years (min 22, max 74) and median follow-up time of 88 months (min 5, max 204). The 28 patients with DM consisted of 24 female and 4 male, with a median age at diagnosis of 52 years (min 17, max 75) and median follow-up time of 80 months (min 4, max 288). The 27 patients with Anti-Jo1 syndrome consisted of 22 female and 5 male, with a median age at diagnosis of 50 years (min 22, max 63) and median follow-up time of 117 months (min 5, max 311).  

Overall survival rates of the whole group were 91%, 83%, and 76% for 1, 5, and 10 years, respectively. The survival rates at 1, 5 and 10 years from the diagnosis were respectively 88%, 82%, and 82% for PM, 89%, 80%, and 80% for DM, and 96%, 88%, 74.5% for Anti-Jo1 syndrome. But there was no significant difference between the survival rates of the diagnose groups (p=0.734). Also there wasn’t a significant difference between the survival rates of sex and age groups (p=0.503, p=0.112). But the survival rates were significantly lower in patients with the time from diagnose less than 8 years (p=0.000).

**Conclusions:** Our study involved 74 patients followed up for a median of 7.7 years and is one of the largest cohorts of patients with inflammatory myositis in Turkey. Survival was quite similar with the literature. Usually mortality has been expected in the first years after the diagnosis.  

**Disclosure of Interest:** None declared  

**DOI:** 10.1136/annrheumdis-2017-eular.5956

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**SAT0339**  
**LUNG TRANSPLANTATION IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH ANTISynthetase AND ANTI-MDA5 SYNDROMES. EXPERIENCE FROM A REFERENCE SPANISH HOSPITAL**  
E. Trallero-Araguás 1, C. Berastegui 2, M. López-Corbeto 1, I. Bello 3, A. Román 2, A. Selva-O’Callaghan 1, 1Rheumatology Unit; 2Pneumology Department; 3Thoracic Surgery Department; 4Internal Medicine Department, Hospital Vall d’Hebron, Barcelona, Spain

**Background:** Interstitial lung disease (ILD) is the most characteristic feature and prognosis determinant of patients with antisynthetase (AS) and anti-MDA5 syndromes. Despite immunosuppressive treatment, ILD sometimes progresses to an end-stage lung disease, for which lung transplantation (LT) is the only therapeutic option. There is scarce data about post-LT outcome in this group of patients.  

**Objectives:** To describe clinical characteristics and post-LT outcome of patients with ILD associated to AS and anti-MDA5 syndromes included in the LT program of the Vall d’Hebron Hospital of Barcelona.  

**Methods:** We performed a review of patient records listed in the LT program.  

**Results:** From 1990 to 2016 ten patients (6 women) with ILD related to AS or anti-MDA5 syndromes were included in the LT program (3% of patients with ILD accepted for LT). Nine patients (2 anti-MDA5, 4 anti-Jo1, 2 anti-PL12 and 1 anti-PL7) received LT while 1 patient (anti-Jo1) was still in list at the end of this study. Median age (range) of disease diagnosis was 39 years (25–55). Six patients had clinical myopathy [2 dermatomyositis (DM) and 4 polymyositis] whereas 1 patient was diagnosed with amyopathic DM.  

Four patients had associated pulmonary hypertension. Time between disease diagnosis and patient inclusion in LT list was higher in anti-Jo1 patients [median (range) 8.8 years (8.3–17.6)] than in the rest of the cohort [anti-MDA5 –1 year; anti-PL12 0.7 and 3.9 years; anti-PL1 7.1 years] (p<0.05). Four patients underwent bilateral LT and one patient received a single LT. Three patients received an urgent LT (2 anti-MDA5 and 1 anti-Jo1). Six patients presented an anatomico mediated rejection 8 and 10 months from LT respectively; 4 patients suffered chronic lung allograft dysfunction (CLAD), 2 of whom are still alive; Infection was diagnosed in 6 patients. One patient developed Aqueous skin disease and his myositis disease was observed after LT in any case. Four patients (44%) died; 2 of an acute respiratory failure in the immediate postoperative period (1 caused by suture dehiscence and 1 by refractory ACR); 1 of an invasive aspergillosis, 17 months after LT; and 1 of CLAD after 54 months. Median follow-up (range) of the rest of the cohort was 35 months (8–70). All patients who survived more than 45 days recovered an optimal functional capacity for daily activities with no request for long-term oxygen therapy.  

**Conclusions:** LT should be considered a valid option to treat patients with end-stage or severe and rapidly progressive ILD associated to AS and anti-MDA5 syndromes. An early remission to LT referral centers for evaluation should be considered especially in non-Jo1 patients. No relapse of myositis or ILD was observed after LT. Mortality could not be attributed to the primary disease.  

**Disclosure of Interest:** None declared  

**DOI:** 10.1136/annrheumdis-2017-eular.6320

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**SAT0340**  
**SUBCLINICAL CARDIOVASCULAR DISEASE IN SCLERODERMA: A STUDY WITH CARDIOVASCULAR RISK CHARTS, CT CORONARY CALCIUM SCORE AND CAROTID ULTRASONOGRAPHY**  
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**Background:** Recently published population-based cohort studies had shown a high prevalence of cardiovascular (CV) disease in Systemic Sclerosis (SSc) patients.  

**Objectives:** The aim of this study is to compare different methods to measure CV risk in patients with scleroderma.  

**Methods:** We conducted a cross-sectional study in a single center that included 43 SSc patients without CV events. We used both CV risk assessment charts SCORE for populations with low CV risk and REGICOR algorithm adjusted to Spanish subjects. Coronary Computed Tomography (CT) with coronary arterial calcium score (CACscore) was performed considering several cut-off points as predictors of CV risk. Carotid doppler ultrasound was performed to measure the Carotid Intima Media Thickness (CIMT) and for the detection of cholesterol plaques, according to Mannheim consensus criteria.  

**Results:** Risk factors and SSc related features are described in table 1. None of the patients were catalogued as high risk according to SCORE chart (<5%). According to REGICOR chart, 17 patients (39.5%) were catalogued as intermediate risk and none as high risk. Twenty-two patients (51.2%) had carotid plaques (CP) and the CACscore of these patients was 283.4. In patients without CP CACscore was 53.2 (p<0.05). Based on the presence of CP we performed ROC curve with CACscore. The AUC was 0.778. The best cut off point was 28 with a sensibility of 71% and a specificity of 82%. Kappa’s coefficient was 0.54. Twenty patients (46.5%) had CP CACscore was 53,2 (p<0.05).  

**Disclosure of Interest:** None declared  

**DOI:** 10.1136/annrheumdis-2017-eular.5956
PILOT STUDY: HOME MANAGEMENT OF ILOPROST IN THE INTERVENTION GROUP

Background: Evaluate the effectiveness of Raynaud’s phenomenon and on digital ulcers, safety and side effects, during intravenous infusion of iloprost therapy in patients with limited subset classification, and limited subset classification.

Methods: 10 patients with the Raynaud's phenomenon, there was a reduction in the daily number of episodes of Raynaud's phenomenon, evaluation of digital ulcers disappeared in 6 patients, they were unchanged in 5 patients, improved although present in 1 patient. In 7 patients capillaroscopic framework remained unchanged, in 5 patients improved capillary density. 10 patients had no pulmonary hypertension, 2 patients had pulmonary hypertension, no change in the two groups at T0 and T12. None of the patients experienced side effects during the infusion.

Conclusions: The cyclical infusion therapy iloprost prevented the onset of ulcers in patients at T0 not presented or the appearance of new ulcers; it has contributed to the reduction in the daily number of Raynaud’s phenomenon and also allowed to reach the same effective dose of a vial of iloprost to dilute in 50 cc of saline solution, allowing the patient to perform at home therapy with greater compliance.

Disclosure of Interest: None declared


SAT0341 PILOT STUDY: HOME MANAGEMENT OF ILOPROST IN THE MICROPUMP/24 HOURS, IN PATIENTS SUFFERING FROM SCLERODERMA, FOLLOWED FOR 12 MONTHS


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Background: Evaluate the effectiveness on Raynaud’s phenomenon and on digital ulcers, safety and side effects, during intravenous infusion of iloprost therapy in patients with limited subset classification, and limited subset classification.

Methods: Enrolled consecutively for a period of 12 months, 12 patients, 9 women and 2 men, 9 suffering from diffuse scleroderma (positive Scl70) and 3 suffering from limited scleroderma (positive anticientromere), middle age 52.91 years, mean age of disease 7.8 years, 11 non-smoking. They were selected based on the infusion of iloprost 1/2 vial diluted in 25 cc of saline solution to 0.6 ml/h, in micropump Infnode for 24 consecutive hours, for 4 days a month for 12 months, 10 patients with peripheral lines and 2 with central venous access.

Results: Of 12 patients with the Raynaud’s phenomenon, there was a reduction in the daily number in 4 patients, unchanged in 8 patients. Digital ulcers disappeared in 6 patients, they were unchanged in 5 patients, improved although present in 1 patient. In 7 patients capillaroscopic framework remained unchanged, in 5 patients improved capillary density. 10 patients had no pulmonary hypertension, 2 patients had pulmonary hypertension, no change in the two groups at T0 and T12. None of the patients experienced side effects during the infusion.

Conclusions: The cyclical infusion therapy iloprost prevented the onset of ulcers in patients at T0 not presented or the appearance of new ulcers; it has contributed to the reduction in the daily number of Raynaud’s phenomenon and also allowed to reach the same effective dose of a vial of iloprost to dilute in 50 cc of saline solution, allowing the patient to perform at home therapy with greater compliance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.15990

SAT0342 TRANSTHORACIC ECHOCARDIOGRAPHY TO QUANTIFY PULMONARY VASCULAR RESISTANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: One of the major causes of systemic sclerosis (SSc)-related death is pulmonary arterial hypertension, which develops in 12–15% of patients with SSc and accounts for 30–40% of deaths. Consequently, monitoring of pulmonary arterial pressures (PAP) is essential in patients with SSc. Abbas formula performed by transthoracic echocardiography (TTE) was reported as a good tool to quantify pulmonary vascular resistances (PVR).

Objectives: Explore the accuracy of TTE and Abbas formula to quantify PVR in patients with SSc.

Methods: All consecutive patients with SSc, diagnosed according to the 2013 ACR/EULAR criteria, or the LeRoy and Medsger criteria for diffuse or limited subsets classification, had within 24H a Doppler echocardiographic examination and right-heart catheterization were performed. The ratio of peak tricuspid regurgitation velocity (TRV, m/s) to the right ventricular outflow tract time–velocity integral (TVI右), cm) obtained by Doppler echocardiography (TRV/TVI右) was then correlated with invasive PVR measurements using regression analysis. An equation was modeled to calculate PVR in Wood units (WU) using echocardiography, and the results were compared with invasive PVR measurements.

Results: Thirty-three consecutive patients were included, 13 (39.4%) were male and the mean age was 64.6±12.1 years. Most were classified as limited cutaneous SSc (cSSc; n=29, 87.9%). All patients tested positive for antinuclear antibodies, 18 (21.2%) for anti-scleroderma-70, 7 (24.5%) for antirecombatere antibodies and 2 (6.1%) for anti-RNA polymerase III antibodies. Mean and systolic PAP were 31±6 and 53±16 mmHg respectively. There was a good correlation between right ventricle to right atrium gradient pressure assessed by TTE and RHC (R=0.620, P<0.001). RVP assessed by Abbas formula (2.6±1.0 wood units) were well correlated with RVP assessed by RHC (R=0.822; R=0.446, P=0.013).

Conclusions: Doppler echocardiography using Abbas formula may provide a reliable, noninvasive method to determine PVR in SSc patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.20881

SAT0343 SCREENING OF PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS USING DETECT ALGORITHM – VALIDATION IN THE COHORT OF JAPANESE SINGE CENTER

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Background: Pulmonary arterial hypertension (PAH) complicated with systemic sclerosis (SSc) has the worst prognosis in PAH associated with other connective tissue diseases (1) and is one of leading cause of death in patients with SSc (2). To improve prognosis in SSc patients, earlier detection and diagnosis of PAH by annual screening is recommended even in asymptomatic patients (3). To effectively detect PAH in patients with SSc at earlier phase, DETECT algorithm is reported as a good tool to identify candidates who need right heart catheterization (RHC), with high sensitivity (4). However, its usefulness has not been validated in Japanese cohorts.

Objectives: To validate the effectiveness of DETECT algorithm in the Japanese single center cohort.

Methods: Patients with SSc who visited Keio University Hospital between 2005 and 2016 were included in the study. Patients over 18 years old, disease duration more than 3 years, and DLCO predicted less than 60% were selected and clinical information was retrospectively collected from records. The sensitivity, specificity, and negative and positive predictive values of the algorithm based on the result of RHC evaluation were calculated in a cohort of PAH patients and non-PAH patients, in whom RHC data were available. Validation with patients with data minimally-required for algorithm were also examined.

Results: Three hundred four cases were visited our hospital during from 2005 to 2016. Patients who fulfilled criteria and had data minimally-required for algorithm were 126 cases. Of 126 cases, 50 were examined RHC evaluation and patients diagnosed as pulmonary hypertension were 26 (21%) and 21 (15%) were PAH. When a cohort of PAH patients and non-PAH patients with RHC data was applied to DETECT algorithm, referral rate to RHC evaluation was 78%, missed diagnosis of PAH was 0%, sensitivity/specificity for detecting PAH patients were 100%/42%, and positive/negative predictive values were 60%/100%, respectively. Evaluation of 126 patients with data minimally-required for algorithm was also examined. Referral rate to RHC evaluation was 43%, missed diagnosis of PAH was 0%, and sensitivity/specificity and positive/negative predictive values for detecting PAH patients were 100%/72%, 43%/100%, respectively. However, there was a patient who was initially excluded at Step 1, but developed PAH one year later.

Conclusions: The DETECT algorithm was reassured as a good tool to effectively screening tool for PAH in SSc patients. However, we have to keep in mind that unnecessary of RHC referral judged by this algorithm does not guarantee the patient to be free from future development of PAH.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.15061

References:
SAT0344 | DISEASE RELATED MALNUTRITION IN SYSTEMIC SCLEROSIS AND ASSOCIATED FACTORS: A CROSS-SECTIONAL STUDY
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Background: The risk of malnutrition increases in patients with systemic sclerosis (SSc) which has a negative prognostic effect. Additionally malnutrition is a significant cause of morbidity and mortality.

Objectives: The aim of this study was to evaluate the associations between malnutrition and clinical features of the disease, depression in SSc patients.

Methods: Concomitant SSc patients followed in our outpatient and inpatient clinics were enrolled in the study. Skin involvement was assessed with modified Rodnan skin score (mRSS), joint/tendon involvement with finger-tip to palm distance (FTP). Intestinal lung disease (ILD) and heart involvement were evaluated with clinical and radiological methods. Patients were questioned for dysphagia and gastrointestinal involvement was diagnosed with endoscopy. Heart involvement was evaluated with electrocardiogram, and heart consumption and diastolic filling were determined with echocardiography. Malnutrition was assessed with Subjective Global Assessment (SGA) method. HAQ-DI, Beck Depression Inventory (BDI), and dietary history were used in the evaluation of malnutrition. Malnutrition risk was higher with patients with bowel involvement, and diarrhea, constipation and bloating as bowel involvement. Interincisal distance measurement was used to assess the maximal mouth opening capacity. Malnutrition risk was assessed by the Malnutrition universal screening tool (MUST). The Beck Depression Inventory (BDI) was used for measuring the severity of depression. The examinations associated between malnutrition risk and clinical features of the disease, depression in SSc patients.

Results: Ninety eight SSc patients with 69 diffuse and 29 limited type of the disease were enrolled in the study. 94.7% of the patients were female and the mean age was 52.67±11.28 years. According to MUST scores 61.2% of patients have low, 15.3% medium and 23.5% high risk for malnutrition. We found no difference between the malnutrition risk among genders (p=0.065). mRSS and FTP were significantly different between malnutrition risk groups (p=0.005, 0.050 respectively). Malnutrition risk was higher with patients with ILD than the patients without ILD (p=0.044). Malnutrition risk was higher with patients with bowel involvement than the patients without bowel involvement (p=0.021). Interincisal distance was significantly different between malnutrition risk groups (p=0.003). 78.7% of SSc patients have BDI scores ≥10, 54.3% of SSc patients have BDI scores ≥17. BDI scores were significantly different between malnutrition risk groups (p<0.001). Factors affecting malnutrition risk were evaluated with logistic regression analysis. Interincisal distance and bowel involvement were found to be the most relevant factors for malnutrition risk. SSc patients with bowel involvement have 2.519-fold increased risk of malnutrition compared to patients without bowel involvement (95% CI 1.039–6.105). Every 1 mm decrement in interincisal distance was associated with 1.101 fold increase in malnutrition risk of SSc patients (95% CI 1.032–1.176).

Conclusions: Malnutrition is common in SSc patients. Malnutrition risk is associated with skin, tendon involvement, bowel involvement, microstomia and depression severity.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6162

SAT0346 | SYSTEMIC SCLEROSIS’S EARLY STAGES AND ITS SIGNIFICANCE IN DAILY PRACTICE

Background: Systemic Sclerosis (ScS) is an autoimmune disease, characterized by skin and internal organs fibrosis. Its clinical manifestations are heterogeneous, hence, the definitive diagnosis of SSc rely on scores, such as American College of Rheumatology (ACR) for SSc. Leroy and Medsger, proposed the potential criteria for the classification of early stages of SSc, due to the insufficient sensitivity previous methods. Lately EUSTAR proposed the concept of Very Early SSc, defined by the presence of 3 red flag – RF, Puffy Fingers and ANA; if ≥2 of these are present, capillaroscopy and specific antibody must be accessed; if one of the last positive, further search for Systemic involvement must be taken in account.

Objectives: We propose to: analyse a group of patients that had been diagnosed with early stages of SSc; study the presence of systemic involvement (at the time of diagnosis and throughout the follow-up), and the possible predictors for progression to definite SSc.

Methods: The patients were selected by consulting the clinical data from patients followed in our hospital with diagnosis of early stages of SSc. Very Early SSc criteria were used to define early stage SSc. The data concerning red flags, capillaroscopy, specific auto-antibodies, systemic involvement (Gastrointestinal, Pulmonary, Cardiac, Kidney, Musculoskeletal).

Results: We obtained a sample of 70 patients, 65 being female subjects (92,9%), with mean age of diagnosis 47.9 years (SD 13.6). 16 patients (22.9%) were classified as Pre-scleroderma at the admission, 16 as Early SSc (22.9%), 15 (21,4%) as Very Early SSc, 16 (22.9%) as possible SSc, 6 (8,6%) as Limited SSc (despite not scoring to ACR criteria) and 1 (1,4%) as Sin Scleroderma SSc. 69 patients (90%) had RP, 15 (21,4%) had puffy fingers, 63 (90%) ANA positivity – 11 patients (15,7%) had 1 red flag, 45 (63,4%) had 2 red flags and 13 (18,6%) had 3 red flags.

Conclusions: Physical components associated to specific SSc autoantibodies; 47 patients (71.2%) had capillaroscopy compatible with SSc in different stages (17.1% Early, 12.9% Active, 4,3% Late and 32.9% compatible). 54 patients (77,1%) scored for Very Early SSc.

At the moment of the diagnosis, 56 patient (81,2%) had systemic involvement. 34 patients (48,6%) scored to the definitive diagnosis by ACR 2013 criteria, after 2,56 years in mean (SD 2,51) of first diagnosis. No correlation was found in what concerns to predictors of progression to SSc or systemic involvement.

Conclusions: This study shed a light on the importance of the recognition of SSc’s early stages, since a significant part of these patients have systemic involvement at the moment of diagnosis, yet not scoring to ACR 2013 criteria. Almost half of the patients scored to definite diagnosis of SSc at the moment of the last appointment. The importance of these findings rely on the possibility to delay systemic involvement and address it in time to prevent/delay further disease progression.

References:

SAT0345 | THE IMPACT OF GASTROINTESTINAL INVOLVEMENT IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS
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Background: Apart from skin involvement, the gastrointestinal (GI) system is the second most commonly involved organ in systemic sclerosis (SSc), affecting over 80% of the patients. Although rarely being a direct cause of death, it is associated to a high morbidity and to a significant impairment in health-related quality of life (HRQoL) and vascular disease. Considering the influence of GI manifestations in the quality of life of SSc patients.

Objectives: The purpose of this study is to characterize the impact of GI involvement in HRQoL in SSc, and to compare it with that in patients with inflammatory bowel disease (IBD).

Methods: Concomitant SSc patients with GI involvement were selected from a cohort of 44 SSc patients, followed in a single referral centre and classified according to 2013 ACR/EULAR criteria. Comparative analysis was made with 24 consecutive patients with IBD without arthritis (14 Crohn’s disease; 10 - ulcerative colitis). Health Assessment Questionnaire (HAQ-DI) and Short Form 36 (SF36), physical component summary (PCS) and mental component summary (MCS) scales, were used to assess HRQoL in both groups. The UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract 2.0 (UCLA SCTG GIT 2.0) was performed in SSc patients to assess the severity of GI involvement. Clinical data were obtained by medical records review. T-Test and Fisher’s exact test were used to compare binary variables. Pearson’s correlation was used for continuous variables.

Results: The most common GI segments involved in SSc patients were the esophagus in 90%, the stomach in 60% and the bowel in 48%, while the anorectum was involved in a smaller percentage (10.3%). The mean UCLA SCTG GIT 2.0 score was 0.64±1.9 (46.8% with a moderate severity, with higher scores obtained for reflux, distention and emotional wellbeing. The mean HAQ-DI score was 1.13±0.57 (0-best health), and the mean PCS and MCS scores were 35.2±9.4 and 35.3±11.4 (100-best health), respectively. These scores were significantly lower than in SSc patients without GI involvement (HAQ-DI: p<0.001; PCS - p<0.04 and MCS - p<0.005). There was a significant correlation between higher UCLA SCTG GIT 2.0 scores and worse quality of life evaluated by HAQ-DI (r=-0.42, p<0.03), but the same correlation was not found for the SF36 components. Comparing with IBD patients, SSc patients with GI involvement had worse life quality, with statistically significantly higher HAQ-DI (p<0.001) and lower PCS (p<0.001) and MCS (p<0.01) scores.

Conclusions: GI involvement in SSc significantly impaired patient’s quality of life. The impact of GI involvement in HRQoL of SSc patients was more severe than in IBD patients. Although physical components were relevant, with esophagus being most frequently involved, multisystemic involvement associated with GI involvement significantly compromised HRQoL in SSc. Therefore, the assessment of SSc patients using clinical severity measure tools, similar to UCLA SCTG GIT 2.0 score, is crucial for a better characterization of the disease and to an optimized clinical approach.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2496


DOI: 10.1136/annrheumdis-2017-eular.4608

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2496
DISEASE MODIFYING EFFECT OF ILOPROST IN PATIENTS WITH SYSTEMIC SCLEROSIS AND POSSIBLE ROLE OF CXCL4 CHEMOKINE

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Background: Iloprost is a synthetic prostaglandine used for vascular manifestation of Systemic Sclerosis (SSc), in particular it is used for active digital ulcers (DU) and severe Raynaud Phenomenon (RP) (1). It acts on several receptors such as IP and EP receptors and PPRs. Iloprost is also involved in the regulation of gene expression, fibrosis and inflammation (2,3). CXCL4 (CXCL4) is a Platelet Factor 4, a 70Kda CXCL chemokine synthesized in megakaryocytes and plasmacytoid dendritic cells, released after platelet activation. In SSc, it seems to be higher in patients with early diffuse SSC and it correlates with mRSS and presence of PAH (4).

Objectives: To evaluate the effect of iloprost on vascular manifestations, on disease activity and on serum levels of CXCL4 at baseline (T0) and after 1 month (T1), 3 months (T3) and 6 months (T6) of therapy.

Methods: 30 patients (M/F = 1:29; mean age =58.2 ± years; mean disease duration = 12.8± 5 yrs) with established SSc according to ACR criteria, were enrolled. At T0, T1, T3 and T6 treatment with iloprost at standard dosage we used RPMY, a number of DU, European Scleroderma Study Group Activity Index (EScSGAI) and serum levels of CXCL4, measured using commercially available immunoassay kit (human CXCL4/PF4 R&D SYSTEMS®). All patients underwent to a complete clinical, instrumental and laboratory evaluation.

Results: Regarding RP VAS, we found a statistically significant increase (p<0.04) at T3, corresponding to the colder winter period, while it decreased, although not significantly at T1 and at T6, where this reduction was significant compared to T3 values (p=0.0008). Concerning the number of active DU, we highlighted the same trend of the RP VAS. EScSGAI values showed a statistically significant reduction (p<0.03) comparing T3 to T6. Regarding CXCL4, we found significantly higher levels in SSc patients respect to a group of healthy controls (HC) (p<0.047). No significant difference was found in serum levels of CXCL4 at T0, T1,T3 and T6. Evaluating patients with higher levels of CXCL4 at baseline, respect to the average of HC values (CXCL4>25,000 pg/ml) (11/30 patients), we found that 7 subjects had a significant improvement in disease activity at T6 evaluated by EScSGAI (p=0.015). In these patients we also detected a significant reduction in T3 CXCL4 values (p<0.043) persisting and at T6, although not reaching statistical significance. Moreover more basal levels of CXCL4 in patients with disease duration less of 60 months (p=0.05) and in patients with pericardial effusion (p=0.037) were detected. Besides we found significantly lower levels of CXCL4 in patients with DU history (p=0.049) and esophageal involvement (p=0.008).

Conclusions: Our study confirms the efficacy of Iloprost on vascular manifestation of Systemic Sclerosis in particular it is indicated for active digital ulcers (DU) and esophageal involvement (p=0.008). In these patients we also detected a significant reduction in T3 CXCL4 values (p=0.043) persisting and at T6, although not reaching statistical significance. Moreover more basal levels of CXCL4 in patients with disease duration less of 60 months (p=0.05) and in patients with pericardial effusion (p=0.037) were detected. Besides we found significantly lower levels of CXCL4 in patients with DU history (p=0.049) and esophageal involvement (p=0.008).

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Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5747

EVALUATION OF STANDARD SWALLOWING FUNCTION IN ASSESSING ASPIRATION RISK FOR PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Swallowing dysfunction is a common symptom of systemic sclerosis, which usually induce aspiration pneumonia to aggravate lung progress. It is necessary to screen swallowing disorders effectively at an early stage.

Objectives: To investigate the value of standard swallowing function assessment (SSA) in aspiration screening for inpatients with Systemic sclerosis.

Methods: SSA and Video fluoroscopic swallowing study (VFSS) were performed in 120 inpatients with Systemic sclerosis from March 2014 to September 2016. The sensitivity, specificity, positive predictive value and negative predictive value of SSA in the diagnosis of aspiration in patients were calculated by taking VFSS examination as the gold standard. The incidence of pneumonia in SSA-positive and SSA-negative patients were compared.

Results: The diagnostic sensitivity of SSA was 81.2%, the specificity was 75%, the positive predictive value was 68.6% and the negative predictive value was 90.3%. The incidence of pneumonia in SSA positive patients was higher than that in SSA negative patients (54.1% vs 28.3%) (P<0.01).

Conclusions: SSA is a valuable screening tool for the evaluation of aspiration risk in patients with Systemic sclerosis.

References:


DOES A SYMPTOMATIC SCLEROSIS PATIENTS’ CLINICAL PHENOTYPE DEMONSTRATE HIS AUTOANTIBODY STATUS?


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Background: Although antibody status has shown to critical in clinical setting in Systemic Sclerosis (SSc), it is far from perfect. For optimal clinical setting as well as for evaluating the possible pathogenic role of SSc specific antibodies, it is relevant to know to what extent clinical SSc phenotypes are determined by presence of these antibodies.

Objectives: To evaluate 1. if clinical relevant subsets of SSc patients are distinguishable using only clinical data, 2. how SSc specific autoantibodies are distributed among these subsets, and 3. whether adding antibody status to cluster analysis improves recognition of SSc subsets.

Methods: Using data from SSc patients of the Combined Care In Systemic Sclerosis (CCIS) cohort, Leiden University Medical Center, hierarchical clustering based on Ward Method was performed on the first obtained factor of principal compoment analysis of 7 organ systems (skin, lung, heart, kidney, muscle, vascular, gastro-

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6927

ASSOCIATION OF VITAMIN D DEFICIENCY WITH REDUCED IL-10-PRODUCING REGULATORY B CELLS IN SYSTEMIC SCLEROSIS

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Background: IL-10-producing regulatory B cells (Bregs), also known as B10 cells, are decreased and function impaired in patients with systemic sclerosis (SSc), particularly in those with SSc-associated interstitial lung disease (1). As serum 25-OH-vitamin D (vitD) levels are associated with clinical aspects in patients with SSc (2), we investigated whether there is any link between vitD levels and Breg levels.

Objectives: To assess whether or not vitD deficiency in SSc is associated with the percentages of circulating IL-10-producing Breg cells.

Methods: PBMCs and serum samples were isolated from 55 patients with systemic sclerosis. Serum VitD levels were measured using a commercially available sandwich ELISA kit. Phenotypic analysis of CD19, CD24, CD27, CD123 and intracellular expression of cytoklasmic IL-10 following bacterial CpG (ODN2006) and PMA/ionomycin stimulation was examined by flow cytometry using specific fluorochrome-conjugated monoclonal antibodies (BD Biosciences).

Results: Systemic Sclerosis patients were divided into two groups (vitD deficient or not) based on a serum concentration cut of value of 20 ng/ml. The mean vitD levels in the deficient group were 14.1±3.6 ng/ml (n=17) whereas the mean vitD levels in the non-deficient group were 37.5±12.9 ng/ml (n=38). IL-10-producing B cells (B10 cells) were significantly decreased in vitD deficient patients compared to those with medium/high levels (p=0.02). CD19+CD27+ (memory) B cells were also significantly reduced with vitD deficiency (p=0.004). In addition the ratio of naïve/memory B cells was significantly higher in vitD deficient patients (p<0.05). Within the memory B cell fraction, the CD19+CD27+CD24hi cells also known as phenotypic memory Bregs, were mostly decreased (p=0.001). There was no significant association between CD19+CD38hiCD24hi (transitional) Bregs and VitD levels.

Conclusions: Our data suggest that vitamin D deficiency may account for reduced B10 cells in systemic sclerosis.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.5747

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intestinal) and time since non-Raynaud phenomenon. Clinical characteristics and prevalence of auto-antibodies within clusters was evaluated. We assessed whether adding autoantibody status as additional factor improved clinical subsetting.

**Results:** Of 407 SSc patients included, 371 patients (91%) fulfilled ACR/EULAR 2013 criteria. Prevalence of anti-centromere (ACA) was 37%, anti-topoisomerase (ATA) 24%, anti-RNAPIII 5%, anti-fibrillarin 4%, anti-Pm/Scl 5%. Cluster analysis identified clinically recognisable clusters of SSc patients based on absence of skin involvement (cluster 1), peripheral vascular involvement (cluster 2), fibrotic complications (cluster 4), and severe vascular complications (pulmonary arterial hypertension [PHT], renal crises; cluster 5). Except for cluster 4, where ATA was diagnostic, in all clusters ACA was the most prevalent auto-antibody. No cluster associated with any of the more rare SSc specific auto-antibodies. Adding of auto-antibodies resulted in increased clinical overlap, with a frequency of PH between 6 – 8% and a frequency of digital ulcers between 24 – 39% in clusters 2, 4 and 5.

Table 1. Clustering of SSc patients based on clinics

<table>
<thead>
<tr>
<th>Cluster 1</th>
<th>Cluster 2</th>
<th>Cluster 3</th>
<th>Cluster 4</th>
<th>Cluster 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=66</td>
<td>n=50</td>
<td>n=129</td>
<td>n=81</td>
<td>n=81</td>
</tr>
<tr>
<td>Age in years, mean (SD)</td>
<td>53 (14)</td>
<td>54 (14)</td>
<td>54 (14)</td>
<td>53 (16)</td>
</tr>
<tr>
<td>Female, % (n)</td>
<td>90 (60)</td>
<td>86 (43)</td>
<td>85 (110)</td>
<td>72 (58)</td>
</tr>
<tr>
<td>Time since non-Raynaud, median (range)</td>
<td>3 (3–14)</td>
<td>10 (3–44)</td>
<td>2 (0–20)</td>
<td>3 (0–27)</td>
</tr>
<tr>
<td>dcSSc, % (n)</td>
<td>0 (0)</td>
<td>2 (1)</td>
<td>17 (22)</td>
<td>65 (53)</td>
</tr>
<tr>
<td>Mean mRSS (SD)</td>
<td>0 (0)</td>
<td>4 (3)</td>
<td>4 (3)</td>
<td>14 (11)</td>
</tr>
<tr>
<td>PAH, % (n)</td>
<td>3 (2)</td>
<td>4 (2)</td>
<td>0 (0)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Digital ulcers, mean (SD)</td>
<td>70 (18)</td>
<td>66 (15)</td>
<td>70 (15)</td>
<td>61 (28)</td>
</tr>
<tr>
<td>Heart failure, % (n)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Digital ulcers, % (n)</td>
<td>15 (10)</td>
<td>98 (49)</td>
<td>4 (5)</td>
<td>28 (23)</td>
</tr>
<tr>
<td>Anti-centromere, % (n)</td>
<td>5 (3)</td>
<td>15 (7)</td>
<td>22 (28)</td>
<td>48 (37)</td>
</tr>
</tbody>
</table>

Conclusions: Based on clinical data alone, relevant subgroups in SSc can be distinguished. Adding antibody status to cluster analyses increases overlap of clinical features between subgroups. These findings show that solely presence of antibodies does not improve clinical subsetting. Of optimising risk stratification, more complex serological findings as antibody titers might be additive.

DOI: 10.1136/annrheumdis-2017-eular.6004

**SAT0351** DIFFERENCES AMONG PATIENTS WITH INTERSTITIAL LUNG DISEASE ACCORDING TO THEIR SYSTEMIC SCLEROSIS SUBCLASSIFICATION


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**Background:** Systemic Sclerosis (SSc) has been widely studied from a purely global standpoint, but only a few trials have analysed patients with interstitial lung disease (ILD-SSc) as well.

**Objectives:** 1. Describe the clinical features of a cohort of patients with SSc and ILD-SSc. 2. Determine whether there are disparities among different types of ILD-SSc and their progression according to the SSc-specific autoantibody (AAb).

**Methods:** Retrospective study of a cohort of patients with ILD-SSc controlled during an SSc consultation. The following variables were collected: sex, age, SSc and ILD progress in years, type of SSc and ILD, smoking, digital ulcers (DU), gastrointestinal, digestive disorders, cancer. SSc treatment, corticosteroid doses and lastly, lung function tests upon diagnosis, at treatment onset, and 24 months later. Additionally, a record was kept on the types of AAb present in every SSc. Qualitative and quantitative variables were compared in relation to the clinical and immunological sub-classification. Chi-square and Student’s T Tests were performed. A P-value <0.05 was considered significant.

**Results:** of 266 patients with SSc, data from 47 patients with ILD-SSc were gathered; 89.4% were female, with an age range of 66.09±15.1 years old, and 9.85±10.2 and 4.38±9.24 years of progression of their SSc and ILD respectively. 33 out of 47 sustained ILD-SSc, and both Scl-70/ATA (29.8%) and ACA (26.1%) were the most frequently found AAb. Non-specific interstitial pneumonia (NSIP) was the most common ILD radiological pattern (76.6%). Most patients with SSc underwent treatment (51.1%), 24% with mycophenolate mofetil (MMF); 36.2% of the patients had been concurrently administered corticosteroids with a mean prednisone dose of 15.73±10.3 mg/day. Upon comparing patients with ILD-SSc and dcSSc, prevalence of DU was higher in those with dcSSc (p<0.01), MMF was less frequently used (p<0.02), rituximab was more usually employed (p<0.03), and they presented worse values of FEV1/FVC ratio after 24 months of treatment (p<0.03). No differences were observed as to either type of ILD or progression. However, when variables were analysed regarding AAb in SSc, patients with ACA presented both fewer DU (p<0.02) and NSIP pattern (p<0.02), and more frequent compromise of the small airway (p<0.01), they were younger and thus, they had had shorter progression of the disease. ILD diagnosis was made significantly earlier in those patients with RNA polymerase, and later in those with anti-U1RNP. No AAb was observed associated with neoplasia. Considering the types of ILD, patients with NSIP pattern were younger (p<0.054) and presented worse spirometric values.

**Conclusions:** In terms of ILD-SSc patient stratification, sub-classification by AAb appears to be more specific than the clinical sub-classification. ACA is related to less frequency of NSIP pattern. Unlike what has been described for SSc from a global point of view, in patients with ILD-SSc no association between AAb and neoplasia could be established.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6138

**SAT0352** MORTALITY IN IDIOPATHIC INFLAMMATORY MYOPATHY—RESULTS FROM A SWEDISH NATIONWIDE POPULATION-BASED COHORT STUDY

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**Background:** Little is known about mortality in idiopathic inflammatory myopathies (IIM) compared to the general population, especially the risk development since diagnosis. In a recently published study, the 5- and 10-year mortality was lower for IIM than previously reported, suggesting improved outcomes in recent years.

**Objectives:** To assess the mortality following IIM diagnosis in a nationwide population-based cohort of IIM patients diagnosed 2002–2011 compared to the general population.

**Methods:** We used nationwide fully covering health care registers to identify all individuals who were treated by a rheumatologist, neurologist, or dermatologist for IIM and who had a listing of IIM at ≥two visits within 1–12 months between 2002 and 2011, general population comparators, and death during follow up. We calculated crude and cause-specific mortality rates with 95% confidence intervals (CI) and compared the mortality in IIM to that in the general population using Cox proportional hazards models adjusted for age, sex, year of diagnosis, and residential area.

**Results:** During a median follow up of 4 years, 228 (31%) of the 733 IIM patients and during a median follow up of 6 years, 888 (12%) of the 7,340 general population comparators died. This corresponded to a crude mortality of 61/1,000 person-years in IIM, and 20/1,000 person-years in the comparators. The cumulative mortality at 1 year after diagnosis was 10% in IIM and 1% in the general population, at 5 years it was 24% in IIM and 7% in general population, and at 10 years the proportion was 31% and 12%. The overall hazard ratio (HR) (95% CI) of death comparing the NPR cohort and its comparator, was 3.5 (3.0–4.0). When restricting the outcome to cardiovascular disease-, cancer-, pulmonary disease- specific death we noted increased mortality from all outcomes in IIM compared to the risk in the general population. When we stratified on time since diagnosis we noted an increased absolute and relative risk of death in the first year of diagnosis in particular for pulmonary disease and cancer, whereas cardiovascular mortality was a major cause of death also after 10 years after IIM diagnosis (table).

**Conclusions:** IIM patients are still at increased risk of death. The highest mortality
Small Airways Involvement in Scleroderma Patients: Results of a Case-Control Study

M. Bonifazi, L. M. Rodriguez-Padilla, M. A. Mesa-Navas

Methods:
- Consecutive SSc patients were included in the present study according to eligibility criteria; controls were health volunteers. Both cases and controls underwent IOS measurements; cases also underwent pulmonary function tests and HRCT assessment of SA pathological features and ILD extent were provided for reference to cutaneous subtype a SA dysfunction was more prevalent in the following ILD subtypes: NSIP, BO, UIP, and a direct correlation with pulmonary artery systolic pressure estimated. With reference to cutaneous subtype a SA dysfunction was more prevalent in the limited form compared to the diffuse, respectively in 23% and 12%, Radiologic HRCT assessment of SA pathological features and ILD extent were provided for 77 patients; 19 (24.7%) presented at least one sign of SA disease. An underlying ILD was detected in 40 patients, characterized by NSIP pattern in 37.

Conclusions: A significant involvement of SA was found in a substantial proportion of SSc patients, compared to healthy controls. Moreover, this seemed to be associated with more severe functional obstructive and restrictive impairment, and with higher PAPs values. Therefore, our findings suggest that SA may be a potential, less known, target of disease, and further studies are needed to assess prognostic and therapeutic implications of this pathologic feature.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5385

Neuropathic Pain: Is It an Underestimated Symptom in Systemic Sclerosis?

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Methods: Diffuse and Limited SSc patients diagnosed by American College of Rheumatology 2013 criteria were included in the study. Pain was evaluated with Visual Analogue Scale (VAS); painful body regions and pain intensity with Brief Pain Inventory (BPI); presence of neuropathic pain with The Leeds Assessment of Neuropathic Symptoms and Signs (LANNS) questionnaire; disease activity with Medsger Disease Severity Scale (MDSS). Mixed-effects regression analysis was used to assess the associations of NPS with sociodemographic and clinical factors.

Results: One hundred twenty patients were included in the study (mean age 53.6 ± 14.4 years, female/male 83.3% ± 16.7%). Total pain frequency was found 69.2% and NPS was 35.9% in the whole patient group. Mean VAS in the study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4075

Small Airways Involvement in Scleroderma Patients: A Preliminary Observational Study

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Background: The prevalence of Raynaud’s phenomenon (RP) has been reported between 3–22%. When associated with systemic autoimmune diseases (SAD), especially systemic sclerosis (SSc), it is the sentinel event of irreversible organic damage. NAILfold videocapillaroscopy (NVC) is a non-invasive and safe procedure that allows two observation of the microcirculation. Between 15–20% of SAD cases who have RP with videocapillaroscopic alterations and certain autoantibodies will develop a SAD over two years. In addition, 90% of individuals with SSc and 85% with mixed connective tissue disease (MCTD) had RP as the first symptom.

Objectives: To evaluate the role of NVC in the differential diagnosis of RP, as well as in the early detection of SAD, in a cohort of Colombian patients.

Methods: A prospective, longitudinal, analytical study was conducted in subjects with RP over 18-year-old, not active smokers, without previous connective tissue disease, secondary causes or aggravating factors. OptiNVC with OptiPix software was used (Optilia Instruments, Solentuna, Sweden). Qualitative variables were described by means, as well as absolute and relative frequencies; quantitative variables, according to the distribution of data, were reported by means or median, with standard deviation (SD) and interquartile range (IQR), respectively. We are reporting the baseline characteristics of these individuals.

Results: Fifty-eight individuals were included; 91.4% were female. The mean age was 40.9 years (SD: 14.1). RP was biophasic in 63.6% of the patients, with a median of 30 episodes per month (IQR: 8–30). In 41 subjects (available data), antinuclear antibodies were positive; the most common patterns were: speckled (41.5%) and centromere (26.8%). The median of erythrocytosis rate (ESR) was 9 (IQR 4–13). Ten individuals (19.2%) were diagnosed with SSc in the first NVC: Seven patients with limited SSc, two with MCTD, and one with diffuse SSc. The patterns observed in the individuals with SSc were: early (n = 3), active (n = 3), late (n = 2), and minor and unspecific abnormalities in subjects with MCTD (n = 1 each). The most frequent NVC alterations in subjects with SAD were: megacapillaries (n = 10), microhemorrhages (n = 10), avascular zones (n = 8), neovascularization (n = 6), and capilar disorganization (n = 6). In these subjects, the mean capillary diameter was 76.7 ± 33.9 mm; the median of capillary number per mm was 7 (IQR: 6–8).

Conclusions: The frequency of systemic autoimmune disease was similar to the published reports in the literature. We highlight the following aspects: 1) The normal erythrocytosis rate in subjects with a rheumatologic diagnosis, a particular finding when compared to previous data; 2) The importance of subjects with a specific diagnosis in the first NVC: capillaroscopy; one possible explanation could be a undiagnosed disorder; this fact could be possibly demonstrated by the large capillary diameter found.

References:

Acknowledgements: Clinica Universitaria Bolivariana. Universidad Pontificia Bolivariana.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4075
group of patients with and without NPS were 5.4±2.0, 3.4±2.1; respectively (P<0.001). Pain was most frequently seen in wrist-hand (50.6%) and ankle-foot (43.4%) regions; albite, NPS rates were highest in face (94.4%), lower leg (87.5%) and gluteal (78.6%) regions. SF-36 scores were lower in patients with NPS than the patients without NPS but the difference has not reached to a statistically significant level (P=0.05). The most associated factors with NPS were Medsger Disease Severity Score for muscle and drug consumption of the patient's quality of life. Extensive studies are necessary to confirm and improve our data into clinical practice.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5456

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**SAT0357**  
**FEATURES ASSOCIATED WITH MODERATE TO HIGH RISK OF MALNUTRITION IN A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS**

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1Rheumatology; 2Nutrition, IARI; 3Rheumatology, Military Hospital; 4Rheumatology, Lanari Institute; 5Rheumatology, Central Hospital of San Isidro; 6Rheumatology, Diagnostic system-CM; 7Rheumatology, Ramos Mejia Hospital, Buenos Aires; 8Rheumatology, HIGA, la plata; 9Rheumatology, HIGA, Mar del plata, Argentina

**Background:** It is estimated that about 28% of Systemic Sclerosis (SSc) patients have moderate to high risk of malnutrition.

**Objectives:** To evaluate differences between SS patients with moderate to high risk of malnutrition and those with low risk.

**Methods:** Cross-sectional, observational, multicentric study. We included patients with SS according to ACR-EULAR 2013 classification criteria. Patients were classified in groups depending on whether they were in low or moderate/high risk of malnutrition, according to the screening method for detection of adult malnutrition (MUST). Were evaluated: disease duration, disease subtype (limited or diffuse), presence of microstomia, xerostomia, active or past digital ulcers, amputations, arthritis, Rodnan Score, gastroesophageal and bowel involvement, anxiety and depression, and hands functionality by Duruöz Index. Continuous variables were described as median (IQR) or mean (SD) and percentages for categorical variables. Mann Whitney or t-test was used for continuous variables, and Fisher exact test or chi-square for categorical variables. A p<0.05 was considered significant. A multivariate analysis was made taking MUST as a dependent variable.

**Results:** 116 patients were included. Thirty percent were at moderate to high risk of malnutrition. These patients experienced significantly higher frequency of diffuse SSc (49% vs 21%, p<0.003), bowel involvement (49% vs 27%, p=0.02), gastroesophageal involvement (74% vs 48%, p=0.009), higher cutaneous involvement (median 12 vs 6, p=0.01, microstomia (40% vs 15%, p=0.003), worst hand functionality (median 11 vs 3, p=0.02), and moderate-severe depression (37% vs 16%, p=0.012). Also, men experienced a higher moderate-high risk of malnutrition (20% vs 6%, p=0.02). In the multivariate analysis, the male sex (OR 4.55, 95% CI 1.11–20, p=0.03), the Rodnan score >9 (OR 3.13, 95% CI, 95% CI, p=0.01), and gastroesophageal involvement (OR 2.87, 95% CI 1.07–7.73, p=0.03), were independently and statistically significant.

**Conclusions:** These results highlight the importance of assessing the nutritional status of our SS patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6535

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**SAT0358**  
**DECREASED BODY FAT, LEAN BODY MASS AND BONE MINERAL DENSITY IN PATIENTS WITH SYSTEMIC SCLEROSIS ARE ASSOCIATED WITH DISEASE ACTIVITY AND PHYSICAL ACTIVITY**

S. Oreska 1, M. Spiritovic 1,2, P. Ccesa 1, M. Ccesa 2, K. Storkanov 1, K. Kubonov 1, M. Klein 1, L. Vernerova 1, O. Ruzickova 1, H. Mann 1, K. Pavelka 1, L. Senoti 1, J. Vencovsky 1, R. Becvar 1, M. Tomcik 1, 2, 3

1Department of Rheumatology, 1Medical Faculty, Charles University, Institute of Rheumatology, 2Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic

**Background:** Systemic sclerosis (SSc) is characterized by fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal involvement, which limit mobility/self-sufficiency of patients, and can have a negative impact on body composition.

**Objectives:** To assess body composition and physical activity of SSc patients and healthy controls (HC).

**Methods:** 59 patients with SSc (50 females, 9 males; mean age 52.1; disease duration 6.7 years; limited cutaneous (lcSSc,36)/diffuse cutaneous (dcSSc,23) and 36 age-/sex-matched HC (30 females, 6 males, mean age 51.4) without rheumatic/tumor diseases or manifest cardiovascular event were included. SSc patients fulfilled EULAR/ACR 2013 criteria. Anthropometric parameters and body composition were assessed (by densitometry-IDXA Lunar, and by bioelectric impedance-BIA-2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Disease activity was evaluated by EUSTAR SSc activity score. Data are presented as means±SD.

**Results:** Compared to HC, patients with SSc had significantly lower body-mass index (BMI: 26.4±3.3 vs. 22.4±4.3 kg/m², p<0.0001) and body fat % assessed by both IDXA (BF%: 37.2±6.6 vs. 32.6±8.2%, p=0.0014) and BIA (BF%: 31.3±6.4 vs. 34.8±6.8%, p=0.0014). These results highlight the importance of assessing the nutritional status of our SS patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2017
THE COURSE OF MOUTH OPENING AND ITS RELATIONSHIP TO DISEASE CHARACTERISTICS, GLOBAL FUNCTIONING, HEALTH-RELATED QUALITY OF LIFE AND MOUTH HANDICAP IN PATIENTS WITH SYSTEMIC SCLEROSIS


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Background: Systemic sclerosis (SSc) is a fibrotic disease which can lead to reduced maximal mouth opening (MMO). Previous cross-sectional research showed that reduced MMO in SSc correlated with higher disease severity and lower oral quality of life. Interpretation of interventions that possibly influence MMO is difficult, as the natural history of MMO in SSc is not well described.

Objectives: To evaluate in SSc 1) the course of MMO 2) disease characteristics predictive for decreasing MMO and 3) the relationship between the course of MMO and global functioning, health-related quality of life (HRQoL) and mouth handicap.

Methods: SSc patients from the Leiden Combined Care In Systemic Sclerosis (CCIS) cohort, Leiden University Medical Center were included if at least one annual clinical assessment was available. Annual clinical assessment includes MMO measurement, global functioning (HAQ), HRQoL (Short Form-36; SF-36), mouth handicap (Mouth Handicap in Systemic Sclerosis scale; MHISS). We assessed mean MMO, prevalence of microstomia (MMO<30.0 mm) and decreasing MMO (decline >5.00 mm/year) over time. Predictors for decreasing MMO were assessed by a linear mixed model (LMM), including baseline clinical parameters HRQoL, mouth function, quality of life, skin, heart, gastrointestinal, lung, renal, musculoskeletal). Additionally, MMO over time was correlated with baseline HAQ, SF-36 and MHISS in separate LMMs adjusted for gender, Body Mass Index, age and disease characteristics correlated significantly (p<0.05) with the course of MMO.

Results: 382 patients were included with mean age 54±14 years, 83% female and 25% diffuse cutaneous SSc. Mean MMO during 6 years of follow-up ranged from 39.4 to 42.5 mm. The annual mean percentage of patients with microstomia was 9%, range 6 to 12% (Figure 1a). A decrease in MMO between two consecutive annual measurements was observed in 17% of patients, mean 12% (Figure 1b). More extended cutaneous involvement, peripheral vasculopathy, pulmonary and gastrointestinal involvement at baseline were predictive for decreasing MMO over time (Table 1). Baseline HAQ (β=-1.6, 95% CI=-2.7 to -0.6), SF-36 physical component (β=0.1, 95% CI=0.0 to 0.1) and MHISS (β=-0.2, 95% CI=-0.2 to -0.1) correlated with longitudinal MMO.

Conclusions: Over time, MMO is relatively stable in the majority of SSc patients. Microstomia is seen in 9% and important decrease of MMO in 12% is associated with more severe organ involvement. Even though this concerns only a small subgroup of SSc patients, a significant association with global functioning and HRQoL was demonstrated, underlining the need for treatment strategies improving MMO.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4873

Table 1. Multivariate mixed model to determine the association between Maximal Mouth Opening (MMO) and baseline disease characteristics in SSc patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>p-value</th>
<th>Lower limit</th>
<th>Upper limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non cutaneous SSc (3)</td>
<td>ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited SSc (2)</td>
<td>-2.2</td>
<td>0.036</td>
<td>-4.2</td>
<td>-0.2</td>
</tr>
<tr>
<td>Diffuse SSc (3)</td>
<td>-4.1</td>
<td>0.004</td>
<td>-6.9</td>
<td>-1.4</td>
</tr>
<tr>
<td>Gastrointestinal vasculopathy</td>
<td>-2.6</td>
<td>0.001</td>
<td>-4.1</td>
<td>-1.1</td>
</tr>
<tr>
<td>Pulmonary vasculopathy</td>
<td>-1.8</td>
<td>0.032</td>
<td>-3.4</td>
<td>-0.2</td>
</tr>
<tr>
<td>Peripheral vasculopathy</td>
<td>-2.3</td>
<td>0.003</td>
<td>-3.8</td>
<td>-0.8</td>
</tr>
</tbody>
</table>

Figure 1: Mean Maximal Mouth Opening (MMO), percentage of microstomia and change in MMO over time in SSc patients

1b). More extended cutaneous involvement, peripheral vasculopathy, pulmonary and gastrointestinal involvement at baseline were predictive for decreasing MMO over time (Table 1). Baseline HAQ (β=-1.6, 95% CI=-2.7 to -0.6), SF-36 physical component (β=0.1, 95% CI=0.0 to 0.1) and MHISS (β=-0.2, 95% CI=-0.2 to -0.1) correlated with longitudinal MMO.

Conclusions: Over time, MMO is relatively stable in the majority of SSc patients. Microstomia is seen in 9% and important decrease of MMO in 12% is associated with more severe organ involvement. Even though this concerns only a small subgroup of SSc patients, a significant association with global functioning and HRQoL was demonstrated, underlining the need for treatment strategies improving MMO.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6245

SAT0360 MYOSITIS-SPECIFIC AND MYOSITIS-ASSOCIATED AUTOANTIBODIES IN PATIENTS WITH DERMATOMYOSITIS / POLYMYSITIDIS: COMPARISON BETWEEN LINE BLOT AND ENZYME-IMMUNOASSAY ASSAYS

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Background: MESCUP™ test (enzyme-immunoassay assays; TIF1γ, MDA5, Jo-1, EJ, PL-7, PL-12, and KS; MBL) (MESA) is used for a diagnosis of idiopathic inflammatory myopathies (IMMs) in Japan. On the other hand, EUROLINE myositis Profile 3 (line blot; EUROMMUN) (EURO) can analyze plural Myositis-specific autoantibodies (MSA) and that of EURO haven’t be disclosed.

Methods: We enrolled 58 patients diagnosed PM/DM in our facility. Polymyositis (PM) and dermatomyositis (DM) were diagnosed according to Bohan and Peter’s criteria. Of the MAA and MSA were analyzed using MESA and EURO. In case of MESA (+), MSA (anti-Jo1, anti-PL7, anti-PL12, anti-KS) were identified by specific ELISA. When those results were different, we analyzed by immunoprecipitation. And we analyzed the association between the line autoantibody and clinical features. Results: MSA and MAA were detected in 43/58 (74%) (anti-PL7: 12, anti-Jo1: 7, anti-EJ: 3, anti-PL12: 1, anti-OJ: 0, anti-Ro52: 27, anti-Pm-Scl70: 7, anti-Ku: 6, anti-Pm-Scl100: 1) by EURO. On the other hand, MAA and MSA were detected in 30/58 (52%) (anti-PL7: 9, anti-Jo1: 7, anti-EJ: 4, TIF1γ: 4, MDA5: 3, U1RNP: 3) by MESA. Five patients were MESA (+) and EURO (-). In the case of ARS positive patient, Two of EURO (+) patients was positive in MESA, respectively Jo1 and EJ. Three of MESA (-) patients was positive in EURO. Although MESA(+) and EURO(+) patients had plural MSA and MAA (PL7+Jo1, PL7+PL12, PL7+Ku), MAA and MSA weren’t detected by immunoprecipitation in MESA(-) and EURO(-) patients. Two of patients that detected plural MSA or MAA had rapid progressive ILD.

(association between clinical manifestations and MSA, MAA) All patients with anti-ARS (anti-Jo1, anti-PL7, anti-PL12 and anti-EJ) had ILD. In addition, anti-ARS were associated with arthritis and mechanic’s hands. Anti-MI-2 positive patients didn’t have ILD. Patients detected anti-Pm-Scl75, anti-Pm-Scl100, anti-Ku were almost overlap syndrome. All of Anti-SPR positive patients was PM.

Conclusions: EURO is a convenient and reliable method useful for detection of MAA and MSA. It was suggested the patients of plural antibodies were detected by EURO have unique clinical course in others.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4762
Table 1. Associations between scleroderma esophagus and various SSc manifestations

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Scleroderma esophagus</th>
<th>No scleroderma esophagus</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>(n=32)</td>
<td>(n=22)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>52 (51, 11.9)</td>
<td>52 (51.1, 9)</td>
<td>0.362</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>28 (87.5)</td>
<td>21 (94.8)</td>
<td></td>
</tr>
<tr>
<td>Diffuse SSc (n, %)</td>
<td>12 (55.5)</td>
<td>14 (43.8)</td>
<td>0.646</td>
</tr>
<tr>
<td>Pulmonary fibrosis (n, %)</td>
<td>25 (78.1)</td>
<td>15 (68.1)</td>
<td>0.750</td>
</tr>
<tr>
<td>Cutaneous ulcers (n, %)</td>
<td>19 (59.4)</td>
<td>12 (54.5)</td>
<td>0.854</td>
</tr>
<tr>
<td>Anti-Scl-70 (%, n)</td>
<td>23 (71.9)</td>
<td>12 (54.5)</td>
<td>0.540</td>
</tr>
<tr>
<td>CT cororal diameters ≥ 9 cm (n, %)</td>
<td>10 (76.9)</td>
<td>7 (77.8)</td>
<td>0.045</td>
</tr>
<tr>
<td>Presence of symptoms (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– dysphagia</td>
<td>18 (56.3)</td>
<td>13 (39.1)</td>
<td>0.914</td>
</tr>
<tr>
<td>– heartburn</td>
<td>25 (78.1)</td>
<td>21 (95.4)</td>
<td>0.620</td>
</tr>
<tr>
<td>– regurgitation</td>
<td>28 (87.5)</td>
<td>19 (86.4)</td>
<td>0.126</td>
</tr>
<tr>
<td>– chest pain</td>
<td>13 (56.3)</td>
<td>7 (31.8)</td>
<td>0.653</td>
</tr>
</tbody>
</table>

Data in 26 SSc patients (13 with and 13 without esophageal symptoms).

Conclusions: Scleroderma esophagus diagnosed by HRM was present in less than 2/3 of symptomatic patients with SSc and associated only with esophageal dilation (>—5mm) in CT. Although further studies are needed, esophageal dilation on chest CT may be a non-invasive alternative for evaluation of SSc patients with esophageal symptoms.

Disclosure of Interest: None declared


SAT0362

RISK FACTORS AND OUTCOME OF THAI PATIENTS WITH SCLERODERMA RENAL CRISIS (SRC): A DISEASE DURATION-MATCHED CASE CONTROL STUDY

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Background: Data regarding the prevalence, risk factors and outcome of scleroderma renal crisis (SRC) in Asian patients with systemic sclerosis (SSc) are limited.

Objectives: To determine the prevalence, risk factors and outcome of SRC in Thai SSc patients.

Methods: Medical records of all SSc patients, fulfilling the 1980 American College of Rheumatology classification criteria for SSc, seen at the Division of Rheumatology, Maharaj Nakorn Chiang Mai Hospital, Thailand, from January 1990 and December 2015 were retrospectively reviewed. Patients younger than 18 years old or overlapping with rheumatoid arthritis, systemic lupus erythematosus or mixed connective tissue disease were excluded. Cases of SRC were identified based on the international Scleroderma Renal Crisis Study criteria 1. Controls were selected from consecutive SSc patients without SRC from our database that was ranked closest to the cases based on esophageal dilation and matched for disease duration from the first non-Raynaud’s phenomenon, by ±1 year. The ratio for SRC patients to control patients was 1:4.

Results: Of 608 SSc patients seen during the study period, 19 SRC were identified resulting of the SRC prevalence of 3.13% and there were 76 matched controls. Of the 19 cases, mean±SD age and median (IQR1, 3) disease duration was 56.2±13.8 years and 9 (5.0, 16.0) months, respectively. Seventeen patients (89.5%) had dSSc. There were 12 (63.2%) patients with hypertensive renal crisis (HRC) and 7 (36.8%) patients with normotensive renal crisis (NRC). Univariate conditional logistic regression analyses showed that current myositis (OR2.01, 95% CI 1.02 – 3.98, p=0.049), WBC≥10,000 cell/mm³ (OR2.69, 95% CI 0.99 – 7.26, p=0.050), serum albumin <3.0 mg/dl (OR11.08, 95% CI 3.02 – 40.6, p=0.001), and current prednisolone used≥15 mg/day (OR19.36, 95% CI 2.29 – 163.6, p=0.007) were associated with SRC. Digital gangrene tended to show an association with SRC in the univariate analysis (OR8.00, 95% CI 0.72 – 88.2, p=0.090). Variables with p<0.15 in univariate conditional logistic regression analysis were included in the multivariate conditional logistic regression analysis. When multivariate conditional logistic regression analysis was adjusted, digital gangrene (adjusted odd ratio [AOR]31.41, 95% CI 1.16 – 852.23, p=0.041), current prednisolone use≥15 mg/day (AOR31.22, 95% CI 1.59 – 613.85, p=0.024), serum albumin <3 mg/dl (AOR9.97, 95% CI 1.49 – 42.56, p=0.015) and cardiac involve (AOR6.62, 95% CI 0.18 – 40.63, p=0.041) were confirmed to be independent risk factors for SRC. During a median (IQR 1, 3) follow-up of 1 (0, 2) months, 15 (78.9%) patients required hemodialysis, including 9 of 12 (75.0%) patients with SRC and 6 of 7 (85.7%) with NRC. Twelve (63.2%) patients received ACEI, including 9 of 12 (75.0%) patients with SRC and 3 of 7 (42.9%) patients with NRC. Ten (52.6%) patients died, including 5 of 12 patients (41.7%) with SRC and 5 of 7 (71.4%) patients with NRC. Current myositis was an uncommon complication in Thai patients with SSc, but associated with high mortality. Digital gangrene, current prednisolone used≥15 mg/day, serum albumin<3 mg/dl and cardiac involvement were independent risk factors of SRC.


Disclosure of Interest: None declared

sclerosis (SSc) and it substantially contributes to prominent features of the disease such as digital ulcers (DUs). History of DUs (HDUs) has been shown to correlate with disease severity, new cardiovascular events, new DUs and overall poor prognosis [1]. Microvascular abnormalities as assessed by nailfold videocapillaroscopy (NVC) and power Doppler ultrasound (PDUS) have been demonstrated to be predictive of new DUs occurrence [2,3].

**Objectives:** To study the severity of microvascular involvement at the 3rd and 4th finger of the dominant hand in patients with SSc with or without HDUs as assessed by NVC and 22-MHz PDUS.

**Methods:** 100 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 XVG by means of linear array transducer (10–22 MHz). Power Doppler settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PRF 75 Hz). PDUS measurements included sagittal scan of nailbed and fingertip and capillarity were not significantly associated with the presence of HU. NVC and capillarity density were significantly different in the two groups as shown in the table below:

<table>
<thead>
<tr>
<th>Presence of HDUs</th>
<th>Absence of HDUs</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillarity density</td>
<td>3.023</td>
<td>3.884</td>
</tr>
<tr>
<td>RI</td>
<td>0.740</td>
<td>0.792</td>
</tr>
</tbody>
</table>

**Conclusions:** A significant lower RI of ulnar and radial proper digital arteries reported in patient with HDUs is novel. By contrast PDUS grading of nailfold and fingertip were not significantly different in patients with or without HDUs. The finding of a significant lower capillary number assessed by NVC in patients with HDUs is consistent with previous results [2]. Adequately longitudinal studies exploring the predictive value of PDUS parameters are required to fully ascertain its role in SSc.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3844

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**SAT0365 MUSCULOSKELETAL US AND MRI FINDINGS IN JUVENILE SCLERODERMA**

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**Background:** Musculoskeletal (MS) involvement and clinically evident arthritis occurs in up to 85% of patients with Juvenile Systemic or localized Scleroderma (JSc). It may be the first manifestation preceding even the onset of Raynaud or skin manifestations; patients presenting with arthritis, tenosynovitis or enthesis may suffer from Sc. On the other hand clinical examination often underestimates MS involvement in JSc. US and MRI can help distinguish arthritis with effusion from tendinosis, tendon-sheath synovitis and muscular fascia thickening and enhancement (black arrows), and contractures (thin white arrow) very characteristic of scleroderma, helped identify sclerodermatous musculoskeletal involvement in the absence of skin induration. Focal bone marrow edema depicted as high signal intensity in fluid sensitive sequences (curved arrow) was found in 2 cases; 1 with generalized morphea without apparent overlying skin sclerodermatous lesion, 1 with linear scleroderma with atrophic lesions in all overlying structures.

**Objectives:**

1. To describe the spectrum of MRI and US features in juvenile scleroderma with MS involvement.
2. To provide insight into disease extent and to allow for disease monitoring.
3. To emphasize the role of MRI and US in the diagnostic work-up and the management of juvenile scleroderma.

**Methods:**

1. We describe MRI and color Doppler MSUS findings of clinically affected children with arthritis and/or JSc. MSUS is a feasible and non-invasive method for follow-up of patients in whom disease activity is of interest.
2. MRI and US were performed with a 1.5 T Siemens Avanto scanner (Siemens AG, Erlangen, Germany) and a 28–8 MHz linear transducer with a 13–5 MHz dedicated probe (Aloka SSD–5000, Tokyo, Japan). MSUS and MRI in Juvenile scleroderma led to earlier definition of the diagnosis and assisted the evaluation of disease extension.

**Conclusions:** Musculoskeletal imaging features of juvenile scleroderma involving the skin, fascia, musculature and bones reflect pathomorphologic changes of this rare disorder and enable a complete assessment of the disease extent, including depth of infiltration and disease activity. In the described cases, implementation of MSUS and MRI in Juvenile scleroderma led to earlier definition of the diagnosis and assisted the evaluation of disease progression.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5393

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**SAT0366 SMOKING BEHAVIOUR AND THE PROGRESSION OF ORGAN MANIFESTATIONS IN SYSTEMIC SCLEROSIS: A LONGITUDINAL EUROPEAN SCLERODERMA TRIALS AND RESEARCH GROUP STUDY**

V.K. Jaeger, G. Valentini, E. Hachulla, L. Czirjak, E. Siegert, D. Diester, L.M. Bambara, E. Rosato, Y. Allainore, M. Matsuuchi, P. Airo, U. Walker on behalf of EUSTAR co-authors. 1University Hospital Basel, Basel, Switzerland; 2Second University of Naples, Naples, Italy; 3Université de Lille, Lille, France; 4University of Pécs, Pécs, Hungary; 5University Hospital Charité, Berlin, Germany; 6University Hospital Zurich, Zurich, Switzerland; 7University of Verona, Verona; 8Sapienza University of Rome, Rome, Italy; 9Paris Descartes University, Paris, France; 10University of Florence, Florence, Italy; 11Spedali Civili, Brescia, Italy

**Background:** Systemic sclerosis (SSc) is a rare, multisystem autoimmune disorder. It is characterised by generalized microangiopathy, in which hypoxia and oxidative stress have been implicated in its pathogenesis. Tobacco inhalation increases free radicals and strongly promotes vascular damage. So far, data available with regards to a role of tobacco exposure with SSc severity and progression are scarce.

**Objectives:** We aimed to assess the effects of smoking on the speed of worsening of organ manifestations, namely lung involvement (forced vital capacity, FVC; forced expiratory volume, FEV1/FVC ratio; diffusing capacity for carbon monoxide corrected for alveolar volume, DLCO/VA), skin involvement (modified Rodnan skin score; mRSS), and digital ulcers (DU) in the European scleroderma trials and research (EUSTAR) database.

**Methods:**

1. We included 9,885 SSc patients from the EUSTAR cohort with a follow-up visit 12±4 months after their baseline visit and available data on their smoking habits were included.
2. The associations of smoking behaviour (never smokers vs ex-smokers vs current smokers) with the disease manifestations at follow up were assessed after adjusting for potentially confounding covariates using multivariable linear or logistic regression analyses.

**Missing data were imputed using multiple imputations.**

**Results:** Of the 3,023 patients included (mean age 57 years, SD 13; 85% female), 66% stated that they never smoked, 23% were ex-smokers and 11% were current smokers. On average, ex-smokers had smoked for 19.5 years (SD 12) while current smokers smoked for 29.1 years (SD 13). Ex-smokers had smoked on average 17.3 pack-years (SD 20) and current smokers 29.3 pack-years (SD 36). The mean time since smoking cessation in ex-smokers was 15.8 years (SD 12). Smoking was associated with decreased FEV1/FVC ratio (p<0.001), increased mRSS (β=-2,8, p=0.001). Similarly, the DLCO/VA diminished faster in current smoking SSc patients than in never smokers (β=-2,8, p=0.001).
SAT0367 | CAPILLAROSCOPY PATTERNS AMONG SYSTEMIC SCLEROSIS PATIENTS WITH GASTROINTESTINAL INVOLVEMENT AND MALNUTRITION EVALUATED BY SELF-REPORTED QUESTIONNAIRES
Y. Yalcinkaya, Z. Erturk, A.U. Ünal, S. Kaymaz, P. Atagündüz, H. Direskeneli, N. İnanç. Department of Internal Medicine, Division of Rheumatology, Marmara University, School of Medicine, Istanbul, Turkey

Background: Gastrointestinal system (GI) is commonly involved in systemic sclerosis (SSc) beginning after early stages of disease.

Objectives: We aimed to investigate capillaroscopic findings among the SSc patients with GI involvement and malnutrition.

Methods: GI involvement was evaluated by UCLA SCTG CIT 2.0 questionnaire (Khanna D.) (7 multi-item; reflux, distension, soilage, diarrhea, social functioning, emotional wellbeing and constipation) in SSc patients ACR/EULAR classification criteria (2013). To report the nutrition status of the patients “malnutrition universal screening tool (MUST)” (sum of the scores of body mass index, weight loss in last 3–6 months and acute disease effect) scores were calculated. Simultaneously, nail fold video-capillaroscopy (NVC) was performed in all patients to determine ealy, active late scleroderma patterns (Cutolo et al.).

Results: In 58 SSc patients (51 female); the mean age, mean duration of Raynaud’s, non-Raynaud symptom (year) and follow-up (month) were 46±13, 54±50, 10±9 and 7±7, respectively. Limited cutaneous form, positive ANA and anti-Scl70, telangiectases, dysphagia, digital ulcers, lung disease were found in 40 (71%), 10 (17%), 45 (78%), 39 (67%), 33 (57%), 23 (40%) in patients, respectively. Of the NVC patterns, early was found in 16 (28%), active was in 11 (19%), late was in 28 (48%) and normal in 3 (5%). Scores of disease activity, severity and GI were shown to be higher in patients with late pattern. NVC might be useful to predict the severity of GI and malnutrition and allow to direct the patients to required procedures earlier.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2729

Table 1. The scores of disease activity and severity and UCLA SCTC GIT 2.0 in SSc patients

<table>
<thead>
<tr>
<th>NVC (early)</th>
<th>NVC (active)</th>
<th>NVC (late)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.31±0.5</td>
<td>3.69±0.6</td>
<td>3.06±0.8</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>0.06±0.01</td>
<td>0.09±0.02</td>
<td>0.04±0.02</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>4.12±0.4</td>
<td>4.63±0.6</td>
<td>6.52±0.6</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>0.06±0.01</td>
<td>0.07±0.02</td>
<td>0.03±0.03</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>0.40±0.2</td>
<td>0.75±0.3</td>
<td>0.55±0.5</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>0.01±0.005</td>
<td>0.01±0.005</td>
<td>0.00±0.005</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>0.01±0.005</td>
<td>0.01±0.005</td>
<td>0.00±0.005</td>
<td>P&lt;0.001*</td>
</tr>
</tbody>
</table>

SAT0368 | THE PREVALENCE OF OSTEOMYELITIS IN INFECTED DIGITAL ULCERS IN SYSTEMIC SCLEROSIS PATIENTS
Y. Braun-Moscovici 1, Z. Keidar 2, M. Braun 3, D. Markovits 1, K. Toledano 1, V. Tavor 1, F. Sazz Bian 1, A. Roini 1, K. Dolnikov 1, A. Balbir-Gurman 1
1Rheumatology Department, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion; 2Department of Nuclear Medicine, Rambam Health Care Campus Rappaport Faculty of Medicine Technion, Haifa; 3Liver Institute, Belinson Hospital Petach-Tikva, Sacker School of Medicine, Tel Aviv University, Petach-Tikva, Israel

Background: Skin ulcers, particularly digital ulcers occur in at least 50% of systemic sclerosis (SSc) patients (pts) and cause significant morbidity. They are often complicated by local infection which can lead to contiguous osteomyelitis.

Objectives: Our aims were to evaluate the accuracy of clinical diagnosis of osteomyelitis and to assess the sensitivity and specificity of clinical parameters that may improve the precision of the clinical diagnosis.

Methods: We retrospectively analyzed the clinical data of consecutive SSc patients hospitalized for skin ulcers in a tertiary referral center for SSc. Our cohort is part of the EUSTAR cohort. The patients were evaluated by rheumatologists skilled in managing SSc skin lesions. All the patients with infected ulcers and suspected for contiguous involvement of underlying bone had bone scans. All the positive scans were followed with 99m-Technetium-Tc-labeled white blood cells (WBC) scintigraphy, in order to differentiate true osteomyelitis fromacro-osteodystasis or soft tissue infection. We collected demographic data, disease type, extent and severity, routine lab data (Glias, CRP, creat, L. Nat), laboratory protein, CRP, erythrocyte sedimentation rate (ESR), alkaline phosphatase (ALKP), albumin) and wound culture. Each hospitalization was considered a separate event. Statistical analysis: descriptive, student’s T test, Mann-Whitney test.

Results: During the years 2003–2016, 220 SSc pts with skin/digital ulcers were hospitalized in our department for ilomedin treatment (993 hospitalizations). Most of the pts were hospitalized several times due to recurrent ulcers. Ulcer scan was performed in 39 pts (59 admissions) with infected ulcers (32 females, mean (SD) age 48 (15), disease duration 9 (6.6) years, 25 with diffuse SSc, skin suspected cases, WBC scans confirmed osteomyelitis in 18 pts in 23 occasions. Osteomyelitis occurred twice in 5 pts in different locations. No statistically significant differences were found between the group with positive scans and the group with negative scans regarding demographic, clinical and lab data. 9 pts had 25 admissions for infected ulcers, osteomyelitis was confirmed in 75% or the patients with positive Tc bone scans.

Conclusions: The prevalence of osteomyelitis among our SSc pts admitted for digital ulcers was 10%. The prevalence of confirmed osteomyelitis by scintigraphy in clinically highly suspected cases was 39%. Even when contiguous osteomyelitis was suspected by highly skilled rheumatologists, bone scan ruled out the diagnosis in 61% of the cases, thus avoiding unnecessary prolonged antibiotic therapy. No clinical predictors to rule osteomyelitis in or out could be identified.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6474

SAT0369 | HETEROGENEITY IN THE UNDERLYING PATHOGENESIS IN PATIENTS WITH CONNECTIVE TISSUE DISEASE-ASSOCIATED BORDERLINE MEAN PULMONARY ARTERIAL PRESSURE AND ITS DISTINCTIVE HEMODYNAMIC CHARACTERISTICS FROM THOSE WITH NORMAL PULMONARY ARTERIAL PRESSURE
Y. Yamasaki 1, Y. Asari 1, K. Tsuchida 1, K. Suzuki 2, Y.J. Akashi 2, T. Okazaki 2, S. Ozaki 3, H. Yamada 3, Y. Braun-Moscovici 1, Z. Keidar 2, M. Braun 3, D. Markovits 1, K. Toledano 1, V. Tavor 1, F. Sazz Bian 1, A. Roini 1, K. Dolnikov 1, A. Balbir-Gurman 1

Background: Borderline mean pulmonary artery pressure (PAP) (21–24 mmHg) may comprise a transition phase from normal pulmonary hemodynamic condition to pulmonary arterial hypertension (PAH), which is one of the fatal complications in connective tissue diseases (CTD) [1]. The accumulated evidence is not enough to conclude that treatment for PAH in this stage may be associated with improving clinical outcomes. On the other hand, CTD-associated PH is caused by various cardiopulmonary comorbidities. It is possible that borderline mean PAP, like overt PAH, is caused not only by pulmonary vasculopathy but also by cardiac and pulmonary complications [2].

Objectives: To clarify whether patients with borderline mean PAP associated with CTD have distinctive hemodynamic characteristics from those with normal mean PAP and its underlying pathogenesis is heterogeneous as those with manifest PAH.

Methods: We retrospectively investigated 76 CTD patients who underwent right heart catheterization from 2008 through 2016. Of the 76 patients, 25 (33%) and 16 (21%) had manifest PH and borderline mean PAP, respectively. The rest of the 35 patients had normal mean PAP. Systemic sclerosis was the most common
EVALUATIONS OF EXERTION DYSPNEA IN PATIENTS WITH BONE FRACTURE RISK ASSESSMENT IN PATIENTS WITH CLINICAL AND SEROLOGICAL ASSOCIATIONS OF Y. Nobuhara

Results: The values of tricuspid regurgitation pressure gradient (TRPG) were correlated with serum biomarkers in borderline patients with borderline mean PAP (31.1±7.8 mmHg) and normal mean PAP (28.3±6.9 mmHg) (P=0.1572) but its value became significantly higher in patients with borderline mean PAP (39.1±8.0 mmHg) than in those with normal mean PAP (32.8±7.4 mmHg) after exercise echocardiography (P=0.0391). Pulmonary arterial wedge pressure was significantly elevated in patients with borderline mean PAP (12.5±3.1 mmHg) compared with that in normal mean PAP (7±3 mmHg) (P=0.0001) and its value was comparable to those with overt PH, suggesting the heterogeneity on the cause of borderline mean PAP among CTD patients. The clinical course of 10 patients with borderline mean PAP was studied. Five were treated for precipi-capillaroscopic pattern and 2 for interstitial lung disease (ILD). Normalization of mean PAP was seen in 3/4 and 3/3 of the patients treated for precipi-capillaroscopic and postcapillary disease, respectively. Deterioration of TRPG was seen in one patient after receiving pulmonary vasodilators. One with severe ILD developed PH.

Conclusions: The pathogenesis of borderline mean PAP could be clearly distinguished from normal mean PAP, which was heterogeneous as that of manifest PH in CTD patients. Though the clinical course may be altered with appropriate therapeutic intervention, repeated assessment is needed.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3592

SAT0371 EVALUATION OF EXERTION DYSPNEA IN PATIENTS WITH CONNECTIVE TISSUE DISEASE (CTD) BY CPET (CARDIOPULMONARY EXERCISE TESTING) FOR EARLY DETECTING ASSOCIATED PULMONARY HYPERTENSION (PAH)

Y. Nebuhara, Y. Kamei, Y. Fujikawa, T. Nakazawa. Rheumatology, Osaka sakesei nakatsu hospital, Osaka, Japan

Background: Patients with CTD often complain of exertion dyspnea, due to lung diseases, heart diseases, musculoskeletal disorders and/or PAH. Although imaging and physiological tests could reveal pathophysiology, some of them remain unknown. Especially PAH is rarely diagnosed in WHO functional class I or II, because pulmonary vasculopathy (PV) cannot be detected until two-thirds of pulmonary blood vessels deteriorated,1 with cardiac ultrasonography (UCG) or right heart catheterization (RHC) at rest. Pathophysiological considerations suggest that the haemodynamic/mechanical impairment in APH may be observed during exercise before the disease becomes evident at rest.2,3 We evaluated exertion dyspnea of unknown origin to find early PAH with CPET.

Objectives: We determined the PAH in patients who complained of exertion dyspnea and tried to detect early PV.

Methods: From June 13th in 2015 to October 28th in 2016, we performed CPET and evaluated their clinical state in 28 patients, 17–80 years old (mean 26.1+18.8 years), 5 mixed connective tissue disease (MCTD), 15 SSC, 3 SLE, 2 Sjogren’s syndrome, 3 dermatomyositis. We undertook UCG, pulmonary function testing (PFT), 6-minutes walk test, and nailfold capillaroscopy by Cuto’s method.4

Results: Twenty cases presented decreased peak VO2. VE/VCO2 ratio, which represented increased ventilation-perfusion mismatch, elevated in 12 cases. 8 cases, with decreased peak VO2 but normal VE/VCO2, were regarded that muscle weakness mainly induced exertion dyspnea, and advised exercise. Twelve cases with decreased peak VO2 and elevated VE/VCO2 were estimated to have APH or/and interstitial lung disease (ILD). Seven of them underwent RHC and 1 case was classified as PAH, and another 1 case as postcapillary PHT. A 34 years MCTD woman without ILD showed an active capillaroscopic pattern, her peak VO2 decreased (13.9±7.8 ml/kg/min.) and nadir VE/VCO2 elevated (39). Although her mean PAP was normal, we suspected she had early PV and administered PDE5 inhibitor to her and her dyspnea had gone soon and CPET parameters improved. CPET was also useful for early detections of therapeutic gains in APH. A SSC woman, diagnosed as APH by RHC, was performed CPET only 9 days after administration of PDE5 inhibitor. Her peak VO2 decreased (13.3±16.4 ml/kg/min.) and nadir VE/VCO2 decreased (43.4 to 38.9) promptly. Thirteen patients showed an early capillaroscopic pattern, 7 an active pattern and 3 a late pattern. Median values of minimum VE/VCO2 ratio significantly differed (p<0.05) in the three capillaroscopic groups, being progressively worse from early to late capillaroscopic pattern.

Conclusions: CPET was useful for early diagnosis in every patient safely. Although more research is required, CPET may provide valuable information notably in patients with PAH.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3448

SAT0372 CLINICAL AND SEROLOGICAL ASSOCIATIONS OF ANTI-BICD2 AUTOANTIBODIES TO BICD2 AS A NOVEL MARKER FOR SYSTEMIC SCLEROSIS

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Background: Anti-nuclear antibodies (ANA), which are present in approximately 90% of systemic sclerosis (SSc) sera, play an important role in establishing the diagnosis and predicting prognosis of SSc. Recently, a novel autoantibody has been described in SSc patients targeting Cytoskeleton-Like Bicaudal D Protein Homolog 2 (BICD2).

Objectives: The aim of this study was to assess the prevalence and titers of anti-BICD2 antibodies in SSc and controls and to study the clinical associations of this new antibody.

Methods: A total of 502 samples from SSc patients enrolled in the Canadian Scleroderma Research Group (CSRG) cohort were included in this study. Clinical associations were assessed either as anti-BICD2 antibody positivity
with and without other autoantibodies present using 451 SSc patients with complete dataset. Autoantibodies to several scleroderma-related autoantibodies were detected using commercial or research use only kits (Inova Diagnostics, San Diego, USA). P-values below 0.05 were considered significant. 

**Results:** The sensitivity and specificity of anti-BICD2 antibodies were determined as 22.1% and 99.0%, respectively. Receiver operating characteristic (ROC) analysis showed an area under the curve of 0.79 (95% CI 0.75–0.84). The likelihood (LR) and odds ratios (OR) were 17.7 (LR+) and 0.8 (LR-) and 20.4 (OR). The prevalence of all these autoantibodies was equally distributed between limited diffuse form of SSc (22.8% and 24.0%). When SSc patients without the classification criteria markers anti-Scl-70, anti-Centromere and anti-RNA Pol III negative (n=184) were compared with controls, similar performance was obtained as seen classification criteria markers anti-Scl-70, anti-Centromere and anti-RNA Pol III (n=184) were compared with controls, similar performance was obtained as seen.

Several statistically relevant clinical associations were found for anti-BICD2 as summarized in table 2 below.

**Conclusions:** Our data confirm the presence of anti-BICD2 antibodies in SSc patients that may help to differentiate SSc from other systemic autoimmune rheumatic diseases and to stratify SSc patients into more defined subsets of the disease.


SAT0373 EVALUATION OF AMERICAN COLLEGE OF RHEUMATOLOGY PROVISIONAL COMPOSITE RESPONSE (CRiSS) INDEX IN THE FASCIINATE TRIAL

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**Background:** Treatment with tocilizumab (TCZ) in early systemic sclerosis (SSc; FaSScinate trial) resulted in consistent, but not statistically significant, improvements in skin sclerosis (mRSS) at wks 24 and 48. CRiSS index has been proposed as a composite index for trials in SSc2. CRiSS is a 2-step process that assigns a probability of improvement for each subject ranging from 0.0 [no improvement] to 1.0 [marked improvement]. Step 1 assesses clinically meaningful disease activity in cardio-pulmonary-renal involvement and assigns a probability of 0.0. For remaining subjects, 5 variables are used to calculate probability of improvement. These are: FVC%, mRSS, patient (PT GA) and physician globals (MD GA), and HAQ-DI.

**Objectives:** To assess the performance of CRiSS index in the FaSScinate trial.

**Methods:** In FaSScinate, pts <18 y with active SSc were randomized 1:1 to TCZ or placebo (PBO) for 48 wks. Step 1 CRiSS was captured using review of serious adverse event data. Non-parametric Wilcoxon test was used to assess significant differences between the CRiSS scores in both arms. Analyses were carried out for subjects who had complete data at baseline and 24 weeks and at baseline and 48 weeks.

**Results:** 87 pts (43 TCZ, 44 PBO) were enrolled. Baseline characteristics were similar between arms. 4 subjects in the PBO group and none in TCZ met the predefined definition of worsening in Step 1 and were given a score of 0. For remaining subjects, we calculated probability score for each subject. Using CRiSS as a continuous measure, the median score was statistically significant favoring TCZ at wk 48.

**Conclusions:** In this post-hoc analysis, CRiSS index was able to discriminate TCZ from PBO, supporting its validity in an independent cohort.


**Disclosure of Interest:** D. Khanna Grant/research support from: NIH/NIAMS, NIH/NIAD, BMS, Pfizer, Consultant for: Actelion, Bayer, BMS, Boehringer Ingelheim, Genentech/Roche, Sanofi-aventis, GSK, Corbus, Cytox, EMD Serono, V. Berrocal. None declared, C. Denton Consultant for: Actelion, Bayer, GSK, CSL Behring, Merck-Roche, Genentech-Roche, Inventiva, Sanofi-Aventis, Boehringer Ingelheim, A. Jaheris Shareholder of: Roche stock and options, Employee of: Genentech, H. Spotwood Employee of: Roche, C. Lin Employee of: Genentech, J. Siegel Employee of: Genentech, D. Furst Grant/research support from: Amgen, BMS, NIH, Novartis, Pfizer, Roche/Genentech, Consultant for: AbbVie, Amgen, BMS, Cytox, Novartis, Pfizer, Roche/Genentech, UCB

SAT0375 | METABOLOMICS OF SERA REVEALS POTENTIAL BIOMARKERS OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS THAT CORRELATE WITH PRO-FIBROTIC GENE EXPRESSION IN SKIN BIOPSIES
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Background: There is an unmet need for biomarkers in Systemic Sclerosis (SSc). Despite its shortcomings, the modiﬁed Rodnan skin score (mRSS) has remained the standard disease assessment tool for SSc. Expression of certain genes, cartilage oligomeric matrix protein (COMP), thrombospondin-1 (THS1), interleukin-1α (IL1α) and collagen 1 (COL1A1), and, more recently, Tenascin-C (TNSC) have been shown to correlate with skin ﬁbrosis. However, assessment of the expression of these genes requires a skin biopsy. Hence, we used an open-ended approach to identify a serum-based biomarker of SSc.

Objectives: To identify small molecules in serum that correlate with mRSS and proﬁbrotic genes that are upregulated in skin of SSc patients.

Methods: We obtained serum and skin biopsies from 25 consenting adult patients with SSc and serum from 25 age- and sex-similar controls. mRNA levels of ﬁve genes: COMP, THS1, IFI44, SIG1, and TNSC were estimated as fold-changes relative to glyceraldehyde 3-phosphate dehydrogenase (GAPDH). Glyceroldehyde 3-phosphate dehydrogenase (GAPDH), a housekeeping gene. H^1NMR (Nuclear Magnetic Resonance) based metabolomics studies were performed on the sera using standard protocols. Principal component analysis (PCoA) and Partial Least Squares Discriminant Analysis (PLSDA) were used to delineate metabolites that were different between patients and healthy controls. The signiﬁcance of associations (α) of the metabolites with mRSS and the fold-expression of the ﬁve pro-fibrotic genes were estimated.

Results: H^1NMR based metabolomics identiﬁed 126 peaks that were different between patients and controls. Out of these, the levels of glycine had the best correlation with pro-fibrotic gene expression (p=0.5, p<0.05 for IFI44; p=0.04, p<0.05 for SIG1).

Conclusions: Glycine was shown to have a signiﬁcant correlation with proﬁbrotic gene expression in serum samples from SSc patients, as well as with the mRSS score. This suggests that serum glycine levels may be useful as a potential biomarker for skin ﬁbrosis in SSc.

DOI: 10.1136/annrheumdis-2017-eular.2742

SAT0376 | ANTI-NT5C1A AUTOANTIBODIES ARE FREQUENT IN JUVENILE MYOSITIS AND ASSOCIATED WITH INCREASED ILLNESS SEVERITY
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Background: Autoantibodies (Abs) against 5'-nucleotidase, Cytosolic 1A (NT5C1A) have been portrayed as a potential diagnostic aide in distinguishing inclusion body myositis (IBM) and polymyositis (PM) in adults. However, 46% of dermatomyositis (DM) patients also have Abs to NT5C1A.

Objectives: The prevalence and clinical features of anti-NT5C1A Abs in juvenile-onset myositis (IIM) patients is unknown, so we sought to examine this in a large cohort.

Methods: We screened 384 juvenile IIM patients meeting probable or deﬁnite Bohan and Peter criteria for anti-NT5C1A Abs by immunoblotting for the full length NT5C1A protein in transfected and non-transfected lysates. Clinical characteristics and HLA typing were compared between juvenile IIM patients who were anti-NT5C1A positive (Ab+) and those who were anti-NT5C1A negative (Ab-).

Results: In this cohort, 29% (103) of juvenile DM, 15% (3) of juvenile PM, and 37% (15) of juvenile overlap myositis patients tested positive for anti-NT5C1A Abs. Compared with anti-NT5C1A Ab- patients, anti-NT5C1A Ab+ juvenile IIM patients showed a similar distribution of race, gender, and association with myositis-specific Abs. However, NT5C1A Ab was associated with anti-p155/140 Abs (p=0.05). The only observed clinical difference was an increased frequency of V- or shaw-sign rashes ever present (44% vs. 26%, p=0.002). Disease severity was increased in anti-NT5C1A Ab+ patients, based on more frequent hospitalizations (p<0.001), more medications used (p<0.001), and more treatment trials per year (p<0.001). Additionally, pulse steroids (p<0.001) and intravenous immunoglobulin therapy (p=0.008) were prescribed more frequently in anti-NT5C1A Ab+ than Ab- patients. The HLA alleles DRB1*07 (20% vs. 9%, p<0.05) and DQA1*0201 (21% vs. 7%, p<0.01) were present more frequently in anti-NT5C1A Ab- compared to Ab+ patients.

Conclusions: Anti-NT5C1A Abs are commonly present in juvenile DM and juvenile overlap myositis patients, and are present more frequently in patients with anti-p155/140 Abs, but are also seen in association with other myositis specific Abs. Consistent with data in adult IIM patients, anti-NT5C1A Abs have few distinguishing clinical features in juvenile myositis, but are associated with increased illness severity marked by increased hospitalizations and receipt of additional therapy.

from: The Myositis Association, I. Targoff Consultant for: Oklahoma Medical Research Foundation Clinical Immunology Laboratory regarding myositis autoantibody testing, F. Miller: None declared, L. Rider: None declared, A. Mammen: None declared
DOI: 10.1136/annrheumdis-2017-eular.6246

**SAT0377 RELIABILITY OF A NEW AUTOMATED SYSTEM FOR ABSOLUTE CAPILLARY NUMBER COUNTING (AUTOCAPI) ON SYSTEMIC SCLEROSIS NAILFOLD VIDEOCAPILLAROSCOPIC IMAGES**

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**Background:** Nailfold capillary density is a useful measure in systemic sclerosis (SSc) classification and evaluation. Its manual detection may be time-consuming, hampering its use in largescale investigations. We evaluated a new automated system to assess the absolute nailfold capillary number.

**Objectives:** To attest the instrumental reliability of automatic counting in SSc patients using nailfold video capillaroscopy (NVC) images.

**Methods:** 75 NVC random images, from SSc patients, were blindly analyzed by four raters (2 less and 2 more experienced; raters: 1,2,3,4) from two European centers. Each rater was asked to define the region of interest (ROI) on the NVC image in order to manually count the number of capillaries, according to the following instructions: upper bound placed on top of the longest capillary head and lower bound placed on half of the length of that longest capillary (figure 1); if the common branch of an abnormal shape (neangiogenesis) is in ROI it is counted as being one; if the common branch is out of ROI it is counted as separate capillaries; if the capillary is on the edge of the vertical line of ROI, it is only counted when the head of the capillary is half in ROI; if the capillary head is on the edge of lower bound, it is counted as soon as the “head” part is in the ROI; all “heads” in the ROI are counted (not only distal row). The dedicated automated system (AUTOCAPI-ds medica, IT) also counted the number of capillaries in the same ROI (figure 1). Reliability between the manual and automatic counting was investigated per rater through intraclass correlation coefficient (ICC) and reported with 95% confidence interval (CI). External validation was obtained by multi-rating tests and laboratory tests (antibody profile, RF, CRP, Creatine phosphokinase) and disease activity (by Valentini index) were done.

**Results:** By multiple logistic regression analysis taking into account all clinical and laboratory variable, we found that MRI bone marrow oedema of the hand was associated and probability for the occurrence of MRI bone marrow oedema was higher for the SSc pts with digital ulcers (OR=6.081;95%IP:1.295–28.550; p<0.05), HAQ<1.5 (OR=6.448; 95%IP:1.714–24.257; p<0.01) and active disease (OR=3.377; 95%IP:1.175–9.706; p<0.05).

**Disclosures of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.4522

**SAT0379 NAILFOLD CAPILLAROSCOPY FINDINGS IN PATIENTS WITH INFLAMMATORY MYOPATHY AND/OR SPECIFIC OR ASSOCIATED ANTIBODIES**

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**Background:** Nailfold videocapillaroscopy (NVC) is an easy, fast and non-aggressive tool, useful in the study of autoimmune diseases. The use of NVC in inflammatory myopathy (IM) is not clearly established.

**Objectives:** 1. To evaluate capillaroscopic findings in patients with IM and/or with presence of specific or associated antibodies with this pathology. 2. To analyze possible relationships with clinical characteristics of the patients.

**Methods:** Retrospective review of a cohort of patients with IM and/or with presence of specific or associated antibodies, followed in Rheumatology Unit of a University Hospital. Patients underwent a NVC at 200x, being evaluated for the presence of: loss of capillary density, enlarged and giant capillaries, ramified capillaries, haemorrhages, thrombosis, tortuous capillaries, avascular areas, disorganization of capillary architecture and subpapilar venous plexus. The following variables were also collected: sex, age, active smoking, muscle weakness, CK elevation at diagnosis, compatible muscle EMG and biopsy, skin findings, cardiac disease, dysphagia, lung disease, Raynaud’s phenomenon, cancer history and overlap syndromes. For the comparison of qualitative and/or quantitative variables Fisher’s exact Test or T-test was performed when necessary.

**Results:** Twenty patients were included at least one NVC (45% with 2), 65% female, with a mean age of 58 years ±11.6 were included. The characteristics of the patients are detailed in table 1.

- 65% of patients had some capillaroscopic alteration. The findings in NVC-1 and NVC-2 were: loss of capillary density 30% and 33%, tortuous capillaries 90% and 89%, enlarged capillaries 40% and 45.6%, giant capillaries 65% and 66.7% (giant 30% and 30%), ramifications 40% and 55.6%, disorganization 10% and 33%, haemorrhages 25% and 44%, thrombosis 20% and 0%, avascular areas 25% and 22%, visible venous plexus 40% and 55%.

**Disclosures of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.3191
density (p<0.02) and haemorrhages (p<0.01) in the initial NVC, as well as the presence of ramifications in the control NVC (p<0.05). It was observed that patients with normal capillary organization presented better value of FVC (p<0.01), TLC (p<0.01), and lower FEV1/FVC ratio (p<0.02), the latter finding also found in control NVC (p<0.03). As additional data, we found that patients with anti-Ku+ presented better values of FVC (p<0.04) and TLC (p<0.05), but although they all had normal capillary organization, the association of this antibody with NVC was not statistically significant. We also did not find a statistically significant relationship between the alterations in NVC and the presence of Raynaud’s phenomenon, the other clinical variables, cancer history and the presence of overlap syndromes.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>N</th>
<th>Age at diagnosis (years)</th>
<th>Time of evolution (years)</th>
<th>Active smoking</th>
<th>Muscle weakness</th>
<th>CX elevation at diagnosis</th>
<th>EMG findings compatible with IM</th>
<th>Muscle biopsy compatible with IM</th>
<th>Skin findings</th>
<th>Cardiac disease</th>
<th>Diabetic disease</th>
<th>Lung disease</th>
<th>Comorbid cancer</th>
<th>Raynaud’s phenomenon present</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
<td>55±11.7</td>
<td>2.9±1.8</td>
<td>5 (25%)</td>
<td>7 (35%)</td>
<td>8 (40%)</td>
<td>5/6 (83.3%)</td>
<td>7/8 (87.5%)</td>
<td>6 (30%)</td>
<td>1 (5%)</td>
<td>5 (25%)</td>
<td>7 (35%)</td>
<td>1 (5%)</td>
<td>11 (55%)</td>
</tr>
</tbody>
</table>

Conclusions: Patients with capillary disorganization in NVC showed worse values of FVC, TLC and FEV1/FVC. We found a statistically significant association between esophageal disease and haemorrhages, loss of capillary density and ramifications. Prospective studies with larger sample sizes are required to define the usefulness of NVC in the diagnosis, prognosis and follow-up of these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6730

SAT0380 | CLASSIFICATION, CATEGORISATION AND ESSENTIAL ITEMS FOR DIGITAL ULCER (DU) EVALUATION IN SYSTEMIC SCLEROSIS (SSC): A DESSCIPHER/EUSTAR SURVEY

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Conclusions: DU in episodic, recurrent and chronic.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6815

SAT0381 | CORRELATION BETWEEN THREE DIFFERENT METHODS TO ASSESS DERMAL THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS WITH DIFFERENT PATTERNS OF NAILFOLD MICROANGIOPATHY


The aim of this study was to identify possible correlations between US, mRSS and PST to evaluate DT in SSC patients with different patterns of nailfold microangiopathy. This study demonstrates a relationship between different methods to evaluated cutaneous involvement in SSC patients (6). Several studies have reported the capability of high frequency skin ultrasound (US) to reflect the overall severity of the skin damage in SSC patients (4–5). The plicometer skin test (PST) is another method to evaluated cutaneous involvement in SSC patients (6).

Objectives: The aim of this study was to identify possible correlations between US, mRSS and PST to evaluate DT in SSC patients with different patterns of nailfold microangiopathy.

Methods: Sixty-three SSC patients (mean age 64±11SD years, mean disease duration 7±6 years, 43 lSceSSc and 20 dcSSc) and 63 sex and age matched healthy subjects were enrolled after written informed consent. All subjects were assessed by mRSS, US and PST to evaluate the DT in the seventeen skin areas of the body usually evaluated by mRSS (zygoma, fingers, hands, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, feet) (1–6). Nailfold videocapillaroscopy (NVC) was used to assess the proper pattern of microangiopathy and to calculate the microangiopathy evolution score (MES) (7–8). Statistical evaluation was performed by non-parametric tests.

Results: As expected, the group of SSC patients had a statistically significant higher DT, as evaluated by the three methods, at level of all areas when compared to the control group (p<0.0001). All methods demonstrated a progressively higher DT in patients with "Late" vs. "Active" vs. "Early" pattern of nailfold microangiopathy (p<0.005), and a positive correlation was observed with MES (r=0.71 p<0.0001). A positive correlation was observed in SSC patients between the method to evaluate DT (PST vs mRSS r=0.98, p<0.0001; PST vs US r=0.53, p<0.0001; US vs mRSS r=0.53, p<0.0001).

Conclusions: This study demonstrates a relationship between different methods to assess DT (US, mRSS and PST) in SSC patients and a relationship between skin damage and microangiopathy impairment.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6815

SAT0382 | PROSPECTIVE STUDY TO ASSESS THE VALUE OF THE SKIN THICKNESS ASSESSMENTS IN SSC PATIENTS WITH PROGRESSIVE DIGITAL ULCE
Changes in volumetric bone mineral density and bone microarchitecture in patients with ankylosing spondylitis: A five-year prospective study using HRpQCT


Background: Studies have demonstrated increased prevalence of osteoporosis in patients with ankylosing spondylitis (AS) in the hip and lumbar spine assessed by conventional DXA but the peripheral skeleton is less studied. The peripheral skeleton can be studied in detail by high-resolution peripheral quantitative computed tomography (HRpQCT) demonstrating data of the volumetric bone mineral density (vBMD) and bone microarchitecture. We have previously shown that patients with AS from Western Sweden had lower vBMD measured by HRpQCT in radius and tibia compared with healthy controls [1]. No prospective study in this matter has been published in AS.

Objectives: To investigate changes over 5 years in the peripheral vBMD and microarchitecture in patients with AS.

Methods: HRpQCT of ultra-distal radius and tibia was performed in male AS-patients (NY criteria) at baseline and at the five-year follow-up. The patients were also assessed with BASDAI and BASFI. The images had common regions.

Results: Of the 69 patients included at baseline 57 (83%) patients were re-examined at the five-year follow-up. Baseline characteristics of the 57 patients (median [IQR]: age 48 (35 to 61) years, symptom duration 21 (11 to 34) years, ESR 10 (5 to 17) mm/h, CRP 3 (1 to 7), ASDASCRP 1.8 (1.3 to 2.8) and BASDAI 2.3 (1 to 4.2). 23% used TNF-inhibitors, 75% used NSAIDs and 2% bisphosphonates. All measurements at baseline had good quality and matched images had common regions >80%. The radius of 12 patients had to be excluded due to insufficient quality. At tibia, the total, cortical and trabecular vBMD decreased significantly. In the microarchitecture an increase in the trabecular separation was seen (Table). Changes in vBMD were negatively and significantly correlated; Spearman’s correlation coefficient between -0.3 and -0.4, to Δ-values (difference between follow-up and baseline) for ESR, CRP (cortical vBMD), ASDASCRP (total vBMD and cortical vBMD) and BASDAI (total vBMD). At radius, no significant change in vBMD was observed; however, less power for analyses of radius. An increase was seen in the cortical thickness and the trabecular number while the trabecular thickness decreased (Table). Changes in cortical vBMD was negatively and significantly correlated, r = -0.3, to Δ-ASDASCRP.

Table.

Conclusions: Over five years, this group of male patients with AS decreased in the vBMD of tibia, both trabecular and cortical. Even though there were alterations in the microarchitecture, no significant change in vBMD of radius was seen. Increases in inflammatory markers and disease activity had a negative impact on the cortical vBMD. The difference in the development of vBMD and microarchitecture in loaded and unloaded skeleton as well as factors associated with the changes needs to be further investigated.

References:
OBJECTIVES: 1) To assess the future risk of newly recorded MI and CVA events among incident cases of AS compared to non-AS controls from the general population by utilizing physician billing, medication, and hospitalization data that covers the entire province of British Columbia (BC), Canada.

METHODS: Our data includes all outpatient visits and hospitalizations (1990–2012) and all residents of BC (1996–2012) for all BC residents. We conducted a retrospective matched cohort study of all patients >18 years of age satisfying the following criteria: 1) two ICD-9 or 10 codes (720.0 or M45) for AS at least two months apart and within a 2-year period by any physician or hospitalization; 2) all AS cases had at least a 7-year run-in period before the 1st ICD code for AS in order to consider the case as incident. Each AS patient was matched with up to 10 controls by birth year, sex, and entry cohort time. The outcomes were a newly recorded MI (ICD-9-CM: 410 or ICD-10-CM: I21) or CVA (ICD-9 codes: 433–434, ICD-10 codes: I63–I68) event from hospital or death certificates. We estimated incidence rate and rate ratios (with 95% CI) for each ICD code using a Cox proportional hazard model.

RESULTS: 7,107 adult patients (48.7% female, mean age of 45.8 yrs), 7,148 and 7,107 were free of previous CVA/MI, respectively. The age-, sex-, and entry-time-matched RR for CVA was 1.60 (95% CI, 1.25–2.03) and MI was 1.52 (95% CI, 1.24–1.85). When adjusted for cardiovascular risk factors (obesity, angina, COPD, hospitalizations in year before index date, Charlson’s comorbidity index, diabetes, cardiovascular medication, HRT, contraceptives, fibrates, statins, NSAIDs, and Cox-2 inhibitors), the estimated RR was 1.34 (1.04–1.73) for CVA and 1.21 (0.98–1.49) for MI.

Table 1. Relative risk of incident CVA and MI according to AS status

<table>
<thead>
<tr>
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<th>AS (N=7,148)</th>
<th>Non-AS (N=71,033)</th>
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<tbody>
<tr>
<td>CVA events, n</td>
<td>80</td>
<td>492</td>
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<tr>
<td>Incidence Rate of CVA/1000 Person-Years</td>
<td>1.83</td>
<td>1.13</td>
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<tr>
<td>Incidence Rate Ratio of CVA (95% CI)</td>
<td>1.60 (1.25–2.03)</td>
<td>1.0</td>
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<tr>
<td>Multivariable RR of CVA (95% CI)</td>
<td>1.34 (1.04–1.73)</td>
<td>1.0</td>
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<th>AS (N=7,107)</th>
<th>Non-AS (N=71,032)</th>
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<tr>
<td>MI events, n</td>
<td>115</td>
<td>748</td>
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<tr>
<td>Incidence Rate of MI/1000 Person-Years</td>
<td>2.62</td>
<td>1.73</td>
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<tr>
<td>Incidence Rate Ratio of MI (95% CI)</td>
<td>1.52 (1.24–1.85)</td>
<td>1.0</td>
</tr>
<tr>
<td>Multivariable RR of MI (95% CI)</td>
<td>1.21 (0.98–1.49)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Conclusions: This large population-based study demonstrates an increased risk of CVA, but not for MI. These findings support that increased monitoring for this potentially fatal outcome and its modifiable risk factors is warranted for AS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8544
**RESULTS:**
The final list was produced. Support the recommendations, items without sufficient basis were removed, and for the management of comorbidity launched by the same panel, a list of Not to do recommendations was issued. A multidisciplinary group was selected [10 rheumatologists, 1 internist, 11 cardiologists, 11 gastroenterologists, and 11 pneumologists].

**Objectives:**
To recognize what prescriptions, risk assessments, or preventive aids of the GECOAx project, the importance of avoiding certain situations was highlighted.

**Methods:**
A summary list of Not to do recommendations (Table 1) was issued. A multidisciplinary group was selected [10 rheumatologists, 1 internist, 11 cardiologists, 11 gastroenterologists, and 11 pneumologists].

**Results:**
We recruited 183 patients diagnosed with IB (57.4% women), 117 with CD and 66 with UC, with a mean age at diagnosis of 37.0±14.0 years old; 29 of them have axial affection and 51 peripheral affection, and simultaneously in 22 cases. We observed no statistical differences in axial or peripheral affection according to the IBD diagnosis. 79 cases were on biological therapy, and these treatments were conducted by Rheumatology in 44% of cases and by Digestive Department in the 66% of cases. We observed that patients with axial affection present higher probability that the treatment has been conducted by Rheumatology (P<0.007), and broken down axial affection AS diagnosis had the most probability to be conducted by Rheumatology (n=36 P=0.019). Related to peripheral manifestations, uveitis diagnosis had the most probability to be conducted by Rheumatology (n=14 P=0.037).

**Conclusions:**
In our patient series with IB and musculoskeletal manifestations, the most common were peripheral affection. Among patients with IB and axial and/or peripheral manifestation, 44% were conducted by Rheumatology, and are cases with axial predominance, where IBT treatment does not improve musculoskeletal disease and a primary spondyloarthropathy treatment is needed.

**Disclosure of Interest:**
None declared.

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**SAF3083**

**ANALYSIS OF THE MUSCULOSKELETAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE PATIENTS AND ITS RELATIONSHIP WITH BIOLOGICAL TREATMENT**

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**Background:**
Crohn’s disease (CD) and ulcerative colitis (UC) are the main entities of inflammatory bowel disease (IBD). Both present extraintestinal manifestations that do not always depend on the IBD activity. The most common manifestations involve the musculoskeletal system and they are included in the seronegative spondyloarthropathy group. If there is active or known IBD, treatment of this is priority because it usually improves joint disease. However, joint disease can also have an independent course of the intestinal manifestations as in patients with IBD and anklyosing spondylitis (AS).

**Objectives:**
To analyze the prevalence of extraintestinal manifestations in IBD patients and treatment provided.

**Methods:**
Retrospective observational analysis of IBD patients that have been remitted to the rheumatology department of HUP La Fe with musculoskeletal manifestations. Demographic, clinical and treatment data of patient were collected. Biostatistical analysis with R (3.3.2) was performed.

**Results:**
We recruited 183 patients diagnosed with IB (57.4% women), 117 with CD and 66 with UC, with a mean age at diagnosis of 37.0±14.0 years old; 29 of them have axial affection and 51 peripheral affection, and simultaneously in 22 cases. We observed no statistical differences in axial or peripheral affection according to the IBD diagnosis. 79 cases were on biological therapy, and these treatments were conducted by Rheumatology in 44% of cases and by Digestive Department in the 66% of cases. We observed that patients with axial affection present higher probability that the treatment has been conducted by Rheumatology (P<0.007), and broken down axial affection AS diagnosis had the most probability to be conducted by Rheumatology (n=36 P=0.019). Related to peripheral manifestations, uveitis diagnosis had the most probability to be conducted by Rheumatology (n=14 P=0.037).

**Conclusions:**
In our patient series with IB and musculoskeletal manifestations, the most common were peripheral affection. Among patients with IB and axial and/or peripheral manifestation, 44% were conducted by Rheumatology, and are cases with axial predominance, where IBD treatment does not improve musculoskeletal disease and a primary spondyloarthropathy treatment is needed.

**Disclosure of Interest:**
None declared.

Diffusion Weighted Imaging (DWI) is a new Magnetic Resonance Imaging (MRI) sequence proposed for spondyloarthritis (SpA) diagnosis. Whether it is more useful than the traditional short tau inversion recovery (STIR) sequence in disease diagnosis had not been evaluated.

Objectives: By comparing with traditional STIR sequence in a group of back pain patients newly referred to rheumatology clinics, we evaluated the usefulness of DWI in SpA diagnosis at different stages.

Methods: All new patients referred to the rheumatology clinics with persistant back pain were recruited. DWI and STIR MRI were performed. Conventional radiographs of the pelvis were assessed according to the modified New York criteria for ankylosing spondylitis. Bone marrow edema (BME) and active sacroiliitis according to the ASAS definition were evaluated in STIR and DWI by two independent observers.

Results: One hundred and thirty-three patients were recruited. Ninety patients (67.7%) had a clinical diagnosis of SpA. Average back pain duration was 8.5±8.9 years. The presence of Human Leukocyte Antigen (HLA) B27 was found in 42.9% of the study population. Inter-observer correlations were excellent (STIR 95.4%, p<0.0001; DWI 69.5%, p<0.0001). DWI was found to be comparable to STIR in disease diagnosis (sensitivity DWI 34.1% vs STIR 34.3%; specificity DWI 85% vs STIR 93.8%) and when applied to the Assessment of SpondyloArthritis international Society (ASAS) criteria for axial SpA (sensitivity DWI 78.9% vs 76.7%; specificity DWI 95.6% vs 78.9%). DWI is better than STIR in non-radiographic axial SpA group (sensitivity DWI 37.8% vs STIR 33.8%; specificity DWI 85.3% vs STIR 95.6%). In the group with disease duration less than 3 years, sensitivity DWI 78.9% vs STIR 63.6% (p<0.001) was better compared to longer than 3 years. When applied to the Assessment of SpondyloArthritis in Cardiovascular Disease (ASCO) criteria for axial SpA, patients with lower disease activity scores tended to experience poorer well-being and quality of life. Although both groups represent different aspects of the same disease, they respond similarly to treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3366

The diagnostic accuracy of existing grading criteria of sacroiliac joint CT in ankylosing spondylitis

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Background: Imaging modalities are essential for the diagnosis of ankylosing spondylitis (AS) due to the absence of specific clinical manifestations. Sacroiliac Joint (SIJ) CT has been used to identify sacroiliac for decades with a higher diagnostic accuracy than radiography in detecting structural changes, and not reducing the specificity like MRI. However, no well-accepted grading system for SIJ CT existed.

Objectives: We evaluated the reliability of 3 grading criteria of sacroiliac CT in SIJ and compared them with the SARA clinical activity score of AS patients.

Methods: In the 6 months of the study, CT scans were sent to a radiology center for grading. Three radiologists independently graded the CT scans. Internal consistency reliability analysis was performed using reliability statistics of the unweighted average kappa.

Results: A total of 2714 patients had received CT scanning for any reasons with complete SIJ structures displaying between June 2012 and December 2015 were included. The CT scans were read by 2 rheumatologists together who had received the same training in radiology. Patients with sacroiliitis were selected and bilateral SIJs of each patient were evaluated separately by the 1984 modified New York (mNY) criteria, the criteria proposed by Lee (Lee criteria) and the criteria from Innsbruck workshop report (Innsbruck criteria) respectively. The grading differences among these criteria were analyzed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2575

Lumbar flexion-relaxation phenomenon in patients with axial spondyloarthritis

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Background: Surface electromyography (sEMG) has been used in several studies to assess muscle activity in patients with low back pain (LBP). It has also been analyzed the lumbar flexion-relaxation phenomenon (FRP) defined by reduced erector spinae muscles (ES) muscle myoelectric activity during full trunk flexion in healthy individuals. FRP is observed through the flexion relaxation ratio (FRR). In LBP patients, this relaxation, compared to the peak reached at the flexion phase, is smaller and even non-existent. There are very few studies that analyze this effect in patients with Axial Spondyloarthritis (axSpA).

Objectives: To evaluate muscular activity at the erector spinae muscles using sEMG in patients with axSpA before and after FRP.

Methods: 39 subjects were included: 25 patients with axSpA (49.3±5.6 years, 75% men) and 14 healthy subjects (46.7±8.7 years, 71% men) as control group. Demographic data, conventional metrology, advanced metrology using motion capture (UCOTrack) and PRO questionnaires were collected. Electrodes were placed on left and right side, at L4-L5 level and separated 2cm from the spinous process, on the ES. Muscle activity values were obtained in 4 phases (standing, flexion, relaxation and extension). With the values of flexion and relaxation, the FRR index and its inverse 1/FRR were calculated. Student t tests were used for differences between groups.

Results: There were no significant differences between the right and left sides of the measurements at ES, so mean values were considered for the analysis. There were also no significant differences in age and gender between the control group and patients. Results obtained in each of the phases are shown in the graph. The FRP appeared in healthy individuals, but not in patients, as show the FRP line in the graph: in axSpA, sEMG values at the Flexion phase are above values at the stand phase, and in control group is the opposite, so there is a truely relaxation. There were significant differences between patients and control group in flexion, relaxation, and in the FRR and 1/FRR ratios.

Conclusions: In our study, there were differences between healthy and patients with axSpA in the FRP, as in other studies with LBP patients. The 1/FRR index shown the best results in correlation with other parameters and it was where major differences between groups appeared. There was good correlation with the patient global score (BASG) and with the functional BASFI index, so assessment with sEMG could be an objective and quantitative test to evaluate the patient's functional status. It would be very interesting to analyze, in future studies, the sensitivity to change to treatments which would give us a good indicator to assess their effectiveness.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2173
Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic diseases which mainly affects the spine and sacroiliac joint. So far, the pathogenesis of AS remains elusive, making it difficult to improve early diagnosis and treatment. Proteomics is a new enabling technology to screen disease associated proteins which can be used in diagnostics or therapeutics.

Objectives: The surface-enhanced laser desorption ionization/time of flight mass spectrometry (SELDi-TOF-MS) and protein chip screening specific biomarkers in serum of patients with ankylosing spondylitis (AS) are used to diagnose and assess the disease as well as to anticipate the program of disease.

Methods: The serum samples of 69 AS patients, 10 rheumatoid arthritis (RA) and 12 patients with ankylosing spondylitis (AS) are used to diagnose and assess the disease.

Results: The contents of 30 proteins were significantly different. Of these proteins, 14 were up-regulated and 13 were down-regulated in the AS patient. The diagnostic model made up of 10259, 7972, 2048, 2154 and 2954 could be used to distinguish AS from RA, which the sensitivity and specificity were 100% and 100% respectively.

Conclusions: The protein fingerprinting set up by SELDI-TOF-MS could screen new biomarkers in AS, which is expected to become a screening platform in diagnosis and assessment of disease.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3242
left HJ (Table 1). There were no statistical differences between MRI symptoms of the impairment HJ and US symptoms of coccyx at baseline and after 2 years (Table 2).

Radiographic progression (BASRI-hip > 1 stage) after 2 years follow-up founded in 7 (31.8%) pts with MRI symptoms of the impairment HJ. There are radiographic progression from baseline to bilateral HJ stages (7.99%) pts. from sacrifice stage 1 to bilateral stage 2 in 2 (28.6%) pts. Mean NSAID index in pts with radiographic progression (31.8%) amount 62.2%, while in pts without radiographic progression – 72.5% (p>0.2).

Conclusions: 1. In patients with early axial spondyloarthritides in two years of observation radiographic progression observed in 31.7%, pts independent on regular intake of NSAIDs. 2. Further studies of the impairment HJ are required in patients with axial SpA.

Disclosure of Interest: None declared


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Background: Previously, some differences between non-radiographic and radiographic axial spondyloarthritis (axSpA) – such as a higher prevalence of females and a lower level of acute phase reactants in non-radiographic axSpA (nr-axSpA) – have been reported in national observational studies, mostly from Europe.

Objectives: To compare demographic and clinical characteristics of patients (pts) with nr-axSpA and radiographic axSpA (ankylosing spondylitis, AS) in a large multinational cohort of pts with recently diagnosed axSpA.

Methods: PROOF is a large prospective observational study. Among all consecutive pts of 29 countries, the pts with axSpA fulfilling ASAS classification criteria were only if diagnosed ≤ 1 year prior to study enrolment. Investigator’s confidence with the diagnosis of axSpA was ascertained on a numeric rating scale (NRS 0–10) at enrolment and end of follow-up. At baseline, demographic and clinical data related to the diagnosis, disease activity, quality of life and work productivity, as well as conventional radiographs of the sacroiliac joints were collected. Classification as nr-axSpA or AS was based on the results of the assessment of sacroiliac radiographs. Available radiographs were assessed first by a local reader and then by a central reader according to the grading system of the modified New York criteria.

In the case of a disagreement in the classification (nr-axSpA or AS), the radiograph was evaluated by the 2nd central reader, who was blinded to the previous assessments and the final classification was made based on the decision of 2 out of 3 readers.

Results: Of the 2126 pts enrolled in PROOF, 1281 (60.3%) pts were classified to AS and 845 (39.7%) as nr-axSpA. The confidence with the diagnosis of axSpA was ascertained on a numeric rating scale (NRS 0–10) at enrolment and end of follow-up. At baseline, demographic and clinical data related to the diagnosis, disease activity, quality of life and work productivity, as well as conventional radiographs of the sacroiliac joints were collected. Classification as nr-axSpA or AS was based on the results of the assessment of sacroiliac radiographs. Available radiographs were assessed first by a local reader and then by a central reader according to the grading system of the modified New York criteria.

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Results: Of the 2126 pts enrolled in PROOF, 1281 (60.3%) pts were classified to AS and 845 (39.7%) as nr-axSpA according to investigators. The confidence with the diagnosis of axSpA was ascertained on a numeric rating scale (NRS 0–10) at enrolment and end of follow-up. At baseline, demographic and clinical data related to the diagnosis, disease activity, quality of life and work productivity, as well as conventional radiographs of the sacroiliac joints were collected. Classification as nr-axSpA or AS was based on the results of the assessment of sacroiliac radiographs. Available radiographs were assessed first by a local reader and then by a central reader according to the grading system of the modified New York criteria.

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In the case of a disagreement in the classification (nr-axSpA or AS), the radiograph was evaluated by the 2nd central reader, who was blinded to the previous assessments and the final classification was made based on the decision of 2 out of 3 readers.
population. We found that AS was more active in patients who were diagnosed as IDA. We suggest that AS activity may cause mucosal inflammation and subsequently may result as IDA. Also we found that mucosal inflammation in AS patients is not related to NSAIDs because there was no difference about mucosal lesions between NSAID taking and non-NSAID taking group. No study was met in the literature concerning AS and IDA. Our findings should be supported by further studies.

References:

Disclosure of Interest: None declared

SAT0397 RISK FACTORS FOR DEVELOPMENT AND PERSISTENCE OF CHRONIC WIDESPREAD PAIN, IN ANKYLOSING Spondylitis and undifferentiated SPONDYLOARTHRITIS

E. Moger 1, E. Lindqvist 1, A. Bremander 2,3, S. Bergman 2,4.

To study the development of CWP in patients with SpA, and to predict the outcome.

Objectives:
- To study non-steroidal anti-inflammatory drugs (NSAIDs) for rheumatic diseases: the EVIDENCE study of European routine practice.
- To analyze frequency of anemia of inflammation in patients with ankylosing spondylitis requiring anti-TNFα drugs and therapy-induced changes.

Methods:
- A cohort study with baseline and 2.5-year follow-up postal surveys.
- 644 patients (47% women) with ankylosing spondylitis (AS) and undifferentiated spondyloarthritis (SpA) answered both surveys, and were categorized as no chronic pain (NCP), chronic regional pain (CRP), and CWP.
- Logistic regression analyses, with CWP as the main outcome were performed. Due to multicollinearity, each risk factor candidate (disease duration, BMI, smoking, and different patient-reported outcome measures; PROMs) were analysed in separate logistic regression models together with a base model (age, sex, and SpA-subgroup).

Results:
- At follow-up, prevalence estimates for NCP, CRP and CWP were similar to those at baseline, but 38% of the patients had transitioned between the groups. A large group, 72% of the patients with initial CWP, also reported persistent CWP at follow-up (Figure). Risk factors (OR and 95% CI) for development of CWP from initial NCP/CRP were more pain regions (1.36; 1.20–1.53), pain intensity (1.35; 1.20–1.52), fatigue (1.25; 1.13–1.38), global health (1.35; 1.19–1.54), EQ-5D (0.50; 0.40–0.60), BASDAI (1.25; 1.07 – 1.45), BASFI (1.32; 1.16 – 1.50), ASAS pain (0.97; 0.96 – 0.99), ASAS symptom (0.98; 0.97 – 0.99), and HADb (1.10; 1.02 – 1.19). The risk factors for persistent CWP compared to patients transitioning to NCP or CRP, were similar to those predicting development of CWP, but in addition, also higher age (1.02; 1.00–1.04), and female sex (1.82; 1.06–3.10), predicted the outcome.

Conclusions: The total prevalence of CWP did not change over the study-period, although a substantial transition between the pain-groups were found. More pain regions, higher pain intensity, fatigue and worse self-reported health predicted the development into CWP, and persistent CWP. Also, higher age and female sex were risk factors for persistent CWP in SpA. Special attention in patients who report increased pain and related symptoms is essential, to early identify the development of CWP in patients with SpA.

References:
[1] Dougados M et al. The European Spondyloarthritis Study Group pre-

SAT0398 PREGNANCY OUTCOMES IN KOREAN WOMEN WITH ANKYLOSING SPONDYLOPHTHYSIS

E.H. Park 1, J.K. Jun 2, S.M. Lee 3, Y.W. Song 3, E.B. Lee 1, 1Division of Rheumatology, Department of Internal Medicine; 2Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea, Republic Of

Background: Ankylosing spondylitis (AS) is a chronic, systemic, inflammatory disease that primarily affects the sacroiliac joints and spine. Despite overwhelming prevalence of AS in men, it can also occur in women. Since AS mainly affects the sacroiliac joints, a special attention should be paid to the normal labor and pregnancy outcomes in these female patients. However, very little is known about the impact of AS on pregnancy outcomes due to rare occurrence of the disease in women.

Objectives: To investigate the pregnancy outcomes in Korean female patients with AS.

Methods: All of the 27 deliveries from 20 AS female patients who had been cared at Seoul National University Hospital between February 1994 and June 2016 were retrospectively evaluated through medical record review. After matching the sacroiliac joints of the AS women with the pregnancies of the control group on a 1 to 4 ratio based on maternal and gestational age, pregnancy outcomes of AS patients were compared with those of the control group. Pregnancy outcomes included cesarean section (CS) rate, preterm birth, low birth weight infant, fetal growth restriction (FGR), fetal malformations and pre-eclampsia. Each pregnancy was considered as a separate observation, and outcomes between the groups were compared by regression models estimated using Generalized Estimating Equations (GEEs) to account for the matched nature of the data. For zero events in either group in which GEE models do not converge, Fisher’s exact test or Chi-square test were used.

Results: Cesarean section (CS) was performed in 44.4% of deliveries among women with AS compared with 20.4% in controls (p=0.002) (Table 1). The indications of CS included previous uterine surgery, breech position, placenta previa, placental abruption, fetal distress, and cephalopelvic disproportion (CPD). Caesarean section (CS) was performed in 1 case (8.3%) of AS women, while there was no case in the controls (p=0.353). Interestingly, the severity of sacroiliitis in AS patients did not show any association with CS (p=0.342). Women with AS had a higher frequency of LBW compared to the controls (22.2% vs 8.3%, p=0.024). However, there was no statistically significant difference in other adverse pregnancy outcomes, including preterm birth, FGR, fetal malformations, and pre-eclampsia.

**Table 1. Overall pregnancy outcomes**

<table>
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<tr>
<th>Characteristics</th>
<th>AS (n=27)</th>
<th>p-value*</th>
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<tr>
<td>Cesarean section delivery, n (%)</td>
<td>12(44.4)</td>
<td>22(88.5)</td>
</tr>
<tr>
<td>Fetal loss, n (%)</td>
<td>0(0.0)</td>
<td>-</td>
</tr>
<tr>
<td>Maternal death, n (%)</td>
<td>0(0.0)</td>
<td>-</td>
</tr>
<tr>
<td>Pre-eclampsia, n (%)</td>
<td>4(14.8)</td>
<td>-</td>
</tr>
<tr>
<td>Fetal malformations, n (%)</td>
<td>3(11.1)</td>
<td>-</td>
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<tr>
<td>Preterm birth, n (%)</td>
<td>7(25.9)</td>
<td>-</td>
</tr>
<tr>
<td>Hospital stay, days (mean)</td>
<td>4.1(2.9)</td>
<td>5.7(3.8)</td>
</tr>
<tr>
<td>Total length of pregnancy, weeks (mean)</td>
<td>39.4(3.4)</td>
<td>40.8(4.1)</td>
</tr>
<tr>
<td>1 min Apgar Score, n (%)</td>
<td>9(33.3)</td>
<td>9(33.3)</td>
</tr>
<tr>
<td>1 min Apgar Score &gt;7, n (%)</td>
<td>16(59.3)</td>
<td>16(59.3)</td>
</tr>
</tbody>
</table>

*P value calculated from regression models estimated using GEEs to account for the matched nature of the data.

Conclusions: Although pregnant women with AS are concerned about CPD during their labors due to the involvement of the sacroiliac joints, vaginal deliveries
can be tried in patients with AS. The obstetric and perinatal outcomes in women with AS were also comparable to normal pregnant women. Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.12511

SAT0399 | HEADACHE AS A CLINICAL COMPLAINT AT INITIAL PRESENTATION AND DURING THE DISEASE COURSE IN PATIENTS WITH SPONDYLOARTHRITIS INDICATES CONCOMITANT / SECONDARY FIBROMyalGia

E. Roussou, M. Karella, A. Georgiou. Rheumatology, Barking, Havering and Redbridge University Hospitals NHS Trust, London, United Kingdom

Objectives: To evaluate the symptom of headache as being able to clinically distinguish associated secondary fibromyalgia in patients with spondyloarthopathies (SpA). To compare the incidence of MSK complaints (related to SpA) in patients with headache to those that did not. To assess headache during the SpA disease course.

Methods: Registry data from 776 patients seen in clinic with SpA were analysed with reference to headache as symptom at presentation. The data of those patients presented with headache were compared with data of those patients who did not report headache with regards to demographics and disease characteristics. In addition, other MSK complaints, fatigue and pain during disease course were also analysed.

Results: From a total of 776 patients (m: f=265:508) age 48.3 (SD +14.1), 13 were excluded as no answer was recorded. 117/ 763 patients (15.08%) representing 28 males and 89 females (23.9% vs 76.1% ratio 1:3.1) reported headache at disease onset.

During the disease course, 13 patients out of the initial 117 did not record an answer to the question and were excluded. From remaining 104 patients, 95 patients (91.3%) continued to describe headache as a symptom. From those not reporting headache as initial symptom, (n=659) 148 did not answer and were excluded. From the remaining 511 patients, 194 (37.9%) reported headache during the disease course.

From those not reporting headache during the disease course, (n=659) 148 did not answer and were excluded. From the remaining 511 patients, 194 (37.9%) reported headache during the disease course. From those patients who did not have headache at disease onset, 38% report headache during the disease course. From those patients who did not have headache at presentation, 38% report headache during the disease course. Patients presenting with headache at presentation worse disease, more fatigue and a greater percentage describe pain at pressure points and MSK system.

### Table 1. Prevalence of items related to headache in patients with spondyloarthritis

<table>
<thead>
<tr>
<th>Item</th>
<th>RA with headache (n=124)</th>
<th>RA without headache (n=122)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>47.7 (13.16)</td>
<td>48.3 (14.3)</td>
<td>0.1</td>
</tr>
<tr>
<td>Gender (M:F ratio)</td>
<td>29.6% (12.3)</td>
<td>219.4% (11.9)</td>
<td>0.3</td>
</tr>
<tr>
<td>Disease duration (y)</td>
<td>11.4 (12.1)</td>
<td>10.9 (10.8)</td>
<td>0.4</td>
</tr>
<tr>
<td>Delay in diagnosis (y)</td>
<td>6.43 (8.9)</td>
<td>6.3 (6.1)</td>
<td>0.7</td>
</tr>
<tr>
<td>ESR (mean ± SD)</td>
<td>15.5 (14.8)</td>
<td>18.2 (18.8)</td>
<td>0.7</td>
</tr>
<tr>
<td>CRP (mean ± SD)</td>
<td>10.4 (36)</td>
<td>8 (2.8)</td>
<td>0.4</td>
</tr>
<tr>
<td>BASDAI score (mean ± SD)</td>
<td>7.31 (3.7)</td>
<td>6.06 (2.08)</td>
<td>0.09</td>
</tr>
<tr>
<td>BASFI score (mean ± SD)</td>
<td>5.6 (2.07)</td>
<td>5.07 (2.07)</td>
<td>0.09</td>
</tr>
<tr>
<td>Butt pain (%</td>
<td>31.6</td>
<td>12.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Back pain (%</td>
<td>82.5</td>
<td>58.4</td>
<td>0.125</td>
</tr>
<tr>
<td>Neck pain (%</td>
<td>72.6</td>
<td>24.4</td>
<td>0.005</td>
</tr>
<tr>
<td>Knee pain (%</td>
<td>63.2</td>
<td>30.6</td>
<td>0.005</td>
</tr>
<tr>
<td>Shoulder (%</td>
<td>70.9</td>
<td>23.7</td>
<td>0.012</td>
</tr>
<tr>
<td>Hip (%)</td>
<td>55.5</td>
<td>19.9</td>
<td>0.021</td>
</tr>
<tr>
<td>Eye (%)</td>
<td>23</td>
<td>4.3</td>
<td>0.012</td>
</tr>
</tbody>
</table>

### Table 2. Clinical features in patients with AxSpA and without headache

<table>
<thead>
<tr>
<th>Item</th>
<th>RA with headache (n=124)</th>
<th>RA without headache (n=122)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI score (mean ± SD)</td>
<td>7.31 (3.7)</td>
<td>6.06 (2.08)</td>
<td>0.09</td>
</tr>
<tr>
<td>BASFI score (mean ± SD)</td>
<td>5.6 (2.07)</td>
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<tr>
<td>Butt pain (%</td>
<td>31.6</td>
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<tr>
<td>Back pain (%</td>
<td>82.5</td>
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<td>Neck pain (%</td>
<td>72.6</td>
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<tr>
<td>Knee pain (%</td>
<td>63.2</td>
<td>30.6</td>
<td>0.005</td>
</tr>
<tr>
<td>Shoulder (%</td>
<td>70.9</td>
<td>23.7</td>
<td>0.012</td>
</tr>
<tr>
<td>Hip (%)</td>
<td>55.5</td>
<td>19.9</td>
<td>0.021</td>
</tr>
<tr>
<td>Eye (%)</td>
<td>23</td>
<td>4.3</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Conclusions: Headache can clinically represent secondary FM among SpA patients. A proportion of patients (representing 15%) report headache at presentation. The majority of those patients (>90%) continue to describe headache during the disease course. From those patients who did not have headache at presentation, 38% report headache during the disease course. Patients describing headache at presentation have more MSK complaints at presentation.


SAT0401 | PREVALENCE OF ULTRASONOGRAPHIC LOWER AND UPPER ENTHESITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Spondyloarthritis (SpA) occurs in up to 20% of patients with inflammatory bowel disease (IBD) [1]. Symptomatic enthesitis is a characteristic feature of SpA and represents an early sign of SpA [2]. The prevalence of enthesitis in patients with IBD is not known.

Objectives: This study was designed to evaluate whether patients with IBD showed an increased prevalence of enthesal involvement, even in the absence of clinical symptoms.

Methods: Thirty-five IBD patients (25 M and 10 F, median age 41 yrs), 25 with Crohn’s disease (CD) and 10 with ulcerative colitis (UC), all with moderate intestinal activity, and 22 (13 M and 12 F, median age 44 yrs) control subjects with irritable bowel syndrome underwent a thorough clinical evaluation followed by entheses ultrasonography of upper limb (shoulder) and lower limb (quadriceps, proximal and distal rotuleus, Achilles tendon and plantar fascia).

The Madrid sonographic entheses index (MASEI) was used to score enthesopathies [2]. Correlation between IBD features (type, duration and 22, and 23 patients) and statistical analysis was performed using the Chi-Square test.

Conclusions: The remarkable finding in this study is that half of patients with AxSpA had a history of whiplash injury. These results suggest that trauma may influence the course of AxSpA through the immunological system or hypothalamic-pituitary-adrenal axis.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.3953

SAT0400 | IS WHIPLASH INJURY A TRIGGERING OR EXACERBATING FACTOR FOR AXIAL SPONDYLOARTHRITIS?

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Background: Axial spondyloarthritis (AxSpA) can be triggered by infection and environmental factors, and some cases involve trauma. Whiplash injury in a traffic accident may lead to exacerbation of symptoms of AxSpA.

Objectives: The aims of this study are to survey the prevalence of trauma before or after onset of AxSpA and to examine the prevalences of neck trauma and other trauma in patients with a history of AxSpA.

Methods: The patients completed a questionnaire, and clinical presentation, inflammatory markers (ESR, CRP), radiographs, MRI of sacroiliac joints, Bath and ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), and Bath ankylosing spondylitis metrology index (BASMI) were assessed. Onset of symptoms was evaluated using European criteria for spondyloarthritis and patients were asked about mechanical stress (spinal trauma, extremity trauma, and internal organ injury). Patients with rheumatoid arthritis (RA) were included as controls and underwent the same evaluation. Patients with neck trauma were divided into four groups based on a short (<3 years) (group A) or long (>3 years) (group B) period between disappearance of trauma symptoms and onset of inflammatory back pain (IBP); continuous IBP after trauma (group C); and a gradual change from minor symptoms to severe IBP after trauma (group D).

Results: The subjects were 124 patients with AxSpA and 102 with RA. Trauma occurred at a significantly higher rate in patients with AxSpA than in those with RA (66 (53.2%) vs. 12 (11.8%), p<0.0001). Neck trauma was also significantly more frequent in patients with AxSpA (63 (53.2%) vs. 9 (8.8%), P<0.001) (Table 1). There were no significant differences in clinical background between patients with AxSpA with and without trauma (Table 2). Regarding the period from neck trauma to onset of IBP in patients with AxSpA, there were 4 (6.3%), 22 (34.9%), 14 (22.2%), and 23 (36.3%) cases in groups A, B, C, and D, respectively.

Conclusions: The remarkable finding in this study is that half of patients with AxSpA had a history of whiplash injury. These results suggest that trauma may influence the course of AxSpA through the immunological system or hypothalamic-pituitary-adrenal axis.

activity), age, sex and MASEI score was assessed with nonlinear Spearman's rho. Significance of differences was assessed by chi-square test. The level of statistical significance of differences was set at p<0.05.

**Results:** All of 35 patients with IBG presented at least one entheses alteration with a mean MASEI of 5.43 (thickness 57.1%, enthesisophyseal 42.8%, bursitis 0%, erosion 1%, PD abnormalities 14.2%) vs 3 patients of control group (enthesisophyseal 14%) (p=0.001).

**Conclusions:** 1) IBG patients showed a significantly higher prevalence of early entheses involvement, even in the absence of clinical symptoms; 2) the entity of entheses alteration as assessed by MASEI did not correlate with type, duration and activity of IBG; 3) age was the only variable which significantly correlated with ultrasonographic entheses involvement; 4) we speculate that IBG patients should undergo ultrasonography evaluation of entheses and, if any alteration, be followed up for early detection of SpA.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4869

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**SAT0402**  
**FREQUENCY AND HLA PHENOTYPE OF REACTIVE ARTHRITIS, UVEITIS, AND CONJUNCTIVITIS IN JAPANESE PATIENTS WITH BLADDER CANCER FOLLOWING INTRAVESICAL BCG THERAPY: A 20-YEAR, TWO-CENTER RETROSPECTIVE STUDY

**H. Nishikawa**  
[1] Hoshikawa1 Y. Taniguchi1 Y. Kiose1 Y. Yoshinaga2 Y. Terada1  

**Background:** Intravesical instillation of Bacillus Calmette-Guérin (BCG) is used as an effective immunotherapy of bladder cancer. However it may have, as an adverse event, a reactive arthritis (ReA) and the frequencies are known as about 0.5 to 1% in Western countries.

**Objectives:** To evaluate the frequencies and HLA phenotype of reactive arthritis (ReA), uveitis, conjunctivitis and other adverse events in Japanese patients with bladder cancer following BCG therapy.

**Methods:** The clinical findings of Japanese patients who received BCG (n=555 [250 and 305 in Kochi Medical School Hospital (KMSH) and Kurashiki Medical Center (KMC), respectively]) for bladder cancer from March 1997 to February 2016 were retrospectively assessed, with specific attention to patients with ReA and conjunctivitis/uveitis. We also looked at human leukocyte antigen (HLA) phenotypes of patients with ReA.

**Results:** Patient age was 73±10 and 70±11 years and male/female ratio was 198/52 and 240/65 in KMSH and KMC, respectively. 91/555 (16.4%), 121/555 (21.8%), and 196/555 (35.3%) of all enrolled patients presented with fever, haematuria, and dysuria, respectively. Of the 555 cases, ReA, uveitis and conjunctivitis were revealed in 11/555 (2.0%), 4/555 (0.7%) and 33/555 (5.9%), respectively. The frequency and the protocol of BCG therapy were stable over the 20 years. Notably, HLA-B27, -B35, -B39 and -B51 positivity was more frequent in ReA patients (9.1%, 36.3%, 36.3% and 63.6%, respectively) (p<0.05) than in healthy subjects without ReA.

**Conclusions:** Of BCG treated Japanese patients exceeds that in Western countries. HLA phenotype, especially HLA-B51 and -B39 alleles in addition to -B27, may be a risk factor in iBCG-induced ReA in Japanese patients.

**Disclosure of Interest:** None declared


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**SAT0403**  
**ARTERIAL HYPERTENSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS – RESULTS OF 10-YEARS FOLLOW-UP

**I.Z. Gaydukovs, A. Aparikna, E. Chkondkaryan, A. Rebrov. Hospital Therapy, Saratov State Medical University, Saratov, Russian Federation**

**Background:** Spondylarthropathy (SpA) (ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are associated with increased cardiovascular risk [1]. Destabilization of arterial pressure in chronic inflammation and anti-inflammatory treatment could be one of the reasons of early cardiovascular events onset.

**Objectives:** The purpose of this work is evaluate the occurrence and risk of arterial hypertension (AH) onset in patients with AS and PsA.

**Methods:** 663 patients were involved in the study: AS patients fulfilled mNew-York criteria (1984). PsA patients fulfilled CASPAR criteria (2006). Study included cross-sectional analysis where 159 AS and 85 PsA patients participated, and 10-year prospective follow-up part, included 278 AS patients, 109 PsA patients. 276 patients were excluded due to lose the follow-up. In follow-up part of the study were involved SpA patients without AH at baseline. 182 healthy volunteers participated in the study like controls, 32 of them lost the follow-up. New cases of AH were registered during 10 years. Statistics was performed in SPSS17 and GraphPadPrizm. All the results were adjusted to cardiovascular risk factors.

**Results:** Characteristics of the patients and controls with 10-years follow-up are presented in table 1.

**Table 1. Baseline characteristics of the patients, involved in the study**

<table>
<thead>
<tr>
<th></th>
<th>AS, n=278</th>
<th>PsA, n=109</th>
<th>Controls, n=150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (M ± SD)</td>
<td>40.3±11.4</td>
<td>40.5±10.6</td>
<td>39.0±11.2</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>212 (76.25)</td>
<td>41 (48.2)</td>
<td>84 (56)</td>
</tr>
<tr>
<td>Disease duration, years (M ± SD)</td>
<td>13.7±10.3</td>
<td>14.8±14.4</td>
<td>–</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td>82 (2.15)</td>
<td>24 (28.2)</td>
<td>22 (14.7)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>151 (54.31)</td>
<td>30 (35.2)</td>
<td>46 (26.70)</td>
</tr>
</tbody>
</table>

**AS, ankylosing spondylitis; PsA, psoriatic arthritis; “–”, absence of data.** p<0.001 for the difference with controls.

The relative risk (RR) of AH onset in patients with AS compared to healthy individuals is 2.22 (95% confidential interval (CI) 1.59 - 3.1); RR in PsA patients is 3.08 (95% CI 2.19 - 4.03), difference between risk of AH development in PsA and AS is significant, p<0.0001. Median to new AH cases in AS and PsA is 10±2.57 years from the first SpA symptoms appearance.

**Conclusions:** AH is frequently presented in PsA patients than in AS. Risk of new AH onset in patients with AS and PsA is superior compared with the healthy individuals. The number of new cases of hypertension increases with time, and in 10 years from diagnosis half of PsA/AxS patients without cardiovascular disease will be in the risk of hypertension.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6325

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**SAT0404**  
**RELATIONSHIP OF SCLEOSTIN AND DICKKOPF-1 SERUM LEVELS WITH DISEASE ACTIVITY AND INFLAMMATORY MRI LESIONS IN PATIENTS WITH SPONDYLOARTHROSIS**

**I. Shyrnykura1, O. Iaremkenko1, D. Fedkov1, K. Iaremkenko1, B. Bogomolots National Medical University; 2Olexandrivska Kyiv City Hospital, Kyiv, Ukraine**

**Background:** Dickkopf-1 (Dkk-1) and sclerostin (Scl) are likely to play important roles in the process of ankylosis in Spondylarthropathy (SpA) [1]. Their serum levels are associated with the formation of new syndesmophytes [2]. But the relationship between these biomarkers and disease activity including active inflammatory lesions in sacroiliac joints (SIJ) on magnetic resonance imaging (MRI) still not clear.

**Objectives:** To estimate the relationship between the SIJ and Dkk-1 and sclerostin serum levels and active inflammatory MRI lesions in SpA, disease activity and functional status.

**Methods:** Serum levels of ScI and Dkk-1 (pmol/l; ELISA) were measured at baseline in 79 cases with SpA. Mean age of pts (63.3% male) was 75.1±13.3, mean disease duration – 10.7±9.44 yrs. Radiological sacroiliitis defined according to Kellgren grade was: 0 – 1.6%, I – 22%, II – 49.2%, III – 13.6% and IV – 13.6%.

**Results:** Disease duration, years (M±SD) 13.7±10.03 14.8±14.4 – 0.001 for the differ-

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6325
In SpA pts with lower activity by SPARCC score significant correlation between Dkk-1 and inflammatory lesions in SIJ (r=0.400, p=0.043) and a negative correlation between Dkk-1 and BASDAI (r=-0.513, p=0.017) were found. There was no correlation between Scl and Dkk-1 levels among all pts and different subgroups.

Conclusions: Scl level is significantly higher in pts with lower disease activity by SPARCC MRI SIJ score and ASDAS-CRP Dkk-1 significantly correlates with disease activity due to CRP level and SPARCC score, but not to BASDAI.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2430

SAT0405 | CLINICAL, BIOLOGICAL AND GENETIC FACTORS, PREDICTORS OF TREATMENT NONRESPONSE TO TNF INHIBITORS (TNFi), IN ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PSA)
J. Pole y La Borda, J. Campos, J. Sanz, J. Muñoz, A. Sánchez. Reumatología, Instituto de Investigación Biomédica, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain

Background: TNF inhibitors (TNFi), effective in controlling the activity of spondyloarthritis, but there is a proportion of patients, who have to stop treatment due to its ineffectiveness or to the appearance of adverse events. In addition, these therapies imply high economic costs. To identify predictors of response, would help us to make decisions and to improve the risk/benefit ratio, in patients candidates who are candidates to initiate TNFi.

Objectives: To determine clinical, biological and genetic predictors of nonresponse to treatment with TNFi in patients with AS and PsA.

Methods: We analyzed 118 patients [49 AS and 69 PsA (24 axial and peripheral involvement and 45 only peripheral)], under treatment or who were to start treatment with TNFi. Data were collected before the start of the TNFi and at the last scheduled visit to the Rheumatology Service of the Hospital Puerta de Hierro, during the period 2013–2014. A clinical response was defined as the reduction ≥50% of the initial BASDAI, in patient with axial involvement, and if the final DAS 28 PCR was <2.6, in those patients with only peripheral involvement. A total of 73 men and 45 women, mean age 53±11.2 years, and a median duration of illness of 15 years (IQR 10–23) were included. The baseline ESR and CRP were (10 mm/hr IQR 5.0–27.0 and 2mg/l IQR 0.0–9.0) respectively. The mean and SD of BASDAI, DAS28 CPR and BASFI were (6.0±1.9, 3.0±0.6 and 5.4±2.5) respectively. An univariate analysis was performed using a Cox proportional hazard regression model which included: Smoker status, axial pain, peripheral arthritis, sacroiliitis, IBD, uveitis, psoriasis, HLA B27, VSG, PCR, BASFI, BASFI, the number of TNFi and 45 single nucleotide polymorphism (SNPs) previously reported to be associated with response to TNFi; SNP genotyping was performed using de Sequenom MassARRAY platform.

Results: A trend of significance (P<0.065) for the association between DKK-1 and BASDAI (HR 1.80, P=0.001), BASFI (HR 1.47, P=0.001) and the number of TNFi used (P<0.001). There was a trend of significance (P<0.10) for females, with a 2.13-fold lower response rate than males (P=0.065). The SNPs associated were: rs4240847 of the MAPKAPK2 gene (allele T, HR 1.47, P=0.035). The multivariable analysis showed in the following table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Private Hazard Ratio</th>
<th>95% CI Hazard Ratio</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASFI at the start of treatment</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>rs11591741 (GG/CC)</td>
<td>0.023</td>
<td>0.13</td>
<td>1.21</td>
<td>1.12</td>
</tr>
</tbody>
</table>

Conclusions: Female gender, basal BASFI elevated and SNP rs11591741 (GG) of CHUK gene were identified as predictors of nonresponse to TNFi treatment in these patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3142

SAT0406 | PREVALENCE OF VERTEBRAL FRACTURES IN AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES
J. C. Nieto-González 1, R. Cubero 2, S. Castañeda 3, J. Ramírez 4, L. Carmona 5
1 Rheumatology, Hospital G.U. Gregorio Marañón; 2 Statistics, Instituto de Salud Musculoesqueletica; 3 Rheumatology, Hospital la Princesa, Madrid; 4 Rheumatology, Hospital Clinic, Barcelona, Spain

Background: Some studies have described a higher rate of osteoporosis in axial spondyloarthritis (AxSpA). However, there are still some doubts about whether vertebral fractures (VF) should be a concern in AxSpA patients.

Objectives: To evaluate the prevalence and incidence of VF in AxSpA.

Methods: A systematic review was performed in Medline, Embase and Cochrane Library databases limited to studies published from Jan/2006 to Dec/2015 in Spanish, Italian and English. Search strategy combined synonyms of AxSpA, vertebral fractures, plus a filter study type. We selected cross-sectional or longitudinal studies estimating the prevalence and/or incidence of VF in adult AxSpA patients.

Results: The search retrieved 3944 references which after screening by title and abstract ended in 90 studies to study in depth. Finally, 12 studies were included. The majority of the studies evaluated the VF prevalence, and only 2 studies evaluated the incidence of VF. Prevalence estimates depended on VF definitions, varying between 4.1% (clinically diagnosed VF) and 32.4% (morphometric fracture by Genant definition). Table 1 shows all studies included and their data.

Conclusions: The published studies that focus on VF in AxSpA are very heterogeneous, but in general showed a slight increase in the VF prevalence. More studies are needed focused on VF incidence in AxSpA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3574

Table 1

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country/ies</th>
<th>Design</th>
<th>N</th>
<th>Population</th>
<th>Primary objective</th>
<th>Vertebral fracture</th>
<th>Incidence or Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang 2014</td>
<td>South Korea</td>
<td>Prospective</td>
<td>298</td>
<td>AS</td>
<td>VF incidence</td>
<td>Clinically diagnosed VF</td>
<td>4.1% at 2 years</td>
</tr>
<tr>
<td>Robinson 2013</td>
<td>Sweden</td>
<td>Cross-sectional (survey)</td>
<td>17764</td>
<td>AS</td>
<td>VF prevalence</td>
<td>Clinically diagnosed VF</td>
<td>4.1%</td>
</tr>
<tr>
<td>Feldkeller, 2006</td>
<td>Germany</td>
<td>Retrospective survey</td>
<td>1080</td>
<td>AS</td>
<td>VF prevalence and incidence</td>
<td>Clinically diagnosed VF</td>
<td>5.7% (4.3% after trauma)</td>
</tr>
<tr>
<td>Jun 2006</td>
<td>South Korea</td>
<td>Cross-sectional</td>
<td>68</td>
<td>AS</td>
<td>VF prevalence</td>
<td>Genant</td>
<td>16.2%</td>
</tr>
<tr>
<td>Klingberg 2013</td>
<td>Sweden</td>
<td>Cross-sectional</td>
<td>69</td>
<td>AS</td>
<td>VF prevalence</td>
<td>Genant</td>
<td>12%</td>
</tr>
<tr>
<td>Montaña 2011</td>
<td>Spain</td>
<td>Cross-sectional</td>
<td>176</td>
<td>AS</td>
<td>VF prevalence</td>
<td>Genant</td>
<td>32.4% (25.9–39.3%)</td>
</tr>
<tr>
<td>Rossini 2015</td>
<td>Italy</td>
<td>Cross-sectional</td>
<td>71</td>
<td>AS</td>
<td>VF and relation with bone remodeling</td>
<td>Genant</td>
<td>29%</td>
</tr>
<tr>
<td>Van der Weijden 2012</td>
<td>Holland</td>
<td>Cross-sectional</td>
<td>113</td>
<td>AxSpA</td>
<td>EsSpAx</td>
<td>VF prevalence</td>
<td>Genant</td>
</tr>
<tr>
<td>Mitra 2000</td>
<td>England</td>
<td>Cross-sectional</td>
<td>80</td>
<td>AS</td>
<td>VF prevalence and relation with BMD</td>
<td>Mc Closkey</td>
<td>16.7%</td>
</tr>
<tr>
<td>Mehmet 2007</td>
<td>Turkey</td>
<td>Cross-sectional</td>
<td>59</td>
<td>AS (Males)</td>
<td>VF prevalence</td>
<td>Tourisot</td>
<td>31%</td>
</tr>
<tr>
<td>Ulus 2013</td>
<td>Turkey</td>
<td>Cross-sectional</td>
<td>86</td>
<td>AS</td>
<td>VF prevalence</td>
<td>Tourisot</td>
<td>28%</td>
</tr>
<tr>
<td>Ulus 2014</td>
<td>Turkey</td>
<td>Cross-sectional</td>
<td>50</td>
<td>AS</td>
<td>VF prevalence</td>
<td>Tourisot</td>
<td>32.5%</td>
</tr>
</tbody>
</table>

Abstract SAT0406 – Table 1
RISE IN THE DIAGNOSIS OF NON-RADIOGRAPHIC FORM OF AXIAL SPONDYLOARTHROPATHY IN NORTHERN ISRAEL OVER TIME

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Background: Approach to the diagnosis of axial spondyloarthritides (axSpA) has changed in the last decade, with the aim of diagnosing the disease in its early form.

Objectives: The objective of this study was to explore change in the diagnostic pattern of axSpA in Northern Israel over the last 15 years.

Methods: Patients with the clinical diagnosis of axSpA from six rheumatology practices affiliated with the Rheumatology Unit of the Bnai Zion Medical Center in Haifa, Israel were included to the study. Ankylosing Spondylitis (AS) was diagnosed in the presence of sacroiliitis grade 2 or more on X-ray films; all other patients were considered as having non-radiographic axSpA. All patients were subdivided by time periods to 5 groups, and percentages of patients diagnosed in the non-radiographic stage of the disease, as well as patient demographic data were compared using exact Fisher test.

Results: One hundred twenty five patients were subdivided to 5 groups by periods of diagnoses (before 2000, 2001–2004, 2005–2008, 2009–2012, 2013–2016). Gradual increase in a proportion of patients diagnosed with non-radiographic axSpA was observed over years, with statistical significance achieved in 2013–2016 (<p>0.05) (Fig 1). Patients’ gender and age distribution did not differ significantly among the groups.

Conclusions: Progressive increase in the proportion of patients diagnosed with non-radiographic form of axSpA over years was observed in this study. This finding, made on the basis of real life data, reflects change in the diagnostic approach to spondyloarthritides during the last decades.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5666

POSITIVE CORRELATION BETWEEN INFLAMMATION ON SACRIOCILIAC JOINT MRI AND SERUM C-TERMINAL TEOPEPTIDE OF TYPE-I COLLAGEN IN ANKYLOSING SPONDYLITIS BUT NOT IN NON-RADIOGRAPHIC AXIAL SPONDYLITIS

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Background: The MRI-determined inflammatory score was suggested as a functional index, or MRI-determined SIJ inflammation. Erythrocyte sedimentation rate, C-reactive protein, and ASAS correlated with MRI inflammatory scores in nr-axSpA but not in AS. sCTX-I correlated with MRI-determined SIJ inflammatory scores in AS only. BASDAI and BALP levels did not associate with MRI inflammatory scores in either group. Multivariate analysis showed that sCTX-I associated independently with MRI inflammatory score in AS (<p>0.047, p=0.038).

Conclusions: Inflammatory markers and ASDAS correlated with active sacroiliitis on MRI in nr-axSpA only. In AS, only sCTX-I correlated with active inflammation on SIJ MRI. sCTX-I may be useful as a marker of objective inflammation in AS.

Disclosure of Interest: None declared


HLA-B27 ROLE IN ANKYLOSING SPONDYLITIS PHENOTYPE: RESULTS FROM THE REGISPONSER DATABASE

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Objectives: To assess if there are different phenotypical patterns of Ankylosing Spondylitis (AS) patients depending on the positivity or negativity of HLA-B27.

Methods: This is a multicentric, observational, transversal and descriptive study of AS patients from the spanish database REGISPONSER. We compared HLAB27 positive and HLAB27 negative patients regarding clinical and demographical data, disease activity and structural damage. In order to assess disease activity we used the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and acute phase reactants (VSG and PCR). Functional disability was measured by Bath Ankylosing Spondylitis Functional Index (BASFI), and structural damage by Bath Ankylosing Spondylitis Radiology Score (BASRI). For qualitative variables we used the Chi square test and for quantitative ones the t test. An univariate
and multivariate comparative analysis was performed, in order to define which variables were related to the negativity or positivity of HLAB27.

Results: Data of 1235 AS patients were analysed. Of them 1029 (83.3%) were HLAB27 positive and 206 (17.7%) HLAB27 negative. 924 (74.8%) were men. AS patients with HLAB27+ presented significantly more familiar history of spondyloarthropathy (p=0.002), axial pain, enthesopathy, enthesis, no radiological signs and diagnosis (p<0.001), with a longer disease duration (p=0.037) and a trend to a higher percentage of uveitis compared to those with HLAB27−. On the other hand, AS patients with HLAB27+ also presented significantly more peripheral arthritis (p=0.002), dactylitis (p=0.001) and extraarticular manifestations (p<0.001), presenting no radiological signs of the disease (p<0.001) compared with those of HLAB27−. AS patients with HLAB27+ also presented higher scores of BASDAI and BASFI (p=0.047 and p=0.005 respectively). The study didn’t show differences between both groups of patients regarding sex distribution, age at diagnosis, family history of inflammatory arthritis (p>0.05), age at diagnosis (OR 0.97, IC95% 0.96–0.98, p<0.001), the presence of dactylitis (OR 0.16, IC95% 0.05–0.56, p=0.004), extraarticular manifestation specially IBD (OR 0.22, IC95% 0.12–0.40, p=0.001) and peripheral arthritis (OR 0.53, IC95% 0.32–0.89, p=0.016) were the variables independently associated with the presence of HLAB27.

Conclusions: The presence of HLAB27 in AS patients is associated to an earlier disease onset, a higher frequency of familiar history of spondyloarthropathy, and a lower frequency of dactylitis, extraarticular manifestations and peripheral arthritis.


**SAT0411** CORRELATION BETWEEN DISEASE ACTIVITY SCORES AND QUALITY OF LIFE IN SPONDYLOARTHITIS


Background: Spondyloarthritides (SpA) is a group of chronic inflammatory rheumatism and it is known to be one of the leading causes of disability.

Objectives: This study aimed to investigate the quality of life and the psychological disorders (depression, anxiety and insomnia) in patients with SpA.

Methods: A total of 60 patients were included with the diagnosis of SpA meeting the Amor and New York modified criteria, in a prospective study. In a questionnaire, the characteristics of the disease and sociodemographic patient were collected. Also psychiatric assessment was done using the insomnia severity index score (ISI) and the Hospital Anxiety and Depression scale (HAD). In addition, patients answered to the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and the SF-12.

Results: The sex-ratio (men:women) was 3.28 (46/14), the average age was 37.95 years (18–70). The average duration of disease progression was 11.5 years (1–30). The mean value of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 5.11 and the Bath Ankylosing Spondylitis Functional Index (BASFI) was 5.22. Uveitis was reported in 11.7% of patients, otoporosis in 35%, enthesis in 36.7% and coxitis in 36.7%. 78.3% of patients received NSAID and 30% were treated with biotherapy. On the psychological level, 25% of patients had an anxiety, 20% had depression. According to the ISI, 35% of patients had sub threshold insomnia, 20% had moderate insomnia and 10% had severe insomnia. The mean value of the ASQoL was 9 (0–16). The mean value of the physical health was 37.13 (19.34–60.41) and for the mental health was 41.65 (14.9–60.35). A significant positive correlation was found between the disease activity and the ASQoL (p<0.001), the physical health (p<0.001) and the mental health (p=0.002). Also, we found a significant positive correlation between the BASDAI and depression (p=0.01) and insomnia (p=0.001).

Conclusions: SpA is a chronic inflammatory disease that contributes to significant physical disability. It decreased quality of life in a significant number of patients. The treatment of those patients must consider the improvement of quality of life, as part of a global approach.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6394

**SAT0412** ASSOCIATION BETWEEN SMOKING WITH SPINAL LEVEL OF STIFFNESS AND FUNCTIONAL LIMITATION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SPANISH ATLAS

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Background: Smoking has been associated with greater disease activity and radiographic progression in patients with axial spondyloarthritis (axSpA). In addition, radiographic damage has been linked to greater functional limitation. However, clarification is still being sought as to whether or not this association exists.

Objectives: To investigate the association between smoking and both the area of spinal stiffness and functional limitation in patients with axSpA.

Methods: A sample of 680 patients diagnosed with axSpA was interviewed between 2016 as part of the Spanish Atlas, which aims to promote early referral and improve healthcare and the use of effective treatments in patients with axSpA. Tobacco consumption was recorded as: Smoker (62.4%), Occasional Smoker (8.9%) and Non-Smoker (28.7%). Spinal stiffness was assessed in the three different vertebral areas: cervical, dorsal and lumbar. To determine the degree of functional limitation we used a composed index which includes the sum of the degree of limitation in the 18 daily activities well established (dressing, grooming, bathing, tying shoelaces, moving around the home, stairs, getting to/out of bed, toilet, shopping, preparing meals, eating, cleaning, walking, using public transportation, going to the doctor, driving, physical exercise, sexual relations) using an ordinal variable (0=noone, 1=little, 2=moderate and 3=moderate).

A descriptive analysis was used to compare the level of stiffness (chi-squared test) in the different groups of smokers consumptions. Regression analysis was also used to assess the relation between smoking and degree of limitation (0–54).

Results: 53% were females, mean age 46 years and 77.1% were HLA-B27+.

The percentage of patients with stiffness in the lumbar region was significantly higher in habitual/occasional smokers than in non-smokers (89.0%, 93.8%, 83.5% respectively; p<0.01) (Table). The mean level of functional limitation increased with tobacco consumption, although this difference was not statistically significant (47.9±12.1 vs. 45.1±11.5 vs. 44.8±13.7 respectively; p=0.2). However, regression analysis showed a statistically significant correlation between smoking and functional limitation (r=0.096; p=0.02).

Declaration of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6519

**SAT0413** INFECTIOUS PROFILE IN A TUBERCULOSIS-ENDEMIC POPULATION WITH SPONDYLOARTHROPATHIES

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Background: Screening latent tuberculosis (TB) and other opportunistic infections in patients with spondyloarthropathies (SpA) with biologic or immunosuppression therapy is important in highly endemic populations (1,2).

Objectives: To assess the prevalence of latent and active TB, hepatitis B, hepatitis C and HIV among patients with spondyloarthropathies (SpA) by means of CHI-square tests, Mann-Whitney test, and logistic regression analyses.

Methods: A cross-sectional study was conducted in 621 patients with SpAs, in whom TB, hepatitis B, hepatitis C, HIV and syphilis screening was analyzed based on type of diagnosis. Differences among immunomodulatory therapies were assessed. Statistical association was examined by means of CHI-square tests, Mann-Whitney test, and logistic regression analyses.

Results: The prevalence of latent and active TB in this cohort were 63.1%, 2.9%, respectively. Significant differences were found in proportions of latent and active TB among types of SpAs, indicating a positive association with AS. A high
Spondyloarthropathies (SpAs) are a group of auto-inflammatory diseases with overlapping symptoms, that include ankylosing spondylitis (AS), psoriatic arthritis (PsA), undifferentiated spondyloarthropathy (Und SpA), enteropathic arthropathies, and reactive arthritis (1). Historically, SpAs have been viewed as diseases that predominantly affected men (2).

Objectives: To analyze the influence of gender on disease patterns and therapeutic approach in a large cohort of Colombian patients with SpAs.

Methods: A cross-sectional study was conducted in 621 patients with SpAs, in whom clinical and therapeutic characteristics were analyzed based on gender. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses.

Results: The male-to-female ratio was 1.1:1 in this cohort. Younger age at diagnosis was found in males. AS was the most frequent disease (54.7%), followed by PsA (35.7%), and undifferentiated SpA (9.5%). The male gender was positively associated to the presence of AS (OR 2.29 95%IC 1.31–4.04), sacroilitis (OR 3.46 95%IC 1.82–6.56), HLAB27 positivity (OR 1.95 95%IC 1.31–2.91), low back pain (OR 1.85 95%IC 1.34–2.54) and axial involvement (OR 1.98 95%IC 1.42–2.77). According to the therapeutic profile, female gender was positively associated to the use of conventional DMARD therapy (i.e., methotrexate [p=0.03], leflunomide [p=0.0057], chloroquine [p=0.013]), while male patients were more associated to the use of biologic therapy.

Conclusions: In this Colombian large sample with SpA, male patients have a younger onset of disease, higher proportion of axial involvement, HLAB27 positivity, evidence of radiographic sacroiliitis and higher use of anti-TNF therapy. References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6844
HLA-B27 positive. In total, 254 (66%) patients started TNF-α inhibitors and 139 (34%) patients received conventional treatment. Patient characteristics were comparable between both groups, except higher disease activity, more often peripheral arthritis, and worse physical functioning in patients starting TNF-α inhibitors. NSAID use and disease activity reduced significantly after starting TNF-α inhibitor and remained low and stable during follow-up. In the conventional treatment group, disease activity was low and NSAID remained stable at all visits. GEE analysis over time showed that NSAID use was significantly associated with disease activity (Table 1). In the TNF-α inhibitor group, a significant association of all NSAID parameters with ASDAS was found: NSAID use yes vs. no, \( \alpha \), GEE analysis over time showed that NSAID use was significantly associated with treatment group, disease activity was low and NSAID remained stable at all visits. 

**Table 1. Association between ASDAS and NSAID use over time in AS patients.**

<table>
<thead>
<tr>
<th>NSAID use</th>
<th>Complete group</th>
<th>NSAID use index</th>
<th>NSAID use index 10</th>
<th>NSAID use index 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current use</td>
<td>0.260 (0.05-0.385)</td>
<td>0.001</td>
<td>0.173</td>
<td>251</td>
</tr>
<tr>
<td>ASAS-NSAID index</td>
<td>0.098 (0.0-0.032)</td>
<td>0.001</td>
<td>0.173</td>
<td>251</td>
</tr>
<tr>
<td>TJC &gt;90%</td>
<td>0.011 (0.00-0.031)</td>
<td>0.001</td>
<td>0.173</td>
<td>241</td>
</tr>
<tr>
<td>12-6 weeks</td>
<td>0.065 (0.00-0.037)</td>
<td>0.001</td>
<td>0.333</td>
<td>248</td>
</tr>
<tr>
<td>CRP</td>
<td>0.093 (0.070-0.090)</td>
<td>0.001</td>
<td>0.173</td>
<td>251</td>
</tr>
<tr>
<td>BASDAI</td>
<td>0.650 (0.621-0.680)</td>
<td>0.001</td>
<td>0.173</td>
<td>251</td>
</tr>
</tbody>
</table>

**Conclusions:** In this observational cohort of established AS patients, NSAID use over time was significantly associated with ASDAS, which was most pronounced in the TNF-α inhibitor group, a significant but less prominent association of NSAID parameters with disease activity in the conventional treatment group, a significant but less prominent association of NSAID parameters with clinical parameters (ASAS 5/6/4/3/2/1), and the combination of NSAID use and disease activity in the conventional treatment group, a significant but less prominent association of NSAID parameters with clinical parameters (ASAS 5/6/4/3/2/1).

**References:**


**SAT0417** | GRADUAL PROGRESSIVE CHANGE TO EQUAL PREVALENCE OF ANKYLOSING SPONDYLITIS AMONG MALES AND FEMALES IN SWITZERLAND: DATA FROM THE SWISS ANKYLOSING SPONDYLITIS SOCIETY (SVMB)

H. Baumberger, 1M. A. Khan 2, PhD. First president of, Schweizerische Vereinigung Morbus Bechterew, Zurich, Switzerland; 2Professor Emeritus of Medicine, Case Western Reserve University, Cleveland OH, United States

**Background:** Classic ankylosing spondylitis (AS) with radiographic sacroiliitis has long been considered to be more common in men than women. But this difference has gradually decreased with increasing recognition of this condition in women so that the more recent data suggest a range of 2:1 to 1:1 ratio in favor of men [1].

**Objectives:** To document greater disease recognition in women during the last 30 years in Switzerland as reflected by AS patient membership in the Swiss Ankylosing Spondylitis Society (SVMB) since its foundation in 1978 [2].

**Methods:** We reviewed the Society's quarterly newsletters that have kept record since 1980 not only of the number of members, but also the percentage of males and females AS patients. We calculated yearly AS patient membership and also change in the male/female patient ratio (M:F).

**Results:** There has been a progressive decline in the M:F ratios since 1980 as shown in the Figure. There were 44 female forming 28% of the patient population, with a M:F ratio of 2.57 in 1980. At the end of 2016, there are 1731 females forming 49% of the total number of patients, and the M:F ratio is now 1.03.

**Conclusions:** AS is now being recognized as often in females as in males, as reflected in the membership of SVMB over the last 36 years. There can be various reasons for this observation, one of them being the availability of better imaging tools to recognize AS/axial spondyloarthritis (axSpA), especially among women whose disease is clinically and radiologically less pronounced and is therefore often overlooked [2]. For example, the use of MRI (for early detection of spinal inflammation) and the ASAS criteria have resulted in > 50% females in a German cohort of patients with nonradiographic axSpA [3]. SVMB has played a major role in achieving greater disease recognition in Switzerland by increasing disease awareness and educating patients and their families, the general public, the governing bodies and the allied health professionals about AS, and by interacting closely with rheumatologists. Other possible factors influencing our data include: women outliving men, forming a little greater percentage of the general population, and possibly more likely to join patient self-help groups and societies. We did not investigate any gender difference in disease severity and clinical presentation. In conclusion, AS/axSpA almost equally afflicts men and women in Switzerland.

**References:**


**SAT0418** | ANXIETY AND DEPRESSION ON DISEASE ACTIVITY AND QUALITY OF LIFE OF SPONDYLOARTHRITIS PATIENTS UNDER BIOLOGIC THERAPIES

N. Madeira 1, J. Borges 1, A. Cardoso 2, L. Miranda 1, F. Barcelos 1, C. Miguel 1, C. Silva 1, S. Fernandes 1, R. Trincão 3, D. Medeiros 1, R. Campanilho-Marques 1, H. Santos 1, R. Leitão 1, A. Faustino 1.

**Background:** Rates of anxiety and depression in ankylosing spondylitis (AS) or related spondyloarthritis (SpA) range from 5 to 70% and are more prevalent in females than males. It is not clear whether this is due to the disease or other factors such as socioeconomic status. This study aimed to evaluate disease activity and quality of life (QOL) among AS or SpA patients with and without anxiety or depression.

**Objectives:** The aim of this study was to evaluate the association of anxiety and depression with disease activity and QOL parameters in AS and related spondyloarthropathies (SpA). Also, to compare the disease experience of ANXIETY and DEPRESSION on DISEASE ACTIVITY AND QUALITY OF LIFE OF SPONDYLOARTHRITIS PATIENTS UNDER BIOLOGIC THERAPIES.

**Methods:** We conducted a cross-sectional analysis of 771 patients with AS or related spondyloarthropathies. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). Disease activity was assessed using the BASDAI and ASDAS. QOL was evaluated using the SF-36 and EQ5D. Statistical analysis was performed using logistic regression.

**Results:** Anxiety and depression were more prevalent in women than in men (64% vs. 36%) and in patients with radiographic sacroiliitis (76% vs. 24%). Anxiety and depression were associated with higher disease activity (BASDAI, ASDAS) and lower QOL (SF-36, EQ5D). Treatment with biologics was associated with lower anxiety and depression.

**Conclusions:** Anxiety and depression are common in AS and related spondyloarthropathies. They are associated with higher disease activity and lower QOL. Treatment with biologics is associated with lower anxiety and depression.
Objectives: To assess disease activity and quality of life in anxious and depressed SpA patients.

Methods: Observational, retrospective, cross-sectional study of SpA patients on bDMARDS, registered at Reuma.pt, Portuguese Rheumatology registry, with ≥1 clinical evaluation from November 2015 to July 2016. Demographic and clinical outcomes including BASDAI, BASFI, ASDAS, BASDI, DAS 28–3V, ESR in peripheral psoriatic arthritis, tender and swollen 44 joints count (TJC, SJC), patients’ pain and global assessments, physician’s global assessment, CRP, ESR, ASO, EQ-5D, FACIT-F for fatigue and HADS scale with 2 domains, HADS-A for anxiety and HADS-D for depression (a cutoff of 0 defining these symptoms), were collected. Statistical: Mann-Whitney test, p<0.05, SPSS® v.17.

Results: 160 patients were included, 41.9% were male, with mean current age 50.7±11.9, age at diagnosis 36.9±11.96, at 1st bDMARD 46.2±11.8, time from diagnosis 18.5±10.3. Years. The mean DAS 28–3V ESR was 3.2±1.4, BASDAI 2.98±2.2, BASDI 2.4±1.5, BASFI 2.68±2.26, BASMI 3.36±1.7, patient’s global assessment 28.9±6.1, physician’s global assessment 14.5±15.2, ESR 18.8±18.1 mm/h, CRP 6.7±16.01 mg/L, ASQol 6.2±6.5, FACIT-F 37.2±10.1 and EQ-5D 0.417±0.19. The mean HADS-A was 5.96±4.01 and HADS-D was 5.05±4.1 (HADS-A ≥8 in 39.5% and HADS-D ≥8 in 28.3% patients). Comparison of anxious vs non-anxious and depressive vs non-depressive groups appears on table 1.

Conclusions: These results suggest that anxious and depressed patients may have higher disease activity, more functional limitations and worse quality of life. These symptoms should not be underestimated, but instead, they should be controlled to achieve clinical improvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6011

**SAT0419** SIMILARITIES AND DIFFERENCES BETWEEN HLA B27 POSITIVE AND HLA B27 NEGATIVE SPONDYLOARTHRITIS: RESULTS FROM THE ESPERA COHORT

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**Background:** The diagnostic relevance of HLA B27 for spondyloarthritis (SpA) vs non-anxious and depressive vs non-depressive groups appears on table 1.

**Objectives:** To investigate the influence of HLA B27 status on disease manifestations in patients with recent-onset SpA.

**Results:** A total of 291 patients (75% B27+ and 25% B27-) were classified as axial SpA (86% [33% B27+ and 67% B27-] as peripheral SpA. Results (mean –standard deviation- and relative frequencies) are presented in the table. In axial SpA, B27+ patients were younger, more frequently males and with a family history of SpA while B27- patients had more frequently psoriasis, IBD and poorer quality of life. In peripheral SpA, B27- had more frequently psoriasis and reported higher BASDAI.

**Conclusions:** In patients with SpA, HLA B27 status influences on the presentation of the disease. In axial SpA, the presence of B27 is associated with an earlier onset, male predominance and more frequency of family history of SpA. In peripheral SpA, the presence of B27 is linked with lower subjective parameters of disease activity. In both, axial and peripheral SpA, the absence of B27 is associated with psoriasis, IBD and poorer quality of life.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5053

**SAT0420** RELATIONSHIP BETWEEN HEALTH-RELATED QUALITY OF LIFE WITH DISEASE ACTIVITY AND FUNCTIONAL STATUS, IN PATIENTS WITH ANKYLOSING SPONDYLITIS

P. Chiowchanwisawikij, V. Sinronprasert, W. Katchamart

1SpA features) was used. Inclusion period in the program was 2008–2011. For this study, 377 fulfilling the ASAS classification criteria for SpA were included. A descriptive analysis was used to compare demographic and clinical characteristics between HLA B27+ and HLA B27- patients for both subgroups, axial SpA and peripheral SpA. Chi-square test for qualitative variables and Student-t test for quantitative variables were employed to compare variables among groups.

**Results:** A total of 291 patients (75% B27+ and 25% B27-) were classified as axial SpA (86% [33% B27+ and 67% B27-] as peripheral SpA. Results (mean –standard deviation- and relative frequencies) are presented in the table. In axial SpA, B27+ patients were younger, more frequently males and with a family history of SpA while B27- patients had more frequently psoriasis, IBD and poorer quality of life. In peripheral SpA, B27- had more frequently psoriasis and reported higher BASDAI.

**Conclusions:** In patients with SpA, HLA B27 status influences on the presentation of the disease. In axial SpA, the presence of B27 is associated with an earlier onset, male predominance and more frequency of family history of SpA. In peripheral SpA, the presence of B27 is linked with lower subjective parameters of disease activity. In both, axial and peripheral SpA, the absence of B27 is associated with psoriasis, IBD and poorer quality of life.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6011

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**Table 1.** Multivariable linear regression analysis of factors associated with the health utility

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Periperal SpA</th>
<th>Axial SpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.4±7.1</td>
<td>33.8±6.5</td>
</tr>
<tr>
<td>Male</td>
<td>48.9 (50.6)</td>
<td>36.4 (56.9)</td>
</tr>
<tr>
<td>Symptoms duration (months)</td>
<td>12.8 ±6.7</td>
<td>13.3 ±6.7</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>44.2 (20.1)</td>
<td>9 (12.5)</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>48.9 (19.1)</td>
<td>9 (12.5)</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>13.5 (5.9)</td>
<td>3.4 (2.2)</td>
</tr>
<tr>
<td>EAMs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Uveitis</td>
<td>20 (9.1)</td>
<td>3 (4.2)</td>
</tr>
<tr>
<td>– Psoriasis</td>
<td>18.2 (25.0)</td>
<td>20 (6.8)</td>
</tr>
<tr>
<td>– IBD</td>
<td>4.1 (8.5)</td>
<td>5 (6.9)</td>
</tr>
<tr>
<td>Diarrhea, cervicitis, urethritis</td>
<td>9.4 (1.4)</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>Inflammatory back pain</td>
<td>83.7 (39.9)</td>
<td>29 (40.3)</td>
</tr>
<tr>
<td>Family history</td>
<td>84.3 (18.4)</td>
<td>17 (23.6)</td>
</tr>
<tr>
<td>ARPs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– ESR (mmHg)</td>
<td>13.6±13.2</td>
<td>15.3±14.2</td>
</tr>
<tr>
<td>– CRP (mg/L)</td>
<td>11.3±15.3</td>
<td>9.4±14.9</td>
</tr>
<tr>
<td>Sclerosis</td>
<td>0.3±1.5</td>
<td>0.2±0.8</td>
</tr>
<tr>
<td>Vas (0–10)</td>
<td>2.2±2.2</td>
<td>2.3±2.2</td>
</tr>
<tr>
<td>Vas (10–20)</td>
<td>4.0±2.7</td>
<td>4.6±2.6</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.7±2.3</td>
<td>4.2±2.2</td>
</tr>
<tr>
<td>BASFI</td>
<td>0.2±0.2</td>
<td>2.1±1.1</td>
</tr>
<tr>
<td>ASQol</td>
<td>5.3±4.7</td>
<td>7.0±4.8</td>
</tr>
</tbody>
</table>

**Model Adjusted**

<table>
<thead>
<tr>
<th>Disease activity, Beta (95% CI)</th>
</tr>
</thead>
</table>
| HU, while using BASFI instead of HAQ in the same model yielded slightly lower predictive value of 70.7%. **Conclusions:** Disease activity and functional status were significantly factors related to QoL and HU in patients with AS. To improve QoL, the aim of treatment should be to achieve remission or at least low disease activity and improve at least maintain function.

**Disclosure of Interest:** P. Chiowchanwisawikij Grant/research support from: Siriraj Research fund, V. Sirinonprasert: None declared, W. Katchamart: None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.5155
SAT0421

FAT MASS NEGATIVELY AFFECTS THE RESPONSE TO TNF-α BLOCKERS IN ANKYLOSING SPONDYLITIS PATIENTS

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1Rheumatology Department, Clinica Alemana de Santiago; 2Rheumatology department, Hospital Padre Hurtado, Santiago, Chile; 3Amsterdam Rheumatology and Immunology Center, Reade; 4Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands

Methods: All AS patients with vitamin D level of < 20 ng/ml who consecutively attended the outpatient rheumatology clinic were enrolled. C-reactive protein, erythrocyte sedimentation rate, Bath AS disease activity index (BASDAI), Bath AS Functional Index (BASFI), TNF-α, IL-1, IL-6, ADMA, symmetric dimethylarginine (SDMA), NG-monomethyl-L-arginine (LNMMA), arginine, arginine/ADMA ratio and citrulline levels were analyzed when vitamin D level was < 20 ng/ml and ≥ 20 ng/ml after replacement.

Results: The study population was represented by 82 patients, 48 women (59%), mean age 39 years old and mean disease duration 5.5 years. When vitamin D levels were increased to normal levels, levels of IL-1 (4.8±9.7 and 3.1±4.0 p=0.001), IL-6 (7.1±14.1 and 4.7±2.1 p=0.009), ADMA (0.8±0.2 and 0.4±0.2 p=0.001), SDMA (0.9±0.2 and 0.4±0.2 p=0.001), LNMMA (0.08±0.02 and 0.06±0.02 p=0.001), arginine (385.8±160.4 and 269.5±79.0 p=0.001) and citrulline (91.5±34.3 and 75.3±23.5 p=0.001) were reduced. Levels of arginine/ADMA ratio was increased (498.7±136.5 and 576.7±170.7 p=0.001) (Table 1). Also BASDAI, BASFI and erythrocyte sedimentation rate were decreased but it was statistically meaningless. In Pearson correlation analysis, ADMA, SDMA, LNMMA, arginine and citrulline were negatively correlated with vitamin D levels. Multiple regression analysis showed that SDMA, arginine and citrulline were significantly related with vitamin D levels. Negative correlation between ADMA and vitamin D levels was shown in Figure 1

Table 1. Multivariate logistic regression analysis results*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Variable</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically important or major improvement of ASAS CRP</td>
<td>Body Fat % at baseline</td>
<td>0.8 (0.7–0.98)</td>
</tr>
<tr>
<td></td>
<td>Fat Mass Index at baseline</td>
<td>0.7 (0.4–0.99)</td>
</tr>
<tr>
<td></td>
<td>FMI percentile at baseline</td>
<td>0.9 (0.8–0.99)</td>
</tr>
<tr>
<td>BASDAI MCI**</td>
<td>FMI percentile at baseline</td>
<td>0.95 (0.91–0.99)</td>
</tr>
</tbody>
</table>

*aControlled for gender, age, years with symptoms, days of follow up, use of DMARDs and NSAIDS and baseline outcome value. **Percentiles according to the reference population tables, stratified by age and gender. *Only for patients with a BASDAI ≥ 4 at baseline. CRP = C-reactive protein, ASAS = Ankylosing Spondylitis Disease Activity Score, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, MCI = minimum clinically important improvement, FMI = Fat Mass Index.

Conclusions: Vitamin D replacement in AS with low vitamin D levels improves antioxidant status via ADMA pathway and shows anti-inflammatory effects on IL-1 and IL-6. In literature, there is no other study investigating the effects of increased vitamin D levels on disease activity, inflammatory parameters and ADMA pathway in AS.

References:

Disclosure of Interest: None declared

SAT0422

EFFECTS OF VITAMIN D REPLACEMENT ON THE DISEASE ACTIVITY AND INFLAMMATORY PARAMETERS SUCH AS IL-1, IL-6, TNF-α, ASYMMETRIC DIMETHYLARGININE (ADMA) AND ARGinine/ADMA RATIO IN ANKYLOSING SPONDYLITIS

S. Ergülü Esen1, S. Yilmaz2, L. Kebapcilar3, A. U nú4, S.H. Ipeki3, A. Abusoglu4, I. Rheumatology, Internal Medicine, Konya Education and Research Hospital; 2Rheumatology, Internal Medicine; 3Endocrinology and Metabolic Diseases, Internal Medicine; 4Biochemistry, Selcuk University, Konya, Turkey

Background: Asymmetric dimethylarginine (ADMA) levels in AS patients were found to be higher than controls (1). The relationship between vitamin D level and disease activity was shown in AS (2). But the effects of vitamin D replacement on the disease activity, inflammatory parameters and ADMA pathway were not investigated in AS.

Objectives: To determine the effects of vitamin D replacement on the disease activity, inflammatory parameters and ADMA pathway in AS.

Methods: All AS patients with vitamin D level of < 20 ng/ml who consecutively attended the outpatient rheumatology clinic were enrolled. C-reactive protein, erythrocyte sedimentation rate, Bath AS disease activity index (BASDAI), Bath AS Functional Index (BASFI), TNF-α, IL-1, IL-6, ADMA, symmetric dimethylarginine (SDMA), NG-monomethyl-L-arginine (LNMMA), arginine, arginine/ADMA ratio and citrulline levels were analyzed when vitamin D level was < 20 ng/ml and ≥ 20 ng/ml after replacement.

Results: The study population was represented by 82 patients, 48 women (59%), mean age 39 years old and mean disease duration 5.5 years. When vitamin D levels were increased to normal levels, levels of IL-1 (4.8±9.7 and 3.1±4.0 p=0.001), IL-6 (7.1±14.1 and 4.7±2.1 p=0.009), ADMA (0.8±0.2 and 0.4±0.2 p=0.001), SDMA (0.9±0.2 and 0.4±0.2 p=0.001), LNMMA (0.08±0.02 and 0.06±0.02 p=0.001), arginine (385.8±160.4 and 269.5±79.0 p=0.001) and citrulline (91.5±34.3 and 75.3±23.5 p=0.001) were reduced. Levels of arginine/ADMA ratio was increased (498.7±136.5 and 576.7±170.7 p=0.001) (Table 1). Also BASDAI, BASFI and erythrocyte sedimentation rate were decreased but it was statistically meaningless. In Pearson correlation analysis, ADMA, SDMA, LNMMA, arginine and citrulline were negatively correlated with vitamin D levels. Multiple regression analysis showed that SDMA, arginine and citrulline were significantly related with vitamin D levels. Negative correlation between ADMA and vitamin D levels was shown in Figure 1

Table 1

<table>
<thead>
<tr>
<th>Vitamin D (ng/ml)</th>
<th>TNF-α (pg/mL)*</th>
<th>IL-6 (pg/mL)*</th>
<th>IL-1 (pg/mL)*</th>
<th>SDMA (μmol/L)*</th>
<th>LNMMA (μmol/L)*</th>
<th>Arginine (μmol/L)*</th>
<th>Arginine/ADMA ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>19.0±14±3.9</td>
<td>19.36±8.18</td>
<td>4.7±2.5</td>
<td>0.041</td>
<td>0.009</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>≥ 20</td>
<td>7.1±14.1</td>
<td>4.7±2.5</td>
<td>0.8±0.2</td>
<td>0.001</td>
<td>0.001</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Vitamin D replacement in AS with low vitamin D levels improves antioxidant status via ADMA pathway and shows anti-inflammatory effects on IL-1 and IL-6. In literature, there is no other study investigating the effects of increased vitamin D levels on disease activity, inflammatory parameters and ADMA pathway in AS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3290

SAT0423

INCREASED PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS AMONG INDIVIDUALS WITH ANKYLOSING SPONDYLITIS IN CANADA: RESULTS FROM THE RHUMADATA® MULTICENTRE REGISTRY

S. Szabo1, S. Chebah2, L. Coupal3, D. Chouquette1, 3Broadstreet HEOR, Vancouver; 2Novartis Pharmaceuticals Canada; 3Institut de Recherche en Rhumatologie de Montréal, Montreal, Canada

Background: Among populations with ankylosing spondylitis (AS), the frequency and severity of extra-articular manifestations (EAMs) vary widely, due to underlying geographic and genetic differences, individual characteristics, and the impact of treatment with anti-tumour necrosis factor (TNF) agents. The frequency of EAMs

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among Canadians with AS has not previously been examined, using data from a large clinical registry.

**Objectives:** To estimate the prevalence of EAMs, including uveitis, inflammatory bowel disease (IBD), dactylitis, and enthesitis, in a population of Canadians undergoing active management for AS.

**Methods:** This retrospective cohort study used RHUMADATA®, a multicentre registry developed by rheumatologists of the IRMM and Centre d’ostéoporose et de rhumatologie de Québec to evaluate the effectiveness and safety of rheumatologic therapies. Up to 15 years of real-world observational data on the broad set of patients treated in clinical practice are available. The proportion with EAMs was estimated according to type. The frequency of EAMs was compared according to age at cohort entry (<40 vs >40 years), sex, AS severity (by BASDAI score), and status of treatment with anti-TNFs (anti-TNF-naive, anti-TNF-treated [without switching], and anti-TNF treated [with switching]).

**Results:** Median (SD) age at cohort entry was 39.0 (12.6) years, and 60.0% were male. Of the 944 patients, 268 (28.4%) were ever diagnosed with an EAM over a median of 9.66 (10.58) years of follow-up. Prevalence was 14.7% for uveitis, 5.8% for IBD, 4.3% for dactylitis, and 9.0% for enthesitis (Table). The proportion with EAMs was: slightly higher among females versus males (31.0% vs. 26.7%), among older versus younger patients (29.5% vs. 25.9%), among those with more severe disease (from 29.2% [mild AS] vs. 34.1% [severe AS]), and among anti-TNF treated patients (18.8% [anti-TNF-naive] vs 47.0% [treated with anti-TNFs, with switching]).

Table 1. EAMs among Canadian Patients from the Rhumadata database; overall, and according to levels of treatment status, key clinical, and demographic characteristics

<table>
<thead>
<tr>
<th>N</th>
<th>Uveitis n</th>
<th>IBD n</th>
<th>Dactylitis n</th>
<th>Enthesitis n</th>
<th>Any EAM n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>944</td>
<td>14.7</td>
<td>5.8</td>
<td>4.3</td>
<td>9.0</td>
</tr>
<tr>
<td>Males</td>
<td>566</td>
<td>81</td>
<td>14.3</td>
<td>29</td>
<td>4.1</td>
</tr>
<tr>
<td>Females</td>
<td>378</td>
<td>58</td>
<td>15.3</td>
<td>26</td>
<td>6.9</td>
</tr>
<tr>
<td>≤40 years at cohort entry</td>
<td>401</td>
<td>65</td>
<td>16.2</td>
<td>29</td>
<td>4.7</td>
</tr>
<tr>
<td>&gt;40 years at cohort entry</td>
<td>293</td>
<td>98</td>
<td>33.8</td>
<td>66</td>
<td>22.4</td>
</tr>
<tr>
<td>Missing AS severity</td>
<td>166</td>
<td>12</td>
<td>7.2</td>
<td>7</td>
<td>4.2</td>
</tr>
<tr>
<td>Mid AS (BASDAI &gt;3.5)</td>
<td>271</td>
<td>47</td>
<td>17.3</td>
<td>16</td>
<td>5.9</td>
</tr>
<tr>
<td>Moderate AS</td>
<td>350</td>
<td>62</td>
<td>17.1</td>
<td>26</td>
<td>7.4</td>
</tr>
<tr>
<td>Severe AS (BASDAI &gt;6.0)</td>
<td>255</td>
<td>36</td>
<td>14.1</td>
<td>22</td>
<td>7.8</td>
</tr>
<tr>
<td>Anti-TNF naive</td>
<td>490</td>
<td>97</td>
<td>19.8</td>
<td>37</td>
<td>7.7</td>
</tr>
<tr>
<td>Anti-TNF treated [no switching]</td>
<td>286</td>
<td>51</td>
<td>17.8</td>
<td>21</td>
<td>7.3</td>
</tr>
<tr>
<td>Anti-TNF treated [with switching]</td>
<td>168</td>
<td>41</td>
<td>24.4</td>
<td>16</td>
<td>9.5</td>
</tr>
</tbody>
</table>

**Conclusions:** Underdiagnosed axial disease is frequent in PsA, women having higher risk and IBD criteria being less sensitive in women. More complex patients (eg with higher enthesitis and peripheral arthritis) have a higher risk of being underdiagnosed. These patients are less frequently treated with biologic treatments, which could be the right treatment choice if were diagnosed. Axial disease needs to be ruled out using imaging modalities, even if back pain does not clinically suggest an inflammatory pattern.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3022

**SAT0424**

**AXIAL DISEASE IN PSORIATIC ARTHRITIS: BURDEN OF UNDERDIAGNOSED DISEASE AND RISK FACTORS IN REAL LIFE**

S.Z. Aydin1, U. Kalyoncu2 on behalf of the PsART study group. 1University of Ottawa, Ottawa, Canada; 2Hacettepe University, Ankara, Turkey

**Background:** The frequency of axial disease in Psoriatic Arthritis (PsA) is around 24–78% with additional patients with subclinical disease who have spondylitis-like changes or sacroiliitis in the absence of clinical findings. Despite that most of the physicians do not perform routine imaging with the argument that subclinical changes or sacroiliitis in the absence of clinical findings. Despite that most of the physicians do not perform routine imaging with the argument that subclinical disease has no effects on management decisions.

**Objectives:** To examine barriers for diagnosing axial disease in PsA and its implications in real life.

**Methods:** PsART (Psoriatic Arthritis Registry of Turkey) is a prospective, multicentre registry where PsA patients are consecutively recruited. Radiographs of the spine and sacroiliac joints were scored by one central reader, whenever available. Patients with axial disease according to the physician were compared with patients with imaging findings of Bacchus disease when appropriate.

**Results:** Among 1195 patients, 35% had axial disease according to the physician who were more frequently men (41.2% vs 32.2%; p=0.04), younger (44.4 (12.2) vs 47.7 (11.8); p=0.04), and inflammatory back pain (44.6% vs 34%; p=0.001), more on anti TNFs (37.1% vs 29.4%; p=0.01) and had more nail involvement (49.9% vs 43.2%; p=0.03). Within the IBD criteria, the ASAS criteria had the lowest sensitivity (59.7%) which was even lower in women (53.1%). Forty-nine (15.7%) patients were classified as having axial disease according to the rheumatologist despite not fulfilling any of the IBP criteria which was more frequent for women (21.1%) than men (8.2%; p=0.002). Among 71 patients that had syndesmophytes, 20 patients (28.2%) were not classified as having axial disease according to the physician. This higher was for women (15/42, 35.7%) then men (5/29, 17.2%). There were 126 patients who had sacroiliac fulfilling the ASAS criteria, despite being categorized as having axial disease by the clinician. The risk of being underdiagnosed was higher for women (30.8% vs 18.4%; p=0.003). These patients had higher Leeds enthesis scores, tender and swollen joint counts (table) and were less using anti-TNF medications (14.6% vs 38.7%; p=0.001).

The PROs and the physician global assessment were similar, suggesting a similar disease activity stage according to the patients and physicians in diagnosed and undiagnosed groups.

Table 1. Comparison of outcomes in patients with axial disease according to the clinician and axial disease by imaging only

<table>
<thead>
<tr>
<th>Axial disease according to the Clinician (n=415)</th>
<th>Axial disease by imaging only (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient global assessment</td>
<td>47 (24.8)</td>
</tr>
<tr>
<td>Pain</td>
<td>46.4 (28.7)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>47.1 (27.7)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>4.5 (2.5)</td>
</tr>
<tr>
<td>BASFI</td>
<td>3.3 (2.5)</td>
</tr>
<tr>
<td>Physician’s global assessment</td>
<td>38.7 (23.3)</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>3.4 (4.7)</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>1.3 (2.5)</td>
</tr>
<tr>
<td>Leeds enthesis index</td>
<td>0.3 (0.8)</td>
</tr>
</tbody>
</table>

**Conclusions:** Underdiagnosed axial disease is frequent in PsA, women having higher risk and IBP criteria being less sensitive in women. More complex patients (eg with higher enthesitis and peripheral arthritis) have a higher risk of being underdiagnosed. These patients are less frequently treated with biologic treatments, which could be the right treatment choice if were diagnosed. Axial disease needs to be ruled out using imaging modalities, even if back pain does not clinically suggest an inflammatory pattern.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5021
SAT0426  HIGH LEVELS OF EMPLOYMENT BUT PERSISTING WORK PLACE IMPAIRMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS ON BIOLOGIC THERAPY

SAT0427  ASAS HEALTH INDEX: VALIDITY AND RELIABILITY IN ARGENTINEAN PATIENTS WITH SPONDYLOARTHRITIS

SAT0428  WHICH CRITERIA FOR INFLAMMATORY BACK PAIN IN SPONDYLOARTHRITIS ARE OPTIMAL? DATA FROM THE SCREENING FOR AXIAL SPONDYLOARTHRITIS IN PSORIASIS, IRRITIS, AND COLITIS STUDY (SASPIC)

Background: Criteria for inflammatory back pain (IBP) in spondyloarthritis (SpA) include the Calin, Berlin, and Assessments in SpA International Society (ASAS) criteria, although no studies have undertaken comparative validation to determine which are optimal versus the rheumatologist expert opinion gold standard assessment.

Objectives: We aimed to compare IBP criteria in unselected patients presenting with undiagnosed back pain to rheumatology practice.

Methods: The Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis Study (SASPIC) is aimed at the development and validation of a triage strategy for detection of axial SpA in patients presenting with undiagnosed back pain. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any of one psoriasis, acute anterior uveitis, or colitis diagnosed by the relevant specialist undergo routine clinical evaluation by a rheumatologist for axial SpA. The rheumatologist then uses the presence or absence of IBP (defined as ≤5 or ≤5 on 0–10 scale, respectively) and axial SpA (yes/no) after the clinical evaluation and review of labs (B27, CRP) and imaging (x-ray, MRI). Clinical and laboratory data, radiographs and MRI scans are also assessed centrally for diagnosis of axial SpA (yes/no). We assessed sensitivity and specificity of each
of the IBP criteria for diagnosis of IBP according to the local rheumatologist, diagnosis of axial SpA by local rheumatologist, diagnosis of axial SpA by central assessment, and concordant diagnosis of axial SpA by both local and central assessment.

Results: We recruited 185 patients (48.6% male, mean age 27.6 years, mean back pain duration 7.0 years) with iritis (30.3%), psoriasis with arthritis (34.9%), Crohn’s disease (18.9%) and ulcerative colitis (18.9%). IBP and/or axial SpA were considered present in 65.2% and 47.3%, respectively, of all patients by the local rheumatologist. By central assessment axial SpA was considered present in 32.7% whilst among patients with a concordant diagnosis by both local and central assessment 37.2% were considered to have axial SpA. Sensitivity was comparatively high for all IBP criteria but specificity was poor. The Berlin criteria consistently performed best when the Calin criteria consistently performed worst (Table).

<table>
<thead>
<tr>
<th>Gold standard</th>
<th>IBP criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR−</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBP by local rheumatologist</td>
<td>ASAS</td>
<td>83.8</td>
<td>58.8</td>
<td>2.03</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>Berlin</td>
<td>88.9</td>
<td>76.5</td>
<td>3.78</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
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<td>94.0</td>
<td>37.3</td>
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<tr>
<td>Axial SpA by local rheumatologist</td>
<td>ASAS</td>
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</tr>
<tr>
<td></td>
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<td>51.3</td>
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<td>Axial SpA by central assessment</td>
<td>ASAS</td>
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<td>37.5</td>
<td>1.28</td>
<td>0.53</td>
</tr>
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<td>Berlin</td>
<td>80.0</td>
<td>38.9</td>
<td>1.31</td>
<td>0.51</td>
</tr>
<tr>
<td></td>
<td>Calin</td>
<td>94.3</td>
<td>20.8</td>
<td>1.19</td>
<td>0.27</td>
</tr>
<tr>
<td>Axial SpA by central and local assessment</td>
<td>ASAS</td>
<td>86.2</td>
<td>44.9</td>
<td>1.56</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Berlin</td>
<td>86.2</td>
<td>51.0</td>
<td>1.76</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>Calin</td>
<td>93.1</td>
<td>22.4</td>
<td>1.30</td>
<td>0.21</td>
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</table>

Conclusions: IBP criteria lack specificity for rheumatologist diagnosed IBP or axial SpA but the Berlin criteria have consistently better performance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5151

SAT0429 | THE PERFORMANCE OF MAGNETIC RESONANCE IMAGING USING THE VIBE TECHNIQUE TO DETECT STRUCTURAL CHANGES IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS IN COMPARISON TO CONVENTIONAL RADIOGRAPHY AND COMPUTED TOMOGRAPHY

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Background: Magnetic resonance imaging (MRI) is the gold standard for detection of inflammation in the sacroiliac joints (SIJ) of patients (pts) with axial spondyloarthritids (axSpA), while for chronic, structural changes (erosions, sclerosis and ankylosis) conventional radiographs (CR) and computed tomography (CT) are often preferred. The 3D volumetric interpolated breath-hold sequence (VIBE) is an MRI technique, easy to acquire in daily practice, that can visualize cartilage especially well because of its good contrast to synovial tissue.

Objectives: To compare the ability of the VIBE technique to detect structural changes in comparison to CR and CT in SIs of axSpA patients in relation to symptom duration and age.

Methods: Complete sets of MRI (T1 and VIBE techniques), CT and CR of SIs of 109 AS patients were available. Two readers evaluated all images independently, blinded to demographic data and in separate, 82% HLA-B27+, 58 pts (53%) had a disease duration <3y. Agreement for positive and negative findings between MRI and CT was generally high (ICC=0.979–0.997). Overall, MRI detected significantly more SIJ erosions in pts <45y (n=134) and in pts with disease duration <3y (n=125) as compared to CT (n=91, p=0.002 and n=90, p=0.003, respectively) and in pts with age <45y (n=61, p<0.001) as compared to CR, while there were no differences between MRI and CT in pts >45y or disease duration >3y. Linear regression analysis showed that the sensitivity of MRI was superior in the disease duration ≤45y (n=134) but weak in pts >45y (B=0.032, p=0.001). However, CT detected significantly more SIJ half erosions in all subgroups and more SIJ with sclerosis in pts with disease duration <3y (n=64 vs. n=37, respectively, p=0.006), and it also detected more so with sclerosis in pts <45y (n=67 vs. n=38, p=0.001) and disease duration >3y (n=64 vs. n=40, p=0.003) as compared to MRI, while no differences were found in the assessment of ankylosis.

Conclusions: MRI in the T1 and VIBE technique is more sensitive in the detection of erosions as compared to CT and CR in axSpA pts with short disease duration and younger age. This is due to its ability to identify structural damage in the SIJ cartilage that has not yet extended to the underlying bone. These differences are not found in pts with longer disease duration or older age. This data suggests a more prominent role for MRI also for the early detection of structural changes in the SIJ of axSpA pts.

Disclosure of Interest: None declared


SAT0430 | THE RELATIONSHIP BETWEEN EXOSOMAL miRNA21-5P AND ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) affects human health seriously, which is difficult to diagnose in the early stages. It is reported that MicroRNAs (miRNAs) may serve as novel biomarkers for AS. Exosome can function as vehicles to deliver miRNAs in body fluids including saliva and plasma. Our previous study shows that exosomal miRNA21–5P is higher expressed in AS patients, compared with healthy subjects. However, the relationship between exosomal miRNA21–5P and AS has yet to be determined.

Objectives: The aim of the present study is to explore the relationship between exosomal miRNA21–5P and AS.

Methods: AS patients who fulfilled the modified New York criteria were enrolled in our study. Healthy subjects were also enrolled as control group. BASDAI, BAVSI, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were evaluated. Quantitative reverse-transcription PCR (qRT-PCR) was used to confirm the expression of exosomal miRNA21–5P, and receiver-operator characteristic (ROC) curve was used to evaluate the diagnostic value of exosomal miRNA21–5P for AS. According to the cut off value, AS patients were divided into exosomal miRNA21–5P low value group (<cut off value) and exosomal miRNA21–5P high value group (>cut off value), and the difference of AS patient’s clinical characteristics between the two groups were explored.

Results: Twenty healthy subjects and 64 AS patients were enrolled in the study. The qRT-PCR results indicated that the expression level of exosomal miRNA21–5P in AS patients was (2.041±0.975) times higher than that of healthy subjects. ROC curve analysis showed that exosomal miRNA21–5P had significant diagnostic value for AS with the AUC of 0.809 (CI95%; 0.691–0.921). In addition, the cut off value was 1.310, with the specificity of 80.0% and sensitivity of 76.32%. According to the cut off value of exosomal miRNA21–5P, AS patients were divided into the low exosomal miRNA21–5P group (<1.310) and the high exosomal miRNA21–5P group (>1.310). Among the 38 AS patients, 12 cases were in the low exosomal miRNA21–5P group and 26 cases were in the high exosomal miRNA21–5P group. Comparations of the clinical characteristics of the two groups showed that BASDAI, BAVSI, CRP and ESR were significantly increased in exosomal miRNA21–5P high value group.

Conclusions: Exosomal miRNA21–5P was significantly increased in AS patients, which may be used as a biomarker for AS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6836

SAT0431 | THE RELATIONSHIP OF SEASONAL VARIATION, THE ONSET AND THE SYMPTOMS OF ANKYLOSING SPONDYLITIS MEASURED BY SELF-ADMINISTRATED QUESTIONNAIRES IN CHINESE PATIENTS

Y. Jiang, M. Yang, Z. Lin, Q. Wei, S. Cao, J. Gu. Rheumatology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease which mainly results in pain, functional limitation and even less life expectancy. Seasonal variation was found in rheumatoid arthritis and gout [1,2]. No reports had been focused on seasonal variation of AS onset or symptoms in AS patients.

Objectives: Our study was to investigate the relationship of seasonal variation and the onset and symptoms of AS in Chinese patients.

Methods: Adult AS patients diagnosed with the modified New York criteria for AS whose disease duration was over 2 years were enrolled from several provinces all over China. Participants were required to complete a set of questionnaires and examinations, including demographic and clinical information. Questions included ‘in which season(s) did you have the initial symptoms of AS’, and ‘in which season(s) were the symptoms aggravated/improved’. The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis.

Results: Of all the 859 AS patients, 75.1% were male patients. 47.8% were married. Mean age was 30.60±9.50 years. Mean disease duration was 7.43±6.92 years. 27.7% of the patients had an onset of the disease in summer, while the lowest incidence happened in autumn (12.5%, p<0.05). 29.6% of the patients could not recall the exact season. 29.5% of the patients’ symptoms got worse in winter,
while only 2.6% of the patients felt worse in autumn, in comparison of 10.3% in winter and 6.0% in summer. 24.4% of the patients felt relieved in summer, while only 2.6% felt better in spring, with a overall 2.7% felt better in spring, with a lower rate of the first in autumn.

Conclusions: More patients had an onset of AS in summer, compared to other seasons. More patients felt worse in winter and better in summer. Nearly half of AS patients considered that there were no seasonal differences in the deterioration or improvement of the symptoms.

References:

Disclosure of Interest: Y. Jiang: None declared, M. Yang: None declared, Z. Lin: None declared, O. Wei: None declared, S. Cao: None declared, J. Gu Grant/research support from: Guangzhou Science and Technology Plan Projects [grant number 200622-Z0221] and 5010 Subject of Sun Yat-sen University (2009–2010)

DOI: 10.1136/annrheumdis-2017-eular.4167

SAT0432 | CORRELATION BETWEEN THE SPINAL MRI FINDINGS AND NEW BONE FORMATION FACTOR (DKK-1) IN PATIENTS WITH SPONDYLOARTHRITIS

Z. Zhao, G. Wang, Y.Y. Wang, J.S. Yang, J. Zhu, F. Huang. Rheumatology. Chinese PLA General Hospital, Beijing, China

Background: Recent prospective data suggest that spinal inflammatory damage in patients with ankylosing spondylitis will eventually convert into fat. In these complex inflammatory lesions, bone formation and inflammation are not synchronized. The molecular basis responsible for new bone formation in SpA patients is still unclear. Serum level of dickkopf-1 (Dkk-1), the natural inhibitor of Wnt protein, is a main factor in limiting new bone formation.

Objectives: In this study, we aimed to assess the correlation between the secreted protein Dkk-1 and abnormal findings on spinal MRI through a prospective study of SpA.

Methods: Thirty patients with active axial SpA (axSpA) who fulfilled the ASAS axSpA criteria were enrolled. All patients received an injection of recombinant human TNF receptor-antibody fusion protein (YISAIPU) at a dosage of 50 mg/week for 6 months. Patient report outcome measure questionnaires and physical examination, blood tests were completed according to the study protocol. All patients were scored for bone marrow edema and fat infiltration on spinal MRI using the SPARCC scoring system by two blinded reviewers.

Results: Before treatment After treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR (mm/h)</td>
<td>23.7±12.27</td>
<td>5.0±4.63**</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>2.59±0.90</td>
<td>0.40±0.52**</td>
</tr>
<tr>
<td>BASDAI</td>
<td>6.23±1.29</td>
<td>2.52±1.84**</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.78±1.44</td>
<td>2.69±1.72**</td>
</tr>
<tr>
<td>BASMI</td>
<td>2.46±1.91</td>
<td>0.69±1.21**</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>3.77±0.83</td>
<td>1.58±0.74**</td>
</tr>
<tr>
<td>Dkk-1 (ng/ml)</td>
<td>98.23±13.41</td>
<td>51.88±41.90*</td>
</tr>
<tr>
<td>Spine-BME</td>
<td>20.2±21.53</td>
<td>6.08±6.09*</td>
</tr>
<tr>
<td>Spine-FAT</td>
<td>10.0±10.38</td>
<td>13.81±15.34</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01.

Table 1. Clinical indexes, serum Dkk-1 and spine imaging scores before and after treatment.

Conclusions: Our findings show that biological therapy in patients with RA or AS is associated with a 13 to 35 fold increase in prevalence of PPP. While the prevalence of biological-associated PV is lower than the prevalence of PV in the general population. In this study PV and PPP are different from each other regarding prevalence, time to onset and consequences for biological treatment, and therefore should be considered as separate entities.

 references:
Disclosure of Interest: None declared

**SAT0434** NETWORK META-ANALYSIS ON THE EFFICACY OF NOVEL THERAPEUTIC AGENTS IN PATIENTS WITH PSORIATIC ARTHRITIS

T.T. Cheung, M.F. Tsoi, Y. Fei, C.S. Lau, B.M.Y. Cheung. Medicine, The University of Hong Kong, Hong Kong, Hong Kong

**Background:** Novel therapeutic agents are more effective than DMARDs in the management of psoriatic arthritis. However, direct comparisons of efficacy between these novel therapeutic agents are lacking.

**Objectives:** This network meta-analysis aims to compare the relative efficacies between different novel therapeutic agents.

**Methods:** Literature searching was conducted in MEDLINE, EMBASE, Scopus, ISI Web of Science, Cochrane Library, Clinicaltrial.gov and recent rheumatology conference abstracts up to Nov 2016. 2 independent researchers analysed the articles. For inclusion, randomised, placebo-controlled trials must report the proportion of patients achieving ACR20, ACR50, ACR70 and PASI75 responses. The outcomes of this network meta-analysis were the proportion of patients achieving ACR20, ACR50, ACR70 and PASI75 responses with reference to placebo and etanercept.

Results were analysed using random effect model by R statistics (version 3.3.1) with statistical package netmeta (version 0.9–2). The heterogeneity of the study results was determined by the I² statistics.

**Results:** 18 trials were included into this study. In general, all novel therapeutic agents demonstrated superior efficacy than placebo. With reference to etanercept, apremilast and ustekinumab were associated with less proportions of patients achieving ACR20 response (odds ratio [95% confidence interval]: golimumab: 3.51 [0.44–28.2]; adalimumab: 0.33 [0.13; 0.86]; 5mg Tofacitinib BID: 0.25 [0.08; 0.81]; 45mg Ustekinumab: 0.26 [0.09; 0.75]; 30mg Secukinumab 0.77 [0.21; 2.80]; 30mg Apremilast: 0.24 [0.09; 0.63]; 20mg Apremilast BID: 0.18 [0.07; 0.49]; Placebo: 0.10 [0.04; 0.22]; 0.09 [0.03; 0.35]).

Conclusions: Apremilast and ustekinumab were less efficacious than etanercept in terms of ACR20 response. All the novel therapeutic agents demonstrated comparable efficacies in terms of ACR50, ACR70 and PASI75 responses.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5096

**SAT0435** IL17 CORRELATES POSITIVELY WITH TGF-BETA 1 AND DKK1 AND INVERSELY WITH BMP2 AND 4 IN SYNOVIAL MEMBRANE OF PATIENTS WITH PSORIATIC ARTHRITIS


**Background:** Immune and non-immune cells contribute to the pathology of chronic arthritis and they can contribute to tissue remodeling and repair as well as disease progression. An important role for their products such as TGF-beta 1, IL17 or BMPs has been suggested in homoeostatic and remodeling mechanisms in arthritis. BMP signaling could have an anti-inflammatory role in the control and maintenance of low levels of pro-inflammatory factors in healthy joints or the early stage of RA.

**Objectives:** To analyze and compare serum levels, gene expression and immunohistochemistry (IHC) in synovial membrane of inflammation and bone destruction/regeneration biomarkers in patients with psoriatic arthritis (PsA), undernourished seronegative arthritis (USA), Osteoarthritis of the knee (kOA) and ankylosing spondylitis (AS).

**Methods:** We recruited 45 consecutive patients with chronic knee arthritis referred for undergoing arthroscopies (17 PsA, 12 USA, 12 kOA, 4 AS). Synovial membrane was processed for IHC analysis and quantification of mRNA expression. Synovial levels of TGF-beta 1, IL6, IL17 and IL22, DKK1, Sclerostin, BMP2, BMP4, Wnt1 and Wnt5a were measured (ELISA). We analyzed and compared these data with the demographic, clinical, analytical and radiological characteristics of the patients. Data were analyzed using the SPSS version 17.0 software and statistical significance was defined as P<0.05.

Conclusions: Synovial membrane samples from 41 patients were collected for biomechanical, IHC and RNA extraction from 29 patients for mRNA expression and flow cytometry from 38 patients for protein levels measurement. IL17 gene expression was higher in PsA patients (p=0.027) and correlated positively with DKK1 (r=0.424, p=0.022) and negatively with BMP2 (r=-0.396, p=0.030) and BMP4 (r=-0.472, p=0.010). IL17 reactivity for TGF-beta 1 in synovial tissue was higher in patients with psoriatic arthritis compared to placebo (p=0.010) and correlated positively with IL17 (r=0.389, p=0.012) and DKK1 (r=0.388, p=0.012). Moreover, serum levels of TGF-beta 1 were significantly increased in PsA with erosions (p=0.044).

Disclosure of Interest: None declared

**SAT0436** DURABILITY OF APREMILAST RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS: LONG-TERM (208-WEEK) RESULTS FROM THE PALACE 1 TRIAL

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**Background:** Optimizing treatment choice in psoriatic arthritis (PsA) necessitates an understanding of the long-term effects of therapies across varied manifestations of this complex disease. Data from 4 years of apremilast (APR) treatment in PALACE 1 were used to examine disease control across markers of active inflammation, such as SJC, as well as improvements in patient (pt) functionality, as assessed using the HAQ-DI.

**Objectives:** Evaluate long-term outcomes with APR treatment after ≥1 DMARD or biologic in pts with active PsA.

**Methods:** Pts were randomized (1:1:1) to placebo (PBO), APR 30 mg BD (APR30), or APR 20 mg BD (APR20). The PBO-controlled phase continued to Wk 24, at which time all remaining PBO pts were re-randomized to APR30 or APR20.
Conclusions: APR30 demonstrated sustained, clinically meaningful improvements in signs and symptoms of PsA, physical function, and associated psoriasis over 208 wks. APR30 continued to demonstrate a favorable safety profile and was generally well tolerated.

Disclosure of Interest: A. Kavanaugh-Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, D. Gladenman/Grant/research support from: Abbvie, Amgen, BMS, Celgene Corporation, Janssen Novartis, Pfizer, UCB, Consultant from: Abbvie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, J. Gomez-Reino/Grant/research support from: Boehringer Ingelheim, Centocor, GSK, MSD, Pfizer, Sanofi Aventis, Sanofi Pasteur, Schering-Plough, Serono, Weyth, Speakers bureau: Boehringer Ingelheim, GSK, MSD, Pfizer, Roche, Sanofia Aventis, Schering-Plough, Weyth, E. Lespesailles Grant/research support from: Amgen, Eli Lilly, Janssen-Cilag, Novartis, Pfizer, Roche, Consultant for: Abbott, Amgen, Biogen Idec, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Servier, P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Schutt Grant/research support from: Abbott, Celgene Corporation, Roche, UCB, Consultant for: Abbott, Celgene Corporation, Roche, UCB, M. Mcrath Grant/research support from: Celgene Corporation, N. Delev Employee of: Celgene Corporation, Paris Employee of: Celgene Corporation, L. Tallroth Consultant for: Abbvie, Novartis, Pfizer, Roche, J. Wollenhaupt Grant/research support from: Abbvie, BMS, MSD, Pfizer, Roche, Consultant for: Abbvie, BMS, MSD, Pfizer, UCB, DOI: 10.1136/annrheumdis-2017-eular.3001
SAT0438  PSORIATIC ARTHRITIS AND NODAL OSTEOARTHRITIS CAN BE DIFFERENTIATED USING HAND RADIOGRAPHS: A NOVEL METHOD

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Background: One of the difficulties of rheumatology practice is the differentiation of Psoriatic Arthritis (PsA) and Nodal Osteoarthritis (NOA) in some patients with distal interphalangeal joint involvement. MRI and ultrasound imaging, have recently been demonstrated to be very valuable in some cases (1,2). This differentiation is critical, as treatment for these debilitating conditions is completely different.

Objectives: To establish a scoring system of radiographic joint and soft tissue features to differentiate PsA from NOA.

Methods: We devised a scoring system for hand radiographs of interphalangeal joints, soft tissue and bone features, allocated major and minor weighting. The scoring system was then tested in a single blind analysis of hand radiographs from 48 patients with PsA, 50 with NOA and 1 with RA (incorrectly classified as PsA at study entry) seen between 2008 and 2016. Anonymised patient images were assessed by a Musculoskeletal (MSK) Radiologist, blind to clinical information. Radiological diagnosis was then compared with clinical diagnosis. We taught the method to 2 rheumatology and 1 radiology trainees over 1 hour, who then independently assessed the same radiographs.

Results: The MSK radiologist reported normal hand radiographs in 5 patients. Of the remaining 53 patients, the scoring system correctly allocated 100% of images into PsA, NOA or RA. Notably, 2 patients with NOA who subsequently developed PsA several years later, and 1 patient with seropositive RA, initially misclassified as PsA, were correctly identified by the MSK radiologist.

Conclusions: We taught the method to 2 rheumatology and 1 radiology trainees over 1 hour, who then independently assessed the same radiographs.

SAT0439  INTEGRATED SAFETY SUMMARY OF TOFACITINIB IN PSORIATIC ARTHRITIS CLINICAL STUDIES

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Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA).

Objectives: To describe the safety profile of tofacitinib from integrated Phase (P)3 and long-term extension (LTE) studies.

Methods: Data were analysed for patients (pts) who received ≥1 dose of tofacitinib 5 or 10 mg BID or placebo (PBO), integrated across 2 P3 studies (OPAL Broaden [12 months; NCT01877668], OPAL Beyond [6 months; NCT01824399]) and 1 LTE study (OPAL Balance [ongoing, database not locked; NCT01976364]). Common adverse events (AEs; occurring in ≥2% of tofacitinib pts in any group) were analysed in the PBO-controlled portion (Months 0–3) of the P3 studies (Cohort 1 [C1]). Serious AEs (SAEs) and discontinuations due to AEs were analysed over 12 months in pts randomised to tofacitinib 5 or 10 mg BID in P3 studies (Cohort 2a [C2a]; pts randomised to PBO were excluded from this analysis. Deaths and AEs of special interest (serious infections [SI], herpes zoster [HZ], opportunistic infections [OI]) including HZ, major adverse cardiac events [MACE], malignancies, non-melanoma skin cancer [NMSC]) were evaluated in all tofacitinib-treated pts in the P3 and LTE studies (Cohort 3 [C3]). Incidence rates (IR; pts with events/100 pt-years [PY]) and 95% confidence intervals are reported. Laboratory results will be reported in future publications.

Results: C1 included 474 tofacitinib- and 236 PBO-treated pts; C2a included 474 tofacitinib-treated pts, and C3 included 783 tofacitinib-treated pts (exposure: 776 PY). Nasopharyngitis (5.9%) and headache (8.5%) were the most commonly reported AEs at Month 3 in pts receiving tofacitinib 5 or 10 mg BID, respectively (Table). In pts randomised to tofacitinib 5 or 10 mg BID, over 12 months (C2a), the IRs for SAEs were 7.92 (4.09, 13.84) and 8.11 (4.19, 14.17), respectively. Discontinuation due to AEs occurred in 11 (4.6%) and 11 (4.7%) pts randomised to tofacitinib 5 and 10 mg BID, respectively. The IRs for SIs of 17.5 (3.68, 13.08), respectively, over 12 months (C2a). Across all tofacitinib-treated pts in the P3 and LTE studies (C3), SIs occurred in 11 pts (1.4%; IR 1.40 [0.70, 2.50]). HZ was reported in 16 pts (2.0%; IR 2.05 [1.17, 3.33]) receiving tofacitinib. All 3 cases of multidermalar HZ were adjudicated as OIs; these were the only OIs (0.2%; IR 0.38 [0.08, 1.11]). In C3, 2 deaths occurred (0.3%; IR 0.25 [0.03, 0.91]); all were considered unrelated to the study drug. MACE were reported in 3 pts (0.4%; IR 0.38 [0.08, 1.11]), malignancies (excluding NMSC) in 5 pts (0.6%; IR 0.63 [0.21, 1.48]) and NMSC in 4 pts (0.5%; IR 0.51 [0.14, 1.30]).

Table: Common adverse events (≥2% occurrence in any group, all causalties) at Month 3 in patients receiving tofacitinib 5 or 10 mg BID or placebo

<table>
<thead>
<tr>
<th>Common Adverse Events, n (%)</th>
<th>Tofacitinib 5 mg BID (N=238)</th>
<th>Tofacitinib 10 mg BID (N=226)</th>
<th>Placebo (N=236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>(8.0)</td>
<td>(9.3)</td>
<td>(1.0)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>(5.2)</td>
<td>(2.0)</td>
<td>(2.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>(6.2)</td>
<td>(5.2)</td>
<td>(7.0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>(0.0)</td>
<td>(7.0)</td>
<td>(1.0)</td>
</tr>
<tr>
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<tr>
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<td>(13.5)</td>
<td>(6.2)</td>
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<td>Urinary tract infection</td>
<td>(3.1)</td>
<td>(6.2)</td>
<td>(5.2)</td>
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<tr>
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<td>(9.8)</td>
<td>(20.5)</td>
<td>(11.7)</td>
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<tr>
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<tr>
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<tr>
<td>Hypertension</td>
<td>(4.1)</td>
<td>(5.2)</td>
<td>(3.3)</td>
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Conclusions: Tofacitinib was well tolerated in pts with PsA, with a safety profile consistent to that seen in RA; no new risks were identified. Longer-term follow-up and larger pt populations will provide further information on the safety profile of tofacitinib in pts with PsA.

Acknowledgements: These studies were sponsored by Pfizer Inc. Editorial support was provided by C. Viegelmann of CMc and was funded by Pfizer Inc.


DOI: 10.1136/annrheumdis-2017-eular.6350

SAT0440  DO DEPRESSION AND ANXIETY INFLUENCE THE CHANCE OF REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS? REAL LIFE DATA FROM THE NOR-DMARD STUDY

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Background: Depression and anxiety are frequent comorbidities in psoriatic arthritis (PsA). The potential influence of depression/anxiety on achievement of remission remains unexplored.

Objectives: To investigate the predictive value of baseline depression/anxiety on the likelihood of achieving remission in PsA, as well as the associations between
baseline depression/anxiety and the components of the remission criteria at follow-up.

Methods: From the prospective multi-center observational NOR-DMARD study we included PsA patients starting first-time methotrexate/tumor necrosis factor inhibitors between year 2006 and 2012. The following criteria for depression/anxiety were assessed: 1) the Medical Outcomes Survey Short Form-36 (SF-36) Mental Health subscale (MH); 2) SF-36 Mental Component Summary score (MCS); 3) The predictive value of baseline depression/anxiety on remission at 3 and 6 months was explored in prespecified logistic regression models adjusted for age, sex, disease duration and smoking, and the associations between baseline depression/anxiety and the components of the remission criteria at follow-up in prespecified multiple linear regression models adjusted for age, sex, disease duration and smoking.

Results: 805 PsA patients were included (mean (SD) age 48.0 (12.4) years, median (25th-75th percentile) disease duration 1.0 (0.07–6.8) years, 50.8% females, 28.6% current smokers). According to the SF-36MH;SF-36MCS;38 criteria 15.6/25.2% of the patients had depression/anxiety at baseline, respectively. Lower percentages of patients with vs. without baseline depression/anxiety achieved remission at 6 months (unadjusted analyses:figure). Patients with baseline depression/anxiety had consistently lower point estimates for achievement of remission at follow-up, but did not reach significance for all the analyses (adjusted analyses: table).

Baseline depression/anxiety was associated with increased patient’s global assessment and joint pain at follow-up, but not with swollen joint count or levels of acute phase reactants.

Objectives: To investigate the merits of different potential remission definitions using data from the PRESTA study.

Methods: Remission was investigated for disease activity index for PsA for 3 definitions: very low disease activity (VLDA), Disease Activity in PsA (DAPSA), and clinical (c)DAPSA. VLDMA index was defined as 7/7 met criteria of the minimal disease activity (MDA) cut-off points: tender joint count (TJC) ≤ 5, swollen joint count (SJC) ≤ 7, psoriasis activity and severity index (PASI) ≤ 1, patient global visual analog scale (PtVAS) ≤ 20mm, Pt pain VAS ≤ 15mm, health assessment questionnaire (HAQ) ≤ 0.5, tender enthesal point ≤ 1. VLDMA remission was defined as VDCA ≤ 4 (TJC, SJC, physician global VAS [cm], Pt VAS [cm], C-reactive protein [CRP]) and cDAPSA remission was defined as cDAPSA ≤ 4 (DAPSA without CRP).

Results: At Week 24, the proportion of patients achieving remission was 9.6%, 31.0%, and 34.7% for VLDMA, and cDAPSA remission, respectively. Discordance between VLDMA and DAPSA or cDAPSA remission was 21.7% or 25.1%, respectively. Only 0.2% of the patients that achieved VLDMA did not achieve DAPSA remission and 21.5% vice versa (Kappa coefficient 0.38) and 0.0% in the case of cDAPSA remission and 25.1% vice versa (Kappa coefficient 0.33). At the end of the study, residual levels of dactylitis and enthesitis appeared to be similar among all definitions (all ≤3.0%); however, patients achieving DAPSA and cDAPSA remission had higher proportions of patients with PASI > 3 versus patients achieving VLDMA remission (PASI > 2.5: VLDMA 0.0% vs DAPSA 4.6% vs cDAPSA 47.2%; PASI ≥ 10: VLDMA 0.0% vs DAPSA 5.8% vs cDAPSA 6.4%).

Raised CRP values (upper limit of normal >8.9 mmol/L) were 7.8%, 4.8%, and 7.3% for VLDMA, DAPSA, and cDAPSA, respectively.

Conclusions: VLDMA remission is a more stringent target than DAPSA and cDAPSA remission, with the advantage of including an measurement for psoriasis. Therefore, VLDMA is more useful than DAPSA or cDAPSA in assessing a remission state in patients with PsA and extended skin lesions. Measurement of CRP levels does not appear to provide further information on current disease activity level in these patients and exclusion of this laboratory marker should facilitate remission assessment in clinical practice.


measurement. As cost data were not normally distributed, standard errors (SEs), 95% confidence intervals (CIs) and P-values were estimated by bootstrap resampling (10,000 samples).

**Results:** Data were available for 95 PsA patients (female: n=43). Mean HAQ-DI score was 0.81 (SE 0.08); mean age at HAQ-DI measurement was 56.8 (SE 1.04). Mean total usual healthcare costs, excluding medication costs, were €1,588 (SE 172.3). Regression modelling indicated that a 1-point increase in HAQ-DI score was associated with an increase in total costs, excluding medications, of £547.49 (SE 222.7; 95% CI 191.1–1,103.8; P=0.004) (Table). Subgroup analyses suggested trends for higher cost increases within the lower HAQ-DI cohort (HAQ-DI ≤1) and for those with greatest disease duration (>10 years). Costs associated with secondary care consultations seemed to be the primary factor in the association between HAQ-DI and total costs.

**Conclusions:** Models incorporating total healthcare costs were highly significant; this association appears to be driven mainly by secondary care consultation costs. Costs in this study were similar to previous studies in RA populations. A study limitation was that only direct medical costs were considered, which may underestimate the true burden of PsA on healthcare systems and the wider society.

**References:**

**Disclosure of Interest:** A. Maguire Grant/research support from: Cogentia Healthcare Consulting Ltd, UK, I. Handel Consultant for: Visible Analytics Limited, W. Tillett: None declared, F. Mughal Employee of: Celgene Ltd, J. Morris Grant/research support from: Celgene Ltd, N. Hawkins Grant/research support from: Celgene Ltd, C. Cavill Grant/research support from: Celgene Ltd, E. Korendowych Grant/research support from: Abbvie, Celgene and Pfizer Consultant for: Janssen, Abbvie, Novartis, Pfizer and Celgene, Speakers bureau: Janssen, Abbvie, Novartis, Pfizer and Celgene, N. McHugh Grant/research support from: Celgene Ltd.

DOI: 10.1136/annrheumdis-2017-eular.5332

**SAT0443 IDENTIFICATION OF PREDICTORS OF MINIMAL DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS**

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**Background:** Psoriatic arthritis (PsA) is a systemic inflammatory disease with articular and extra-articular features, the disease activity ranges from mild oligoarthritis to destructive polyarthritis. Hence, establishing the prognosis of a patient with PsA is very important to better define the treatment strategy. Furthermore, minimal disease activity (MDA) is a validated composite outcome measure since it correlates well with long-term outcomes (e.g. development of joint damage)1. The aim of our study was to explore the short-term effects of secukinumab on bone.

**Methods:** Consecutive PsA patients attending the outpatient Early Arthritis Clinic in Udine or Verona in the last two years, were assessed. All the included patients had: I) CASPAR score ≥2; II) new diagnosis of PsA III) a complete clinical data and follow-up of at least 12 months. The GRAPPA recommendations on the management of PsA were followed. Statistical analysis included T-test, ANOVA and Pearson’s test in order to find possible predictors of MDA.

**Results:** Eighty-one early PsA patients were included in the study. 47/81 (58.2%) reached MDA at 12 month of follow up; 68/81 (83.9%) were in c-DMARDs while 11/81 (13.6%) were in b-DMARDs. Two variables at baseline were selected according to the groups based on achievement of MDA. These were: 1) lower LEI score was significantly lower at baseline in patients reaching MDA (0.43 Vs 0.86, p=0.001); and 2) a lower baseline CRP (1.2 mg/dl vs 2.8 mg/dl, p=0.008). Of note, neither the baseline disease activity evaluated with DAPSA nor the time to referral were selected by statistical analysis.

**Conclusions:** Baseline lower LEI score and lower CRP were identified as clinical predictors of MDA after 12 months of treatment in PsA. Therefore, patients with a more active enthesitis or higher inflammation may have a less responsive disease. This may be relevant to select proper treatments at baseline, and indirectly confirms that enthesitis is a key therapeutic target in PsA.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4987

**SAT0445 DETECTION OF PSORIATIC ARTHRITIS AT EARLY ONSET: A MULTI-PROTEOMIC APPROACH TO DEVELOPING A NEW BLOOD TEST**

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**Background:** Psoriatic Arthritis (PsA) is an inflammatory arthritis (IA) frequently associated with psoriasis. Clinically, it is a complex heterogeneous disease and there are no diagnostic tests or criteria [1]. At first presentation, PsA may resemble other disease types - especially rheumatoid arthritis (RA), Making an accurate and early diagnosis is particularly important to ensure that individual patients receive effective and safe medication and so optimise long-term patient outcomes. Thus, it is widely acknowledged by physicians and patients alike that a new diagnostic test is urgently needed to facilitate the early and specific diagnosis of PsA [2].

**Objectives:** To (i) identify and verify candidate biomarkers with the potential to segregate patients with PsA from those with RA; and (ii) explore the value of combining different proteomic discovery platforms.

**Methods:** Serum samples were obtained from a cohort of 64 patients (32 PsA (<12 months); 32 RA defined as disease onset <12 months, and DMARD naïve). Individual baseline samples were analysed with label free LC-MS/MS (n=64), the Luminex xMAP (n=62) and an aptamer based platform called SOMAscan (n=36). The random forest test was applied to each individual data set as well as to a combined-matched data set (n=36). To verify MS data, a multiple reaction monitoring (MRM) assay was developed for 54 of the most discriminatory proteins to be applied to both pooled (PsA n=9, RA n=9) and individual patient samples (n=64).

**Results:** In this study, it was possible to quantify 387, 48 and 1129 proteins from LC-MS/MS, Luminex and SOMAscan analysis, respectively. Proteins with the ability to segregate PsA patients from those with RA were identified by random forest analysis; LC-MS/MS (AUC 0.94), Luminex (AUC 0.69) and SOMAscan (AUC 0.73). The application of the random forest model to the (i) combined data and (ii) MRM data set is part of ongoing work.

**Conclusions:** To date, statistical analysis revealed LC-MS/MS identified proteins were the most discriminatory. An MRM assay has been developed to top the 54 LC-MS/MS proteins and this assay has been applied to the discovery cohort (data analysis ongoing). The assay will next be applied to additional evaluation cohorts that include patients with spondyloarthropathy and psoriasis. Discriminatory proteins verified here represent candidates for inclusion in a blood based multi-analyte test that could ultimately be used in the diagnosis of PsA.

**References:**


**Disclosure of Interest:** None declared


**SAT0445 SHORT-TERM EFFECTS OF SECUKINUMAB ON BONE TURNOVER MARKERS AND WNT SIGNALING PATHWAYS IN PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized also by increased levels of cells producing IL-17 [1], and these levels have been shown to correlate with measures of disease activity and structural damage and bone loss [2]. Secukinumab is a monoclonal antibody licensed with the treatment of PsA which selectively binds to and neutralizes interleukin-17 (IL-17). Currently, data about the effects on the activity of either bone-reabsorbing cells and bone-forming cells secondary to the inhibition of the IL-17 pathway are completely absent.

**Objectives:** The aim of our study was to explore the short-term effects of secukinumab on bone turnover markers and Wnt signaling pathways in patients with PsA.

**Methods:** We enrolled 28 patients with PsA, classified with the CASPAR criteria and 43 healthy controls (HC). For the PsA group DAS28 was recorded and serum samples were stored at baseline and then at the first, third and the sixth month of therapy. Intact N-propeptide of type 1 collagen (PINP) and C-terminal
IXEKIZUMAB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PREVIOUS INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR-INHIBITORS

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Background: Ixekizumab (IXE), a monoclonal high affinity antibody that selectively targets interleukin-17A, was superior to placebo (PBO) in achieving clinical responses and improving health related quality of life (HRQoL) for psoriatic arthritis (PsA) patients who were biologic-naive.1 Herein, results are presented from a phase 3 trial (SPIRIT-P2; NCT02349295) with IXE in patients with active PsA and previous inadequate response to tumour necrosis factor-inhibitors (TNF-ı).

Objectives: To explore the impact of IXE on patient reported HRQoL outcomes up to 24 weeks (wks) in patients with active PsA.

Methods: In this phase 3, multicentre, double-blind study, 363 adult patients with active PsA were randomly assigned in the ratio of 1:1:1 to subcutaneous administration of either 80-mg IXE every 4 wks (Q4W; N=122) or every 2 wks (Q2W; N=123) following a 160-mg starting dose at Wk 0 or PBO (N=118). All patients entering the study had an inadequate response to one or two TNF-ı or were intolerant to TNF-ı. At baseline and Wk 24, HRQoL was measured by the Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS), European Quality of Life 5 Dimensions Visual Analog Scale (EQ-5D VAS), Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP; absenteeism; presenteeism, work productivity, and activity impairment), the tich Numeric Rating Scale (NRS), and the Dermatology Life Quality Index (DLQI), Iitch NRS, DLQI, and Psoriasis Area Severity Index (PASI) responses were assessed in patients with baseline psoriatic lesion involving ≥3% body surface area (BSA; N=203). Treatment comparisons were made by a mixed model for repeated measures for continuous data and by a logistic regression model for categorical data with missing values imputed by nonresponder imputation.

Results: Mean baseline (±SD) scores for HRQoL measures indicated impaired physical and mental function, quality of life, and work productivity (Table). At Wk 24, clinical efficacy was shown by 50.6% and 58.1% of IXE-treated patients achieving ACR20 and PASI75 responses, respectively. Patients receiving IXE (Q4W or Q2W) reported significantly greater improvements in SF-36 PCS and MCS, EQ-5D VAS, and WPAI-SHP (presenteeism, work productivity, and activity impairment) than patients treated with PBO (Table; p<.05). For PsA patients with co-morbid psoriasis (≥3% BSA), IXE treatment (Q4W or Q2W) resulted in significantly greater improvements in Iitch NRS and DLQI than PBO treatment (Table; p<.001). Finally, 51.5% of IEXEQ4W patients and 50.0% of IEXEQ2W patients reached a DLQI total score of 0 or 1 at Wk 24, which is significantly greater than patients treated with PBO (9.0%, p<.001).

Conclusions: In patients with active PsA and previous inadequate response to TNF-ı, IXE provided significant improvement through 24 wks in all joint and skin associated HRQoL outcomes, including physical and mental function, quality of life, work productivity, DLQI, and Iitch.

References:


DOI: 10.1136/annrheumdis-2017-eular.2734

SAT0446
Background: To date, published studies suggest that a significant proportion of patients with Psoriatic Arthritis (PsA) present asymptomatic sacroiliitis; that is to say, an inflammatory back pain (IBP) absence. This fact could account for the underdiagnosis of axial involvement in these patients (1).

Objectives: To evaluate the prevalence of radiographic sacroiliitis in patients with PsA and to determine its association with clinical, analytical and demographic factors.

Methods: A cross-sectional, observational, and uncentre study in which clinical, analytical and demographic data from 359 patients belonging to a PsA monotherapy (PsA) were collected. The x-ray image performed showed sacroiliitis in 127 patients (35.4%). Univariate analysis showed that radiographic sacroiliitis is predominantly associated to the presence of IBP, the positive HLA-B27 antigen and psoriatic cutaneous involvement greater than 25%. The multivariate analysis showed that radiographic sacroiliitis in these patients is predominantly associated to the presence of IBP, the positive HLA-B27 antigen and gender (men). However, sacroiliitis is not associated to the onset age of PsA (p=0.05).

Conclusions: The prevalence of radiographic sacroiliitis in our population is 35.4%, higher than in other series due to the fact that the sacroiliac x-ray images were performed on all patients, regardless of the clinical. The radiographic sacroiliitis in patients with PsA is related to the presence of IBP, HLA-B27 antigen and gender. However, the time of evolution of arthropathy and the onset age of PsA are not related to sacroiliac radiographic involvement.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3572
SAT0449 SEX, METABOLIC CO-MORBIDITIES AND LINE OF THERAPY PREDICT TNF-INHIBITOR THERAPY PERSISTENCE IN PSORIATIC ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Although tumour necrosis factor-alpha inhibitor (TNFi) therapy has proven efficacy in the management of psoriatic arthritis (PsA), relatively little is known about predictors of TNFi persistence. Such knowledge would assist the application of stratified medicine.

Objectives: To determine baseline clinical characteristics associated with TNFi persistence in patients receiving their first-line, and to compare TNFi persistence in first versus second-line users.

Methods: A retrospective cohort study was performed of all patients with PsA attending a single-centre between 2003–2016. Demographic, clinical and laboratory characteristics were compared with TNFi persistence, using Kaplan-Meier survival analysis and multivariable Cox proportional hazards models.

Results: A total of 188 PsA cases had used TNFi therapy as first-line over a period spanning 7.820 person months; 46% male; mean age at TNFi initiation 47.27 (SD 11.36) years; median disease duration at initiation 11 (IQR 7.16) years. Etanercept was used by 102 and adalimumab by 86. Concomitant DMARDs were used by 121/186 (65%) and 87/186 (46%) had metabolic co-morbidities (hypertension, dyslipidaemia, type-2 diabetes, obesity). TNFi therapy was terminated in 65/188 (35%) of cases (35% due to primary inefficacy, 22% secondary inefficacy, 43% adverse events), with a median duration of TNFi persistence of 26.5 (IQR 10.5, 62.0) months. Multivariable Cox proportional hazards modelling found the following parameters at TNFi therapy initiation to be associated with shorter (poorer) TNFi persistence in first line users: female sex (hazard ratio, HR 2.57; 95% CI 1.05, 6.12; p=0.04), presence of metabolic co-morbidity (HR 2.65; 95% CI 1.24, 5.69; p=0.01); with a non-significant statistical trend towards younger age at TNFi initiation (HR 0.94; 95% CI 0.88, 1.00; p=0.06) and older age at PsA onset (HR 1.05; 95% CI 0.99, 1.12; p=0.08). Parameters not statistically associated with TNFi persistence included: choice of TNFi agent (adalimumab vs. etanercept), concomitant DMARD/methotrexate use, tender/swollen joint counts, patient global assessment (PGA) of disease activity, CRP, ESR and disease duration. Of 32 cases proceeding to a second TNFi (19 adalimumab, 13 etanercept), persistence was 14/32 (44%) over 954 person months. TNFi failure was two-fold more likely in second versus first-line users (HR 2.02; 95% CI 1.20, 3.42; p=0.009) [Figure 1], with no significant contribution from other co-variables.

Conclusions: Patients with PsA who are female and have metabolic co-morbidities appear to be more likely to fail first-line TNFi therapy. Contrary to observations in rheumatoid arthritis, and somewhat challenging the few studies in PsA, choice of TNFi agent (humanised monoclonal antibodies vs. TNFi) and is poorly diagnosed. Careful identification of IBP together with MRI of SIJs will help to better define spinal involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3178

SAT0451 THE ONE-YEAR RADIOGRAPHIC PROGRESSION AND MINIMAL DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS PATIENTS TREATED ACCORDING TO TREAT-TO-TARGET STRATEGY (RESULTS OF AN ONGOING OPEN-LABEL REMARCA STUDY)

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Background: Treat-to-target (T2T) strategy has benefit in early psoriatic arthritis (PsA) treatment, its influence on radiographic progression has limited data.

Objectives: To investigate radiographic outcomes and minimal disease activity (MDA) after 1-year of T2T strategy in patients with PsA.

Methods: 40 (M:18/F:22) DMARD-naive pts with active PsA, according to the CASPAR criteria, mean age 38.4±11.1 yrs., Psa duration 11.9±6.6 months, psoriasis duration 73.8±84.6 months, median DAS 3.8 [3.2; 4.7] from the open-label REMARCA study were included. At baseline all pts were treated by Methotrexate (MTX) subcutaneous (s/c) 20–25 mg/week. Pts that still had medium or high activity after 3–6 months under MTX (MDA) therapy were added to biologic therapy (MTX+ biologic therapy (BT) - anti-TNF or Ustekinumab (s/c)). In the end of the study, 19 pts were treated by MTX-monotherapy. At baseline and after 1-yr. of treatment PsA activity index and digital radiographs of hands and feet were performed. All images were scored according to Sharp/van der Heijde (Sh.-v.d. H) method by a blinded musculoskeletal radiologist. Median total score (TS Sh.-v.d. H) = total erosion score (TES) + total narrowing score (TNS), the proportion of pts with erosion increased up to 26 pts (65%). The median TS Sh.-v.d. H significantly increased from 91.5 [72–108.5] to 91.5 [73.5–111.5] (W-test, p<0.01), TES from 2 [0–4.5] to 2.5 [0–5] (W-test, p<0.05) and TNS from 85 [69–105] to 87 [71–97] (W-test, p<0.05). There was no significant difference between the treatment groups in the value of TS Sh.-v.d. H (W-test p>0.05).

25 of pts (62.5%) had reached MDA by 1 yr. In pts who did not reach MDA (n=15) by 1 yr. TES was significantly higher at baseline compare to those who reached MDA, 3 [2–9] and 0 [5–3] accordingly (U-test, p<0.05). In the group of pts who did not reach MDA 1 yr. treatment was significantly higher (table). In 29 of 40 pts (72.5%) there was no X-ray progression considering both erosion and joint space narrowing. 13 of them (45%) were treated by MTX and 16 pts (55%) by MTX+BT. Negative X-ray progression was found in 11 out of 40 pts (27.5%); 6 of them (54.5%) were treated by MTX and 5 pts (45.5%) by MTX+BT.

Conclusions: Patients with PsA who are female and have metabolic co-morbidities appear to be more likely to fail first-line TNFi therapy. Contrary to observations in rheumatoid arthritis, and somewhat challenging the few studies in PsA, choice of TNFi agent (humanised monoclonal antibodies vs. TNFi) and is poorly diagnosed. Careful identification of IBP together with MRI of SIJs will help to better define spinal involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3044

SAT0405 SILENT AXIAL DISEASE IN THE RUSSIAN COHORT OF EARLY PERIPHERAL PSORIATIC ARTHRITIS PATIENTS

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Background: Axial involvement in early psoriatic arthritis (pPsA) patients (pts) is not well studied so far and has not been studied properly. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJs) helps to better define spinal involvement in pPsA.

Objectives: to study the prevalence of axial involvement in peripheral pPsA pts. Methods: 89 pts (M/F=42/47) with peripheral pPsA according to CASPAR criteria were included; mean age 36.5±10.9 yrs. disease duration 12.1±11.0 mo., disease activity index (DAS) 5.2±2.8, CRP 161 [6.6; 31.0] mg/l, ESR 22.5±19.2 mm/h. All patients were evaluated for the presence of inflammatory back pain (IBP) as ASAS criteria. In pts having IBP disease activity was also measured according to BASDAI. The examination included X-ray of sacroiliac joints (SIJs) (pelvic radiograph), HLA B27 antigen, MRI of SIJs was performed in 79 pts, both with and without IBP, on Signa Ovation 0.35T. Bone marrow edema on MRI (STIR), considered as active MRI sacroilitis (MRI-SI), was evaluated by an experienced musculoskeletal radiologist. MRI of SIJs was performed in 79 pts, of which 58 had IBP disease activity according to BASDAI was 4.5±1.6. Correlation has been detected between MRI-SI and IBP; among the group of pts having MRI-SI IBP was observed in 92.9% cases while out of the group of patients without MRI-SI in 54.9% cases (p<0.0002). An association was found between MRI-SI and long-term IBP (p=0.003) as well as between MRI-SI and short-term IBP (p<0.001). Moderate correlation has been detected between the presence of MRI-SI and IBP (p=0.038). It's worth noticing that among the group of pts having MRI-SI 15 (19.2%) pts never had IBP before. And among the 15 pts having ndMRI-SI, 6 (40.0%) pts never had IBP before. No association was found between the presence of MRI-SI/IBP-R/SI and HLA B27 status.

Conclusions: in the Russian cohort of early peripheral psoriatic arthritis pts, careful examination quite often revealed high prevalence of axial involvement: 65% of pts had IBP (moreover, more than half of them (60%) had short-term IBP), 35% of pts had MRI-SI, half of the pts had R-SI, one third of the pts had definite SI-R. A significant number of patients (40%) developed 2 grade changes in one SIJ without previous IBP. An association was found between IBP and SI revealed by any of the visualization methods used. No association has been detected between the presence of MRI-SI or R-SI and HLA B27 status. These data indicate that in peripheral pPsA pts axial involvement is often asymptomatic and is poorly diagnosed. Careful identification of IBP together with MRI of SIJs will help to better define spinal involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5178
In the Russian cohort of active PsA pts erosive progression was found in 18% at 1 year. Active EPsA pts treated according to T2T strategy during 18 months of therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5269

SAT0452

INFLUENCE OF ANTIRHEUMATIC THERAPY ADMINISTERED IN ACCORDANCE WITH “TREAT TO TARGET” PRINCIPLES ON HEART RATE VARIABILITY AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH ACTIVE EARLY PSORIATIC ARTHRITIS

E. Markelova, D. Novikova, T. Korotaeva, E. Loginova, I. Krillova, L. Denisov, D. Karateev. V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Psoriatic arthritis (PsA) is an inflammatory arthropathy, which is associated with range of co-morbid diseases and risk factors, such as dyslipidemia, obesity, metabolic syndrome, cardiovascular disease (CVD). Lower heart rate variability (HRV) is a well-established risk factor for CVD and all-cause mortality in the general population.

Objectives: to study dynamic of traditional risk factors (TRF) of CVD and parameters of HRV during antirheumatic therapy, administered in accordance with “Treat to target” principles in PsA pts.

Methods: 44 (F:21) DMARD-naïve PsA pts, according to the CASPAR criteria, age 36 [27; 46] years (yrs.), PsA duration – 6 [4; 8] yrs, DAS 4.06 [3.51; 4.74]. TRFs of CVD were assessed according to ESC (2016): arterial hypertension (AH) – 11 (22.9%) pts, obesity (body mass index >30kg/m2) – 11 (22.9%), dyslipidemia – 11 (22.9%), abdominal obesity – 14 (29.2%), diabetes – 31 (64.5%), family history of early CVD – 6 (12.5%), menopausal status – 5 (10.4%), smoking - 16 (33.3%). All pts were assessed for ECG, 24-h ECG monitoring, carotid ultrasound imaging. Antihypertensive therapy received all pts with AH. Metohotrexate (MT) therapy was started in all pts with an escalation of the dose up to 25 mg/week subcutaneously. In case of no remission 3 months later, MT was added with biologic therapy: Adalimumab, Certolizumababep, Ustekinumab. 23 subjects were assessed after 18 months of therapy.

Results: After 18 months of therapy DAS and CRP level decreased significantly, p<0.001. DAS remission was achieved in 82.6% of pts. The incidence rate of AH – 14 (29.2%), dyslipidemia – 31 (64.5%), family history of early CVD – 5 (10.4%) mmol/l and from 3.4 [2.8; 3.8] to 3.3 [2.6; 3.6]

Conclusions: antirheumatic therapy of early PsA pts in accordance with “T2T” principles improves lipid profile but not HRVs parameters. Lower HRV is a risk factor for cardiovascular disease and mortality that demands the further studying its influence on the cardiovascular prognosis in PsA pts.
SAT0454 FINGER FLEXOR TENDON PULLEY COMPLEX INVOLVEMENT IN PSA: A HIGH RESOLUTION ULTRASONOGRAPHIC STUDY

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Background: Psoriatic Arthritis (PsA) is often associated with hand involvement including synovitis and tenosynovitis and dactylitis. At the micro-anatomical level PsA is strongly linked to disease localisation to entheses and other sites of high mechanical stressing. Recently high resolution MRI has shown prominent abnormalities at the mini-entheses of the flexor tendon pulleys, a site of high physical stressing during finger flexion.

Objectives: This study tested the hypothesis that sonographic abnormalities were common at the hand flexor tendon mini-entheses in PsA including the A1, A2 and A4 in patients without active hand arthritis or dactylitis at the moment of ultrasound (US) scanning.

Methods: Consecutive patients affected by psoriasis (PsO) (23 cases), PsA (17) and healthy controls (HC) (19) were collected. The demographic characteristics are shown in Table 1. The cases were matched for sex, age and BMI. We excluded PsA patients with active arthritis or dactylitis at the moment of US study, the majority being under therapy with conventional DMARDs. The 26-40 flexor tendon of the dominant hand were scanned with a high resolution linear probe (10-22 MHz) using an Esaote MyLab Twice machine. The sonographer was expert in muscolo skeletal ultrasound (MSKUS) and was blinded to the clinical details. The following changes were scored: tenosynovitis, A1, A2 and A4 pulley tendon thickness and pseudotendinosynovitis (pertendinous oedema). Pulleys were explored with transverse and longitudinal scan.

Results: The A1, A2 and A4 pulleys were significantly thicker in PsA compared to PsO and healthy controls measuring both longitudinal and transverse scan (Table 2 shows means±SD value of transverse measures). In PsA patients, A1, A2 and A4 pulleys thickness were above than the 95th percentile of HCs values respectively in 84%, 80% and 100% of cases. Considering HCs and PsA we found that having a A1 thickness over the 95th percentile of HCs shows a sensitivity of 82% and specificity of 100% of PsA. Using ROC curve analysis we found that the presence of one A1 thickness over the 95th percentile of HCs have a sensitivity of 82% and specificity of 100% for PsA. Pertendinous oedema evaluated scanning the palmar side of proximal and intermediate phalanx was common in PsA patients (6/17) and absent in PsO and HCs.

Table 1 Demographic data

<table>
<thead>
<tr>
<th></th>
<th>Healthy (n=19)</th>
<th>PsO (n=23)</th>
<th>PsA (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>7/11 (39%61%)</td>
<td>9/14 (40%69%)</td>
<td>12/5 (70%30%)</td>
</tr>
<tr>
<td>Age (y) med ± SD</td>
<td>57±12</td>
<td>56±9</td>
<td>56±6</td>
</tr>
<tr>
<td>BMI med ± SD</td>
<td>25±4.0</td>
<td>25±3.2</td>
<td>28±3.3</td>
</tr>
<tr>
<td>Nail involvement</td>
<td>0 (1%)</td>
<td>1 (4%)</td>
<td>8 (47%)</td>
</tr>
<tr>
<td>Previous dactylitis</td>
<td>0</td>
<td>1 (4%)</td>
<td>8 (47%)</td>
</tr>
<tr>
<td>MD &lt; 30</td>
<td>0</td>
<td>0</td>
<td>9 (53%)</td>
</tr>
<tr>
<td>Previous trigger finger</td>
<td>0</td>
<td>1 (4%)</td>
<td>8 (47%)</td>
</tr>
</tbody>
</table>

Table 2 Transverse measures of pulleys thickness (mm)

<table>
<thead>
<tr>
<th></th>
<th>PsA</th>
<th>PsO</th>
<th>HC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>0.61±0.05</td>
<td>0.40±0.10</td>
<td>0.33±0.08</td>
</tr>
<tr>
<td>A2</td>
<td>0.56±0.11</td>
<td>0.40±0.10</td>
<td>0.34±0.02</td>
</tr>
<tr>
<td>A4</td>
<td>0.50±0.13</td>
<td>0.33±0.05</td>
<td>0.30±0.02</td>
</tr>
</tbody>
</table>

Conclusions: This study suggests that PsA cases as a much higher burden of abnormalities in the mini-entheses of the flexor tendons on the hand. With the involvement resolution and capabilities of MKUS these findings may be relevant to understand the involvement of flexor tendon in PsA especially in sites with high mechanical stressing. Measuring A1, A2 and A4 thickness could be useful in detecting PsA cases without clinical signs of synovitis or dactylitis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6777

SAT0455 IMPACT OF PSORIATIC ARTHRITIS IN THE WORKPLACE: RESULTS OF THE FRENCH SURVEY PSOPRO

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Objectives: The PSOPRO (Psoriasis & PsORessionnal life) survey, run under the auspices of the patient advocacy groups France Psoriasis, was aimed at measuring in comparison to the general population, the impacts of psoriasis occurring alone (PsO) or concurring with psoriatic arthritis (PsO+PsA) on patients’ working life.

Methods: From 13/07/16 to 08/08/16, 714 PsO patients, 18 of whom were under system treatment (PsO-ST), and 84 patients PsO+PsA were surveyed using a questionnaire drawn up by a multi-disciplinary scientific committee and conducted via the Internet. In addition to medical and professional characteristics, patients provided their recent absenteeism and presenteeism data, using a WPAI-PSO standardized self-questionnaire, as well as information about the interactions between psoriasis and their working life. Using the Student, Chi-deux and Fischer tests, patients were compared with a sample of 604 working respondents representative of the French population and questioned about the impact of possible health problems on their working life.

Results: The socio-demographic characteristics of the control group were similar to those of the total patient population with psoriasis, although men were slightly over-represented in the latter group. The duration of disease and cutaneous and rheumatological localisations were in line with those usually found in the literature. The unemployment rate over the previous 5 years and number of days of medical leave over the previous 12 months was higher in the PsO+PsA group as compared to the control group (Table 1). In the subgroup reporting a flare-up at the time of the survey, the impact of the disease on absenteeism, presenteeism and productivity was significantly higher in PsO-ST and PsO+PsA patients (Figure 1). Despite this, PsO-ST and PsO+PsA patients reported greater attachment to their work than did those in the control group (Table 1).

Table 1. Impact of psoriasis and psoriatic arthritis on functioning in the workplace and attachment to work.

Control group PsO PsO-ST PsO+PsA

Unemployment over the past 5 years, % (n) 31 (187) 34 (243) 41 (53) 57 (42) p < 0.05 versus control group respondents. PsO: psoriasis; PsO-ST: psoriasis under systemic treatment; PsO+PsA: psoriasis and psoriatic arthritis.

Number of days of medical leave over past 12 months, n 11 6 6 17* p < 0.05 versus control group respondents. PsO: psoriasis; PsO-ST: psoriasis under systemic treatment; PsO+PsA: psoriasis and psoriatic arthritis.

Work considered more important than other aspects of life, % (n) 8 (45) 10 (62) 20* (28) 25* (17) p < 0.05 versus control group respondents. PsO: psoriasis; PsO-ST: psoriasis under systemic treatment; PsO+PsA: psoriasis and psoriatic arthritis.

Work considered less important than other aspects of life, % (n) 42 (236) 49* (301) 21* (15) 27* (18) p < 0.05 versus control group respondents.

Conclusions: In patients with PsO, placement under systemic treatment or the co-existence of PsA appears to be associated with greater impact on patients' working life, though they also reported higher attachment to their work. Close supervision and appropriate care in PsO patients developing PsA should limit these impacts.

Acknowledgements: This survey was made possible by funding from Celgene France and participation of the patient advocacy groups France Psoriasis.

Disclosure of Interest: P. CLAUCÉPPIERRE Grant/research support from: Abbvie, MSD, Roche, Pfizer, Consultant for: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche, UCB, I. BONNET: None declared, Y. ROQUELAURE Consultant for: Abbott, Celgene, P. LEVY Consultant for: Abbvie, Actelion, Amgen, Anergis, Astellas, Bayer, Becton Dickinson, Biogen, BMS, Conceptus, Dalichi-Sankyo, Eli Lilly, EGS, Gilead, GSK, Hospira, Impeto Medical, Janssen, MSD, Mundipharma, Novartis, Novo Nordisk, Roche, Sanofi Pasteur MSD, Stallergènes. H., R. AUBERT: None declared, H. BACHELEZ Grant/research support from: Pfizer, Consultant for: Abbvie, Actelion, Amgen, Boehringer, Celgene, Eli-Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Takeda, Abbott, Merck Serono, Roche, Schering-Plough, Wyeth

DOI: 10.1136/annrheumdis-2017-eular.4433

SAT0456 THERAPY MODIFICATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH A BIOLOGIC IN THE UNITED STATES – DESCRIPTIVE ANALYSES FROM AN ADMINISTRATIVE CLAIMS DATABASE

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Background: Biologic therapy used for the treatment of active psoriatic arthritis (PsA) can sometimes be augmented by adding non-biologic medications and/or...
escalating the dose of the biologic therapy. Limited data exist on how these therapy modifications are used in patients with PsA receiving biologic treatment in real-world settings.

Objectives: To describe therapy modifications (adding non-biologic medications or dose escalation of the current biologic therapy) in patients with PsA receiving biological therapy in the United States.

Methods: This study used US administrative claims data from the Optum Research Database. Adults with PsA who newly initiated (no evidence of use in the 12 months prior) a biologic between January 1, 2013 and January 31, 2015, and who continuously enrolled in a commercial or Medicare Advantage health plan (with baseline period) and 15 months following the index date, were included. To reduce confounding by patients with an early switch/discontinuation, therapy modifications were identified only in those patients who persisted with their index biologic for ~90 days. Therapy modifications identified included initiation of add-on medications (disease-modifying antirheumatic drugs [DMARDs], nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, corticosteroids, antidepressants, anxiolytics, sleeping aids and topical analgesics) after the first 90 days of persistence, and dose escalation of the index biologic. Dose escalation was defined as a patient receiving a dose >10% above the reference dose from the product package for >90 days.

Results: Of the 1,010 patients included on their index biologic for >90 days, 80.5% initiated a subcutaneous tumor necrosis factor inhibitor (TNF-SC; adalimumab, certolizumab pegol or golimumab) as their index biologic, 12.0% initiated an intravenous TNF (TNF-IV; infliximab) and 7.5% initiated ustekinumab. During the 12-month baseline period, patients had a mean (standard deviation) number of claims of 2.9 (4.3) for conventional synthetic DMARDs (csDMARDs), 2.6 (5.0) for opioids, 2.2 (3.1) for NSAIDs and 2.0 (2.9) for corticosteroids. Overall, 49.5% of patients received ≥1 additional medication during the period from 90 days after the index date to the end of persistence with the index biologic or immediate 12-month post-index period. The most commonly added medications were corticosteroids (22.0%), opioids (17.1%), NSAIDs (12.9%) and csDMARDs (5.3%) (Table 1). Overall, 9.6% of patients had a dose escalation of the index biologic (33.9% for TNF-IV, 6.4% for TNF-SC and 5.3% for ustekinumab) in the immediate 12-month post-index period.

Table 1: Add-on medications initiated after 90 days from the index date to the end of persistence or 12 months among patients with PsA

<table>
<thead>
<tr>
<th>Add-on Medication, n (%)</th>
<th>Total (N=1010)</th>
<th>TNF-SC (n=813)</th>
<th>Infliximab (n=121)</th>
<th>Ustekinumab (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any medication</td>
<td>460 (45.4)</td>
<td>353 (43.4)</td>
<td>82 (61.2)</td>
<td>45 (59.2)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>222 (22.0)</td>
<td>188 (23.0)</td>
<td>37 (30.5)</td>
<td>17 (22.4)</td>
</tr>
<tr>
<td>Opioid</td>
<td>173 (17.1)</td>
<td>126 (15.5)</td>
<td>20 (16.5)</td>
<td>27 (35.6)</td>
</tr>
<tr>
<td>NSAID</td>
<td>130 (12.9)</td>
<td>105 (12.9)</td>
<td>14 (11.6)</td>
<td>11 (14.5)</td>
</tr>
<tr>
<td>csDMARD</td>
<td>54 (5.3)</td>
<td>43 (5.3)</td>
<td>8 (6.6)</td>
<td>3 (3.9)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>49 (4.9)</td>
<td>43 (4.2)</td>
<td>6 (5.4)</td>
<td>3 (3.9)</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>48 (4.8)</td>
<td>41 (4.2)</td>
<td>6 (5.0)</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>Topical analgesic</td>
<td>31 (3.1)</td>
<td>24 (3.0)</td>
<td>3 (3.3)</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td>Sleep aide</td>
<td>22 (2.2)</td>
<td>17 (2.1)</td>
<td>3 (2.5)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>csDMARD</td>
<td>11 (1.1)</td>
<td>9 (1.1)</td>
<td>0 (0.0)</td>
<td>2 (2.6)</td>
</tr>
</tbody>
</table>

Conclusions: In this descriptive, administrative claims-based study, nearly one-half (45%) of patients with PsA receiving biologic therapy initiated an add-on medication, most of which were pain medications. Further research is needed to better understand the reasons for therapy modifications during biologic treatment and the impact of insufficient control of pain in patients with PsA in the United States.

Acknowledgements: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

was also used. In order to confirm the specificity of the new genetic variation associated with PsA risk, we analyzed the association with purely cutaneous psoriasis (PsC, n=614) and rheumatoid arthritis (RA, n=1,191). We performed a pharmacogenetic analysis to investigate the new PsA-specific pathways as a source for drug discovery in PsA.

Results: LDA analysis identified a new association between rs3971712 gene and PsA (P<5e-08). In the GWAS pathway analysis, we identified and validated a total of 14 genetic pathways associated with PsA risk. From these, the glycosaminoglycan (GAG) metabolism pathway was also found to be significantly associated with PsA risk when directly contrasted to the PsC cohort as well as the RA cohort. At a functional level, we detected a significant differential expression of GAG metabolism pathway genes in blood samples from PsA patients compared to PsC patients. The pharmacogenetic analysis identified several FDA-approved drugs likely to modify the GAG pathway.

Conclusions: This study represents an important step towards the characterization of the genetic factors specific to PsA risk.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3685

<table>
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<th>SAT0459</th>
<th>LOW DOSE IL-2 RESTORES IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH PSORIATIC ARTHRITIS</th>
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<tbody>
<tr>
<td>K. Qin1, Q. Chen1, J. Fan1, D. Xu1, X. Li1, C. Wang1, C. Gao2.</td>
<td>1Department of Public Health and Clinical Medicine/Rheumatology, University Hospital, Umeå, Umeå; 2Department of Clinical and Experimental Medicine, Rheumatology; 3Division of Cell Biology, Dept of Clinical and Experimental medicine, Linköping University, Linköping, Sweden</td>
</tr>
</tbody>
</table>

Background: Psoriasis arthritis is one of chronic, relapsing, inflammatory autoimmune disorders with skin lesions and joint damage. A therapeutic revolution of psoriatic arthritis (PsA) is still a considerable unmet need in the past decades. It has been well known that the imbalance of Th17 cells and regulatory T cells (Tregs) may be a pivotal cause of PsA. Correction of this dysfunction can be a potential therapy of PsA.

Objectives: In this study, we measured and compared both absolute numbers and proportions of CD4+CD17+ Th17 cells and CD4+CD25+Foxp3+ Treg cells in peripheral blood of PsA patients and healthy controls to explore the immunopathogenesis of PsA; on the other hand, the effects of low-dose recombinant human IL-2 (rIL-2) on Th17 and Treg cells were investigated in patients with PsA.

Methods: Both absolute numbers and proportions of Th17 and T cells in peripheral blood, defined as the CD4+CD17+Th17 cells and CD4+CD25+Foxp3+ Treg cells in peripheral blood of PsA patients and healthy controls to explore the immunopathogenesis of PsA; on the other hand, the effects of low-dose recombinant human IL-2 (rIL-2) on Th17 and Treg cells were investigated in patients with PsA.

Results: The absolute count of Th17 cells in patients with PsA was very significantly higher than that of healthy controls (P<0.01), but the proportions of Th17 cell were not seen difference between PsA and healthy controls (P>0.05). In contrast with treated-PsA patients, the absolute count of Th17 cells was significantly higher in untreated-PsA patients (P<0.05). After the course of rIL-2 treatment, there was a significant increase in the absolute count of Th17 cells (P<0.05), but no difference in the absolute count of Th17 cells, Th17/Treg was significantly lower and went back to normal.

Conclusions: The results suggest that, the proportion, but the decrease in the absolute count of Th17 cells, defined as the CD4+CD17+ populations, contributes to the pathogenesis of PsA. After the treatment of rIL-2, there was a more significant increase in the absolute count of Treg cells than that of Th17, and consequently the balance of Th17/Treg was restored to normal, leading to the development of new therapies.

References:
[3] Szodoray P, Nakken B, Barath S, et al. Altered Th17 cells and Th17/regulatory T cells may be a pivotal cause of PsA. Correction of this dysfunction can be a potential therapy of PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3685

<table>
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<th>SAT0460</th>
<th>ASSOCIATION BETWEEN INFLAMMASOME-RELATED POLYMORPHISMS AND PSORIATIC ARTHRITIS</th>
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<tr>
<td>K. Juneblad1, A. Kastbom2, S. Rantapää-Dahlgqvist1, P. Söderkvist3, G.M. Aleenius1, 1Dept of Public Health and Clinical Medicine/Rheumatology, University Hospital, Umeå, Umeå; 2Department of Clinical and Experimental Medicine, Rheumatology; 3Division of Cell Biology, Dept of Clinical and Experimental medicine, Linköping University, Linköping, Sweden</td>
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</tr>
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</table>

Background: In recent years, research on the interleukin 1[IL-1 β]–regulating protein complex, called the inflammasome, has shown interesting associations with chronic, inflammatory diseases. E.g. for Rheumatoid Arthritis (RA) (1) and psoriasis (PsO) (2, 3) associations with genetic polymorphisms in genes related to the inflammasome has been discovered. So far, no studies investigating genetic polymorphisms in inflammasome genes in Psoriatic Arthritis (PsA) patients have been published.

Objectives: To examine whether polymorphisms in genes related to inflammasomes confer increased risk for psoriatic arthritis.

Methods: DNA from 771 PsA patients and 793 healthy controls from Sweden were analyzed for different single nucleotide polymorphisms (SNPs) in NLRP3 (rs39298419, rs17531135, rs4553135), CARD8 (rs2045211) and NLRP1 (rs8079304, rs878329).

Results: Significant associations with PsA were found between carriage of allele, C, of rs878329 in NLRP1 (Chi²=2.65, OR (95% CI): 1.25 (1.02–1.53), p=0.028). Genotype distribution was also significantly different between patients and controls and for rs878329 in NLRP1 there was a significant difference in allele frequency (G/C) between patients and controls (Chi²=2.58, OR (95% CI): 1.20 (1.03–1.36), p=0.016). No significant associations with PsA were found for the other SNPs analyzed.

In genotype analysis, a significant higher frequency of genotype GG in rs878329 in PsA was detected (32.9% vs 26.9%, Chi²=2.46, OR (95% CI): 1.34 (1.07–1.71), p=0.011), whilst no significant differences were detected for genotypes GC or CC. For rs4553135, a significantly higher frequency of genotype TG (43% vs 37%, OR (95% CI): 1.66, OR (95% CI): 1.01 (1.05–1.53), p=0.033) and significantly lower frequency of genotype TT (50.5% vs 56.1%, Chi²=2.44, OR (95% CI): 0.80 (0.63–0.98), p=0.028) was seen in PsA, no significant difference was detected for genotype GG.

Conclusions: Carriage of rs878329C in NLRP1 was less frequent in patients with PsA compared with controls indicating a protective effect, but when different genotypes were analysed the difference likely results from an increased risk of PsA with genotype GG. The results are in contrast with the study of Ekman et al, where an increased transmission of rs878329C to family members with PsA was seen (3), indicating that carriage of genotypes may be associated with increased risk for carriers of C, but in agreement with the study of Sui et al on patients with RA, where an association was detected for carriage of C (OR 0.82, p=0.02), with the risk genotype for RA being G (4). Thus, the genotype GG possibly confers risk of arthritic disease whilst the C-allele seems associated with skin disease.

Carriage of rs4553135G in NLRP3 was more frequent in PsA patients compared with controls indicating an increased risk of disease, but only genotype GT was significantly increased in PsA. In the current association analyses were compared between one SNP in NLRP3 and one SNP in NLRP1, indicating a possible involvement in pathogenesis of PsA disease.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3477

<table>
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<th>SAT0461</th>
<th>CHARACTERISATION OF DIFFERENT LOW DISEASE ACTIVITY MEASUREMENTS IN PATIENTS WITH PSORIATIC ARTHRITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>L.C. Coates1, A.B. Gottlieb2, J.F. Merola3, L. Akeman4, A. Szumski5, A. Chhabra 2.</td>
<td>1University of Leeds, Leeds, United Kingdom; 2New York Medical College, New York; 3Harvard Medical School, Boston, United States; 4Pfizer, Walton Oaks, United Kingdom; 5InVentiv Health, Princeton; 6Pfizer, New York, United States</td>
</tr>
</tbody>
</table>

Background: Selection of the correct target to guide treatment is crucial for effective disease management in patients with psoriatic arthritis (PsA).

Objectives: To evaluate the prognostic value of several low disease activity (LDA) targets in PsA and in patients with PsA and psoriasis to assist physicians choose a valid target that facilitates assessment in clinical practice.

Methods: This was a post-hoc analysis from the PRESTA1 clinical study. LDA targets analyzed were: Disease Activity in PsA (DAPSA) LDA ≤14 (tender joint count [TJC], swollen joint count [SJC]), patient global visual analog scale [Pt VAS], C-reactive protein [CRP], clinical (c)DAPSA LDA ≤13 (DAPSA without CRP); and minimal disease activity (MDA) measurement defined as 5/7 cut-offs (TJC ≤1, SJC ≤1, psoriasis activity and severity index [PASI] ≤1, Pt pain ≤15mm, Pt VAS ≤20mm, health assessment questionnaire ≤0.5, tender enthesal points ≤1). Additional MDA measurements were investigated where 5/7
Multiple facets of PsA were demonstrated to distinguish treatment effect, perform better in statistical terms than traditional joint-only indices\(^1\) and could be used as a treatment target in clinical trials in PsA.

**Methods:** Secukinumab provided sustained improvement in the signs and symptoms of PsA over 104 weeks (wks) in the FUTURE 2 study.\(^2\) Here, we report the ability of secukinumab to reach and sustain PASDAS based low disease activity (LDA) up to 104 wks in the FUTURE 2 study using a post-hoc exploratory analysis.

**Results:** PASDAS score (mean [SD]) at baseline was 5.9 (0.9), 6.0 (1.0) and 5.8 (1.0) in the secukinumab 300mg, 150mg and PBO groups. In the overall population at Wk 16, PASDAS LDA was achieved in 37/96 (38.5%) and 34/99 (34.3%) of pts, treated with secukinumab 300mg and 150mg, respectively; vs. 14/87 (16.1%) with PBO. A high proportion of pts treated with secukinumab 300 and 150mg achieved LDA (49/83 [59.0%] and 58/87 [64.4%], respectively) at Wk 104. The proportion of pts achieving PASDAS LDA and remaining in HDA at Wks 16 and 104 by anti-TNF use (naïve/inadequate response [IR]) and disease duration (≤2 years vs. >2 years since diagnosis) and reported using non-mutually exclusive categories at group level and as observed analysis. Secukinumab 75mg data are not reported as this was not considered an effective dose.\(^2\)

**Conclusions:** A higher proportion of secukinumab-treated pts at Wk 16 achieved PASDAS LDA than PBO, with LDA sustained at group level at Wk 104. Discriminatory effect of PASDAS was consistent with that previously reported in the GRACE project.\(^4\) A higher proportion of anti-TNF\(\alpha\)-naïve pts treated with secukinumab achieved and sustained PASDAS LDA than anti-TNF\(\alpha\)-IR pts whereas similar proportion of pts treated with secukinumab achieved PASDAS LDA irrespective of time since diagnosis (≥2 years vs. >2 years).

**References:**


\(^2\) McInnes IB et al, Arthritis Rheumatol. 2016;68 (suppl 10).

Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Celgene, Pfizer, UCB, MSD, Novartis, Lilly, Janssen, Sun Pharma. D. Gladman Grant/research support from: Ame... Shareholder of: AbbVie, Biogen, BMS, Boehringer-Ingelheim, Celltrion, Eli Lilly, Ericus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingeheim, Celtrion, Eli Lilly, Ericus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, P. Conaghan Consultant for: Abbvie, BMS, Lilly, Novartis, Pfizer, Speakers bureau: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, M. Østergaard Consultant for: Abbvie, BMS, Boehringer-Ingelheim.

References:

Conclusions:

- FACIT-F was significantly greater with SEC vs. PBO at Wk 16 in both FUTURE 1 and 2 (P = 0.002; Table 1).
- Improvements were generally somewhat larger in TNF-naive pts than in TNF-IR pts.
- Correlation analyses did not identify any BL factors that consistently predicted a 20% reduction in CRP and the EULAR remission criteria.

Results:

- FACIT-F was 27.8–28.9 and 26.6–29.2 at BL across groups in FUTURE 1 and 2, respectively. Improvements in fatigue seen with all doses of SEC vs. PBO from Wks 4–24 were sustained through 156 wks in FUTURE 1 and 104 wks in FUTURE 2 in both the overall population and subgroups stratified by prior exposure to TNF (Table).
- The numerically higher responses with SEC vs. PBO from Wks 15 vs. 300 mg SC, respectively. At Wk 16, PBO pts with ≥20% reduction in tender/swollen joint count (non-responders) were re-randomized through 156 wks. Improvement in fatigue were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).
- Across both studies, approximately 68% of pts were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).
- Improvement in fatigue were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).
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- Improvement in fatigue were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).

Background:

- Fatigue is a common symptom in patients with PsA and is negatively associated with HRQoL and social functioning. Secukinumab (SEC), a fully human anti-IL-17A mAb, rapidly improved signs and symptoms, physical functioning, HRQoL, and fatigue in TNF-naive and TNF-IR pts in PsA.

Objectives:

- To assess the long-term effects of SEC on fatigue in TNF inhibitor (TNF)-naive PsA pts and those with an inadequate response or intolerance to TNF inhibitor therapy (TNF-IR).

Methods:

- 606 and 397 pts were randomized to SEC or placebo (PBO) in FUTURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and FUTURE 2 (300 mg, 150 or 75 mg SC), respectively, at Wk 16, PBO pts with ≥20% reduction in tender/swollen joint count (non-responders) were re-randomized to SEC or placebo at Wk 15 to 5 mg/kg IV followed by 150 or 75 mg SC (FUTURE 1) and SEC or 300 mg SC (FUTURE 2); responders were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).
- Across both studies, approximately 68% of pts were TNF-naive and 32% were TNF-IR. Fatigue was assessed at baseline (BL) and Wks 4, 8, 12, 16, 24, 52, 104, and 156 (FUTURE 1 only) using FACIT-F (higher score = less fatigue). Fatigue response was defined by an increase in FACIT-F score of >4 from BL (corresponding to the MCID). Correlations between BL characteristics and improvements in fatigue were investigated using a logistical regression model. Only data with approved doses of SEC (300/150 mg) are shown.

Results:

- FACIT-F was 27.8–28.9 and 26.6–29.2 at BL across groups in FUTURE 1 and 2, respectively. Improvements in fatigue seen with all doses of SEC vs. PBO from Wks 4–24 were sustained through 156 wks in FUTURE 1 and 104 wks in FUTURE 2 in both the overall population and subgroups stratified by prior exposure to TNF (Table).
- The numerically higher responses with SEC vs. PBO from Wks 15 vs. 300 mg SC, respectively. At Wk 16, PBO pts with ≥20% reduction in tender/swollen joint count (non-responders) were re-randomized through 156 wks. Improvement in fatigue were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).
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- Improvement in fatigue were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436).

Acknowledgments:

- Background: Recommendations on psoriatic arthritis (PsA) state that the target of treatment should be remission or inactive disease. Multiple potential targets have been developed and proposed, each with a different composition of clinical measurements.

Objectives:

- Our aim is to use an existing real life dataset of a large group of patients in a low disease activity state, to compare different targets and provide further evidence to choose a target.

Methods:

- This analysis uses data from a cross-sectional real life cohort of 250 PsA patients (EULAR16–2124). All patients were considered in an acceptable disease state according to the treating rheumatologist, defined by the fact that the rheumatologist did not consider to modify the current treatment. Remission/inactive disease targets were the DAPSA [TJC; SJCP; patient global visual analogue scale (Pt VAS); pain VAS; CRP] and clinical (c)DAPSA [(DAPSA minus CRP) remission] (<4), very low disease activity (VLD) [7/7 of TJC ≤1; SJCP ≤1; Pt pain ≤16; Pt VAS ≤20; HAQ ≤0.5; tender enthesal points ≤1], and PASDAS <1.9 or near remission (NR).

Results:

- 113 pts were in cDAPSA remission, 107 in DAPSA remission, 56 met VLD and 37 in PASDAS NR. There was a very high percentage exact agreement between DAPSA and cDAPSA (96%) reflecting the similarity of the two definitions. DAPSA/cDAPSA and VLDA show high correlation (Pearson 0.611 and 0.590 resp) but VLDA is more stringent in comparison with both DAPSA scores. The correlation between NR and DAPSA/cDAPSA/VLDA was lower, (Pearson 0.400, 0.403 and 0.412 resp). Again PASDAS NR was generally more stringent than DAPSA/cDAPSA remission but greater dissimilarities are seen between PASDAS NR and VLDA where 14 patients are in VLDA but not PASDAS NR and 29 are in PASDAS NR but not VLDA.

Discussion:

- Although presence of active joint disease was similar across the different measures, VLDA presents as a more stringent cutoff with less residual disease in PASI, TJC and less impact on DLOQ and HAQ. All targets had similar % of patients...
with a raised CRP. The DAPSA measures which do not include an enthesis measure show more patients with an active enthesis.

There was a limited consequence on QoL measures when residual disease activity was allowed in certain domains in these remission states. In those patients with active enthesis or skin disease, no differences were found on PROs on quality of life and functionality. The severity of active skin disease pooled–reported pooled PASI-2 (present in 20/110 pts achieving DAPSA) was reflected by an impact on DLQI (2.85 (SD2.9) vs. 1.23 (p=0.003). This effect was not seen when the cutoff of for PASI-1 was used.

Conclusions: This comparison of the different remission targets shows that VLA4 presented as the most stringent target. Inclusion of laboratory markers seems not to be a necessity although the exclusion of a skin domain might result in a significant understatement of skin disease in some patients despite an impact on their QoL.

Disclosure of Interest: L. Van Mens: None declared, A. van Kuijk Grant/research support from: UCB, Pfizer, MSD, Janssen, Consultant for: Foravits, Celgene, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim. This cohort was funded by an unrestricted grant from Pfizer to DB. Consultant for: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, Employee of: UCB, L. Coates: None declared

DOI: 10.1136/annrheumdis-2017-eular.2926

SAT0465 AN INTEGRATED SAFETY DATA ANALYSIS ACROSS ALL PHASE II AND PHASE III CLINICAL PROGRAMS FOR USTEKINUMAB IN PSORIATIC ARTHRITIS, CROHN'S DISEASE, AND PSORIASIS


Objectives: Therapeutic decisions are based on efficacy, but clinicians need to consider medication safety in this process. Here, we report ustekinumab (UST) integrated safety data in patients (pts) with psoriatic arthritis (PsA), Crohn's disease (CD), and psoriasis (PsO). We also compare a subset of PsA pts with & without baseline methotrexate (MTX).

Methods: Integrated safety data from 3 PsA, 5 CD, & 4 PsO trials were analyzed. PsA studies included the Ph2 trial (CNTO743T10) & the 2 Ph3 trials (SUMMIT 1 & 2) with 222, 615 & 312 pts exposed to UST, respectively. The percentage of pts in the Ph3 study that received MTX was 20.5%. No concomitant DMARDs with the exception of MTX (approximately 50% of pts in each study) were permitted in the 2 Ph3 studies. In the 5 CD studies (Ph2/3Ph3), 1749 pts were exposed to UST. In the 3 Ph3 CD studies, pts received one dose of UST 130mg or ∼6mg/kg IV at induction (UNIT1-1 & UNIT1-2), then 8 weeks later, entered the maintenance phase (IM UNIT1) and received UST 90mg SC q8w or q12w for 44 weeks. The percentage of pts on background MTX in UNIT1-1 was 9.2% & in UNIT1-2, 4.8%. In the PsO studies (1Ph2/3Ph3), a total of 3117 pts received UST 45mg or 90mg SC; no concomitant DMARD therapy (including MTX) was permitted. The PsO studies were completed through 5-years of follow-up. All pts who received at least 1 dose of UST were included in this analysis. Safety events are reported in events per 100-pt years. 95% CI for events per 100 PY were estimated.

Results: Through 1 year of follow-up, a total of 1018 PsA pts were treated with UST, of which 465 were co-treated with MTX. Of the 1749 CD pts treated with UST, 193 received MTX. Discontinuation rates of UST due to adverse events (AEs) were comparable across disease states irrespective of MTX use (Table). AE rates (95% CIs for events/100 PY) were noted to be comparable in the UST vs PBO groups for all diseases pooled irrespective of MTX use (240.39, 432.45) vs PBO (534.50, 170.40). Serious adverse event rates (SAEs) were also comparable in the UST vs PBO groups for all diseases pooled–reported UST (14.25, 16.56) vs PBO (24.05, 32.18). Infections and Serious infections (SIs) had numerically lower event rates in UST vs. PBO groups for all diseases pooled–reported UST (122.16, 128.72) vs PBO (120.94, 138.27) and UST (2.10, 3.05) vs PBO (2.76, 6.00), respectively (Table). Major adverse cardiovascular events (MACE) did not appear to significantly differ in both PBO & UST pts in PsA, PsO and CD. Event rates of malignancy (excluding non-melanoma skin cancer) were comparable across all disease states. No deaths in Pts or CD were reported.

Conclusions: UST demonstrates a favorable safety profile in an integrated safety data analysis across the PsA, CD, & PsO phase 2 & 3 clinical trials. The use of UST in PsA appears to be safe & well-tolerated, with fewer event rates of SAEs & SIs noted vs PBO. Despite higher overall rates of SAEs & SIs observed in CD pts, the data do not suggest an influence of UST on either.


DOI: 10.1136/annrheumdis-2017-eular.1116

SAT0466 PREGNANCY IN WOMEN WITH PSORIATIC ARTHRITIS: PREGNANCY OUTCOMES AND CHANGES IN DISEASE ACTIVITY

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Background: Very little has been published about psoriatic arthritis (PsA) in pregnancy, and it remains unknown whether pregnancy outcomes are impacted by this disease or whether disease activity is changed by pregnancy or delivery.

Objectives: To discover the rate of pregnancy complications for women with psoriatic arthritis, and to determine whether psoriasis and the associated arthritis change during and following pregnancy.

Methods: A retrospective survey was completed by 40 women aged 20–50 years with psoriatic arthritis managed at a university center. Each survey collected information about infertility, pregnancy outcomes and complications, as well as patient-reported assessments of changes in both skin and joint disease activity at the onset of pregnancy, over the course of the pregnancy, and in the months following pregnancy. Simple statistics were used to compare outcomes before and after the diagnosis of PsA.

Results: The survey was completed by 40 women with PsA. The majority (93%) were white, non-Hispanic with a high level of education (40% completed college and another 30% either started or finished a graduate degree); 62.5% were married. The average age at the time of the study was 37.4 (SD 7.9) years and age at PsA diagnosis was 30.9 (8.4) years. Twenty-five women reported they had ever tried to become pregnant, and of those, 9 had been unable to become pregnant after 12 months of trying or had been diagnosed with infertility by a physician (36%). The reasons for infertility or inability to become pregnant included pelvic inflammatory syndrome (44%), problem with ovulation (11%), problem with uterus (11%), elevated prolactin (11%), infection in pelvic area (11%), and/or cervical problems (30%). Infertility was unexplained in 33%.

There were 70 pregnancies to 26 patients, with 37 pregnancies occurring after the diagnosis of PsA (see table). Pregnancy outcomes following PsA diagnosis were worse than those prior to PsA diagnosis, particularly the rate of pregnancy loss (32% compared to 12%; p=0.05) and preterm birth (48% compared to 21%; p=0.002). Only 24% of patients took psoriasis or arthritis medications during pregnancy. The most commonly used medications during pregnancy were TNF inhibitors (16%), corticosteroids (8%), and DMDARs (5%). The large majority of patients had minimal arthritis and psoriasis during pregnancy.

<table>
<thead>
<tr>
<th>Table. Pregnancy outcomes before and after psoriatic arthritis diagnosis</th>
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<td><strong>No.</strong></td>
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<td><strong>Overall</strong></td>
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<tr>
<td><strong>Number of Pregnancies</strong></td>
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<td><strong>Live Births</strong></td>
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<td><strong>Elective Abortions</strong></td>
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<td><strong>Preterm Birth</strong></td>
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<td><strong>Abnormal Infant</strong></td>
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<td><strong>Adverse Pregnancy Outcome</strong></td>
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*Two twin pregnancies.*
Only 12% had moderate and 6% had severe arthritis. Similarly, only 10% had moderate and 7% had severe psoriasis. During and following pregnancy, about half of all patients reported no change in either joint or skin activity during and follow pregnancy, with fairly equal numbers reporting improved and worsened arthritis. On the other hand, 42% had improved psoriasis during pregnancy compared to 6% in whom arthritis worsened. There did not appear to be a significant postpartum flare.

**Conclusions:** Our analysis found that among women with PsA who have tried to become pregnant, 36% experienced infertility, primarily due to PCOS. Compared to pregnancies occurring before the diagnosis of PsA, pregnancies after PsA diagnosis had a lower frequency of live births and a higher frequency of preterm births. Overall, in this cohort of women with mostly mild disease during pregnancy, arthritis pain and psoriasis activity did not appear to substantially worsen during pregnancy.

**Acknowledgements:** This study was funded by Janssen.

**Disclosure of Interest:** None declared.

DOI: 10.1136/annrheumdis-2017-eular.4392

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**SAT0467**

**ALL 10-YEAR CARDIOVASCULAR RISK SCORES ARE SIMILAR IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS**

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**Background:** Psoriatic arthritis (PsA) and Psoriasis (PsO) are associated with higher cardiovascular (CV) risk with higher risk in patients with a severe disease phenotype. Long-term CV risk is evaluated using several methods for the general population.

**Objectives:** The aim of the study was to compare CV risk factors and 10-year CV risk scores between patients with PsA and PsO vs PsO only.

**Methods:** PsA patients fulfilling the CASPAR criteria and PsO with disease duration <10 years were enrolled consecutively from Rheumatology and Dermatology clinics. Fasting bloods were obtained for glucose, insulin and lipids, hypertension (HTN) and metabolic syndrome in PsA group, and completed questionnaires on health and quality of life. Four different CV risk scores were calculated: (1) Framingham Coronary risk score (FCS); (2) American College of Cardiology and American Heart Association (ACC/AHA) 10-year atherosclerotic cardiovascular disease (ASCVD) algorithm; (3) Systematic Coronary Risk Evaluation (SCORE) algorithm; and (4) QRISK2 (2016).

**Results:** 232 patients (100 PsA and 132 PsO) were recruited with mean age 52.4 ± 10.5 for PsA and 39.7 ± 14.4 for PsO. Mean disease duration for PsA was 17.9 ± 10 years. There were significantly more patients with hypertension (HTN) and metabolic syndrome in PsA group, and patients taking DMARDs and/or biologics treatment were also higher compared to PsO. Fasting glucose, insulin, lipids, BMI and waist/hip ratio did not show significant differences. The mean FCS, ASCVD, SCORE, and QRISK2 were significantly higher in PsA as compared to PsO, 4.7 ± 7.0% vs. 4.4 ± 8.2% P < 0.0001; 2.7 ± 1.6% vs. 1.1 ± 1.8%, P = 0.0002; 11.2 ± 9.9% vs. 5.2 ± 6.4%, P < 0.0001, respectively. However, after adjusting for age and sex, all CV risk scores were similar. Multiple regression analysis revealed that waist/hip ratio significantly correlated with all CV risk scores in both PsA and PsO patients.

**Conclusions:** While psoriatic arthritis is associated with higher CV risk, similar CV risk scores were calculated in both PsA and PsO patients.

**Disclosure of Interest:** [Disclosure statements]

DOI: 10.1136/annrheumdis-2017-eular.4404

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**SAT0468**

**PRESENCE OF POOR PROGNOSTIC FACTORS MAY PREDICT RESPONSE TO ABATACEPT IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A POST HOC ANALYSIS FROM A PHASE III STUDY**

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**Background:** Abatacept, a selective T-cell co-stimulation modulator, significantly increased ACR20 response and had an overall beneficial effect on musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA) in the Phase III Active pSoriaTic arthritis RAndomisedEd triAL (ASTRAEA, NCT01860976). Factors that may predict responses to abatacept were explored in this post hoc analysis.

**Objectives:** To evaluate the relationship between baseline characteristics and abatacept response in a post hoc analysis of ASTRAEA.

**Methods:** Pts were randomized (1:1) to SC abatacept 125 mg weekly or placebo for 24 weeks in this trial. Pts without ≥20% improvement in joint counts at Week 16 were switched to open-label abatacept (early escape). ACR20 response rate in pts stratified by baseline variables was investigated in a multivariate analysis and odds ratios (ORs) generated to identify differences in response. Using a cut-off of OR > 1.2, indications in which abatacept appeared to have a meaningful treatment benefit, baseline variables were further investigated in a univariate analysis and estimated differences calculated.

**Results:** Of 424 pts enrolled, 213 received abatacept and 211 placebo. In abatacept-treated pts, the multivariate model showed a difference in ACR20 response (OR 1.29, 95% CI 1.15–1.45) vs baseline CRP (< upper limit of normal (ULN) vs > ULN: OR 1.346 [95% CI 0.668, 2.712], DAS28 (CRP) (>5.1 vs ≤5.1: 1.489 [0.728, 2.836]), dactylitis (≤0 vs > 0: 1.372 [0.708, 2.659]), and median baseline erosions ≤3 vs > 3: 1.924 [1.032, 3.587]). In placebo-treated pts, the OR was 1.2 for CRP > ULN and >5.1. These factors, with their previously identified as indicating poor prognosis in PsA, were balanced between treatment arms at baseline. In the univariate model by poor prognostic factors, the differences in ACR20 response rates with abatacept treatment vs placebo in distinct subgroups were numerically greater in pts who were positive for these prognostic factors at baseline than in those who were not (Figure).

**Conclusions:** These findings identified subgroups of pts with PsA with certain baseline characteristics in whom abatacept is most likely to be effective. The predictive factors identified are aligned with poor prognostic factors in the EULAR and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guidelines, and may indicate pts with the highest unmet medical need.

**References:**


**Disclosure of Interest:** None declared.

DOI: 10.1136/annrheumdis-2017-eular.1641

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**SAT0469**

**INTEGRATED EFFICACY ANALYSIS OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS**


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**Background:** Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA).

**Objectives:** To assess the integrated efficacy of tofacitinib in patients with PsA treated in Phase III clinical trials.

**Methods:** Pts were included in this analysis if they were ≥18 years of age and had ≥10 swollen joints and ≥20 tender joints at baseline. Pts were treated with oral tofacitinib 5 or 10 mg twice daily for up to 1 year in the core studies and up to 2 years in the open-label extension studies. The analysis included all patients from the core studies (ASTRAEA, NCT01860976) and the open-label extension study (ASTRAERETRO, NCT02486831). The population included pts from Phase III studies regardless of discontinuation. Pts were included if they discontinued therapy due to non-response or adverse events, or if they completed at least 1 year of treatment.

**Results:** Of 3162 pts included in the analysis, 1349 (43%) were treated in core studies and 1813 (57%) were treated in the core studies plus 1 year of open-label extension. The majority of pts were female (75% in core studies vs 80% in core studies plus open-label extension). The mean age was 52 years, and most pts (81%) had PsA with active arthritis. The mean baseline CRP was 2.7 mg/L and the median disease duration was 10 years. At Week 16, 41% of all pts achieved ≥20% improvement in swollen joints and tender joints compared to baseline (ACR20). The overall ACR20 response rates were 24% in core studies and 30% in core studies plus open-label extension. Median change in DAS28 (CRP) decreased from 5.2 at baseline to 3.9 at Week 16. A 12-week change in median CRP was -0.33 mg/L from baseline to Week 16. A 12-week change in median ESR was -12 mm/h from baseline to Week 16. The mean change in HAQ-DI was -0.33 from baseline to Week 16.

**Conclusions:** Tofacitinib was associated with improvement in pts with PsA in Phase III trials. The results from this analysis support the use of tofacitinib in the treatment of pts with PsA.

**Disclosure of Interest:** [Disclosure statements]

DOI: 10.1136/annrheumdis-2017-eular.1641
Objectives: To determine efficacy based on pooled data from 2 pivotal Phase 3 studies of tofacitinib in patients (pts) with active PsA.

Methods: Data were pooled from 2 placebo (PBO)-controlled, double-blind, multicentre, global Phase 3 studies (OPAL Broaden [N=422; 12 months; NCT01877668]; OPAL Beyond [N=394; 6 months; NCT01882439]). Pts had active PsA and either inadequate response (IR) to <1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) and were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden), or had IR to disease-modifying antirheumatic drug (csDMARD) and were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Beyond). Pts were randomised to tofacitinib 5 mg twice daily (BID), 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only) or PBO. In addition, to a single, stable background csDMARD. PBO pts advanced to tofacitinib 5 mg or 10 mg BID at Month (M)3. Endpoints included ACR20/50/70 response rates (≥20%, ≥50% and ≥70% improvement) compared with baseline (BL), HAI-2 (Health Assessment Questionnaire Disability Index), HAQ-DI (Health Assessment Questionnaire Disability Index) and enthesis absence, % DSS (Dactylitis Severity Score) and dactylitis absence and %ΔDLQI (Dermatology Life Quality Index). Pts who discontinued treatment were re-randomised for a 3-year extension phase. Efficacy results at Week (Wk) 156 are presented for those pts originally randomised to tofacitinib (n=308) and included ACR20/50/70 (≥20%, ≥50% and ≥70% improvement) vs PBO at M3 were observed for peripheral arthritis and physical function endpoints for tofacitinib 5 mg and 10 mg BID: ACR20, ACR50, ACR70, %ΔHAI-2 (least squares mean [LSM]), and %ΔHAQ-DI response (Table 1).

Results: For pooled data, pts were predominantly white (94.2%) and female (55.4%) with ≥5 peripheral swollen or tender joints (98.0%), enthesitis (LEI≥0; 67.5%), dactylitis (DSS≥0.525%), psoriatic skin body surface area ≥8% (67.7%) and CRP levels above the upper limit of normal (>2.87 mg/L; 62.5%) at BL. Mean age was 49.1 years and PsA duration was 8.0 years. Significant improvements in psoriasis, enthesis and dactylitis endpoints vs PBO were also observed for tofacitinib 5 mg and 10 mg BID at M3: PASI75 (%ΔDSS [LSM], dactylitis absence and %ΔDLQI (Dermatology Life Quality Index). Pts who discontinued treatment were re-randomised for a 3-year extension phase. Efficacy results at Week (Wk) 156 are presented for those pts originally randomised to tofacitinib (n=308) and included ACR20/50/70 (≥20%, ≥50% and ≥70% improvement) vs PBO at M3 were observed for peripheral arthritis and physical function endpoints for tofacitinib 5 mg and 10 mg BID: ACR20, ACR50, ACR70, %ΔHAI-2 (least squares mean [LSM]), and %ΔHAQ-DI response (Table 1).

Table 1. Summary of efficacy results at Week 156

<table>
<thead>
<tr>
<th>Variable</th>
<th>Secukinumab IV 75 mg</th>
<th>Secukinumab IV 150 mg</th>
<th>PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20/50/70 % responders</td>
<td>74.4</td>
<td>78.5</td>
<td>65.0</td>
</tr>
<tr>
<td>PASI75 % responders</td>
<td>95.3</td>
<td>96.4</td>
<td>82.1</td>
</tr>
<tr>
<td>DAS28-CRP, mean change (SD)</td>
<td>2.3</td>
<td>2.3</td>
<td>3.4</td>
</tr>
<tr>
<td>HAQ-DI, mean change</td>
<td>−0.3 (0.6)</td>
<td>−0.3 (0.6)</td>
<td>−0.5 (0.7)</td>
</tr>
<tr>
<td>Resolution of dactylitis</td>
<td>82.4</td>
<td>86.8</td>
<td>76.7</td>
</tr>
</tbody>
</table>

Conclusions: In a pooled analysis of csDMARD-IR/TFN naïve and TNF-IR pts, tofacitinib 5 mg and 10 mg BID were superior to PBO at M3 across four PsA disease domains: peripheral arthritis, psoriasis, enthesis and dactylitis.
TRENDS IN CLINICAL CHARACTERISTICS ASSOCIATED WITH ACHIEVEMENT OF MINIMAL DISEASE ACTIVITY IN RESPONSE TO BIOLOGIC THERAPY IN PSORIATIC ARTHRITIS – ANALYSES FROM THE CORRONA PSORIATIC ARTHRITIS/SPODYLOARTHITIS (PSA/SPA) REGISTRY

P.J. Mease 1, C. Karki 2, M. Liu 2, A. Kavanagh 3, C.T. Ritchlin 4, D.H. Hulsey 5, R. Pandurengan 1, J.B. Palmer 2, J.D. Greenberg 1, 2, 3, 4, 5, 6, 7

Objectives: To retrospectively report the MDA and patient-reported outcomes (PROs) over time (baseline vs first follow-up [FU] visit vs second FU visit) which may contribute to achievement of MDA in responders versus non-responders to biologic treatment.

Methods: This analysis included all patients with PsA in the Corrona registry aged ≥18 years between March 2013 and March 2016 who received biologics (biologic initiation) at enrollment (baseline) and had ≥2 FU visits (at ≥6-month intervals, mean [SD] 2nd FU visit: 15.7 [3.7] months). Responders were defined as patients who achieved MDA at the second FU visit and remained on their index biologic.

Results: Of 148 patients who met the inclusion criteria (mean [SD] age, 54.7 [11.0] years; mean [SD] disease duration, 11.8 [10.1] years), 34 patients (23%) were responders (i.e., patients who had ≥2 MDA assessments/infestations, candida infections, Crohn’s disease, and malignant/unspecified tumors was 1.7 (27), 1.2 (17), 0.1 (2), and 0.9 (14) per 100 pt-yrs, respectively. Conclusions: Secukinumab provided sustained improvements in signs/symptoms and HAQ among clinical domains of active PsA in pts who completed ≥3 yrs of therapy. Secukinumab was well tolerated with a favorable safety profile consistent with that previously reported.1

References:


SAT0471

TRENDS IN CLINICAL CHARACTERISTICS ASSOCIATED WITH ACHIEVEMENT OF MINIMAL DISEASE ACTIVITY IN RESPONSE TO BIOLOGIC THERAPY IN PSORIATIC ARTHRITIS – ANALYSES FROM THE CORRONA PSORIATIC ARTHRITIS/SPODYLOARTHITIS (PSA/SPA) REGISTRY

P.J. Mease 1, C. Karki 2, M. Liu 2, A. Kavanagh 3, C.T. Ritchlin 4, D.H. Hulsey 5, R. Pandurengan 1, J.B. Palmer 2, J.D. Greenberg 1, 2, 3, 4, 5, 6, 7

Objectives: To retrospectively report the MDA and patient-reported outcomes (PROs) over time (baseline vs first follow-up [FU] visit vs second FU visit) which may contribute to achievement of MDA in responders versus non-responders to biologic treatment.

Methods: This analysis included all patients with PsA in the Corrona registry aged ≥18 years between March 2013 and March 2016 who received biologics (biologic initiation) at enrollment (baseline) and had ≥2 FU visits (at ≥6-month intervals, mean [SD] 2nd FU visit: 15.7 [3.7] months). Responders were defined as patients who achieved MDA at the second FU visit and remained on their index biologic.

Results: Of 148 patients who met the inclusion criteria (mean [SD] age, 54.7 [11.0] years; mean [SD] disease duration, 11.8 [10.1] years), 34 patients (23%) were responders (i.e., patients who had ≥2 MDA assessments). The core components of MDA in these patients are shown in Table 1. Among responders, there were significant improvements in clinical characteristics and PROs such as mean TJC (3.4 vs 2.1 vs 0.6; P < 0.04), SJC (3.2 vs 2.0 vs 0.6; P < 0.01), percentage of affected BSA (6.2% vs 2.4% vs 1.4%; P = 0.03), patient pain (34.7 vs 26.1 vs 21.9; P = 0.007) and HAQ scores (0.6 vs 0.4 vs 0.3; P = 0.04); however, there were no significant changes over time for patient global assessment or entheseal counts (P = 0.05). Non-responders failed to have a significant improvement from baseline to the first and second FU visits in TJC, SJC, entheseal points, pain, patient global assessment and percentage of affected BSA (all P ≥ 0.05).

Conclusions: Only 23% of patients achieved MDA on their index biologic at the second FU visit and were considered responders. Over time, responders showed significant improvements in TJC and SJC and percentage of affected BSA, patient pain and HAQ scores; these most likely contributed to achievement of MDA response. A treat-to-target approach may be considered given the low number of patients in MDA.

References:

Acknowledgements: Corrona, LLC has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.
for most characteristics at enrollment, including BMI and PROs. These findings highlight the value of screening for PsA among patients with PsO in order to improve potential future outcomes. References:


Acknowledgements: The Corrona Psoriasis Registry is sponsored by Corrona LLC and is funded by AbbVie, Boehringer Ingelheim, Eli Lilly and Company and Novartis Pharmaceuticals Corporation. Corrona, LLC and is supported through contracted subscriptions in the last two years by AbbVie, Amgen, AstraZeneca, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Disclosure of Interest: M. Focherini has received honoraria for lectures and meeting expenses from Novartis, AbbVie, Janssen, Lilly, Pfizer and UCB.

SAT0473 | PREVALENCE OF ULTRASOUND ABNORMALITIES IN PATIENTS WITH PSORIATIC ARTHRITIS IN A CLINICAL PHASE OF MINIMAL DISEASE ACTIVITY UNDER ANTI-TNF TREATMENT


Table 1. Baseline characteristics of patients with PsO and no diagnosis of PsA stratified by PEST score (0-5)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PEST score 0</th>
<th>PEST score 1</th>
<th>PEST score 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>48.0 (15.5)</td>
<td>46.1 (14.8)</td>
<td>47.9 (13.8)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>27.4 (4.3)</td>
<td>27.6 (4.5)</td>
<td>28.4 (4.3)</td>
</tr>
<tr>
<td>Current employed, %</td>
<td>31.7 (41.0)</td>
<td>29.2 (41.0)</td>
<td>22.2 (31.2)</td>
</tr>
<tr>
<td>BMI, g/m²</td>
<td>22.6 (4.3)</td>
<td>22.8 (4.5)</td>
<td>22.7 (4.3)</td>
</tr>
<tr>
<td>Cigarettes (per day) on enrollment</td>
<td>15.0 (15.0)</td>
<td>14.0 (15.0)</td>
<td>13.0 (15.0)</td>
</tr>
<tr>
<td>Normalized hand US (≥ 25%</td>
<td>126.3 (51.8)</td>
<td>128.1 (51.9)</td>
<td>122.5 (51.6)</td>
</tr>
<tr>
<td>Normalized knee US (≥ 25%)</td>
<td>126.3 (51.8)</td>
<td>128.1 (51.9)</td>
<td>122.5 (51.6)</td>
</tr>
</tbody>
</table>

Results: Sixty-three pts were recruited (mean age 53±13y, mean PA duration 21±11y, mean MDA duration 21±11y). At US examination 66.7% of pts had at least one peripheral joint involved (17.5% had peripheral active synovitis), 47.6% had acute entheses and 95.2% chronic entheses. US bursitis was present in 22.0% of pts. 3.7% had hand extensor tendon involvement.

Table 1 shows clinical and demographic data of the pts and table 2 the US results

Table 2. US abnormalities in 63 pts in MDA

<table>
<thead>
<tr>
<th>Peripheray active synovitis</th>
<th>Joint peripheral involvement</th>
<th>Chronic enthesal alterations</th>
<th>Acute enthesal alterations</th>
<th>Tenosynovitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with abnormality (%)</td>
<td>28.3</td>
<td>42.9</td>
<td>23.9</td>
<td>19.7</td>
</tr>
</tbody>
</table>

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5010

SAT0474 | VERY LOW DISEASE ACTIVITY AND IMPACT OF DISEASE IN A SPANISH POPULATION WITH PSORIATIC ARTHRITIS

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Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain

Background: The target of treatment in psoriatic arthritis (PsA) should be remission or inactive disease. A potential definition that would fit with the Treat-to-Target Recommendations would be MDA meeting all 7 criteria, proposed as a definition of very low disease activity (VLDA) in PsA. Patient reported outcomes (PROs), such as those provided by the novel PsAID questionnaire 2, are also important to evaluate healthcare interventions and to reflect the impact of PsA on patients’ lives.

Objectives: The aims of the present study were to evaluate the prevalence of VLDA in patients with PsA and how much residual active disease is still present, so as to determine whether PsAID could be an additional useful tool to assess PsA interventions in clinical practice.

Methods: This was a post-hoc analysis of data from a cross-sectional observational and multicenter study (MAAPS), aimed at evaluating the prevalence of MDA in a Spanish population with PsA, to describe their characteristics and to evaluate the association between MDA and the impact of the disease as assessed by the PsAID questionnaire in routine clinical practice. The original study included adult patients of both genders diagnosed with PsA according to CASPAR criteria with at least one year of evolution time of disease and on treatment with biological or conventional synthetic disease modifying anti-rheumatic drugs (cDMARD). Patients were considered in VLDA when they met all the MDA criteria:1: tender joint count <1, swollen joint count <1, PASI score ≤0.5, HAQ ≤0.5, tender entheseal points <1, patient global disease activity VAS score ≤1, and PDI ≤1.

The original study included adult patients’ lives.

Results: 227 patients were included, 133 (58.6%) in MDA state and 58 (25.6%) in VLDA state. VLDA patients suffered from a mild impact of the disease according to PsAID: the majority (82.5%) had a PsAID score <4 and a mean total score (SD) of 2.1 (2.6) IC95% [1.55–2.64], while 66.7% of MDA patients had a PsAID score <4 and a mean total score (SD) of 3.3 (3.1) IC95% [2.82–3.87]. Disability, as measured by HAQ was greater in MDA patients (mean SD (0.3) 0.5 IC95% [0.21–0.43]) than in those who reached VLDA state (mean SD (0.2) 0.3 IC95% [0.11–0.25]).

Conclusions: 26% of Spanish PsA patients achieve VLDA state in routine clinical practice. PsA patients who reached this state also had a very low impact of disease according to PsAID. VLDA state could represent a situation of clinical remission of PsA.

References:


Acknowledgements: MAAPS (Minimal Activity in Psoriatic Arthritis) study group: J.C. Torro Alonso; J.A Román Ivorra; J. Sanz; J. Salviaterra; J. Calvo Alén;
RECENT ONSET PSORIATIC ARTHRITIS: BASELINE DATA FROM THE REAPSER STUDY


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Background: The natural history of psoriatic arthritis (PsA) is very little known and the information regarding prospective cohorts is very scarce worldwide, including our country. REAPSER (Spanish Rheumatology Society Registry of Psoriatic Arthritis) is the first registry of Spanish patients with recent onset PsA.

Objectives: To describe the baseline characteristics of patients included in the REAPSER cohort.

Methods: Observational, multicentric study (34 centers), with consecutive inclusion. We included adults of both sexes 18 years of age or older with PsA that met CASPAR criteria, and duration of less than two years since the appearance of symptoms attributed to PsA. Annual follow-up visits will be carried out for 5 years. Measurements: socio-demographic data; employment status and impact of the disease; family history of PsA and other inflammatory diseases; comorbidities and treatment; lifestyle; use of health services; clinical status at the time of diagnosis of PsA; anthropometric data; clinical evaluation of PsA manifestations; radiographic evaluation; analytical determinations; treatment of PsA. The study has been approved by the ethical committees of the participating centers.

Results: Two hundred and fifteen consecutive patients were included, mean age 49.8±13.9 years.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3780

SAT0475

FROM THE REAPSER STUDY


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Background: The purpose of this study is to compare and evaluate the demographic, clinical and laboratory features of elderly-onset psoriatic arthritis (EOPsA) and young-onset (YOPsA) patients.

Methods: One hundred and eighty patients diagnosed with PsA according to CASPAR criteria and followed-up in single center were included in this study. The patients with initial symptoms started after age 65 were accepted as EOPsA. Demographic, clinical, and laboratory data and the medications which the patients received were recorded and retrospectively evaluated.

Results: Nineteen (10.5%) of 180 patients were diagnosed as EOPsA, and 161 (89.5%) patients were evaluated as YOPsA. Mean patient age was 42.1±5 years for YOPsA group and 68.3±8.9 years for elderly onset group. Mean duration of disease was 5.6 years for early onset group and 1.3 years for elderly onset group (p=0.001). Fourteen (73.3%) of 19 EOPsA patients were female and 5 were male. Higher rates of fatigue, pain scores, comorbid diseases and acute phase reactants were detected in EOPsA patients comparing to YOPsA (p=0.000, p=0.000, p=0.001 and p=0.001 respectively). YOPsA patients have more dactilitis, nail involvement, elevated PASI scores, and smoking habits when compared with EOPsA patients (p=0.019, p=0.03, p=0.005, p=0.004 respectively). In terms of the treatment options chosen, there was no significant difference in the use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CS), methotrexate (MTX), and sulfasalazine (SS), but there was a more frequent use of anti-tumor necrosis factor-alpha in YOPsA group.

Conclusions: Herein we showed that YOPsA and EOPsA patients may have different demographic, clinical, and laboratory features. EOPsA patients are characterized with higher rates of fatigue, pain scores, comorbid diseases, and acute phase reactants and less dactilitis, nail involvement and anti-TNF-alpha usage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1378

SAT0476

DEMOGRAPHIC, CLINICAL, AND LABORATORY CHARACTERISTICS OF ELDERLY ONSET PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized with axial and peripheral joints involvement. It is rarely affects patients older than 65 years old.

Objectives: The purpose of this study is to compare and evaluate the demographic, clinical and laboratory features of elderly-onset psoriatic arthritis (EOPsA) and young-onset (YOPsA) patients.

Methods: One hundred and eighty patients diagnosed with PsA according to CASPAR criteria and followed-up in single center were included in this study. The patients with initial symptoms started after age 65 were accepted as EOPsA. Demographic, clinical, and laboratory data and the medications which the patients received were recorded and retrospectively evaluated.

Results: Nineteen (10.5%) of 180 patients were diagnosed as EOPsA, and 161 (89.5%) patients were evaluated as YOPsA. Mean patient age was 42.1±5 years for YOPsA group and 68.3±8.9 years for elderly onset group. Mean duration of disease was 5.6 years for early onset group and 1.3 years for elderly onset group (p=0.001). Fourteen (73.3%) of 19 EOPsA patients were female and 5 were male. Higher rates of fatigue, pain scores, comorbid diseases and acute phase reactants were detected in EOPsA patients comparing to YOPsA (p=0.000, p=0.000, p=0.001 and p=0.001 respectively). YOPsA patients have more dactilitis, nail involvement, elevated PASI scores, and smoking habits when compared with EOPsA patients (p=0.019, p=0.03, p=0.005, p=0.004 respectively). In terms of the treatment options chosen, there was no significant difference in the use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CS), methotrexate (MTX), and sulfasalazine (SS), but there was a more frequent use of anti-tumor necrosis factor-alpha in YOPsA group.

Conclusions: Herein we showed that YOPsA and EOPsA patients may have different demographic, clinical, and laboratory features. EOPsA patients are characterized with higher rates of fatigue, pain scores, comorbid diseases, and acute phase reactants and less dactilitis, nail involvement and anti-TNF-alpha usage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1378

SAT0477

THE COMPARISON OF ULTRASOUND SYNOVITIS AND ENTHESITIS FINDINGS AND CLINICAL FINDINGS IN PATIENTS WITH PSORIATIC ARTHRITIS AND SKIN PSORIASIS

T. Okang1, K. Inui1, Y. Sugioka2, K. Mamoto 1, H. Yoshimura1, T. Koike1,2,3, H. Nakamura1, 1Department of Orthopedic surgery; 2Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, Osaka, 1Search Institute for Bone and Arthritis Disease (SINBAD), Health Foundation for Health and Welfare, Wakayama, Japan

Background: Conventionally, the assessment of affected joint count in patients with psoriatic arthritis (PsA) was relied for the detection of swelling and tenderness in the joints and enthesis by clinical physical assessment. To date, the modern imaging tool such as ultrasonography (US) can detect inflammation in the joint and enthesis more sensitively than clinical assessment.

Objectives: The aim of this study was to research the prevalence of US synovitis and enthesitis findings in patients with PsA and psoriasis (PsO) comparing with clinical assessment.

Methods: Total 101 patients, 54 patients with PsA and 46 patients with PsO, were consecutively included. HI VISION Ascendus (HitachiAloka Medical, Tokyo, Japan) was used with a 18-MHz linear array transducer. US examination was performed in MCP,PIP, DIP and wrist joints in both hand. Grayscale (GS) and power Doppler (PD) US were scored on a 0–3 semiquantitative scale for each joint. Moreover, the US assessment of enthesitis was performed. Lateral epicondyle, ilioitops enthesis, the proximal and distal anterior superior iliac spine, Achilles tendon and fascia plantaris tendon enthesion was scanned in both GS and PD assessment. Abnormal findings of enthesis was defined structure thickness, bursitis eosiion, calcification and power Doppler signal.

Results: US synovitis was found in 81.5% (n=44) and 60.9% (n=28) by GS, and 45.7% (n=21) by PD assessment, respectively in patients with PsA and PsO. Active synovitis (GS grade ≥ 2 and/or PD grade ≥ 1) was found in 37.8% (n=21) and 21.7% (n=12) in patients with PsA and PsO, respectively. Active enthesitis was detected in 25.4% (n=13) and 17.4% (n=9) in patients with PsA and PsO, respectively.
68.5% (n=37) in PsA and 45.7% (n=21) in PsO. US synovitis was more frequently found than clinical assessment. The most common sites of inflammatory synovitis were the wrist. US enthesisopathy was found in 87.0% (n=47) in patients with PsA and 56.5% (n=26) in patients with PsO. US enthesis was also more frequently found than clinical assessment. The most common sites of enthesisopathy were the enthesis in lateral epicondyle, quadriceps and Achilles tendon.

**Conclusions:** Our results showed that US was able to detect a high prevalence of inflammatory synovitis in peripheral joints and enthesis in patients with PsA. Moreover, subclinical inflammatory findings were also found in patients with PsO by US. US examination is useful to detect the inflammatory condition in patients with PsA and PsO than clinical examination.

**Acknowledgements:** We wish to thank Setsuko Takeda, Ayumi Hashimoto and Emi Yamashita for their special efforts as a sonographer and collecting data.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5028

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**SAT0478** Rapid3 Questionnaire has high discriminating ability in minimal disease activity attainment in patients with early psoriatic arthritis treated according to tight control strategy in daily clinical practice (results of one-year open-label REMARCA study)


**Background:** RAPID3 is an instrument based on patient’s report outcomes (PROs) for the assessment of remission and disease activity in rheumatoid arthritis. The advantages of this questionnaire in treat-to-target (T2T) strategy in early psoriatic arthritis (EPA) have not been studied properly.

**Objectives:** To study discriminating ability of RAPID3 in minimal disease activity (MDA) attainment in patients with EPA treated during one year according to tight control strategy.

**Methods:** 61 (M/F–29/32) patients (pts) with active EPA, according to CASPAR criteria, mean age 37±10.6 years, PsA duration 11±3±10.2 months, psoriasis duration 75±8.9 months were included. All pts signed a consent form for participation in the open-label REMARCA study. At baseline and after 1 year (yr.) of therapy all pts underwent evaluation of PsA activity by TJC78, Swollen Joint Count (SJCT76), physician’s global disease activity (PtGDA), VAS, CRP, PGA (mg/l) and by PROs - patient global assessment PGA VAS, Health Assessment Questionnaire (HAQ), and RAPID3. The dose of Methotrexate (MTX) subcutaneous (s/c) was escalated by 5 mg every 2 weeks from 10 mg/wk up to 20–25 mg/wk. If pts did not achieve MDA after 6–9 months of MTX mono-therapy, combination therapy (CoT) of MTX+Adalimumab (ADA) was started in a standard regime; CoT was continued up to 1 yr. The proportion of pts who achieved MDA was calculated. MsSD, Me [Q25,75], %. Spearman rank correlation R, W-test, U-test, ROC-curve analysis were performed. All p<0.05 were considered to indicate statistical significance.

**Results:** By 1 yr. of therapy 36 out of 61 pts (59%) and 25 out of 61 pts (41%) were treated with MTX and with MTX+ADA accordingly. Significant improvements in PsA activity and PROs from baseline up to 1 yr. were observed: DAS 3.93 [3.20–4.58] vs 1.36 [0.82–2.25] (p<0.001), PGA 56 [48–69] vs 17 [10–21] (p<0.001), HAQ 0.81 [0.50–1] vs 0.36 [0.20–0.63] (p<0.001). Among those pts DAS 28 = 2.6 (p<0.05) was the optimal cut off point. RAPID3 based on PROs is a simple instrument for evaluating PsA activity. RAPID3 has shown high discriminating ability in MDA attainment in EPA pts treated according to tight-control strategy, and could be useful in daily clinical practice.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3010

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**SAT0479** Increased carotid intima-media thickness can discriminate significant coronary artery stenosis by coronary CT angiography in patients with psoriatic arthritis

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1Department of Medicine and Therapeutics, the Chinese University of Hong Kong; 2Department of Diagnostic and Interventional Radiology, The Prince of Wales Hospital, Hong Kong, Hong Kong

**Background:** PsA patients have increased morbidity & mortality due to cardiovascular disease (CVD). However, their CV risk was underestimated by various CV risk score1. Subclinical carotid atherosclerosis may be considered as surrogate bulb & proximal ICA bilaterally. Significant coronary artery stenosis was defined as stenosis of the lumen >50%.

**Objectives:** To assess the relationship between carotid artery disease by ultrasound (US) and CAD by coronary computed tomography angiography (CCTA) and identify US parameters predictive of significant CAD

**Methods:** 91 subjects (56 males; age: 56±11 years; disease duration 9.4±9.2 years) underwent CCTA & carotid US (interval between two exams: 2–7 months) were recruited. Carotid intima-media thickness (cIMT) & the presence of plaque were determined by high resolution US in the distal CCA, bulb & proximal ICA bilaterally. Significant coronary artery stenosis was defined as stenosis of the lumen >50%.

**Results:** Carotid plaque was present in 33 (36%) patients & coronary plaque was present in 55 (60%) patients while 9 (10%) patients had significant coronary artery stenosis. 36 (40%) patients had non-zero calcium score (CAC>0) group. The mean cIMT was significantly higher in CAC>0 group compared to CAC=0 group (0.70±0.11mm vs 0.64±0.11mm, p=0.031). There was a trend suggesting the max cIMT increases with increasing CAC score, while the presence of carotid plaque increased significantly with rising calcium score (Table1). The mean cIMT increased significantly with number of coronary vessels harboring plaque, while there was a trend suggesting the max cIMT and the prevalence of carotid plaque may increase in patients with rising number of coronary vessels harboring plaques. The mean & max cIMT were significantly higher in SS+ group than SS- group [mean cIMT: 0.76±0.07mm vs 0.65±0.12mm, p=0.011; max cIMT: 0.93±0.14mm vs 0.80±0.16mm, p=0.020 (Table1)]. The prevalence of carotid plaque was similar between SS+ & SS- group [29 (35.4%) vs 4 (4.4%), p=0.421]. Using multivariate logistic regression, mean & max cIMT were independent explanatory variable of significant coronary stenosis after adjusting age, gender, disease duration & damaged joint count. The OR of significant coronary stenosis of every 0.1mm increase in mean & max cIMT were 1.07 (95% CI: 1.00–1.15, p=0.042) and 1.06 (95% CI: 1.00–1.11, p=0.036). Mean cIMT of 0.66mm was the optimal cut off.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3010

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**Table 1.** Relationship between carotid artery disease by ultrasound and coronary artery disease by coronary computed tomography angiography.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS</td>
<td>0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SJCT78</td>
<td>0.63</td>
<td>0.042</td>
</tr>
<tr>
<td>PGA VAS</td>
<td>0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PGA VAS</td>
<td>0.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP</td>
<td>0.69</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: less compared to pts that did not achieve MDA-2.5 [1.3–5.3] and 8.1 [6.0–15.1] accordingly (U-test, p<0.001). According to the results of ROC-curve analysis RAPID3 score had a high discriminating ability for the presence of MDA - AUC 0.888 [0.808–0.969] (Fig. 1).

**Conclusions:** RAPID3 based on PROs is a simple instrument for evaluating PsA activity. RAPID3 has shown high discriminating ability in MDA attainment in PsA pts treated according to tight-control strategy, and could be useful in daily clinical practice.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3010

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**Figure 1.** ROC-curve analysis: association of RAPID-3 values and presence of MDA.
for discriminating patients with significant coronary stenosis (sensitivity: 100%; specificity: 44%). ROC analyses demonstrated that mean cIMT (AUC=0.801, p=0.003) has higher power than Framingham CVD risk score (FRS) (AUC=0.756, p=0.012).

Conclusions: Increased cIMT is associated with the presence & severity of coronary disease & obstructive coronary disease on CCTA in PsA patients. cIMT measurement can discriminate PsA patients with significant coronary stenosis better than FRS. PsA patients with moderate CVD risk should have carotid US for better CV risk stratification.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1473

SAT0480

COMPARATIVE EFFECTIVENESS OF SECUKINUMAB AND THERAPEUTIC OPTIONS WITH DISCRETE MODES OF ACTION ARE NOW AVAILABLE FOR PSORIATIC ARTHRITIS (PsA). CLINICAL TRIAL DATA


Background: The therapeutic options with discrete modes of action are now available for psoriatic arthritis (PsA). Clinicians require evidence to guide decision-making.

Methods: Placebo arms were also matched; placebo-adjusted comparisons were possible only until week 16 because patients could receive active treatment from this point onwards. Logistic regression was used to determine weights for age, sex, race, body weight, methotrexate use, presence of psoriasis (<3% body surface area), mean PASI score, dactylitis, enthesitis, mean HAQ-DI score and physical NAFLD therapy. Recalculated outcomes from F1 and F2 (SEC, ESS=91; INF, ESS=59) were compared with data from IMPACT 2 (INF, n=100; placebo, n=100). Pairwise comparisons using odds ratios (ORs [95% CIs]) were performed for ACR 20, 50 and 70 responses at nearest-equivalent time points across trials: weeks 6/8, 14/16, 24 and 54/52. Mean changes from baseline in SF-36 Physical and Mental Component Summary (MCS) scores were also compared.

Results: There was no evidence of differences in ACR 20, 50 and 70 responses between SEC and INF at weeks 6/8, 14/16 (both placebo-adjusted) and 24 (non-placebo-adjusted). At week 54/52, ACR 20 and 50 responses were higher with SEC than INF (OR [95% CI]: 4.05 [1.98–8.30], p<0.001 and 1.90 [1.05–3.44], p=0.034, respectively). Improvements in SF-36 MCS scores were greater with SEC (ES=0.34, p=0.065) compared with INF (ES=0.01, p=0.034). A sensitivity analysis that added PsA duration, swollen joint count and CRP levels to the matching parameters yielded similar results.

Conclusions: In this MAIC, SEC showed evidence of superiority for symptomatic improvement (non-placebo-adjusted ACR 20 and 50) over INF for active PsA at 1 year. This was accompanied by greater improvements in SF-36 MCS scores. At earlier time points, there was no evidence of differences in ACR responses between SEC and INF.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5806

SAT0481

THE RELATIONSHIP BETWEEN THE PATIENT ACCEPTABLE SYMPTOM STATE (PASS) AND DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS (PsA)

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Background: PASS is the highest level of symptoms beyond which patients consider themselves well. Psoriatic Arthritis Disease Activity Score (PASDAS) is a recently developed composite disease activity measure that summarizes a patient’s disease in a single 0–10 score.

Objectives: In this study, we aimed to identify the PASDAS cut-off points for PASS, and to examine the agreement between PASS and the PASDAS thresholds for low (<3.2), moderate (3.2–5.4), and high disease activity (>5.4).

Methods: Patients were prospectively recruited from the University of Toronto PsA clinic. A standard protocol including physician assessment and patient-reported outcomes was used to record variables required to calculate PASDAS. In addition, each patient was asked to “think about all the ways your PsA has affected you during the last 48 hours. If you were to remain in the next few months as you were during the last 48 hours, would this be acceptable to you?” to assess PASS. For analysis, the PASDAS threshold for PASS was identified with the ROC analysis to maximize specificity and sensitivity. Furthermore, the agreement between PASS and low, moderate, and high PASDAS disease activity cut-offs were evaluated.

Results: 169 patients [61% male, mean age 56.1, mean disease duration 16.9 years, mean (SD) PASDAS 3.25 (1.1)] were recruited. The PASDAS threshold for the patient acceptable symptoms state (PASS=) was identified to be 3.84 (AUC = 0.88, sensitivity 0.82, specificity 0.94) using ROC curve analysis. 91% of patients with low disease activity (PASDAS <3.2) considered their symptoms state acceptable (PASS+), and 100% of the patients with high disease activity (PASDAS >5.4) considered their symptom state as unacceptable (PASS–). Furthermore, the mean (SD) PASDAS was 4.5 (1.0) in the PASS- group and 2.6 (1.1) in the PASS+ group.

Conclusions: The PASDAS threshold for patient acceptable symptoms state is 3.84, which is within the moderate disease activity range. Thus with a PASDAS of 3.84 or lower, PsA patients consider their symptom state acceptable for the next few months. This cut-off should be considered for shared decision making regarding treatments in PsA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6186

Saturday, 17 June 2017

Scientific Abstracts
SUBCLINICAL ENTHESOPATHY IN PSORIATIC PATIENTS AND ITS RELATION TO OTHER DISEASE PARAMETERS: AN ULTRASOUND STUDY

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Background: Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by reddish, thick patches covered with marked silvery scaling [1]. In about 70% of the patients, psoriasis is present many years before the onset of psoriatic arthritis [2]. The early recognition and therapeutic intervention especially with the new biologic treatments is critical to prevent the destructive and debilitating changes of psoriatic arthritis [3]. Enthesitis is inflammation at the attachment of tendons and ligaments to the bones, has been suggested as being the unifying feature of psoriatic arthritis, and the disease can be considered an enthesitis associated disorder rather than primary synovitic arthropathy [4].

Objectives: We aimed to correlate the subclinical enthesitises in patients with psoriasis detected by means of power Doppler (PD) ultrasonography (US) with other disease parameters. Methods: 50 persons with a definite diagnosis of psoriasis with no clinical evidence of arthritis or enthesitis were selected. All patients completed clinical assessment included Psoriasis severity (PASI) score, body mass index (BMI), PDUS evaluation of Achilles, quadriceps, patellar entheses and planter aponeurosis. US findings were scored according to the Glasgow Ultrasound Enthesitis Scoring System (GUESS).

Results: In 18 of 50 of patients (36%) PDUS found signs indicative of enthesopathy. The Achilles entheses had the highest number of PDUS signs of enthesopathy (33.3%), followed by distal patellar enthesis (22.2%), proximal patellar enthesis (16.7%), quadriceps enthesis (16.7%), and plantar aponeurosis enthesitis (11.1%) with variable enthesial morphostructural abnormalities. The GUESS score was directly correlated with age (p = 0.012), disease duration (p = 0.044), PASI (p = 0.035), BMI (p = 0.011), hyperuricemia (p = 0.011).

Demographic findings of the study population:

<table>
<thead>
<tr>
<th>Character</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (range) mean (SD)</td>
<td>(19-70) 33.8±11.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>31 (62)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>Disease duration</td>
<td>(2-12) 7.7±3.4</td>
</tr>
<tr>
<td>(range) mean (SD)</td>
<td></td>
</tr>
<tr>
<td>PASI score</td>
<td>21 (17.3)</td>
</tr>
<tr>
<td>mean ±SD (range)</td>
<td>29.9±6.4 (19.5-42)</td>
</tr>
</tbody>
</table>
| Rheumatoid factor: N of patients (%) | Positive (>-1/8) 4 (8%)
|                   | Negative 46 (92%) |
| SIUA: N of patients (%) | Normal -6 mg/dl 38 (76%)
|                   | Elevated 12 (24%) |
| Radiographic sacroiliitis: N of patients (%) | Normal 6 (12%)
|                   | Abnormal (arthritis) 18 (36%) |
| Ultrasonographic findings: (%) |          |
|                   | Normal 62 (12%) |
|                   | Abnormal (arthritis) 38 (36%) |

Conclusions: In addition to the importance of PDUS as a complimentary tool in examination of entheses in psoriatic patients, the presence of high PASI score in those with the increased BMI and hyperuricemia in addition to long disease duration could be considered as predictive parameters for the presence of psoriatic enthesitis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1595

CITATION: SAT0482

Osteoarthritis

OSTEOARTHRITIS (OA) AND SOCIO-ECONOMIC STATUS (SES) PREDICTS THE ONSET OF COMORBIDITIES LINKED TO FREQUENT HEALTHCARE CONSULTATION

R. Hayward 1, K. Kaur 2, R. Wilkie 1, 1Research Institute for Primary Care & Health Sciences; 2Medical Student, Keele University, Keele, United Kingdom

Background: OA is the most common joint condition, the fourth leading cause of disability globally and the fastest increasing major health condition. In older adults, OA frequently coexists with other morbidities, but the temporal nature is unclear. There is abundant evidence that markers of low SES are associated with poor outcomes among people with musculoskeletal conditions, however the mechanism linking comorbidity may vary with SES.

Objectives: To examine if OA predicted the onset of comorbidities that are the reason for frequent consultation to primary care, and if this association was moderated by SES.

Methods: Cohort study combining questionnaire data at two time points (2005, 2008) in the North Staffordshire Osteoarthritis Project, and medical record data from 2000 to 2005 (n=3910). OA was defined by consultation to primary care for OA between 2000 and 2005, and the indication of moderate to extreme pain interference in the questionnaire (2005). Logistic regression examined the association between OA and the onset of seven comorbidities (anxiety, depression, widespread pain (WP), insomnia, cognitive impairment, neurosis, stress between 2005 and 2008) and restricted social participation, first unadjusted and then adjusting for putative confounders (comorbidity, socio-demographic and lifestyle factors). Moderation of the association between OA and new onset comorbidity by change in income, education and area-level deprivation was examined by including interaction terms in regression and stratified analyses. Results were reported as odds ratios with a 95% Confidence Interval (OR; 95% CI).

Results: Mean age was 63, 55% were female, and 942 (24%) had OA. In the unadjusted analysis, OA was significantly associated with new onset of seven comorbidities (p<0.05). After adjusting for confounders, OA was associated with the onset of WP (2.49; 1.96–3.17) and insomnia (1.58; 1.14–2.19). There was a significant non-multiplicative interaction between OA and income and new onset cognitive impairment (P=0.047); new onset of cognitive impairment in those with OA whose income remains adequate 29.1% of 38.1% in those with OA whose income remains inadequate), and between OA and education and new onset WP (P=0.012; new onset in those with OA and secondary education only was 37.4% of 50% in those with OA and had more than a secondary education).

Conclusions: OA was more likely to develop new physical and psychological comorbidities that lead to more frequent consultation to primary care than those without OA. Whilst confounders explained some of these associations, OA consultants may benefit from more proactive strategies to prevent further morbidity. Despite no significant multiplicative interactions, there were differences in the prevalence of new onset of morbidity in those with OA when stratified by SES. Onset of cognitive impairment was associated with inadequate income but WP was associated with those with higher education suggesting a “worried well” population seen both in other health surveys and in screening. OA and baseline morbidities were higher with lower SES and further exploration across the life-course will help to establish the role of SES on the natural history OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2106

CITATION: SAT0483

LOW MAGNESIUM INTAKE IS ASSOCIATED WITH INCREASED PAIN IN SUBJECTS WITH RADIOGRAPHIC KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

A. Shmagel 1, N. Onizuka 2, T. Vo 2, L. Langsetmo 3, K. Ensrud 3, A. Foley 1, P. Valen 1,6. 1Rheumatology, University of Minnesota; 2Medicine, VA Medical Center; 3Nephrology/Medicine, University of Minnesota; 4Medicine/Rheumatology, VA Medical Center, Minneapolis, United States

Background: Osteoarthritis pain appears to be caused, at least in part, by alterations in peripheral and/or central nociceptive pathways.[1] As magnesium is a known mediator of nociception, we hypothesized that low magnesium intake may be associated with increased pain in radiographic knee OA.

Objectives: To evaluate whether magnesium intake is associated with knee pain in radiographic knee osteoarthritis.

Methods: We investigated the associations between knee pain and magnesium intake from food and supplements in 2549 participants with prevalent radiographic knee OA (Kellgren-Lawrence score ≥2) in the Osteoarthritis Initiative cohort.[2] WOMAC pain scores in the affected knee were reported annually with total follow up period of 48 months. Magnesium intake was assessed at baseline by food frequency questionnaire and dietary supplement questionnaire, and expressed in gender-specific calorie-adjusted quintiles. Analyses used generalized linear mixed effects models with repeated measures.

Results: Among participants with baseline radiographic knee OA the mean total magnesium intake was 310 mg/day (SD 133) for men, and 288 mg/day (SD...
for women, with 68% of men and 44% of women below the estimated average requirement (EAR). The mean WOMAC pain score at 0, 12, 24, 36, and 48 months of follow up was 3.5 (SD 3.8), median score 2 (IQR 0; 6). After adjustment for age, gender, BMI, caloric intake, physical activity, smoking status, alcohol use, renal insufficiency, and the use of analgesics, subjects in the lowest quintile of magnesium intake (Q1) had, on average, 1 point higher WOMAC knee pain scores than subjects in the highest quintile (Q5): Q1 1.00 (0.61–1.39), Q2 0.69 (0.32–1.06), Q3 0.25 (-0.12–0.62), Q4 0.25 (-0.14–0.64); p<0.0001.

Conclusions: In a cohort of adults with prevalent radiographic knee osteoarthritis, magnesium intake overall was below recommended. Low magnesium intake as baseline was associated with increased pain in the affected knee over 48 months of follow up. These findings may be of growing importance as the average dietary magnesium intake for humans is declining.[3]

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3024

Conclusions: This is the first study to show gene expression alterations in uncultured CD271+ MSCs from OA patients. A notable increase in OPG is suggestive of MSCs’ bias towards inhibition of bone resorption in late hip OA and further incriminates the RANKL/OPG pathway, specifically in MSCs, in OA pathophysiology. Further studies are needed to define the role of native MSCs in lesion associated OA disease progression and to evaluate these as a possible target for treatment.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5937

SAT0486 CATASTROPHIZING IN OSTEOARTHRITIS OF THE KNEE: DOES THE LEQUESNE SCORE TAKE IT IN COUNT? A PROSPECTIVE STUDY

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Background: knee osteoarthritis is a frequent matter of consultation in both general practice and rheumatology. Pain is the main symptom leading to a consultation. This painful experience can be influenced by various factors such as the anxiodepressive state or catastrophizing. Catastrophizing is known to be associated with lower analgesia results in total knee arthroplasty (1).

Objectives: The aim of this study is to evaluate the correlation between the functional status (assessed by the Lequesne score) and the catastrophizing (assessed by the Sullivan score) in patient with osteoarthritis of the knee.

Methods: We included patients consulting for knee osteoarthritis, meeting the OARSI criteria (2), one of the three general practitioners participating in the study or a rheumatologist at University Hospital. We excluded those with surgical indication. For each patient we registered the epidemiological data, the radiographic stage as well as the scores of Lequesne and Sullivan questionnaires. The correlation between the different scores were assessed with a Spearman test.

Results: A total of 100 patients were included, 50 consulting a general practitioner and 50 consulting a rheumatologist, between November 2015 and April 2016. Among these 100 patients, there were mainly women (57%) with a mean age of 64.8±1.77 years old. The mean radiographic stage was 2.66±0.11 on the Kellgren and Lawrence scale. The Mean Sullivan score was 12.96±1.18 and the mean Lequesne score was 10.46±0.47. There was a close correlation (r=0.3, p=0.006) between the Lequesne score and the radiographic scale. There was no correlation between the Sullivan score and the radiographic scale. However, the correlation between the Sullivan and the Lequesne scores was modest (r=0.47, p=0.001) (Figure 1). Thus, the Lequesne score is correlated with the radiographic scale and the Sullivan score. When we compare the two populations, it appeared that the people consulting a rheumatologist are majority of women (72%) and younger (62.58±1.8 VS 67.18±1.38 years, p<0.05) and with a shorter duration of symptoms (6.02±1.12 VS 7.95±1.5 Years, p<0.001). In terms of radiographic and functional impairment, the two populations were similar (Kellgren score of 2.59±0.15 VS 2.7±0.158 and Lequesne score of 11.13±0.67 VS 9.78±0.66, p<0.05) but there was a clear difference for the Sullivan score (16.8±1.67 VS 21±1.4, p<0.001).

Conclusions: Our study is the first to highlight a correlation between the Sullivan and the Lequesne scores in patient consulting for osteoarthritis of the knee. Moreover, unlike the Sullivan, score the Lequesne score is correlated with the radiographic scale. The strength of this study is the inclusion of both patients consulting the general practitioner and those consulting the rheumatologist to avoid a recruitment bias. Indeed, patients consulting the rheumatologist had a catastrophizing score more important for the same functional and radiological impairment than those consulting the general practitioner. Thus, our population is representative of the global population suffering from osteoarthritis of the knee in terms of age, sex-ratio, BMI. The Lequesne score is a global score correlated with structural damage and with psychological factors like catastrophizing.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2617

SAT0485 INCREASED EXPRESSION OF OSTEOPROTEGERIN IN CD271+ MULTIPOTENTIAL STROMAL CELLS FROM FEMORAL HEADS OF PATIENTS WITH HIP OSTEOARTHRITIS

D.C. Ilas 1, S.M. Churchman 1, J. Aderinto 2, P.V. Giannoudis 1, D. McDonnagle 1, E. Jones 1, 1Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; 2Department of Orthopaedics, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Background: Osteoarthritis is a disease of the whole joint, but subchondral bone marrow lesions (BMLs) closely correlate with disease progression [1]. We have previously shown that in OA femoral heads, subchondral bone multipotential stromal cells (MSCs) were 5-fold more abundant in MRI determined BML areas where they also showed reduced mineralisation capacity and altered RANKL expression compared to non-BML areas [2]. This offered novel insight into MSC involvement in the bone remodeling process in OA.

Objectives: The current study investigated a multi-lineage gene expression profile of native CD271+ MSCs from OA femoral heads focusing on osteogenesis and bone remodeling related genes compared to CD271+ MSCs from healthy trabecular bone.

Methods: Femoral heads were obtained from 17 OA patients undergoing total hip arthroplasty. Control samples included healthy iliac crest bone from 12 patients undergoing autograft harvesting for bone reconstruction and healthy femoral neck bone from 2 patients, extracted following core decompression surgery for avascular necrosis of the femoral head. CD271+ MSCs were extracted by enzymatic digestion and purified by FACS, as previously described [3, 4]. MSC cultures were generated by standard methods [4]. Quantitative real-time PCR was performed using TaqMan assays for 12 transcripts and gene expression was normalised to HPRT1.

Results: Sorted CD271+ cells from both groups displayed gene expression profiles indicative of their steady-state osteogenic, adipogenic, bone remodeling and stromal-support functions (Table 1). Three out of 11 transcripts showed significant increases in OA: alkaline phosphatase, melanoma cell adhesion molecule and osteoprotegerin (OPG) (p<0.05, Mann Whitney test). The proportion of CD271+ cells related to total live cells was more variable but on average 2-fold higher in OA (medians of 2.3 and 5.2%, respectively, not significant). Consistent with previous findings [4, 5], gene expression levels for the majority of transcripts were altered following MSC culture expansion (3 up-regulated and 8 down-regulated).

Conclusions: This is the first study to show gene expression alterations in uncultured CD271+ MSCs from OA patients. A notable increase in OPG is suggestive of MSCs’ bias towards inhibition of bone resorption in late hip OA and further incriminates the RANKL/OPG pathway, specifically in MSCs, in OA pathophysiology. Further studies are needed to define the role of native MSCs in lesion associated OA disease progression and to evaluate these as a possible target for treatment.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2617
A RANDOMIZED, BLINDED, COMPARATOR-CONTROLLED TRIAL INVESTIGATING A 4-WEEK COURSE OF LYRICA IN SUBJECTS WITH KNEE OSTEOARTHRITIS WHO EXHIBIT NEUROPATHIC PAIN, COMPARED WITH A 4-WEEK COURSE OF PARACETAMOL

A. Wright1, P. Moss1, H.A. Benson2, R. Will3, P. Chowallour4, 1School of Physiotherapy and Exercise Science, 2School of Pharmacy, Curtin University; 3School of Medicine and Pharmacology, University of Western Australia; 4Department of Rheumatology, Royal Perth Hospital, Perth, Australia

Background: Knee osteoarthritis (OA) has been considered the archetypal model of inflammatory or nociceptive pain [1] but it is apparent that people with knee OA may present with different pain phenotypes including some with features of neuropathic pain [2,3].

Objectives: The aim of the present study was to select people with knee OA who exhibited features of neuropathic pain based on elevated cold pain thresholds (>15°C) and elevated PainDETECT scores (>13) and to determine if pregabalin would be more effective in reducing pain and improving function in this cohort than paracetamol.

Methods: The study used a double-blind, randomized, comparator-controlled design in participants with knee OA to compare the effectiveness of a standard dose of paracetamol (1000mg tid) with a titrated dose of pregabalin (Lyrica) taken daily over 28 days. A cohort of 90 participants with moderate to severe painful knee OA (Pain rating >4/10) who demonstrated features of neuropathic pain were included. Participants were selected from an initial cohort of 271 OA sufferers recruited from the Perth community based on screening of CPT and PainDETECT. Included participants were randomly assigned to receive either a four week course of pregabalin titrated to a maximum dose of 300mg or a four week course of paracetamol (4A,000mg).

Participants were assessed at baseline, 14 and 28 Days. They completed the PainDETECT, WOMAC and POAS questionnaires. Quantitative sensory testing was carried out at three sites (index knee, contralateral knee, ECRB) using standard methods. Cold and heat pain thresholds were tested using a Peltier thermal stimulator and pressure pain using a digital algometer. Stabilometric Physical function was assessed using three timed locomotor function tests (sit-to-stand, walk, stairs).

Results: Participants receiving pregabalin (300mg) exhibited greater reductions in WOMAC Pain scores (P=0.0001) and PainDETECT scores (P=0.0001) at Day 28 compared to the paracetamol group and a greater increase in pressure pain thresholds (reduced tenderness) (P=0.025) at the index knee. There was no significant difference between the groups in cold pain thresholds (P=0.33).

Participants in the pregabalin group completed the physical tests more quickly than the paracetamol group (Sit-to-stand p=0.05, Walk, p=0.001, stair algometer p=0.05).

The pregabalin group also had a significantly increased likelihood of reducing their PainDETECT score below the entry value of 13 compared to the paracetamol group (OR 9.20; P=0.001) but there was no significant difference in the likelihood of reducing their cold pain threshold below the 15°C entry value (OR 2.28; P=0.14).

Conclusions: The group receiving pregabalin 300mg showed greater reductions in pain, reduced features of neuropathic pain and reduced tenderness at the affected knee. Further research is warranted to evaluate pregabalin in this specific patient cohort.

References:

Acknowledgements: The investigators thank Ms Lisa Webster for her contribution to the study.

Disclosure of Interest: A. Wright Grant/research support from: Pfizer Inc, P. Moss Grant/research support from: Pfizer Inc, H. Benson Grant/research support from: Pfizer Inc, R. Will Grant/research support from: Pfizer Inc, P. Chowallour. None declared

DOI: 10.1136/annrheumdis-2017-eular.5656

SAT0489 ASSOCIATION OF CHILDHOOD OVERWEIGHT MEASURES WITH ADULTHOOD KNEE CARTILAGE DEFECTS AND BONE MARROW LESIONS: A 25-YEAR COHORT STUDY

T. Meng 1, S. Thayer2, A. Venn1, F. Cicutiin3, L. March4, T. Dwyer5, A. Halliday1, M. Cross1, L. Laslett1, G. Jones1, C. Ding1,2,2, B. Antony1, M. Menzies1, M. Hough1,2,2, H. Benson Grant/research support from: Pfizer Inc, H. Benson Grant/research support from: Pfizer Inc, R. Will Grant/research support from: Pfizer Inc, H. Benson Grant/research support from: Pfizer Inc, R. Will Grant/research support from: Pfizer Inc, P. Chowallour. None declared

SAT0467 COMPARATIVE EFFECTIVENESS OF AYURVEDA AND CONVENTIONAL CARE IN KNEE OSTEOARTHRITIS – A RANDOMIZED CONTROLLED TRIAL

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Background: Traditional Indian Medicine Ayurveda is used to treat knee osteoarthritis (OA) despite limited evidence.

Objectives: We aimed to evaluate the effectiveness of complex Ayurvedic treatment compared to conventional complex care in knee OA patients.

Methods: According to ACR criteria patients with knee OA were included in a multicenter randomized, controlled trial and treated in 2 hospital outpatient clinics and 2 private outpatient clinics in Germany with 5 physicians and 20 therapists participating. Patients received either Ayurvedic treatment (n=77) or conventional care (n=74) with 15 treatments over 12 weeks. Primary outcome was the change on the European Centre for Osteoarthritis and Rheumatism (WOMAC) Index after 12 weeks (validated German version). Secondary outcomes included the WOMAC subscales; a pain disability index, numeric rating scales for pain and sleep quality, a pain experience scale, a quality-of-life index, a profile of mood index, rescue medication use, and safety issues.

Results: A total of 151 patients (Ayurveda n=77, conventional care n=74) were included. Changes of the WOMAC index from baseline to 12 weeks were more pronounced in the Ayurveda group (mean difference 6.10 [95% CI 52.69;6.6]) than in the conventional group (32.0 [95% CI 21.4;42.6]) resulting in a significant difference between groups (mean difference 0.001). In a clinically relevant effect size (Cohen’s d 0.68 [95% CI 0.35;1.01]). Similar tendencies were observed for all secondary outcomes at week 12. Effects were sustainable at follow-ups after 6 and 12 months.

Conclusions: The results suggest that a complex Ayurvedic treatment might be clinically superior to a complex conventional intervention in the treatment of OA of the knee.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4692

SAT0488 MARROW LESIONS: A 25-YEAR COHORT STUDY

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5668
GENOME-WIDE DNA METHYLATION PROFILING OF OSTEARTHRITIS PERIPHERAL BLOOD MONONUCLEAR CELLS REVEALS SLOWED EPIGENETIC AGING AMONG RAPID RADIOGRAPHIC PROGRESSORS: DATA FROM THE OSTEARTHRITIS INITIATIVE (OAI)

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Background: Extensive evidence has correlated epigenetic alterations in articular tissues with both the pathogenesis and progression of human osteoarthritis, but few analyses of blood cell epigenetic patterns have been done in OA.

Objectives: We examined the DNA methylation aging rate in peripheral blood mononuclear cells (PBMCs) at baseline from knee OA patients with rapid radiographic progression compared to well-matched non-progressors enrolled in the Osteoarthritis Initiative (OAI).

Methods: PBMC DNA was obtained from baseline blood draws of 64 OA patients enrolled in the OAI longitudinal study. All patients had baseline symptomatic and radiographic OA. 32 rapidly-progressive OA patients, defined as ≥1.0mm radiographic joint space loss within 24 month follow-up were compared to 32 non-progressive patients. There were no differences in age, sex, race, BMI, baseline K/L grade, or calculated PBMC subset composition between rapid- and non-progressors. DNA methylation was quantified with Illumina HumanMethylation 450k arrays. Preprocessing was performed in GenomeStudio and normalized to baseline characteristics. Epigenetic age was estimated with the algorithm described by Horvath et. al., using 353 age-associated CpG sites. This epigenetic age was correlated to chronological age to calculate epigenetic-chronological age discordance (∆Age) and group differences compared to a Student t-test. ∆Age was correlated with age at death and BMI. Statistical analyses were performed with the Ingenuity Pathway Analysis (IPA) system.

Results: The baseline DNA methylation aging rate in rapidly progressive (RP) knee OA patients was 5.5±1.4 years less than chronological age (p=0.015). 1165 CpG sites were correlated with ∆Age in rapid progressors, corresponding to 755 genes. Ontologic analysis of highly correlated genes showed association of the STAT3 pathway (p=4E-4), Notch signaling (p=1E-3), axonal guidance signaling (p=7E-3), CREB signaling (p=2E-2), NFAT signaling (p=2E-2), and autophagy (p=4E-2) among others. Associated upstream regulators included FGF2 (p=3E-5), SMAD4 (p=9E-4), SMAD5 (p=1E-3), TNF (p=4E-3), and TGFB1 (p=4E-3), among others.

Conclusions: Our data reveal that a decelerated peripheral blood differential DNA methylation age epigenotype is present at baseline in rapidly progressive knee OA patients, but not in nonprogressive knee OA patients. The genes correlated with this methylation age deceleration cluster in pathways previously associated with OA in articular tissues, suggesting that these pathways may systematically epigenetically dysregulated. Our data reinforce the notion that OA is a heterogeneous disease composed of distinct subgroups, and suggests that future epigenetic investigation of immune cell subsets may be beneficial in OA research.

Acknowledgements: We gratefully acknowledge the assistance of Dr. Michael Nevitt, PhD, MPH, and Dr. John Lynch, PhD, of the University of California San Francisco and the OAI for their assistance in sample selection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3727

INTRAMUSCULAR CORTICOSTEROID INJECTION VERSUS PLACEBO INJECTION IN HIP OSTEOARTHRITIS: A 12-WEEK BLINDED RANDOMIZED CONTROLLED TRIAL

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Background: Several international guidelines recommend intra-articular (IA) corticosteroid injections for patients with hip OA experiencing moderate to severe pain and no responding to oral analgesics. Previous research has shown a systemic effect of an intramuscular (IM) gluteal corticosteroid injection in patients with subacromial impingement shoulder pain. A clinically relevant effect of IM corticosteroid injections could be less complex, alternative treatment for patients’ episodes of increased pain in hip OA.

Objectives: The trial aimed to assess the efficacy of an IM gluteal corticosteroid injection compared to a placebo injection on patients’ reported hip pain severity in patients with hip OA, who were not responding on oral analgesics.

Methods: Patients in primary care or secondary care who met the inclusion criteria, were included. Patients were randomized to receive either an IM gluteal corticosteroid injection on one hip followed by a placebo injection on the other hip or vice versa. Intervention and placebo injections were performed with a standardized technique. Analgesic medication use was recorded at baseline and at every follow-up visit. Primary outcome was a severity of hip pain at 2 weeks, measured with a numerical rating scale (NRS) in rest and during walking (0–10, 0=no pain). Secondary outcomes included hip pain severity (NRS, WOMAC pain, ICOAP, WOMAC function, stiffness (WOMAC stiffness), adverse events, and medical co-interventions at 2, 4, 6, and 12 weeks followed. Statistical analyses were performed based on the intention to treat principle. Linear mixed models with repeated measurements were used to analyze between group differences. The models were adjusted for variables that changed the effect size.

Results: 107 of 422 screened patients were randomized. After informed consent, one randomized patient did not show up at the appointment for baseline measurement and subsequent injection and could, because of lack of data, not be included in the analyses. Finally, 52 patients in the corticosteroid injection group, and 54 in the placebo injection group were included in the analyses. 88% of the patients were female, and 25% were recruited by orthopedic surgeons. Mean age was 64 years (SD 11) and duration of OA was ≥1 year for 70%. At 2 weeks follow-up (table), the corticosteroid injection was statistically significant and clinically relevant associated with hip pain reduction at rest (coefficient -1.3, 95% CI -2.3 to -0.3) compared to placebo. The corticosteroid injection was also associated with significant hip pain reduction at 4, 6 and 12 weeks. Moreover, at almost all follow-up measurements the estimates showed significant differences in favor of the corticosteroid injection on WOMAC pain, function, stiffness and total score, and ICOAP. No significant differences between groups were found for adverse events and medical co-interventions.

Conclusions: An IM gluteal corticosteroid injection was effective in hip pain reduction compared to placebo injection in patients with hip OA at 2 weeks
follow-up. Moreover, the effect of the corticosteroid injection prolonged the entire 12 week follow-up period.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1056

SAT0493 MAINTAINING SUFFICIENT SERUM VITAMIN D LEVELS OVER TWO YEARS IS ASSOCIATED WITH IMPROVED KNEE STRUCTURAL AND SYMPTOMATIC OUTCOMES IN PEOPLE WITH KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS OF THE VIDEO TRIAL

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Objectives: To describe whether maintaining sufficient serum vitamin D levels in people with knee osteoarthritis (OA) and baseline vitamin D insufficiency has an association with change in knee structures and symptoms over two years.

Methods: Participants (n=413, age 63.2%; 50% females) with symptomatic knee OA and vitamin D insufficiency were enrolled in a clinical trial. 340 participants (62.3%; completed the study with 25-hydroxyvitamin D [25(OH)D] measurements at month 0, 3 and 24. Participants were classified as consistently insufficient (serum 25(OH)D <50nmol/l) at month 3 and 24, n=45); fluctuating (25(OH)D >50nmol/l at either point, n=68) and consistently sufficient (25(OH)D >50nmol/l at month 3 and 24, n=228) vitamin D groups. Knee cartilage volume, cartilage defects, bone marrow lesions (BMLs) and erosion-synovitis volume were assessed using MRI at baseline and month 24. Knee symptoms were assessed at baseline, month 3, 6, 12 and 24 using Western Ontario and McMaster Universities Arthritis Index (WOMAC).

Results: The consistently sufficient group had significantly less loss of tibial cartilage volume (β: -2.1%, 95 CI%: -3.3%, 3.9%), less increase in erosion-synovitis volume (β: -2.5mL, 95 CI%: -4.7, -0.2) and less loss of WOMAC physical function (β: -94.2, 95% CI: -183.8, -4.5) compared to the consistently insufficient group in multivariable analyses. In contrast, there were no significant differences in these outcomes between the fluctuating and consistently insignificant groups. Changes in tibiofemoral cartilage defects, BMLs and knee pain were similar between groups.

Table 1. Associations between maintaining sufficient 25-(OH)D levels and changes in cartilage volume and erosion-volume over 24 months in patients with knee osteoarthritis

<table>
<thead>
<tr>
<th>Multivariable analysis</th>
<th>β (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibial Cartilage Volume Change (%/y)</td>
<td>Reference</td>
<td>0.15</td>
</tr>
<tr>
<td>Consistently insufficient</td>
<td>1.5 (-0.5, 3.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Fluctuating</td>
<td>2.1 (0.3, 3.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>P for trend</td>
<td>Reference</td>
<td>0.02</td>
</tr>
<tr>
<td>Erosion-Synovitis Absolute Volume Change (mL)</td>
<td>Reference</td>
<td>0.66</td>
</tr>
<tr>
<td>Consistently insufficient</td>
<td>0.7 (2.5, 3.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>Fluctuating</td>
<td>-2.5 (-4.7, -2.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>P for trend</td>
<td>-0.01</td>
<td></td>
</tr>
</tbody>
</table>

Adjusted age, sex and BMI and change in season of blood sampling.

Conclusions: This post hoc analysis suggests beneficial effects of maintaining vitamin D sufficiency on cartilage loss, erosion-synovitis and physical function in people with symptomatic knee OA.

References:

Acknowledgements: We specially thank the participants who made this study possible, and we gratefully acknowledge the role of Vitamin D Effect on Osteoarthritis Study staff and volunteers in collecting the data. We thank the research assistants Jodi Barling, Kay Ngvo, Judy Hankin and Alice Noone who were involved in the coordination of this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1056

SAT0494 EARLY TOLL-LIKE RECEPTOR 4 BLOCKADE IMPEDES THE BEHAVIOURAL AND HISTOLOGICAL CHARACTERISTICS OBSERVED IN A MIA-INDUCED ANIMAL MODEL OF OSTEOARTHRITIC PAIN

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Background: Contribution of Toll-Like Receptor 4 (TLR4) to pain sensitisation has been demonstrated to occur under chronic pain conditions. We previously described an antinociceptive effect of TLR4-A1, a TLR4 inhibitor, in two chronic pain conditions, peripheral neuropathic pain and osteoarthritis (OA).

Objectives: The aim of this study was to evaluate TLR4-A1 effect on alldynia and hyperalgesia in OA model, and to evaluate whether this effect is correlated with changes in spinal glial activation.

Methods: Wistar rats weighing 200–250g were used. OA was induced by a single intraarticular injection of 2mg of monosodium iodoacetate (MIA) into the right knee joint of anaesthetised rats. TLR4-A1, 10 mg/kg, was intraperitoneally administered during the first five days post-MIA injection. TLR4-A1 was synthesised by Dr Quesada. Vehicle-treatment (ethanol:saline, 1:9) was administered in the same way. At three weeks (day 21 post-MIA injection), animals were sacrificed for tissue collection. L3-L5 spinal segments were collected and embedded in paraffin wax. Eventually, samples were immune-stained with anti-GFAP or Iba-1 antibodies. Photomicrographs were recorded to make montages of the entire spinal cord at a final magnification of 20x (n=3 per lumbar section). Total number of GFAP or iba-1 positive cells were counted separately in laminas II-III, IV-VI and V-VI.

Results: Intraarticular injection of MIA increased microglial expression (Iba-1 labelling) in the ipsilateral spinal cord compared to the contralateral side. Being the difference statistically significant for the superficial (II-III; +72.25%, P<0.01) and deeper (V-VI, +95.31%, P<0.001) laminae of L3 and for the superficial laminae of L4 (+87.5%; P<0.01). In animals treated with TLR4-A1, Iba-1 labelling in the ipsilateral dorsal horn showed a similar pattern to the contralateral dorsal horn. Pre-treatment with TLR4 blocker prevented microglia activation after MIA-injection in L3 and L4 segments. Intraarticular injection of MIA also increased the number of GFAP-positive activated astrocytes in the ipsilateral spinal cord compared to the contra-lateral side; in this case, statistically significant differences were found for the superficial (I-II; +41.88%, P<0.01) and middle (III-IV; +64.3%, P<0.001) laminae of L3 levels. GFAP in TLR4-A1-treated rats showed a similar pattern for the ipsi- and the contra-lateral sides. That is, TLR4-A1 prevented L3 increased activated astroglia following MIA-injection.

Conclusions: Early toll-like receptor 4 blockade hampers spinal glial activation, which correlates with diminished allodynia and hyperalgesia observed in TLR4-A1-treated animals in a model of MIA-induced OA. Although further studies are needed, TLR4 blockade could be a good option in the treatment of osteoarthritis.

Acknowledgements: Franco R and Marquez A for technical support.

Granted: Ministerio de Economía y Competitividad. SAF2012-40075-C02-01.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6022

SAT0495 KNEE FUNCTION AND ENTHESITIS IN LONG STANDING OSTEOARTHRITIS, WHAT ULTRASOUND COULD TELL US?

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Background: The enthesis around the knee including the quadriceps tendon and infrapatellar ligament insertions could be responsible for a significant cause of knee pain functional deterioration in long standing knee osteoarthritis.

Objectives: Ultrasound evaluation of the enthesis at the quadriceps tendon patellar insertion, infrapatellar ligament patellar and tibial insertions in patients with long standing knee osteoarthritis (KOA) and low knee function.

Methods: 410 Patients with KOA attending the outpatient rheumatology clinic of AL-Azhar university hospitals who had met the inclusion criteria: At least 5 years disease duration. Kellegren – Lawrance scale grade III.

Exclusion criteria: Patients with chronic diseases affects the patient function.

Acknowledgements: Franco R and Marquez A for technical support.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1056
Patients with previous knee surgery, recent trauma, or intraarticular intervention.
Patients with knee effusion, active synovitis, or popliteal cysts.

All patients were subjected to ultrasound assessment in gray scale and Power Doppler was performed using a scanner with a multifrequency 12L linear array transducer (General Electric Systems; LOGIQ-E). Ultrasound techniques were used for all patients included in the study. Knee was assessed for the following items in both sides while Patient lying supine with the knee flexed 40 degrees:

1. Superior pole of the patella — quadriceps tendon enthesis: • Quadriceps tendon thickness >6.1 mm • Suprapatellar bursitis • Superior pole of patella erosion • Superior pole of patella enthesophytes
2. Inferior pole of the patella – proximal patellar ligament enthesis: • Patellar ligament thickness >4 mm • Inferior pole of patella erosion • Inferior pole of patella enthesophytes
3. Tibial tuberosity – distal patellar ligament enthesis • Patellar ligament thickness >4 mm • Infrapatellar bursitis • Tibial tuberosity erosion • Tibial tuberosity enthesophytes.

Knee functional status was assessed using KOOS scale for Pain, other Symptoms, Activities of Daily Living (ADL), Sport and Recreation Function (Sport/Rec) and knee-related Quality of Life (QOL). Low knee function was considered if the patient had score 50 or more in any KOOS scale parameter.

Results: 172 (42%) patients were found with low knee function among them quadriceps enthesis found in 114 (66.3%) patients, at the patellar attachment of infrapatellar ligament in 160 (93%) patients, and enthesis at the tibial attachment of infrapatellar ligament in 44 (26%) patients. Good knee function were found in 238 (58%) patients among them quadriceps enthesis found in 76 (31.9%) patients, at the patellar attachment of infrapatellar ligament in 87 (36.3%) patients, and no enthesis at the tibial attachment of infrapatellar ligament were detected.

Conclusions: Entheses at the quadriceps and infrapatellar ligament represent a common ultrasonographic finding in patients with longstanding KOA, and significantly associated with low knee function.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4284

SUN0498 SAFETY OF DIACEREIN IN PATIENTS WITH OSTEOARTHRITIS – A REAL WORLD EXPERIENCE WITH UNEXPECTED RESULTS

A. Malpica, D. Buitrago-Garcia, C. Mendez, P. Santos-Moreno, L. Villarreal.

Background: Osteoarthritis (OA) is a common joint disorder and may occur in any synovial joint in the body, the condition is common in hands, knees, hips and spine. Diacerein is an antraquinone derivate has shown the inhibition of cytokine interleukine 1-B (1). A Cochrane review published in 2014 showed that diacerein could be effective for this condition, however the most frequent adverse event with this medication was diarrhea compared to placebo RR 3.52 (95% CI 2.42 to 5.11) or other symptomatic slow acting drugs for OA 3.20 (95% CI 1.58 to 6.49) (2).

Objectives: To describe the real-world safety of Diacerein in patients with OA in a specialized center in Bogotá, Colombia.

Methods: We performed a cross-sectional study; patients with confirmed criteria of osteoarthritis and treated on a regular basis with Diacerein were included. Patients were followed during a 16 month period. Adverse events were classified according the Common Terminology Criteria for Adverse Events (CTCAE) of the World Health Organization. Descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages were calculated, we analyzed bivariated connections with X2 test.

Results: 1278 patients meet inclusion criteria; mean age was 62 years ± 10 years. 88% were female and 12% male, due to our patient's condition 80% of them were polimedicated. 93% of our patients received diacerein in usual dose of 100 mg daily and remaining 7% in a 50 mg day dose. Regarding safety 7.5% (n=96) of our patients developed adverse, the most frequent event was diarrhea with 50%, followed by nausea and abdominal disturbances among others. According to the CTAE classification the events adverse were mild 98% and only 2% severe; that means only 0.075% of total of patients receiving Diacerein had severe AE. On the other hand, correlation between adverse events and polymedication were statistical significant (P=0.000). For this reason we consider that AE such as diarrhea can be attributed more to patients' polymedication than diacerein.

Conclusions: This evidence showed a low proportion of patients with adverse events taking Diacerein; also most of these patients were polymedicated giving as a result a higher risk of having an adverse event. When we compared our results to other studies diarrhea was the most frequent event, followed by nausea, but only a very low proportion of patients were forced to discontinue medication.

It is important to continue following patients that take diacerein in order to report its true safety and effectiveness.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5272

SAT0497 WHAT ARE THE PATIENTS’ EXPERIENCE, NEEDS AND EXPECTATIONS IN HAND OSTEOARTHRITIS? A QUALITATIVE EVALUATION

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Background: The objective of this study was to evaluate the patients’ experience and needs in relationship with HOA, in order to establish a therapeutic education program for HOA patients.

Objectives: As the subject was about descriptive, not quantifiable elements, qualitative methodology was chosen. Patients were submitted to individual semi-directive interviews. Verbatim were analyzes following the grounded theory until saturation of data.

Methods: Twelve HOA patients accepted to participate to the study. There were 10 women and 2 men, aged 45 to 79 years. Body-mass indexes varied from 18.7 to 31.6 kg/m2. Clinical and radiological severity of HOA varied among patients. They provided data on the experience of HOA, which is influenced by clinical and functional signs and the evolution of the disease. Pain and deformity are the main clinical signs, and lead to severe functional impairment. The functional, psychological, social consequences of HOA also have an impact on the patient experience. Patients develop adaptive strategies, mainly recourse to medical management, and pharmaceutical and non-pharmacological therapies. The needs of HOA patients were also explored, and three main ideas emerged. First, they want to be better informed on HOA. Second, they have a feeling of failure of conventional medicine, and often use alternative medicines. Third, the fear of disability with the course of the disease is very strong. They have difficulty accepting pharmacological treatments, but often do not realize the therapeutic nature of non-pharmacological treatments.

Results: The main concerns of HOA patients are: information, non-pharmacological treatments and evolutionary risks. These themes should be included in the development of therapeutic education programs for HOA.

References:

[1] We thank Pr François Rannou, Pr Pascal Richette and Pr Eric Roulot for providing access to HOA consultation in their centers for recruitment. We thank Dr Laurence Baumann-Coblenz for her advice in qualitative methodology.

Acknowledgements: We thank Pr François Rannou, Pr Pascal Richette and Pr Eric Roulot for providing access to HOA consultation in their centers for recruitment. We thank Dr Laurence Baumann-Coblenz for her advice in qualitative methodology.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1203

SAT0498 THE PERFORMANCE OF URINARY COLLAGEN TYPE II C-TELOPEPTIDE (UCTX-II) IN KNEE OSTEOARTHRITIS: A META-ANALYSIS

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Background: Among the currently available biochemical markers for osteoarthritis (OA), urinary collagen type II C-telopeptide (uCTX-II) is one of the most frequently investigated markers. Much research has been performed into the performance of uCTX-II, but most of it in relatively small cohort studies. Therefore, we performed a meta-analysis to summarize uCTX-II studies in a quantitative way.

Objectives: To perform a meta-analysis of the performance of uCTX-II as a biomarker for diagnosing knee osteoarthritis (kOA) and its association with radio-
graphic KOA severity. Furthermore, to look for patient and study characteristics that determine uCTX-II performance.

**Methods:** Medline and Embase databases were searched for studies into uCTX-II levels in adult subjects with radiographic KOA according to the Kellgren and Lawrence (K&L) classification system. uCTX-II levels were compared between subjects with KOA K&L ≥ 2 versus healthy control subjects and between subjects with KOA K&L 2 versus K&L 3–4 (i.e. moderate vs severe KOA). Controls were either selected based on lack of knee symptoms, based on K&L score, or were randomly selected from the general population. Differences between KOA subgroups were expressed as standardized mean differences (SMD). Subgroup analyses were performed to compare uCTX-II performance between genders, ethnicities, and large and small studies. Differences between subgroups were considered relevant when SMDs differed >25% between groups.

**Results:** 2035 Studies were screened for eligibility, of which ten studies were included. A moderate pooled SMD of 0.52 (95% CI: 0.40–0.64, P < 0.0001) was found for subjects with KOA K&L ≥ 2 versus controls, based on ten SMDs. For K&L≥2 versus K&L2 a moderate pooled SMD of 0.47 (CI: 0.32–0.63, P < 0.0001) was found, based on five SMDs. No indications for publication bias were identified using funnel plots. Subgroup analyses of the K&L ≥2 versus control comparison showed that uCTX-II performs better in women as compared to men and in Caucasian subjects as compared to other ethnicities. Study size did not influence the pooled SMD. Subgroup analysis was considered infeasible for the K&L 2 versus K&L 3–4 comparison due to a limited number of studies.

**Conclusions:** This is the first meta-analysis of uCTX-II performance in subjects with radiographic KOA. It appeared that uCTX-II levels can distinguish with moderate strength between radiographic KOA subjects and controls. Moreover, uCTX-II levels are consistently increased in severe versus moderate radiographic KOA. Female gender and Caucasian ethnicity were found to enhance uCTX-II performance in distinguishing radiographic KOA from controls. Yet, the number of studies was relatively small and criteria for KOA and control subjects differed between studies.

**References:**


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2342

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**SAT0499 | IDENTIFICATION OF BIOCHEMICAL PHENOTYPES IN KNEE OSTEOARTHRITIS: LONGITUDINAL DATA FROM THE FNIH OA BIOMARKER CONSORTIUM**

B. Jeremiasse 1, P.M. Welsing 1, C. Fellows 2, F.P. Lafeber 1, W.E. Van Spil 1, 1Department of Rheumatology and Clinical Immunology, UMC Utrecht, Utrecht, Netherlands; 2School of Veterinary Medicine, University of Surrey, Guildford, United Kingdom

**Background:** It is hypothesized that patients with knee osteoarthritis (OA) can be classified into different phenotypes. Knowledge of these phenotypes may contribute to developing effective targeted treatment strategies.

**Objectives:** To identify different longitudinal phenotypes of knee OA using biochemical markers and to compare these phenotypes with regard to radiographic joint space loss (JSL) and/or pain progression.

**Methods:** Baseline, 1-year, and 2-year biochemical marker data from the FNIH OA Biomarker Consortium were used. This consortium is a nested case-control study of 600 subjects with one symptomatic index knee showing radiographic OA changes of Kellgren and Lawrence grade 1 to 3. Subjects were classified into different subgroups based on clinical, and radiographic parameters (data not shown).

**Conclusions:** Seven longitudinal phenotypes of knee OA could be identified based on biochemical markers representing bone, cartilage and synovial metabolism. These phenotypes showed relevant differences in other characteristics, such as JSL and/or pain progression.

**References:**


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5825

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**SAT0500 | SLEEP DISTURBANCE, KNEE INFLAMMATION, AND SYMPTOMS IN KNEE OSTEOARTHRITIS**

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**Background:** Sleep disturbance has been shown to contribute to systemic inflammation as well as JSL progression, pain, and pain sensitization. The role of sleep disturbance in knee osteoarthritis (OA) has not been established. Sleep disturbance may be an aggravating contributor to and/or a consequence of knee OA symptoms, with inflammation serving as a potential mediator.

**Objectives:** To compare knee symptoms over nine years of follow-up by...
frequency of sleep disturbance at baseline, among participants with or at risk for radiographic knee OA (ROA), and to estimate the association between the presence of inflammation on knee MRI and pain that disturbs sleep among knees that developed ROA.

Methods: Knees from the Osteoarthritis Initiative (OAI) with or at risk for ROA were included in this longitudinal analysis. Self-reported frequency of restless sleep in the past week was assessed using a CES-D Q3 symptom. Knees were assessed annually using the WOMAC. Knees that developed incident ROA (i.e., ≥ 2 Kellgren-Lawrence grade, KLG) through four years of follow-up were assessed for erosion-synovitis on non-contrast-enhanced 3T MRI using the MRI Osteoarthritis Knee Score (MOAKS) from annual clinical visits between four years prior to incident ROA and up to one year after ROA detection. Erosion-synovitis represents a combination of joint effusion and synovial thickening on fluid-sensitive sequences and scored as 0 (normal), 1 (mild), 2 (moderate), or 3 (severe). Annual mean WOMAC total score was estimated using a mixed model with participant and knee treated as random effects, in 5,028 knees at risk for ROA at baseline, and in 3,893 knees with ROA at baseline. Log-binomial regression with generalized estimated equations was used to estimate the association between erosion-synovitis and knee pain in bed that disturbs sleep, adjusted for age, sex, and BMI in a sample of 355 knees with an average of 3.8 MRI assessments.

Results: There was dose-dependent effect, with participants reporting restless sleep 1–2 days, 3–4 days, and 5–7 days in the past week having higher mean WOMAC total scores compared to those who reported 0–1 day of restless sleep (i.e., difference in means: 2.5 [95% CI: 1.3 to 3.8], 5.1 [95% CI: 3.2 to 7.1], and 10.1 [95% CI: 7.6 to 12.6], respectively) among knees with ROA (KLG ≥ 2) at baseline. Differences in average WOMAC total score between groups were relatively persistent over nine years (Figure 1). A similar dose-dependent effect of restless sleep was observed among knees at risk of ROA (i.e., KLG 0 or 1). Among knees that developed incident ROA, those with mild erosion-synovitis had a 52% higher risk of knee pain in bed that disturbs sleep at the same visit (RR=1.52; 95% CI: 1.13 to 2.04), while knees that had moderate/severe erosion-synovitis had more than double the risk of knee pain that disturbs sleep (RR=2.55; 95% CI: 1.67 to 3.47), compared to knees with no MRI-detected erosion-synovitis.

Conclusions: Restless sleep was associated with knee symptoms and disability in a dose-dependent manner, with average levels persistent over nine years of follow-up among knees with and at risk of ROA. Erosion-synovitis was associated with pain that disturbs sleep among knees that developed incident ROA. Sleep disturbance and knee inflammation may be important targets for interventions in knee OA.

Disclosure of Interest: C. K. Kwoh Grant/research support from: Abbvie, EMD Serono, E. Ashbeck: None declared, A. Guermazi Grant/research support from: Boston Imaging Core Laboratory, S. Parthasarathy: None declared

DOI: 10.1136/annrheumdis-2017-eular.2476

SAI0502 A RANDOMIZED, PLACEBO-CONTROLLED, PROOF-OF-CONCEPT EFFICACY STUDY OF A MICROSOMAL PROSTAGLANDIN E SYNTHASE-1 (MPGES1) INHIBITOR AND A PROSTAGLANDIN E RECEPTOR (EP) ANTAGONIST IN THE TREATMENT OF CANINE OSTEOARTHRITIS PAIN

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Background: Inflammation is a known contributor to osteoarthritis (OA) pain in animals and humans. While translation of human treatments to companion dogs is common, translation from companion dogs to humans is less frequent. We present results of a clinical study, in client-owned canines with moderate OA pain, which evaluated the efficacy of 2 molecules targeting the actions of prostaglandin E, either by modulating its production (mPGES1 inhibitor; LYA), or subsequent degradation (EP4 antagonist, LIP).

Objectives: To provide translational and comparative data to inform the potential utility of each of these mechanisms for treatment of chronic OA pain in humans and animals.

Methods: A multicenter, randomized, double-blind, placebo (PBO)- and active-controlled trial in client-owned canine patients with moderate OA pain ≥ 1 hindlimb/forelimb joint. Dogs ≥ 2 years of age with Liverpool Osteoarthritis in Dogs (LOAD) Mobility total score ≥ 13 to ≤ 46 were randomized (1:1:1:1:1 to 2 weeks of LVA (1.5 mg/kg/day), LBV (25 mg/kg/day), carprofen (4.4 mg/kg/day), or PBO. Efficacy versus PBO was assessed by mean change from baseline (CFB) to Week 2 in the Canine Brief Pain Inventory (CBPI) Pain Interference (PI) Score (primary endpoint), and for secondary endpoints: CBPI Pain Severity (PS) and Overall Impression (OI) subscore and LOAD Mobility score. Data were analyzed by mixed-effect model for repeated measures with treatment, time, and interaction of treatment and time as fixed effects, and with baseline score, site, and weight as covariates. Posterior probability of treatments being superior to PBO was calculated with Bayesian methods.

Results: Of 163 dogs randomized, 158 (96.9%) completed the study. Treatment arms were well-balanced for baseline characteristics (mean [standard deviation] age: 9.3 [3.0] years, weight: 54.6% 15–32 kg, 45.4% > 32–50 kg, CBPI PI: 5.1 [2.1]; CBPI PS: 4.2 [1.9]; LOAD Mobility: 24.1 [5.6]). Improvements (CFB) in CBPI PI were observed in all treatment groups after 2 weeks (Table). For LVA,
the probability of superiority to PBO was 80% for CBPI PI and 89% to 96% for secondary endpoints. LYB showed inconsistent separation from PBO across the endpoints, with probability of superiority to PBO 54% to 89%. The separation of carprofen and PBO arms demonstrated assay sensitivity. The incidence of adverse events for LYA (35.9%) was comparable to that of carprofen (25.6%) and the control group (32.6%). For LYB, the incidence was significantly higher versus PBO (59.5%, P<0.01).

**Mean CFQ to Week 2 in primary and secondary efficacy endpoints and probability of being superior to PBO**

<table>
<thead>
<tr>
<th></th>
<th>LYA (n=29)</th>
<th>LYB (n=42)</th>
<th>Carprofen (n=42)</th>
<th>PBO (n=43)</th>
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<tr>
<td>CBPI PI (Primary)</td>
<td>1.85</td>
<td>1.54</td>
<td>1.91</td>
<td>1.54</td>
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<tr>
<td>LS mean CFQ (55% CI)</td>
<td>(2.41, -1.85)</td>
<td>(2.51, -1.75)</td>
<td>(2.67, -1.60)</td>
<td>(2.67, -1.92)</td>
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<tr>
<td>Prob. superior to PBO, %</td>
<td>80</td>
<td>94</td>
<td>93</td>
<td>90</td>
</tr>
<tr>
<td>CBPI PI (0.05)</td>
<td>1.66</td>
<td>1.13</td>
<td>1.66</td>
<td>1.13</td>
</tr>
<tr>
<td>LS mean CFQ (55% CI)</td>
<td>(2.14, -1.16)</td>
<td>(1.87, -0.91)</td>
<td>(2.05, -0.78)</td>
<td>(2.05, -0.88)</td>
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<tr>
<td>Prob. superior to PBO, %</td>
<td>79</td>
<td>93</td>
<td>93</td>
<td>90</td>
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<tr>
<td>CBPI Pt (Primary)</td>
<td>0.56</td>
<td>0.37</td>
<td>0.61</td>
<td>0.37</td>
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<tr>
<td>LS mean CFQ (55% CI)</td>
<td>(0.30, 0.02)</td>
<td>(0.11, 0.03)</td>
<td>(0.35, 0.07)</td>
<td>(0.35, 0.09)</td>
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<tr>
<td>Prob. superior to PBO, %</td>
<td>93</td>
<td>96</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>LOAD Mobility</td>
<td>6.68</td>
<td>5.43</td>
<td>5.68</td>
<td>5.43</td>
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<tr>
<td>LS mean CFQ (55% CI)</td>
<td>(8.38, -3.97)</td>
<td>(7.61, -3.24)</td>
<td>(9.75, -3.28)</td>
<td>(9.75, -3.62)</td>
</tr>
<tr>
<td>Prob. superior to PBO, %</td>
<td>98</td>
<td>98</td>
<td>99</td>
<td>99</td>
</tr>
</tbody>
</table>

**Conclusions:** The study results support an efficacy proof-of-concept signal for the mPGE51 inhibitor mechanism for treatment of chronic OA pain in canine patients.

**Acknowledgements:** We also thank Leijun Hu, Alain Frix, and Claire Smith of Eli Lilly and Company for their contributions to the study.

**Background:** MicroRNAs (miRNAs) are a class of 19–23 nucleotides long non-coding RNAs that post-transcriptionally regulate the activity of target mRNAs. MicroRNAs are involved in cartilage homeostasis and play an important role in the pathogenesis of osteoarthritis (OA). They have been detected in human plasma and in synovial fluid and are considered potential diagnostic biomarkers and therapeutic targets of OA. Balneotherapy is a common non-pharmacological treatment for OA patients. In a previous published prospective single-blind randomized clinical trial in patients with knee OA, we showed that a cycle of mud-bath therapy (MBT) in addition to conventional treatments induced an improvement on pain, functional capacity and quality of life in comparison to standard treatment alone.

**Objectives:** As part of this study we evaluated the whole blood levels of miR-155, 225, 225, 181a, 146a and miR-let-7e, which are involved in the pathogenesis of OA.

**Methods:** Thirty-two patients aged between 50 and 75 years with knee OA defined by the ACR criteria were included for the current analysis, based on the availability of blood sample at basal time and after 2 weeks. Twenty-one patients (MBT group) were daily treated with a combination of daily mud-packs at 42° C and mudbaths in mineral water, at 37° C for 15 min, for a total of 12 applications over a period of 2 weeks, in addition to standard therapy; the other eleven patients (control group) continued their conventional treatment alone.

**Clinical parameters [global pain score by a 0–100 mm Visual Analog Scale (VAS); physical function, total pain score and total stiffness score (WOMAC)] and microRNAs expression were performed at basal time and after 2 weeks.**

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.9462

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**SAT0504**

**PREDICTIVE ABILITY OF BIOMARKERS LINKED WITH SYNOVITIS FOR FUTURE INCIDENCE OF PAINFUL KNEE OSTEOARTHRITIS IN A COMMUNITY-BASED COHORT OF MIDDLE-AGE WOMEN**


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**Background:** Radiographic knee osteoarthritis (RKOA) is associated with the knee pain. However, more than half of the middle-aged individuals with RKOA will report no concurrent knee pain. Specific matrix metalloproteinases (MMPs) generated protein fragments have been associated with knee synovitis and suggested as specific neo-epitope biomarkers of joint remodelling.

**Objectives:** The aim of the study was to evaluate the association between MMP-derived neo-epitope biomarkers measured in serum, and future incidence of either painful RKOA or RKOA without pain, in a cohort of middle-aged women with no RKOA at baseline.

**Methods:** 585 participants (mean age 53.2, mean BMI 25.1) from the Chingford 1000 Women Study Chingford Women Study had serum biomarker levels of MMP- degraded of CRP (CRPM), collagen type II (C2M) and collagen type III (C3M) measured at year 2 or 3 of the study. All participants had a Kellgren Lawrence (KL) score of 0 in both knees at baseline. Ten years following the recruitment, incidence of RKOA was determined as KL≥2 and painful RKOA was defined as the presence of pain on any number of days in the preceding month in the knee with RKOA. Log-transformed normalised biomarker levels were utilised in separate logistic regression models adjusted for age. Outcomes were defined as either without pain or painful RKOA. Further analyses were performed adjusting for both age and BMI.

**Results:** 24.6% of women developed RKOA during 10 years after the recruitment, but only 8.9% of developed RKOA associated with concurrent knee pain. After adjusting for age, statistically significant positive associations were found between C3M and CRPM and the risk of developing painful RKOA with odds ratio (OR) ≥3.4 (95% confidence interval (CI): 1.4 to 8.2), and OR≥2.5 (95% CI: 1.2, 5.2) respectively. After adjusting for age and BMI, only C3M was positively associated with risk of developing painful RKOA with OR≥3.2 (95% CI: 1.3, 7.8).

**Conclusions:** In a population of middle-aged women without knee osteoarthritis, an MMP generated neo-epitope of collagen III previously linked with knee synovitis (C3M) can independently identify high-risk individuals for developing painful RKOA. These findings indicate that targeting MMP activity may be a promising therapeutic strategy in well-targeted populations.

**Disclosure of Interest:** C. Thudium Employee of: Nordic Bioscience, S. Kluzek: None declared, J. Newton: None declared, T. Spector: None declared, D. Hart: None declared, M. Karsdal: None declared, A. Bay-Jensen: None declared, N. Arden: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5761

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**SAT0505**

**SELF-REPORTED KNEE INSTABILITY ASSOCIATED WITH PAIN AND ACTIVITY LIMITATIONS PRIOR TO TOTAL KNEE ARTHROPLASTY IN PATIENTS WITH KNEE OSTEOARTHRITIS**

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**Background:** Sixty to 80% of the patients with knee osteoarthritis (OA) reported self-reported knee joint instability, which was associated with pain and activity limitations. In the previous randomized control trial described the prevalence of retained self-reported knee joint instability after total knee arthroplasty (TKA) (32%). To better understand self-reported knee joint instability in usual care there is a need to replicate and extend the results.

**Objectives:** The aims of the study were to determine (i) the prevalence of self-reported knee joint instability prior and one year after TKA, (ii) the associations between self-reported knee instability, pain, activity limitations and quality of life prior and one year after TKA, (iii) the course of self-reported knee instability over time and (iv) the associations between retained knee instability, pain, activity limitations and quality of life.

**Methods:** The aim of the study was to determine (i) the prevalence of self-reported knee joint instability prior and one year after TKA, (ii) the associations between self-reported knee instability, pain, activity limitations and quality of life prior and one year after TKA, (iii) the course of self-reported knee instability over time and (iv) the associations between retained knee instability, pain, activity limitations and quality of life.
Methods: Consecutive patients with knee OA undergoing primary TKA, extracted from the Longitudinal Leiden Orthopaedics and Outcomes of OsteoArthritis Study (LOAS Study), were included. Self-reported knee joint instability and the Injury and Osteoarthritis Outcome Score (KOOS) Pain, Activity Daily Living (ADL) and QoL subscales (0–100; worst–best) were assessed by questionnaires prior and one year after surgery. Multivariable regression analyses were performed to determine associations between knee joint instability, pain, activity limitations and quality of life, adjusted for potential confounders including age, sex, comorbidities, physical activity and preoperative frailty.

Results: 982 patients were included of which 649 patients (72%) reported knee joint instability (mean age 67 years (SD8.6), 485 females (70%)) and 187 patients (21%) postoperative knee joint instability. Preoperative knee joint instability was associated with preoperative KOOS Pain (B=-2.7;95% CI -10.9–3.5) and ADL (B=-3.8;95% CI -7.5–0.9), but not QoL (B=0.495; CI -2.1–1.1). In addition, postoperative knee joint instability was associated with postoperative KOOS Pain (B=-13.5;95% CI -17.0–10.0), ADL (B=-15.1;95% CI -18.4–11.6) and QoL (B=-11.0;95% CI -13.5–8.5). Among the patients with preoperative self-reported knee joint instability, 65 patients (25%) retained knee instability and among the patients with no preoperative self-reported knee joint instability, 22 (8%) developed knee instability one year after surgery. Adjusting for baseline scores and potential confounders, retained knee joint instability was associated with postoperative KOOS Pain (B=-19.6;95% CI -30.9–8.3), ADL (B=-16.5;95% CI -27.0–5.9) and QoL (B=-13.0;95% CI -19.7–8.1).

Conclusions: In usual care, knee joint instability is prevalent one year after TKA (21%). Reported knee joint instability is associated with more pain, worse physical function (pre- and postoperatively) and worse QoL postoperatively. Besides, retained knee joint instability was associated with worse pain, physical function and QoL. This emphasizes the importance of further research into the genesis of pre- and postoperative knee joint instability.

Acknowledgements: The study was funded by the Dutch Arthritis Foundation (DAF).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5988
**SAT0508**

LACK OF A CLEAR DISEASE MODIFYING ACTIVITY OF ECOCIBOX IN TREATMENT OF END-STANCE KNEE OSTEOARTHRITIS: A RANDOMIZED OBSERVER BLINDED CLINICAL TRIAL


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**Background:** Several studies suggest that celecoxib has beneficial effects on degenerated cartilage (1, 2). Together with effects on synovial tissue and bone, celecoxib was postulated to have disease modifying osteoarthritic drug (DMOAD) activity.

**Objectives:** This study evaluated the DMOAD activity of celecoxib, a selective cyclooxygenase 2 (COX-2) inhibitor compared to no treatment and naproxen, treating end-stage knee osteoarthritis (OA), after in vivo exposure using detailed *ex vivo* tissue analyses.

**Methods:** 172 patients with end-stage knee OA were randomized to 4 groups and treated for 4 weeks prior to knee replacement surgery: celecoxib 2dd200mg, naproxen 3dd250mg, celecoxib 2dd200mg stopped 3 days prior to surgery, or no treatment. To determine if treatment had reached the joint, intra-articular COX-2 expression was determined by Western Blot analysis in the celecoxib until surgery group. Intra-articular content was determined by staining and precipitation of glycosaminoglycans (GAGs) with Alcian Blue. Release of newly formed proteoglycans, as a measure of proteoglycan retention, was determined by loss of 35SO2-labeled GAGs in culture medium by precipitation of GAGs and no treatment group, considering these as most extremes. Proteoglycan expression was determined by Western Blot analysis in the celecoxib until surgery group. Intra-articular content was determined by staining and precipitation of glycosaminoglycans (GAGs) with Alcian Blue. Release of newly formed proteoglycans, as a measure of proteoglycan retention, was determined by loss of 35SO2-labeled GAGs.

**Results:** Intra-articular COX-2 expression was significantly decreased in both cartilage and synovial tissue (figure 1) indicating proper in vivo exposure of the treatment. Despite this reduction, no significant effect on proteoglycan release, retention or cartilage expression was found for none of the treatment groups (table 1). Synovial tissue showed only a small decrease in nitric oxide levels in celecoxib treated patients. No clear clinical effects could be observed as indicated by the WOMAC scores.

**Conclusions:** No effect of a 4-week in vivo celecoxib treatment on joint tissue in knee OA patients could be detected, although decreased expression of COX-2 confirmed its intra-articular availability. Effects on synovial inflammatory mediators and clinical outcome were very limited. No adverse effects were found either. As such the previous reported disease modifying effects of celecoxib in *in vitro* and pilot clinical studies could not unambiguously be confirmed in this randomized trial.

**References:**

**Disclosure of Interest:** E. Van Helvoort: None declared, K. Cooievel: None declared, T.N. de Boer: None declared, A.M. Huismann: None declared, A.A. Polak: None declared. J. Bijlsma Grant/research support from: J.W.J. Bijlsma received a consultancy fee from Pfizer (> 5 000 USD). J. van Laar: None declared, F. Lafeber: None declared, S. Mastbergen: None declared

DOI: 10.1136/annrheumdis-2017-eular.1454
life. Obesity is considered to be associated with the incidence and progression of OA, thus weight loss is of paramount importance in OA management.

**Objectives:** To evaluate the efficacy of pharmacological and non-pharmacological therapy of obesity in pts with knee OA.

**Methods:** The study included 50 female pts aged 45–65 years with knee OA, Kellgren-Lawrence stage II–III, and obesity (BMI ≥30kg/m²). Pts form Group 1 (n=25) were administered orlistat at 120 mg x 3 times a day for 6 months along with low-caloric diet and therapeutic physical exercise. Pts from Group 2 (n=25) adhered to life-modifying therapy only, i.e. low-caloric diet and therapeutic physical exercise for 6 month. Anthropometry data (height, body weight, BMI), as well as WOMAC and quality of life EQ-5D scores were assessed at baseline, at 6 and 12 months (i.e. 6 months after discontinuation of therapy) after initiation of treatment in all pts.

**Results:** After 6 months of pharmacological therapy pts from Group 1 achieved significant mean weight loss by 10.07% (p<0.05), while pts from Group 2 with non-pharmacological therapy demonstrated only <1% (0.84%) (p>0.05) weight loss. Pts receiving pharmacological therapy with orlistat demonstrated the following improvements by WOMAC subscales: pain reduction by 52.5% (p<0.05), stiffness reduction by 47.96% (p<0.05), and 51.55% function improvement, while total WOMAC score improved by 51.49% (p<0.05). Respective WOMAC subscale scores in pts from Group 2 were considerably less impressive vs Group 1. Pts from Group 1 demonstrated statistically significant improvement in the quality of life by 52.27% EQ-5D (p<0.05), EQ-5D score remained unchanged only in 2 pts from Group 1 who failed to lose weight. During the following 6 months after discontinuation of orlistat pts from Group 1 regained 5.6% of their body weight (p>0.05) (Fig.1), which was associated with OA worsening OA (deterioration of pain by 42.63% (p<0.05) WOMAC, and total WOMAC score decrease by 23.15%). After 12 months of follow up pts from Group 2 showed body weight loss by 3.5%, and continuing decrease of pain in knee joints by WOMAC pain subscale, reaching 22.3% (p<0.05) as compared to baseline.

**Conclusions:** The results of our study demonstrate significant >10% weight loss in OA pts induced by orlistat therapy. Such a noticeable weight loss was associated with reduced pain intensity, improved function and quality of life in OA pts. Partial regain of body weight during 6 months after discontinuation of orlistat was accomplished by worsening of OA clinical course. Thus, effective maintenance of optimal body weight in OA pts requires longer pharmacotherapy of obesity.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2819

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**SAT0511 THUMB BASE OSTEOARTHRITIS: ASSOCIATIONS BETWEEN SYNOVITIS ON ULTRASOUND AND PAIN**

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**Background:** Hand osteoarthritis (OA) affects the interphalangeal (IP) joints but also the first carpometacarpal (CMC1) joint in the thumb base. Previous ultrasonography (US) studies of the IP joints have shown that inflammatory and structural features are frequently present and associated with clinical signs and symptoms. Until now, US studies specifically assessing the CMC1 joint have not been performed.

**Objectives:** To investigate associations between inflammatory features, structural damage and pain in CMC1 OA.

**Methods:** Cross-sectional data of 87 hand OA patients participating in the EChography in Hand OA (n=63) and the Etanercept in Hand OA (n=24) study at the Leiden University Medical Center were used in this analysis. Both CMC1 joints were assessed with US for synovial thickening, effusion and power Doppler signal (PDS) on a 0–3 scale by experienced ultrasonographers. Presence of pain upon palpation of the thumb base was assessed by trained research nurses on the same day as the US. Hand radiographs were scored blinded for clinical and US features, according to the Osteoarthritis Research Society International Atlas for osteophytes (0–3), joint space narrowing (JSN, 0–3), sclerosis (0–1) and malalignment (0–1) in the CMC1 joint. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using generalized estimating equations to investigate associations between US or radiographic features and thumb base pain on joint level.

**Results:** Of 87 patients (mean age 60.3 years, 82% women, mean BMI 27.2 kg/m²) 174 CMC1 joints were assessed, of which 54 (31%) were painful. The US features synovial thickening, effusion and PDS were found in 26%, 33% and 25% of the joints, respectively. Radiographic features were present in 55% (osteophytes), 79% (JSN), 20% (sclerosis) and 12% (malalignment) of the joints. No associations were seen between inflammatory US features and pain upon palpation of the thumb base (Table). However, osteophytes and sclerosis were associated with more pain (RR 2.5 [95% CI 1.4 to 4.6] for osteophytes grade 3 versus no osteophytes, and RR 2.0 [95% CI 1.3 to 3.2] for sclerosis). Other radiographic features (JSN, malalignment) showed a trend for increased risk of pain on palpation, and for osteophytes and JSN a dose-response relation was apparent.

**Conclusions:** Radiographic features, especially osteophytes and JSN, were prevalent and more frequently present than US inflammatory features in the CMC1 joints of hand OA patients. In contrast to what is known from studies in IP joints, the presence of inflammatory US features was not associated with pain in the thumb base, but structural damage was. These results suggest differences in etiology of pain in thumb base compared to IP OA, with a larger role for structural damage in thumb base OA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4921

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**SAT0512 MRI PROVIDING INSIGHTS IN ASSOCIATION OF SYNOVITIS AND BONE MARROW LESIONS (BMLS) WITH PAIN IN THUMB BASE OSTEOARTHRITIS (OA)**

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**Background:** Hand OA affects the interphalangeal (IP) and thumb base joints (first carpometacarpal [CMC]1 and scaphotrapeziotrapezoid [STT]). Much is still unknown about the pathophysiology of thumb base OA. Magnetic resonance imaging (MRI) studies have led to new insights in IP OA, but in absence of a scoring system thumb base MRI studies are lacking.

**Objectives:** To investigate the prevalence of MRI synovitis and BMLs in the thumb base, and their association with pain, using the novel OMERACT thumb base OA MRI scoring system (TOMS).

**Methods:** Cross-sectional data of the Hand OSTeoArthritis in Secondary care (HOSTAS) study, including consecutive patients diagnosed by their treating rheumatologist with primary hand OA, were used. Patients with an MRI of the right thumb base at baseline were included in the analysis. MRI were scored by two readers using the TOMS for synovitis and bone marrow lesions (BMLs) in the CMC1 and STT joints (grade 0–3). BMLs were evaluated in the proximal and distal joint parts separately, resulting in a 0–6 and 0–9 sum score for CMC1 and STT, respectively. Pain on palpation of the thumb base was assessed by trained research nurses. Hand radiographs were assessed for presence of osteophytes in the CMC1 and STT joints. Associations between MRI lesions and thumb base tenderness were analysed using logistic regression, presented as odds ratios (ORs) with 95% confidence intervals (CIs), stratified for absence or presence of radiographic osteophytes. For the analyses synovitis and BML scores were
aggregated into a dichotomous total thumb base involvement score (0–1 in both joints vs. ≥2 in at least one joint).

**Results:** 85 out of 202 patients (84% women, mean age 60.1 years) reported pain on palpation in the thumb base. Synovitis was seen in both thumb base joints (CMCJ 42%, STT 37%), although prevalence of grade ≥2 synovitis was low in both joints. MRLs were present in CMCJ 1 and STT in 54 and 53%, respectively, with 18 and 21% having a sum score of 2–3, and 16 and 7% a sum score ≥4. In absence of radiographic osteophytes, presence of synovitis or BMLs in either thumb base joint was not statistically significantly associated with thumb base tenderness (ORs 1.9 [95% CI 0.6–6.4] and 1.5 [0.5–4.3], respectively). However, in absence of synovitis or BMLs, radiographic osteophytes and pain were associated, with increasing ORs when MRI lesions were additionally present (Table). Similar results were found for self-reported thumb base pain (not shown).

**Conclusions:** Synovitis and BMLs are present in the thumb base, although severe MRI lesions were uncommon. Prevalence of synovitis was similar in the CMCJ and STT joints, although higher BML scores were more frequently seen in CMCJ. Radiographic osteophytes seemed more important in predicting thumb base tenderness than MRI inflammation alone. Combined presence of radiographic osteophytes and MRI lesions had a small additive effect. These findings are in contrast to results from IP OA studies, supporting thumb base OA as a distinct hand OA subset. It might also explain why trials investigating intra-articular corticosteroids in thumb base OA have led to equivocal results.

**References:**
2. Disclosure of Interest: None declared

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**Cluster analysis showed that patients with severe functional impairment had also high rate of co-morbidities to baseline. The reduction of OA functional impairment is an important determinant of 5-year improvement of HSU while burden of co-morbidities was not associated with change in hip and knee OA HSU. This result highlights the importance of reducing functional impairment in clinical management of patients with hip and knee OA, and gives clues for interpretation of medico-economic analyses.

**References:**
5. Disclosure of Interest: None declared

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**SAT0514**

**CAN IMMUNOPHENOTYPING OF SYNOVIAL FLUID CELLS HELP DISTINGUISH BETWEEN PATIENTS WITH OSTEOARTHRITIS?**

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**Background:** Osteoarthritis (OA) is a leading cause of chronic pain and functional disability in elder people. It is not a homogeneous but diverse group of joint diseases. This could stay behind the therapeutic inconsistency observed in clinical practice caused probably by different diseases and/or different stages of a single disease. The comprehensive immunophenotyping of immune cells and their cell counts in synovial fluid (SF) might therefore advance our understanding of a particular type/stage of OA. This could have diagnostic value as well as provide novel insights into the pathophysiology of OA.

**Objectives:** To characterize immune cells present in SFs from OA patients in different stages of a disease.

**Methods:** We performed immunophenotyping of SFs from 63 patients with OA and 10 SFs from control patients (non-OA) without clinical/radiographic signs of OA using flow cytometry. We were able to characterize the following immune cells in the sampled SFs: T helper lymphocytes (CD3+/CD4+), T cytotoxic lymphocytes (CD3+/CD8+), NK cells (CD3-/CD16-/CD56+), B lymphocytes (CD19+), T regulatory (Treg) cells (CD4+/CD25+/CD127+), mast cells (CD203c+/CD117+), M1+ (CD14+/CD68+/HLA-DR+), and M2-polarized macrophages (CD14+/CD163+/CD206+), and neutrophils (CD15+). The second largest cell population was macrophages. Despite the dominant mixed-polarized (M1-M2) macrophage subpopulations in both the studied groups, SFs from the OA patients displayed a tendency towards greater M1 activity compared to the controls. A markedly increased percentage of neutrophils found in the OA group was associated with their activated state compared to the controls. No difference was found in percentages of B, Treg and mast cells. Despite the similar numbers of NK cells in both the groups, the activation-associated marker CD69 was up-regulated in NK cells from the OA patients. Representative dot-plots (FCS-SSC) of inter-individual variability of the main immune cell populations in synovial fluids from osteoarthritic patients is shown in Figure 1.

**Results:** A comparison between OA and control (non-OA) SFs revealed phenotypic alterations mainly in T cells, NK cells, macrophages, and neutrophils. T cells were the predominant population in the SFs, with CD4+ T lymphocytes being more prevalent than CD8+ T cells in OA (increased CD4/CD8 ratio). The second largest cell population was macrophages. Despite the dominant mixed-polarized (M1-M2) macrophage subpopulations in both the studied groups, SFs from the OA patients displayed a tendency towards greater M1 activity compared to the controls. A markedly increased percentage of neutrophils found in the OA group was associated with their activated state compared to the controls (increased CD11b). No difference was found in percentages of B, Treg and mast cells. Despite the similar numbers of NK cells in both the groups, the activation-associated marker CD69 was up-regulated in NK cells from the OA patients. Representative dot-plots (FCS-SSC) of inter-individual variability of the main immune cell populations in synovial fluids from osteoarthritic patients is shown in Figure 1.

**Figure 1.** Representative dot-plots (FCS-SSC) of inter-individual variability of the main immune cell populations in synovial fluids from osteoarthritic patients.

**Conclusions:** We were able to distinguish between the OA cases and controls...
in terms of their immune cells profiles (i.e. their numbers, activation status etc.). Additionally, we were able to follow specific immune cell patterns inside the OA group. Our study further emphasized the role of immune cells in the pathogenesis of OA. In particular, the results provide evidence suggesting ongoing activation of innate immunity as well as a shift towards T helper lymphocytes in fluids of the patients with OA. Our findings warrant a rational treatment point to be addressed by the future research for clinically useful biomarkers associated with the OA development and progression.

Acknowledgements: Grant support: MZ CR VES16–31852A, MZ CR VES15–27726A.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4045

SAT0515 SONOGRAPHIC AND CLINICAL EXAMINATION OF TENDON INVOLVEMENT IN HAND OSTEOARTHRITIS


Background: Persistent tenosynovitis and degenerative tendinosis is associated with pain and can lead to dysfunction and tendon damage. While tenosynovitis is a common finding in rheumatoid arthritis, data on tendon involvement in hand osteoarthritis (HOA) is clearly limited. The clinical assessment of tendons is difficult and not fully standardized, but musculoskeletal ultrasound (MSUS) has been used successfully in inflammatory rheumatic disease as a sensitive method to detect tenosynovitis, tendon damage and osteophytes.

Objectives: To characterize tendon involvement in hand osteoarthritis and compare ultrasound with clinical assessment.

Methods: In this cross-sectional observational study 34 patients with HOA underwent MSUS and clinical examination on the same day. Each flexor and extensor tendon of the hand was scored independently for tenosynovitis and tendon damage (presence-absence) respectively by an expert in MSUS, blinded to the results of the clinical examination. Additionally, osteophytes in the proximal and distal interphalangeal joints of the fingers were assessed. Clinical assessment of tendons for tendon involvement included volar or dorsal pain, crepitus and swelling involving the hand, wrist or forearm during active movement of the tendon against resistance according to the Birmingham consensus criteria, by assessors who were blinded to the results of the MSUS. Conventional radiographs (CR) of the hands were also acquired and evaluated by the Interphalangeal Osteoarthritis Radiographic Simplified score.

Results: The majority of patients (30/34, 88.2%) were female, with a mean age of 69.5±8.5 years and a median of 10 (9–22.5) years disease duration. Clinical examination revealed tendon involvement in 21 (61.8%) patients with a median of 3 (1–11) tendons involved. A total of 20/33 (60.6%) patients exhibited sonographic signs of tendon involvement (tenosynovitis/tendon damage) with a median of 2 (1–12) involved tendons. Tendon damage was found more often on the right hand (p<0.05) while tenosynovitis did not significantly differ. Similarly, no significant difference between male and female patients was found. The extensor digitorum and the extensor carpi ulnaris tendons were the most commonly affected tendons under US. Tenosynovitis was found to be more prevalent among extensor tendons (p<0.001), while tendon damage was demonstrated at a higher frequency in flexor tendons (p<0.05) (Fig. 1). The agreement between MSUS and clinical examination was moderate on the patient level and poor on the level of individual tendons. Osteophytes were found in 96.8% patients using MSUS and in 100% of patients assessed using CR. Osteophytes detected on MSUS or CR showed good agreement (p=0.01, Cronbach’s Alpha=0.66).

Fig. 1 Distribution of tenosynovitis and tendon damage

Conclusions: The findings of our study reveal a high prevalence of tendon involvement in patients with hand OA. Sensitivity of MSUS in detecting tendon involvement coupled with the lack of agreement between clinical examination and MSUS on the level of individual tendons may suggest that while clinical examination is able to identify patients with overall tendon involvement, it does not allow the specific identification of involved tendons.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5853

SAT0516 INFLUENCE OF ETHNICITY ON CLINICAL PAIN IN PATIENTS WITH OSTEOARTHRITIS VERSUS RHEUMATOID ARTHRITIS: CONTRIBUTION OF LEVEL OF EDUCATION AND DEPRESSION

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Background: The experience of pain is characterized by inter-individual and group variability, with ethnicity being one potential contributing factor. In a systematic review, it was shown how African Americans (AA) demonstrated lower pain tolerance in experimental studies. Pain is the most common and troubling symptom in patients with osteoarthritis (OA) and in patients with rheumatoid arthritis (RA) – maybe reflecting synovitis- but other pain mechanisms are important.

Objectives: To investigate the influence of ethnicity on clinical pain and other outcomes and to identify potential predictors of higher scores for pain in AA and Hispanic patients with OA or RA seen in routine care.

Methods: As part of their clinic visit, all patients complete a multidimensional health assessment questionnaire (MDHAQ) at 2 academic sites. MDHAQ includes 0–10 visual analogue scales (VAS) for pain, physical function, and a patient global evaluation (PATGL), and a depression score between others. The MDHAQ also include demographic data and patients “self-identify” their ethnicity. One random visit with complete questionnaire data for each OA (ICD-9=714.0) and RA (ICD-9=714.10) patient from each site was included in this analysis. Comparison according to patients’ self-reported ethnicity -White, African-American (AA) or Hispanics- were performed using ANOVA and chi-squared. Multiple regression models were performed to identify independent explanatory variables for clinical pain in AA and Hispanics groups versus White.

Results: The study included 402 OA patients and RA 373. There were no differences in age and gender between ethnicity groups in both diagnostic groups. Years of education were highest in the White followed by AA and then Hispanics in both OA and RA. AA and Hispanics showed statistically significantly higher scores for pain (6.6 vs 5.3 in OA, p<0.001; 5.7 vs 4.4 in RA, p<0.001) and lower physical function (3.2 vs 1.9 in OA, P<0.001; 3.2 vs 1.9 in RA, P<0.001) in comparison with Whites in both diagnostic groups. A lower level of education and a higher level of depression predicted greater pain on a MDHAQ in OA in separate models for AA and Hispanic patients and in RA in Hispanic patients (Table).

Table 1. Multiple regression models predicting clinical pain on a MDHAQ stratified by ethnicity

<table>
<thead>
<tr>
<th>Model</th>
<th>Predictors</th>
<th>Coefficients</th>
<th>p</th>
<th>R squared</th>
<th>Beta</th>
<th>p</th>
<th>R squared</th>
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<tr>
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<td>Age</td>
<td>-0.04</td>
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<td>0.08</td>
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<td>0.10*</td>
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<td>0.03</td>
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<td></td>
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<td>African-Americans</td>
<td>0.12</td>
<td>0.06</td>
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<td>0.94</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
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<td>0.005</td>
<td>-0.09</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>0.19</td>
<td>0.002</td>
<td>0.29</td>
<td>-0.001</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>Age</td>
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<td>0.15*</td>
<td>0.05</td>
<td>0.40</td>
<td>0.16*</td>
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<tr>
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<td>0.07</td>
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<td>Hispanic</td>
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<td>0.03</td>
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<tr>
<td>Depression</td>
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<td>0.30</td>
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</table>

Conclusions: AA and Hispanic patients had higher level of pain than Whites, but these differences are mainly influenced by level of education and level of depression in OA and RA patients. These results support the biopsychosocial-cultural model of pain in which, ethnic group differences may be determined by multiple mechanisms including socio-cultural as education, and psychological as depression, in addition to biological pathways.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3843
Factors Related to Analgesic Use in Patients with Knee and/or Hip Osteoarthrosis Referred to an Outpatient Center: Results from the Amsterdam Osteoarthritis Cohort

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Background: Analgesics are recommended in current guidelines, but non-use or inadequate prescription have been reported in patients with knee and/or hip osteoarthrosis (OA). Furthermore, predictors of analgesic use have not yet been clarified.

Objectives: To (i) describe the use of analgesics; and (ii) determine factors that are related to analgesic use in patients with knee and/or hip OA referred to an outpatient center.

Methods: Data from 656 patients with knee and/or hip OA referred to an outpatient center (Amsterdam Osteoarthritis (AMS-OA) cohort) were used. Self-reported use of analgesic (yes/no) was administered and subdivided into acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs, including coxibs) and opioids. Logistic regressions were performed to analyze the association between analgesic use and disease-related, predisposing, and enabling factors.

Results: Analgesic use was reported by 62% of the patients, with acetaminophen, NSAIDs and opioid use reported by 50%, 30% and 12%, respectively. Factors related to analgesic use were higher pain scores, longer duration of symptoms, higher radiographic hip OA severity, overweight/obesity, and psychological distress. These factors explained 21% of the variance of analgesic use.

Conclusions: Less than two-thirds of patients with knee and/or hip OA referred to an outpatient center reported analgesic use, which seems to be indicative for under-use. Although multiple, mostly disease-related factors were associated with analgesic use, it remained predominantly unexplained. Our findings may indicate that prescription of analgesics should be guided more dominantly by clinical symptoms, rather than by a grading system. Multiple linear regressions were used to explore associations and OA. Hand grip strength was measured using a hand-held dynamometer, and this large, population-based cohort study, we took advantage of the availability of which may also show a one-way effect of reduced muscle strength on OA. In whether grip strength, as a measure of muscle activity, is related to knee OA, is related to specific radiographic features of hand OA, such as osteophytes, Republic Of

DOI: 10.1136/annrheumdis-2017-eular.2286

Association Between Grip Strength and Hand and Knee Radiographic Osteoarthrisis in Older Adults: Data from the Dong-gu Study

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Objectives: Although some studies have shown a negative relationship between grip strength and hand osteoarthrosis (OA), little is known about how grip strength is related to specific radiographic features of hand OA, such as osteophytes, joint space narrowing, and erosion. In addition, no reported study has examined whether grip strength, as a measure of muscle activity, is related to knee OA, which may also show a one-way effect of reduced muscle strength on OA. In this large, population-based cohort study, we took advantage of the availability of subjects without hand pain to evaluate the effect of grip strength on OA using a novel, semi-quantitative grading system. We also examined whether grip strength was related to detailed radiographic features of OA.

Methods: Data from 2,251 subjects enrolled in the Dong-gu study, who had no hand and joint pain, were analyzed to investigate the relationship between grip strength and OA. Hand grip strength was measured using a hand-held dynamometer, and radiographs of the hand and knee were scored according to a semi-quantitative grading system. Multiple linear regressions were used to explore associations between grip strength and radiographic features of OA.

Results: Grip strength in men and women was negatively related to hand (both p<0.01) and knee (men, p<0.001; women, p=0.010) OA after adjusting for confounders. Hand (men, p<0.001; women, p=0.001) and knee (both p<0.001) joint space narrowing showed the strongest associations with low grip strength, regardless of sex. Moreover, the severity of joint space osteophytes in women (p<0.001), knee osteophytes in men (p=0.006), hand malalignment (men, p=0.008; women, p=0.041), and subchondral cysts (men, p=0.001; women, p=0.007) was correlated with low grip strength in both sexes.

Conclusions: Among subjects without hand joint pain, low grip strength was associated significantly with hand and knee radiographic OA, regardless of sex. Among all types of OA radiographic damage, low grip strength showed the strongest association with joint space narrowing.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2355

The Value of High-Sensitivity C-Reactive Protein in Hand and Knee Radiographic Osteoarthrisis: Data from the Dong-gu Study

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Objectives: Due to the inconsistent association between high-sensitivity C-reactive protein (hs-CRP) and osteoarthrisis (OA), we evaluated the relationship between hs-CRP and various radiographic findings in older adults with OA.

Methods: This cross-sectional study recruited 2,400 participants from the population-based Dong-gu cohort. The scores of radiographic features in OA on X-rays of the knees and hands were computed using a semi-quantitative grading system. The hs-CRP levels were measured using a particle-enhanced immunonephelometry assay. Correlations showing the relationship between hs-CRP and radiographic OA were calculated using multiple linear correlation analysis.

Results: The hs-CRP levels were significantly higher in older subjects (p<0.001), with those higher body mass index (BMI) (p<0.001), current smokers (p<0.001), current alcohol drinkers (p=0.012), those who were less physically active (p<0.002), and those with a lower level of education (p<0.036). After adjusting for BMI and other confounders, the total OA scores (knee, p=0.048; hand, p=0.010), erosion scores (knee, p=0.035; hand, p=0.031), and sclerosis (knee, p=0.021; hand, p=0.029) in the knees and hands were all significantly positively correlated with hs-CRP. A significant association was also observed between hs-CRP and the hand malalignment score (p<0.012).

Conclusions: In this large, population-based radiographic study, the hs-CRP level was a significant predictor of radiographic OA. Of the various types of OA radiographic damage, erosion, sclerosis, and malalignment showed significant associations with hs-CRP.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2358

Marked Reduction of Osteoarthrisis Pain with a Hydrogen Sulphide-Releasing Naproxen Derivative

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) remain a mainstay of therapy for osteoarthrosis, but their use is limited by their propensity to cause significant gastrointestinal (GI) bleeding and ulceration. Hydrogen sulfide (H2S) is an endogenous signaling molecule that has been shown to exert protective and pro-healing effects in the GI tract. We developed a series of H2S-releasing NSAIDs, and have now tested the lead drug (ATB-346) in a phase 2a clinical trial in patients with osteoarthritis. ATB-346 is a derivative of naproxen, the most cardiovascular-safe of the NSAID family. Data from a phase 1 clinical trial suggested that ATB-346 was significantly more potent and long-lasting than naproxen in terms of suppressing cyclooxygenase (COX) activity.

Objectives: An open-label phase 2a trial was performed to determine if a low dose of ATB-346 (250 mg; equivolmar to 160 mg naproxen), given once daily, would provide significant pain relief in patients with osteoarthritis. To be admitted to the trial, patients had to exhibit a ≥10 point increase in the WOMAC Visual Analogue Score between the worst score of their current trial and the baseline study entry visit.

Methods: 12 patients with osteoarthritis of the knee who met the inclusion criteria were recruited for the trial (diagnosis of OA ≥2 years; age 40–75; BMI ≤40). The WOMAC subscale pain score (0–20) was the primary endpoint. The patients were off anti-inflammatory medication for 5 days prior to starting this study. After recording the initial WOMAC subscale pain score, they began once daily oral treatment with ATB-346 (250 mg). Pain scores were recorded on the day prior to starting ATB-346 treatment (day `-1`) and on days 4 and 10 of treatment. Blood samples were collected for measurement of COX activity on days `-1`, 4, and 10. Results: ATB-346 was safe and well tolerated. The mean WOMAC subscale pain score the day prior to initiation of treatment was 14.0 ± 0.7. A significant decrease in the WOMAC subscale pain score was observed on day 4 (−4.3±1.0; p<0.01), with an even greater decrease on day 7 (−7.6±1.5; p<0.001). Whole blood COX activity was suppressed by 89% (p<0.01) on the first day of treatment, and continued to be suppressed throughout the study.

Conclusions: The results of this study demonstrate that a low dose of ATB-346, given only once daily, produces a clinically and statistically significant reduction in pain in patients with osteoarthritis, that may exceed what can be achieved with standard doses of naproxen or celecoxib (1,2). The observed suppression and regression of COX activity was consistent with the pain reduction data, supporting the conclusion that ATB-346 is considerably more potent and long-acting than naproxen. Extensive pre-clinical studies have demonstrated that ATB-346 has greatly improved GI profile as compared to naproxen and other commonly used NSAIDs.

Disclosure of Interest: None declared

References:


DOI: 10.1136/annrheumdis-2017-eular.1040
SAT0521 INCREASING PHYSICAL ACTIVITY IN OLDER PEOPLE WITH PAIN. PRELIMINARY RESULTS OF THE IPOPPI PILOT TRIAL

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Background: Chronic (>3 months) pain is associated with physical inactivity in older adults and walking is an accessible form of physical activity with health benefits. We have developed Increasing Physical Activity in Older People with Pain (iPOPPI), a brief intervention to increase walking.

Objectives: To assess the acceptability and credibility of iPOPPI, and to test the feasibility of key processes, in a pilot randomised, controlled trial.

Methods: Eligible respondents to a screening questionnaire (>65 years; consulted their general practitioner for chronic pain; Chronic Pain Grade score ≥2) collected 7-day accelerometer data before randomisation and at the end of follow-up. Participants were randomised to one of Usual primary care; Pedometer, walking diary, pain toolkit (written pain management information); or iPOPPI comprising week 1 face-to-face Health Care Assistant (HCA) consultation to develop a walking action plan, pedometer, walking diary, pain toolkit (written pain management information); or iPOPPI comprising week 1 face-to-face Health Care Assistant (HCA) consultation to develop a walking action plan, pedometer, walking diary, pain toolkit, discussion of walking behaviour and barriers, goal setting; week 2 follow up face-to-face or telephone (participant preferred) HCA consultation to review progress and goals, relapse prevention strategies; 3–10 weekly motivational prompts (participantpreferred postcard, email or text). A follow-up questionnaire was sent 12 weeks post-randomisation.

Success criteria were: 7% of those screened would be eligible, return an accelerometer and be randomised; follow-up rates ≥75% of those randomised; ≥50% of those in iPOPPI would complete week 1 and 2 intervention sessions; and a median score of ≥5/10 across a four-item acceptability and credibility questionnaire.

Results: Of 2326 people mailed, 1256 (54%) responded and 695 (30%) were eligible. After mailing study information to 425 eligible participants, 161 (38%) agreed to participate, 159 (12% of those mailed) returned an accelerometer and were randomised, 7 withdrew, and 136 (86%) returned a follow-up questionnaire. Of those randomised to iPOPPI 82% completed week 1 and 2 intervention sessions; 32% had a face-to-face week 2 follow-up; 48% preferred postcard motivational prompts, 10% email, 22% text, and 20% had no preference. Median (IQR) acceptability and credibility scores were: “how logical is treatment?” 5 (3, 9.8), “confidence in treatment success” 5.5 (3, 8), “would recommend treatment to friend” 5 (3.3, 9), and “treatment would be successful for another pain problem” 5 (3.7, 8). 152 participants were mailed a follow-up accelerometer and 144 (95%) were returned. 147 (91%) baseline and 117 (81%) follow-up accelerometers had usable data.

Conclusions: This data demonstrate the acceptability and credibility of the iPOPPI intervention, and the feasibility of proposed trial processes. The effectiveness of iPOPPI compared with usual care will be tested in a future main trial.

Acknowledgements: Funded by Arthritis Research UK (grant reference 20608), ELH, CJ, and CCG are part funded by the NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands. The views expressed in this paper are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7957

SAT0522 SEARCHING FOR THE OPTIMAL TIMING FOR PREVENTIVE WEIGHT REDUCTION STRATEGIES FOR KNEE OSTEOARTHRITIS DEVELOPMENT

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Background: We previously showed that middle-aged women free of clinical knee osteoarthritis (OA), but at high-risk for future OA development due to a BMI ≥25 kg/m2). MRI scans of both knees was made on a 1.5 Tesla scanner. All MRIs were scored using the semi-quantitative MRI effect of glucosamine over the control intervention in the different subgroups was estimated using multiple imputation methods, within each original study. Subgroup factors were dichotomized, based on consensus of the OA Trial Bank Steering Committee. A systematic search for published randomized controlled trials on the effectiveness of oral glucosamine in clinical relevant subgroups of hip and knee OA patients based on pain severity, BMI, sex, structural abnormalities and inflammation, using individual patient data from published trials.

Methods: A search was performed to include all published randomized controlled trials on the effectiveness of oral glucosamine in clinical relevant subgroups of hip and knee OA patients based on pain severity, BMI, sex, structural abnormalities and inflammation, using individual patient data from published trials.

Results: A total of 9555 trials were identified, of which 257 were randomized controlled trials on the effectiveness of oral glucosamine in clinical relevant subgroups of hip and knee OA patients. Of these, 95 were included in the meta-analysis. Of these trials, 44 were included in the meta-analysis of patients with knee OA. The effect of glucosamine over the control intervention in the different subgroups was estimated using multiple imputation methods, within each original study. Subgroup factors were dichotomized, based on consensus of the OA Trial Bank Steering Committee. Additional, trial registries were searched for ongoing studies. All authors and institutions of all eligible studies were contacted and asked to share the trial data. All shared trials were assessed for their risk of bias, using the criteria recommended by the Cochrane. Missing data for covariates and outcome measures were imputed, using multiple imputation methods, within each original study. Subgroup factors were dichotomized, based on consensus of the OA Trial Bank Steering Committee. A multilevel regression analysis was performed to evaluate the magnitude of the effect of glucosamine over the control intervention in the different subgroups with the individuals nested within each study. Pain at short-term (3 months)
Estimates pooled differences between glucosamine and placebo on a 0-100 scale and p-values for treatment-subgroup interactions.

## Results

### Conclusions

The majority of industry-led glucosamine studies for osteoarthritis did not wish to share data, challenging optimal use of available data. There is currently no evidence for the use of glucosamine for the treatment of hip or knee osteoarthritis and an absence of support for clinically relevant subgroups of OA patients according to baseline pain severity, BMI, sex, and structural abnormalities.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5966

## SAT0525 | THE EFFICACY OF PELOID THERAPY IN MANAGEMENT OF HAND OSTEOARTHRITIS

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**Background:** Hand osteoarthritis (OA) is associated with pain, reduced grip strength, loss of range of motion (ROM), and joint stiffness, leading to impaired hand function and difficulty in performing daily living activities. Various randomized controlled clinical trials were conducted to assess the efficacy and tolerability of mud-pack therapy in patients with knee OA. Data from these trials support the beneficial effect of mud-pack therapy on pain, function, and quality of life in knee OA. However, to the best of our knowledge, in spite of its significant impact on the activities of daily life, there is a lack of adequate randomized controlled studies on peloid therapy in management of osteoarthritis of the hand.

**Objectives:** To investigate the effects of peloid therapy in the patients with hand OA on pain, functional state, grip strength, and the quality of life.

**Methods:** 53 patients aged 35–75 and 78 years, who had been diagnosed with hand OA were included in the study. Patients were randomized into 2 groups with a random number table. Patients in Group 1 (n=33) underwent peloid therapy over 2 weeks, 5 sessions a week, for a total of 10 sessions and home exercise program. Patients in Group 2 (control, n=30) received only the same home exercise program as in Group 1. Patients were evaluated just before, and 2 and 6 weeks after the start of the study with Visual Analogue Scale (VAS), Australian/Canadian Osteoarthritis Hand Index (AUSCAN) Health Assessment Questionnaire (HAQ), Hand Grip Strength (HGS), Pinch strength (PS).

**Results:** Statistically significant improvements were observed in all parameters assessed at week 2 and week 6 in the Group 1 (p<0.05). Statistically significant differences were observed in HGS scores in the Group 2 at week 2, and in AUSCAN scores at week 6 (p<0.05). Intergroup comparisons of the scores revealed significant differences between the peloid therapy group and control group in VAS, HAQ, AUSCAN, HGS and PS scores at week 2 and week 6 (p<0.05).

**Conclusions:** This study demonstrates that peloid therapy is an effective and confident treatment modality in the management of symptomatic osteoarthritis of the hand and provides effective pain control and improvements in the hand functions, quality of life and grip strength.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2310

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**SAT0524 | UTILITY OF TOCILIZUMAB IN CLINICAL MANIFESTATIONS OF EROSIIVE OSTEOARTHRITIS OF HANDS REGIONAL HOSPITAL ISSSTE PUEBLA, MEXICO**

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**Background:** Erosive osteoarthritis (EOA) is a form of severe involvement of osteoarthritis in the hands, characterized by inflammation of the synovium of the proximal interphalangeal joints and distal joints (DIP); the last ones are the most affected in a symmetrical manner. Inhibition of interleukin 6 (IL-6) in joints with osteoarthritis helps to improve the production of the cartilaginous matrix and microstructures of articular cartilage.

**Objectives:** To know if the application of TCZ is useful for the control of the clinical manifestations of EOA of the hands.

**Methods:** Twenty-four patients with EOA were studied, 18 females and 6 males with ages ranging from 42 to 72 years, with an evolution time of 4 to 30 years. The application of TCZ was intravenous (8 mg/kg of body weight per month). Articular pain in the PIF and distal joints was evaluated by the visual analogue scale (VAS) (0 to 10) and joint pain (0 to 60), morning stiffness (0 to 10), and functional limitation (0–90) by the AUSCAN index.

**Results:** The VAS showed improvement of 30% (0% to 100%). The AUSCAN index showed improved pain (16.2%), morning stiffness (0.6%) and functional limitation (17.5%). Decreased ESR, CRP, and IL-6 levels less than 1.56 to 59.1 pg/ml.

**Conclusions:** IV Tocilizumab is useful for the control of the clinical manifestations of EOA of the hands. More precise studies are needed to evaluate the improvement of the cartilaginous matrix in EOA by TCZ.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5483

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**SAT0526 | POSSIBILITY OF CARTILAGE REPAIR WITH PLATELET AUTOLOGOUS PLASMA (PAP)**

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**Background:** The investigations of the platelet-derived biologic agents in osteoarthritis treatment had shown promising but often controversial results.

**Objectives:** To study the efficacy (in clinic & experiment) & safety (in clinic) of the platelet autologous plasma (PAP) in cartilage repair and treatment of early knee OA.

**Methods:** The study was conducted at the Department of Family Medicine and Traumatology and Orthopedic Department and consisted of 2 parts: experimental (20 rabbits with the traumatic damage of the knee cartilages) and clinical (included 146 patients with diagnosed knee OA (radiological stage I-II). Rabbits...
were randomly divided in 4 groups: in 1st and 2nd grs. 10 animals received 3 intra-articular injections of PAP (on 5th, 7th, 14th day after knee trauma) as a control (gr.3) and 4 rabbits received 3 intra-articular injections of 0.9% NaCl at the same days after trauma; histopathology was performed at 45th (1st and 3rd gr.) & at 90th day (2nd and 4th gr.) after trauma. 146 patients - 58 men (39.7%) & 88 women (60.3%), were divided into 2 grs. Gr.1 included 68 patients who consented to receive standard OA treatment and 3 weekly intra-articular injections of PAP (total 2 courses in 12 months) (plasma volume 12–15ml/course, total platelets number per injection 1260±24±22.1±10⁹); Gr.2 consisted of 78 patients with the same diagnosis who received only standard OA treatment (non-steroidal anti-inflammatory drugs, physiotherapy, exercises). Both groups were of comparable age, gender and initial WOMAC data (Gr.1 40.9±0.7 Gr.2 39.7±0.9, p<0.05). WOMAC scale parameters were analyzed before treatment and after 3 weeks; 6 & 12 months after course of treatment in both groups. Results: In all patients who received PAP, significant improvement of joint pain, inflammation and better structure of the knee cartilage after PAP injections comparing with the control group was found (comparing to 4th gr.). Clinical study demonstrated better changes in pain, stiffness and function in 3 weeks after treatment in patients of Gr.1 comparing to Gr.2 (WOMAC had decreased by 35.8% in Gr.2 and by 74.1% in Gr.1), p<0.05. After 6 months of follow-up (before 2 course of PAP treatment), the mean number of OA exacerbations was (0,7±0,02) Gr.1 & (1,6±0,04) Gr.2 (p<0.05) and general WOMAC index in Gr.1 was significantly lower than in Gr.2 (accordingly (22,8±0.3) and (36,5±0,8); p<0.05). In the next 6 months again patients in Gr.1 had less exacerbations (0,51±0,03) then patients in Gr.2 (1,4±0,03),p<0.05; & better WOMAC performance (Gr.1-(17,5±0.8) Gr.2–37,1±0.5 accordingly)p<0.05). Conclusions: 1. Histopathology of the knee cartilage has shown promising results concerning possibility of cartilage repair after trauma and prophylaxis of the early posttraumatic OA after PAP injections in animal model. 2. Repeating intra-articular injections of PAP, added to the standard care in knee OA improves functional activity, reduces pain and number of OA exacerbations in 12 months of follow up. 3. The further studies (both experimental and clinical) are needed to obtain more accurate information and determine the most effective methods of PAP use in OA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2720

SAT0527 ASSESSMENT OF SHORT-TERM EFFECTIVENESS OF FIVE LOCAL TREATMENT MODALITIES IN PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS


Background: Inside the therapeutic algorithm of knee osteoarthritis (OA) it is included the Non-Arthroscopic Joint Lavage (NAJL) since around 1934 Burman reported that arthroscopies improved the symptoms. Current medical treatment strategies are aimed at pain reduction and symptom control rather than disease modification (1). The large variety of potentially interventions available has raised the need to assess their effectiveness.

Objectives: To compare the short-term effectiveness among five treatment strategies in patients with symptomatic knee OA.

Methods: An open, controlled, randomized prospective study involving 150 patients of whom 76.7% were females. The average age was 65.3±7.35. Patients had knee OA according to American College of Rheumatology criteria, with Kellgren-Lawrence radiographic grades II-III. They were randomly assigned to five groups of treatment, 1)NAJL (n=30), 2)NAJL+hyaluronic acid (HA) (n=32), 3)NAJL + corticosteroid (CS) (n=32), 4)HA (n=31), and 5)CS (n=25). Evaluations took place at baseline, one and three months. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Lequesne scores were recorded. Statistical analysis included mixed analysis of variance, with post-hoc comparisons with Sidak’s adjustment, and multiple linear regression (MLR) to identify those possible factors associated to WOMAC total at 3 months.

Results: Regarding WOMAC pain, significative differences were found in NAJL at one month and at 3 months; in NAJL+CS at one month, and at 3 months; in NAJL+HA at one month and 3 months; and in NAJL-CS at one month and 3 months. For WOMAC function, significative differences were found in NAJL at one month and at three months; in NAJL-C at one month; and in HA at 3 months. Regarding WOMAC total, significative differences were found in NAJL at one month (p<0.001) and at 3 months (p<0.001); and in NAJL+CS at one month (p<0.018). For Lequesne, significative differences were found in HA at one month (p<0.003) and at 3 months (p<0.019) versus baseline; and in CS, at one month (p<0.001). The WOMAC function at baseline, NAJL+HA, and infiltration with CS are the variables that show a significant association with WOMAC total at 3 months. The group that received NAJL+HA had poorer outcomes.

Conclusions: One month after treatment, best outcomes were obtained with HA due to the results found in Lequesne scale when comparing HA versus NAJL+HA, and NAJL-CS. Three months after the treatment, the most effective modality treatment was NAJL; since we did find significant differences regarding articular stiffness, physical function and Lequesne scale. The treatment with NAJL+HA appears to be less effective than the other modalities.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3555

SAT0528 MOLECULAR MODIFICATIONS INDUCED BY MUD-BATH THERAPY IN PATIENTS WITH OSTEOARTHRITIS

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Background: Mud-bath therapy (MBT) is a non-pharmacological approach commonly used to treat osteoarthritis (OA). Several data indicate that MBT improve patient’s symptoms (1), exerting a beneficial effect on pain and joint function, although the biological mechanisms involved in the therapeutic response are poorly defined.

Objectives: This study aimed to find molecular changes (proteins and mRNA variations) in patients with OA after MBT treatment.

Methods: The study included 39 patients whit primary diffuse osteoarthritis, assigned to receive a cycle of mud-bath therapy over a period of 2 weeks added to usual pharmacologic treatment. Whole blood and serum were collected before and after standard MBT treatment: for each time points two pools of patients sera were analyzed by the direct antigen-labeling technology (RayBio® Biotin Label-based Antibody Array, RayBiotech) obtaining a broad, panoptic view of protein expression. Using this semi-quantitative technique up to 1000 target proteins was simultaneously detected, making this approach ideally suited for proteomic studies. Again, pooled samples of mRNA were used to investigate genes expression and to perform the transcriptomic analysis using an high-resolution array design that contains >6.0 million distinct probes, covering coding and non-coding transcripts (GeneChip® HTA 2.0, Affymetrix).

References:
REFERENCES:

ACKNOWLEDGEMENTS:
Supported by Fondazione per la Ricerca Scientifica Termale (FORST) grant.

DISCLOSURE OF INTEREST: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6874

SAT0529 PROLONGED TNF-INHIBITOR TREATMENT DURATION IS ASSOCIATED WITH LOWER RISK OF HAND OSTEOARTHRITIS PROGRESSION IN PATIENTS WITH RECENT-ONSET RHEUMATOID ARTHRITIS AFTER 10-YEAR FOLLOW-UP

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BACKGROUND: Increasing evidence indicates involvement of the pro-inflammatory cytokine TNF-α in hand osteoarthritis (OA) pathogenesis. Ten years clinical and radiographic follow-up of the BeSt study, a randomized trial primarily designed to investigate targeted treatment in rheumatoid arthritis (RA) patients, offered the unique opportunity to study the long-term effects of TNF inhibitors (TNFi) on the development and progression of hand OA. The distal interphalangeal joints (IPs) are rarely affected in RA, which allowed to evaluate primary OA separately.

OBJECTIVES: To investigate the effect of TNFi on incidental and progressive radiographic hand OA after 10-year follow-up in recent-onset RA patients.

METHODS: At baseline and 10-year follow-up 262 patients (mean age 52 years, 66% women) were available for radiologic assessment of hand OA. Eighteen interphalangeal joints (IPs) were scored for osteophytes (OP) using the Osteoarthritis Research Society International (OARSI) atlas (0–3; summated score 0–72). Incidental OA was defined as an increase in summated OP score or ≥1 in summated KL score in presence of OA at baseline, and progressive OA as an increase ≥3 in summated OP or KL score in presence of OA at baseline, based on the smallest detectable change. TNFi treatment and disease activity score (DAS) were assessed on standardized visits at a three-monthly interval. Associations between duration of TNFi treatment in months and incidental and progressive OA were analyzed using generalized linear models with Poisson distribution and robust standard errors, while adjusting for age, gender, time averaged DAS, time averaged Sharp-van der Heijde score and hand OA severity at baseline.

RESULTS: Based on the OP score, 126 patients (48%) were classified with OA at baseline in the DPs and 82 patients (31%) in the proximal IPs (PIPs). Incidental OA developed in 33% of patients in DPs and in 42% in PIPs. Progressive OA occurred in 30% of patients in DPs and in 38% in PIPs. Of patients with and without OA at baseline, irrespective of joint location, 63% and 55% were treated with TNFi, with a median treatment duration of 47 and 36 months, respectively. No effect of TNFi treatment duration was seen on incidental hand OA. On progressive hand OA, every month of TNFi treatment resulted in a reduced relative risk (RR) of OA progression in DPs with a RR (95% confidence interval) of 0.987 (0.978–0.996), but not in the PIPs. The results from the analyses with the KL scoring method were comparable to the OP score, as shown in table 1.

CONCLUSIONS: Prolonged TNFi treatment is associated with a reduced relative risk on radiologic hand OA progression in DPs, but not in PIPs, after 10 years. Although the effect sizes are small, these results provide evidence for influence of TNFi in hand OA pathogenesis.

Disclosure of Interest: M. Looi: None declared, F. Kroon: None declared, S. A. Bergstra: None declared, J. van der Pol: None declared, W. Lems: None declared, P. Kerstens: None declared, C. Allaart: Grant/research support from: The BeSt study was designed and the investigators and supported by a government grant from the Dutch Insurance Companies with additional funding from Schering-Plough B.V. and Janssen B.V., M. Kloppenburg: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2337

SAT0530 CENTRAL SENSITISATION IN HAND OSTEOARTHRITIS: THE ANTERIOR CINGULATE CORTEX IS INVOLVED IN PAIN PROCESSING

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BACKGROUND: We have previously shown that people suffering with chronic pain in hand OA have activation of central brain pain processing centres localised to the anterior cingulate cortex, insular cortex and thalamus by functional neuroimaging (1) and algometry (2).

OBJECTIVES: We hypothesised that hand OA subjects will have structural differences in 3 pain-processing regions of the brain - the anterior cingulate cortex (ACC), insular cortex and thalamus - based on activation of brain centres we have found previously (1). Our brain neuroimaging work was part of a randomised, placebo-controlled trial to assess the effect on clinical pain outcomes by intervention with centrally-acting analgesic agents: pregabalin or duloxetine.

METHODS: The primary outcome measures for our clinical trial were hand pain numerical rating scale (NRS) and AUSCAN pain after 12 weeks’ treatment. In secondary outcome analyses, participants with hand OA (n=28) underwent T1-weighted MRI of the brain before and after 12 weeks of treatment with pregabalin, duloxetine or placebo therapy. Grey matter brain structure was compared using FreeSurfer regional volumetric analysis and voxel-based morphometry (VBM) to age-matched controls (n=11), and evaluated for volume changes in the ACC, insular cortex and thalamus.

RESULTS: In our clinical trial, we observed clinically significant improvement in pregabalin, duloxetine and placebo treatment groups after 12 weeks (ANOVA p=0.0078). Most notably, pairwise comparisons for pregabalin vs placebo showed significant improvement for NRS pain and AUSCAN pain outcomes in the ITT analysis (p<0.05), but not for duloxetine vs placebo after 12 weeks’ (p>0.05). Both voxel-wise and regional volumetric analyses demonstrated areas of reduced grey matter volume in the ACC of hand OA subjects, relative to control subjects, but not for duloxetine (p<0.05) Figure 1. The structural differences in the ACC persisted following 12 weeks of treatment with pregabalin, duloxetine or placebo therapy (p<0.05). We did not observe structural differences in the insular cortex or thalamus in any of the three groups.

Conclusions: We found that the ACC volume was reduced in participants with hand OA. The ACC is a key pain-processing region of the brain. Changes in ACC grey matter volume have previously been described in other painful conditions, but not hand OA. ACC grey matter volume reduction is thought to represent neural plasticity in chronic pain states. Our data supports the role of central sensitisation in hand OA and provides a rationale for the further investigation of centrally-acting analgesics in its management. Our trial demonstrated improvement in clinical endpoints for pain for pregabalin vs placebo and duloxetine vs placebo, respectively (p<0.05). However, structural differences in the ACC were still evident following 12 weeks of treatment with pregabalin or duloxetine. This may relate to the relatively short duration of treatment in our study. Alternatively, the baseline differences in the ACC may represent irreversible changes. Longitudinal studies with greater follow-up periods are necessary to further investigate this.

Table 1. Associations between TNFi treatment duration and progressive hand OA in 261* patients, defined by osteophyte score and Kellgren-Lawrence score.

<table>
<thead>
<tr>
<th>Number of patients treated/median duration (IQR)</th>
<th>Adjusted Joint type</th>
<th>Duration of treatment (RR (95% CI))</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with a OP score ≥3 units in presence of OA at baseline</td>
<td>DPs</td>
<td>67/33 (12-72)</td>
<td>0.987 (0.978–0.996)</td>
</tr>
<tr>
<td>Patients with a KL score ≥2 units in presence of OA at baseline</td>
<td>PIPs</td>
<td>47/30 (12-72)</td>
<td>0.995 (0.985–1.005)</td>
</tr>
<tr>
<td>Patients with a KL score ≥2 units in presence of OA at baseline</td>
<td>DPs</td>
<td>51/39 (12-87)</td>
<td>0.991 (0.984–0.998)</td>
</tr>
<tr>
<td>Patients with a KL score ≥2 units in presence of OA at baseline</td>
<td>PIPs</td>
<td>32/36 (12-72)</td>
<td>0.995 (0.986–1.004)</td>
</tr>
</tbody>
</table>

*1 patient missing due to poor quality of hand radiographs at 10 years. *Adjusted for age, gender, time averaged DAS, time averaged VAS, severity of OA at baseline.
References:


Acknowledgements: We acknowledge support from the Rosetree’s Trust and the NIHR Clinical Research Network.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3537

SAT0531

MATRIX ASSISTED LASER DESORPTION IONIZATION IMAGING MASS SPECTROMETRY APPLIED TO HUMAN OSTEOARTHRITIS CARTILAGE REVEALS THE INTRA-TISSUE METABOLIC HETEROGENEITY

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Background: Osteoarthritis (OA) is one of the most common diseases, caused by a chronic degenerative disorder of the joint. OA can be related to the metabolic syndrome or metabolic abnormalities being recently defined as a subtype of the disease. Matrix-assisted laser desorption/ionization (MALDI) imaging mass spectrometry (IMS) technology allows for the investigation of the bimolecular distribution of proteins, lipids or metabolites through the in situ analysis of tissue sections. In order to better understand the metabolic OA phenotype, the study of the endogenous metabolic profiles using MALDI-IMS should be considered.

Objectives: The main goal of this study is to apply MALDI-IMS methodology to study the metabolic spatial distribution of cartilage and to reveal intra-tissue and inter-patient heterogeneity.

Methods: Human OA cartilage was obtained from donors undergoing total knee joint replacement. Samples were heat stabilized by a stabilizer system, before being snap frozen. Cartilage punches were sectioned at 12 μm thickness in a cryostat and deposited on indium tin oxide (ITO) glass slides. 9-Aminoacridine (9AA) and N-(1-Naphthyl) Ethylenediamine DihydroChloride (NEDC) matrices were sprayed on the tissues. MALDI-MS profiling and imaging experiments were performed using different mass spectrometers. Data were analyzed by different software dedicated to mass spectrometry.

Results: Results showed that 9AA and NEDC matrices were both able to extract several and different compounds. MALDI-MS/MS profiling and imaging experiments were performed using different mass spectrometers. Data were analyzed by different software dedicated to mass spectrometry.

Conclusions: MALDI-IMS methodology is a useful technique for metabolic profiling of cartilage and could be employed to study OA patient heterogeneity. This fact will be especially relevant for OA patients suffering of metabolic syndrome.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6498

SAT0532

SLEEP QUALITY IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Objectives: The aim of this study was to investigate sleep quality in patients with knee osteoarthritis (OA).

Methods: One hundred patients with knee OA and age and gender-matched 75 healthy controls were enrolled into the study. Demographic characteristics of the participants were recorded. All patients were examined by a single physician. The findings were recorded. Knee radiographs of the patients were staged according to the Kellgren-Lawrence grading. In addition, to evaluate the clinical status and quality of life of patients, the MOS Sleep Scale and computerized sleep staging system (DreamLab) were used. The Knee Osteoarthritis Outcome Score (KOOS) was also used. The study was approved by the ethical committee of the hospital.

Results: All scores of MOS sleep scale were significantly lower in patients with knee OA than controls (p<0.001). When MOS outcomes of the patients compared with the controls, sleep quality during sleep period (WSTS) (37.2±35.9, 13.1±19.4 p=0.012 respectively) and number of awakeness (NOAW) (9.2±18.2, 6.2±3.5, p=0.05 respectively) were significantly higher. Sleep efficiency (SE) (84.2±21.1, 96.7±6.4 p=0.009 respectively) was significantly lower in patients with knee OA. There were positive correlations between MOS sleep scale and PSG (sleep latency, sleep onset, sleep efficiency). Regression analysis (Multiple and REM latencies) outcomes of the patients were significantly lower in patients with knee OA. There were significant differences of the patients and controls in the MOS sleep scale scores of patients were negatively related with both NHP (pain, emotional reaction, sleep and social isolation subgroup scores) and WOMAC (total and functional disability subgroup scores) whereas in the REM latency subgroup scores.

Conclusions: The sleep quality of patients with knee OA was worse compared to healthy controls. The poor sleep and sleep quality in knee OA had adversely affected the clinical status and quality of life.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2158

SAT0533

ASSOCIATION OF OSTEOARTHRITIS AND PERIODONTITIS BASED ON THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

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Background: Osteoarthritis (OA) is a chronic joint disease with complex etiologies characterized by synovial inflammation, subchondral bone remodeling, and the formation of osteophytes, which leads to cartilage deterioration. Periodontitis (PD) is also a chronic inflammatory disease characterized by loss of periodontal ligament and alveolar bone. Recently, the association between OA and metabolic diseases has been proposed, and the association between several systemic diseases such as rheumatoid arthritis, metabolic syndrome and periodontitis has been unveiled.

Objectives: The aim of this study was to investigate the association between OA and PD in South Korea using data from the Korean National Health and Nutrition Examination Survey (KNHANES) during 2010–2014.

Methods: Cross-sectional data of 7,969 adults who completed the KHANES, and participated in both a periodontal examination and a knee imaging were analyzed. OA of knee was defined when a participant had knee arthralgia and showed radiographic change of Kellgren-Lawrence (KL) grade over 1. OA patients were grouped into mild (KL grade 1–2) and severe (KL grade 3–4) OA. The periodontal status was assessed by the Community Periodontal Index. Binary logistic regression analysis was performed according to the OA and PD status, severity of OA, and subgroups (age, gender) adjusting for the socio-demographics, oral health behaviors and status, smoking, and drinking.

Results: Of the 7,969 participants, 1,408 (17.7%) had OA and 2,987 (37.5%) had PD. OA and PD showed no significant association in overall analysis. However, in subgroup analysis, female patients with severe OA were more likely to have PD (adjusted odd ratio (OR) 1.377, P=0.0316); likewise, OR for severe OA in female patient with PD was 1.367. (P=0.054).

Conclusions: Severe OA and PD were associated with each other especially in
female in the Korean population. Further prospective and experimental studies are necessary to identify the impact and mechanisms of association between severe OA and PD in female.

References:
[2] Kwon YE, Ha JE, Paik DI, Jin BH, Bae KH. The relationship between peri-

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4849

SAT0534 EFFECT OF SUSTAINED-RELEASE SYMPTOMATIC DRUGS ON PROGRESSION OF KNEE JOINT OSTEOARTHRITIS IN PATIENTS WITH LESS THAN 5 YEARS DISEASE DURATION IN A 5-YEAR PROSPECTIVE STUDY

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Objectives: To assess the effect of sustained release symptomatic drugs chondroitin sulfate (CS) + glucosamine hydrochloride (GH) on progression of knee OA in pts with <5 years disease duration during the 5year follow-up period (FUP).

Methods: This 5-year study included 52 female-patients with primary knee OA (ACR criteria), disease duration did not exceed 5 yrs (mean age=59±8,9). On each pts the individual file including 200 parameters was filled. Diagnostic modalities used in each patient included plain radiography of knee joints (progression stage was classified using Kellgren J.-Lawrence J. scale), DEXA subchondral portions of the hip and tibia, ultrasound (US) and MRI examination of knee joints. First OA stage was documented in 22 (42,3%)pts, 2-nd - in 24 (46,2%), 3-d- in 6 (11,5%). During 5 years of FUP 31 (60%) pts were administered the combined CS+GH regimen for more than 6 months a year. OA progression was documented based on radiographic criteria.

Results: During the 5 year FUP radiographic progression (upgrade in radiographic stage) of knee OA was documented in 14 pts (Group 1 - with OA progression), while in 38 pts radiographic stage remained unchanged (Group 2 - without progression). Patients from both groups were comparable in terms of age and disease duration (p=0,05). Although, pts from Group 1 with OA progression had more intense knee pain when walking: 60,4±18,3 vs 48,7±17,8mm, p=0,04; and higher BMI values: 34,5±4,6 vs 28,9±4,9 kg/m 2, p=0,001; US-findings based higher rate of synovitis:57,1% vs 18,4%, OR=5,9, 95% CI 1,6–22,5, p=0,009; bone marrow edema in medial tibia aspect 64,3% vs 13,2%, OR=11,9, 95% CI 2,8–50,3, p=0,0006 based on MRI findings. In pts with OA progression DEXA examination identified significantly higher absolute BMD values in the medial condyle of the tibia (0,9 (0,8–1,2) vs 0,8 (0,7–0,8) g/cm 2, p=0,001) as compared to pts from Group 2. Re-examination in Sysrs showed that statistically significant differences between the two groups still remained. Analysis of 5year therapy revealed, that the majority of pts without OA progression (68,4%) were taking combined CS+GH regimens for more than 6 months a year during 5-year FUP, while only 35,7% of pts who progressed (OR=4,3, 95% CI 1,1–16,3, p=0,003) managed to adhere to this regimen. Discriminant analysis showed that 5-year intake of combined CS+GH therapy for more than 6 months a year should be considered as a predictor of decreased risk of disease progression, while on the contrary, such symptoms as synovitis, bone marrow edema, and high BMD values in the medial condyle of the tibia should be viewed as predictors and risk factors for knee OA progression in pts with <5 years disease duration. Based on identified factors and their coefficients the authors designed a model (with area under the ROC curve equal to 0,93), allowing to predict the future course of the disease in an individual patient with high accuracy, i.e. 85,7% sensitivity and 84,2% specificity.

Conclusions: Use of combined CS+GH regimens for more than 6 months a year during 5 years is an important factor, decelerating the progression of knee OA in pts with <5 years disease duration by the factor of 4. While synovitis, bone marrow edema, and high BMD values in the medial condyle of the tibia are responsible for further OA progression on this group of pts.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3900

SAT0535 IMPACT OF THE METABOLIC SYNDROME ON THE PREVALENCE, SEVERITY INCIDENCE AND PROGRESSION OF KNEE OSTEOARTHRITIS

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Background: The contribution of metabolic factors on the development of OA has not been fully elucidated.

Objectives: The aim of this work is to analyze the influence of metabolic syndrome in the rate of radiographic incidence and progression of knee osteoarthritis, as well as its impact on the prevalence and severity of the disease.

Methods: For this work we used data from the Spanish cohort PROCOAC (PROGnostic Cohort of OsteArthritis A Coruña). This cohort consists of subjects that visited the Rheumatology consultations at different time points and comprises 984 subjects at baseline including radiographic knee and hip KL grade, radiographic hand OA status, demographic and clinical parameters, as well as the necessary information to assess the metabolic syndrome at baseline, that is, abdominal circumference (in cm) in addition to at least two of the following parameters: triglycerides above 200mg/dL, low HDL (<35mg/dL), hypertension and increased glucose blood levels (>110 mg/dL). To assess the severity of the disease, the number of affected joints was coded as 0–1 and 2–3, according to the radiographic information of hands, knees and hips. Appropriate statistical analyses including Cox regression models with Kaplan-Meier survival curves and chi-square contingency tables were performed with SPSS v19.

Results: The mean age of subjects was 63.86 [32–88] years and 75.6% were women. A total of 85% had radiographic hand OA and 11.8% suffered metabolic syndrome at baseline. In those OA patients that experienced radiographic knee OA progression over time (any KL increase from KL=2 at baseline) the metabolic syndrome appeared as a significant risk factor (HR=3.68;95CI:1.085–14.520,p-value=0.037) (Figure 1). Similarly, in those subjects that developed incident radiographic knee OA over time (a new-onset KL grade 2), the metabolic syndrome at baseline also appeared as a significant risk factor with an increased magnitude (HR=12.931;95CI:3.037–55.051,p-value<0.001) (Figure 1). In addition, to have contralateral knee OA at baseline (HR=12.937;95CI:5.044–32.673;p-value<0.001) as well as radiographic hand OA (HR=5.671;95CI:0.854–37.649;p-value=0.07) associates with an increased rate of incident knee OA too. In terms of prevalence and severity of the disease, the metabolic syndrome associate with an increased risk of knee OA (OR=1.865;95% CI=1.080–3.220;p-value=0.024) as well as with increased number of affected joints, though in a non-significant manner (OR=1.582;95%CI=0.916–2.733;p=0.098).

Conclusions: The alterations that underlie the metabolic syndrome condition the severity and prevalence of knee osteoarthritis, as well as the rate of incidence and progression of the disease

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3100

SAT0536 AXIAL ALIGNMENT OF THE KNEE – IMPORTANCE IN CARTILAGE REPAIR? HIGH TIBIAL OSTEOTOMY VS. DISTRACTION

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Background: Opening-wedge high tibial osteotomy (HTO) is primarily indicated in treating varus gonarthrosis. The rationale behind HTO treatment of knee
Influence of meloxicam in orodispensible form on platelet aggregation and von Willebrand factor in patients with osteoarthritis

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Background: Meloxicam, which selectively inhibits COX-2, can cause inhibition of the biosynthesis of vascular endothelium vaso dilator - prostacyclin, without impacting significantly on production of thromboxane, which promotes vascular dysfunction [1]. Meloxicam on the possibility of thrombotic complications need to be learn more accurately.

Objectives: To investigate the effect of orodispensible form of Meloxicam on platelet aggregation and von Willebrand factor in patients with knee osteoarthritis.

Methods: The study included 24 patients with knee osteoarthritis (OA) of the II stage according to the Kellgren-Lawrence. The control group consisted of 15 healthy individuals. Patients were prescribed the orodispensible form of Meloxicam in dose of 15 mg 1 time per day orally during 10 days. The survey was carried out before and after treatment. Patients had all-clinical studies, questionnaires (visual analogue scale (VAS), WOMAC, Lequesne index (WOMAC), questionnaire Lequesne), optical aggregometry with adenosine diphosphate (ADP), collagen, thrombin and ristocetin for revealing the level of von Willebrand factor.

Results: The result of treatment patients had a significant improvement of overall health and reduction of pain in knee joints according to the VAS (before treatment – 54.5 [50 – 71] mm, after treatment – 27 [18 – 41] mm; p<0.05), WOMAC (before treatment – 143 [109 – 187] points, after treatment – 98 [13–168] points; p<0.05), questionnaire Lequesne (before treatment – 16 [13 – 21] points, after treatment – 12 [9 – 18] points; p<0.05). After treatment patients experienced a significant increase in the degree of platelet aggregation with ADP (before treatment – 52.6 [39.6 – 82.0]% after the treatment – 83.5 [41.2 – 127.2]%); p<0.05), which may indicate a probable increase in the initiation of irreversible aggregation of circulating platelets. The degree of platelet aggregation with collagen also increased (before treatment – 84.5 [71.6 – 89.4]% after treatment – 86.8 [87.9 – 115.4]%); p<0.05), indicating the increased adhesion of platelets to collagen of the vascular endothelium. Before and after treatment, patients remained significantly elevated degree of aggregation with thrombin in comparison with the control group (before treatment – 65.6 [32.11 – 42.26]% after treatment – 78 [62.3 – 92.7%], control group – 37.8 [32.11 – 42.26]%); p<0.05) which may indicate the stimulation of the of the endothelin-1 synthesis with further infringements of procoagulants and anticoagulants. Von Willebrand factor, as an indirect indicator of endothelial damage, was significantly increased after treatment (before treatment – 151.4 [138.9 – 224] after treatment – 245.6 [238.6 – 262.5]%), which may indicate increase of endothelial lesions because of meloxicam with further endothelial dysfunction (p<0.05).

Conclusions: Intake of the orodispensible form of Meloxicam in patients with osteoarthritis can cause an increase of platelet aggregation and level of von Willebrand factor that may contribute to the vascular endothelial dysfunction and increase in risk of thrombosis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5348
Results: Altogether, 129 patients (12 male) with symptomatic nodal OA were included in this study and followed between April 2012 and January 2017. Out of these patients, 72 had erosive disease. The disease duration (p < 0.01) was significantly higher in patients with erosive compared with non-erosive disease. Pain (p < 0.05) and the number of clinically swollen joints (p < 0.05) were significantly higher in patients with erosive compared with non-erosive disease at baseline. There were significant progression of pain (p < 0.05) and the number of clinically swollen joints (p < 0.01) at the two years follow up. The progression in clinically swollen joint count was about 21% higher in patients with erosive disease.

According to the AUSCAN, patients with erosive compared with non-erosive disease had more pain (p < 0.05) and stiffness (p < 0.01) at baseline. Pain and stiffness, but not function, got worse (p < 0.01) in patients with erosive compared with non-erosive disease at the two years follow up.

US-images of patients with OA showed, as gray-scale synovitis total score (p < 0.001), intensity of PDS (p < 0.01) and number of osteophytes (p < 0.01) were significantly higher in patients with erosive compared with non-erosive disease at baseline.

There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened at the two years follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups.

Conclusions: The findings of this study show that pain and number of clinically swollen joints associated with US-detected synovial hypertrophy inflammatory signs and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

Acknowledgements: This work was supported by the project (Ministry of Health, Czech Republic) for consensual development of research organization 023728.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2795

**SAT0539**

**DIFFERENTIAL PROFILE OF ENDOGENOUS PEPTIDES DETECTED BY TARGETED PROTEOMICS IN HIP AND KNEE CARTILAGE SECRETOMES FROM OSTEOARTHRITIS PATIENTS**

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Background: Peptidomics can be defined as the comprehensive, qualitative and quantitative study of all native peptides in a sample in a defined space at a defined time under defined biological conditions. LC-MS/MS targeted proteomics have been used to identify and quantify candidate molecular biomarkers in diverse range of samples, including cells, tissues, serum/plasma, and other types of body fluids.

Objectives: In the present work, we have developed a targeted method to detect a panel of endogenous peptides that were identified as released from human healthy (N) and/or osteoarthritic (OA) hip and knee cartilage. Secretomes were obtained separately from the wounded (WZ) and unwounded (UZ) zones of OA cartilage. The enrichment of endogenous peptides was achieved by ultrafiltration and solid phase extraction (SPE). After peptide extraction, the different peptide profiles of these secretomes were relative quantified by target proteomics.

Methods: Proteins secreted from human articular cartilage (secretomes) were obtained by culture of tissue explants [1]. The enrichment of endogenous peptides was standardized using ultrafiltration procedures and solid phase extraction with reversed phase (C18) resins. A method for the targeted identification and relative quantitation of endogenous peptides by Multiple Reaction Monitoring (MRM)-mass spectrometry was developed employing cartilage secretome samples, and then applied on synovial fluid and serum. The peptides were separated by nano-LC coupled to a 5500 QTRAP mass spectrometer using stable isotope-labeled (SI) peptides as external standards. Peptide identifications were searched using the ProteinPilot program. Data analysis was performed using the Skyline software.

Results: 23 endogenous peptides belonging to 9 proteins related with OA, as Cartilage Oligomeric Matrix Protein (COMP), Cartilage Intermediate Layer Protein (CILP), Prolargin (PRELP), Dermcidin (DDC), Fibronectin (FNC) and Oligo Derived Nocin (GDN) among others, were differentially detected and relatively quantified in the cartilage secretomes. Some of the endogenous peptides belonging to COMP, FNC and GDN were found with a significant high release in the UZ of hip cartilage, however in knee cartilage the release is higher in the WZ. On the other hand, certain peptides belonging to proteins like CILP or PRELP were found to be mostly increased in the UZ of both hip and knee OA cartilages when compared to healthy tissue.

Conclusions: A panel of endogenous peptides has been identified in articular cartilage, which are differentially released between OA and healthy patients, and which could be used as potential biomarkers of disease. A panel of OA-specific peptides may be potential biomarkers to differentiate osteoarthritis from hip and knee. Our targeted proteomics approach would be widely applicable to quantify low abundant peptides of interest in complex biological samples as synovial fluid and serum in order to unravel their putative biomarker value for osteoarthritis.

References:


Disclosure of Interest: None declared

**SAT0540**

**THE REDUCTION IN ADRENERGIC AND INFAMMATORY SERUM MARKERS IN OSTEOARTHRITIS PATIENTS AFTER TREATMENT WITH CHONDROTIN SULFATE/GLUCOSAMINE HYDROCHLORIDE AND CELECOXIB IS DIFFERENT ACCORDING TO THE PRESENCE OF BACTERIAL DNA IN BLOOD**

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Background: Inflammation in osteoarthritis (OA) has been characterized by infiltration of immune cells and secretion of cytokines into synovial tissues. Synovial macrophages production of IL-1beta and TNF-alfa is increased in response to glycopolysaccharide (LPS) and associated molecular patterns (PAMPs) in OA development and/or evolution. Adrenergic activity have been associated with subchondral bone loss and increased osteoclast activity. Also, adrenergic activity is a main modulator of immune response to PAMPs in different settings. However, the relationship between activation of adrenergic and immune system with OA progression and treatment response remains still unknown.

Objectives: To assess the adrenergic and immune activation in OA patients according to the presence of bacterial DNA (bDNA) fragments in blood before and after Chondroitin Sulfate/Glucosamine Hydrochloride (CS/GH) or Celecoxib (CE) treatment.

Methods: Serum samples from patients participants in a 6-month controlled, double blind and randomized clinical trial comparing the analgesic efficacy of CS/GH and CE were analyzed to determine cytokines (IL-2, IL-4, IL-6, IL-8, IL-1beta, catecholamines (noradrenaline, adrenaline and dopamine) and the presence of endotoxin or LPS and bDNA. Results are shown as mean±sd or median with ranges (Q25-Q75).

Results: Serum samples from 12 OA patients (age: 62±8yr; BMI: 31±6kg/m² 86 females; VAS: 73±15; WOMAC: 369±43) treated with CS/GH (50) or CE (50) were analyzed. There were no baseline significant differences between the two treatment groups regarding demographics,clinical and experimental variables. Thirty-four patients (17-CS/GH and 17-CE) showing bDNA in blood had significantly higher levels of noradrenaline compared with patients without bDNA (1993 [1354–3183] vs. 1561 [1174–2193]; p=0.0325). IL-8 positive at baseline). Patients with bDNA at 6 months after treatment showed reduced serum noradrenaline levels compared with those observed in patients with bDNA at baseline (1993 [1354–3183] vs. 1561 [1174–2193]; p=0.0002). After 6 months, both groups of treatment showed a similar reduction in VAS and WOMAC score (pain assessment) and serum adrenaline levels independent of presence or absence of bDNA (Table 1). Thirty-three patients showed bDNA presence at the end of the study (23 negative and 10 positive at baseline). Patients with bDNA at 6 months after treatment showed reduced serum noradrenaline levels compared with those observed in patients with bDNA at baseline (1993 [1354–3183] vs. 1561 [1174–2193]; p=0.0325). IL-8 was significantly reduced after 6 months of treatment only in patients without bDNA. There were no significant differences between baseline and 6 months samples in the other experimental variables.

Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
<th>CS/GH</th>
<th>CE</th>
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<tbody>
<tr>
<td>VAS (mm)</td>
<td>73±15</td>
<td>73±15</td>
</tr>
<tr>
<td>WOMAC (points)</td>
<td>369±43</td>
<td>369±43</td>
</tr>
<tr>
<td>Serum Adrenaline (nmol/L)</td>
<td>1993 [1354–3183]</td>
<td>1561 [1174–2193]</td>
</tr>
<tr>
<td>Serum Noradrenaline (nmol/L)</td>
<td>1993 [1354–3183]</td>
<td>1561 [1174–2193]</td>
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<tr>
<td>Serum Dopamine (nmol/L)</td>
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<td></td>
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<tr>
<td>Serum Catecholamines (nmol/L)</td>
<td></td>
<td></td>
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<tr>
<td>Serum IL-6 (pg/mL)</td>
<td></td>
<td></td>
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<tr>
<td>Serum IL-8 (pg/mL)</td>
<td></td>
<td></td>
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<tr>
<td>Serum IL-10 (pg/mL)</td>
<td></td>
<td></td>
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<tr>
<td>Serum TNF (pg/mL)</td>
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<td></td>
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<tr>
<td>Serum IL-1 (pg/mL)</td>
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<tr>
<td>Serum IL-2 (pg/mL)</td>
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</table>

Conclusions: OA patients show bDNA fragments in blood associated to higher noradrenaline levels. Six month treatment with CS/GH or CE reduces significantly and in a similar fashion the pain intensity and adrenaline levels. IL-8 levels were reduced in patients with presence of bDNA fragments in blood. Systemic adrenergic and inflammatory activity in OA patients is influenced by the presence of PAMPs as bDNA in blood and this may be a factor to take into consideration to evaluate the severity, evolution and response to treatments.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6147

SAT0541 INHIBITING αV3 INTEGRIN AND CD47 SIGNALING AMELIORATES THE PROGRESSION OF OSTEOARTHRITIS
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Background: Osteoarthritis is leading cause of disability, and its prevalence is rising due to aging population and obesity epidemic. Despite the substantial morbidity and health costs attributed to osteoarthritis, no treatment has been approved to prevent or slow disease progression, largely because the underlying pathogenic mechanisms remain elusive. Both integrin αV3 and the integrin-associated receptor CD47 are considered important therapeutic targets for a number of diseases, but the potential involvement of these receptors in osteoarthritis remains unclear.

Objectives: Our study aimed at assessing the role of integrin αV3 and the integrin-associated receptor CD47 signaling pathways in the pathogenesis of osteoarthritis, and identifying potential targets for disease-modifying therapy.

Methods: We performed transcriptomic and proteomic analyses of human and murine osteoarthritic tissues to examine the involvement of integrin αV3 and CD47 with osteoarthritis. Further, we evaluated the effects of genetic deficiency in and pharmacological modulations of integrin αV3 subunits, CD47, and their downstream signaling molecules Fyn and FAK on the degenerative meniscus (DMM) mouse model. Additionally, we used microPET/CT imaging of the DMM mouse model to assess the ligand-binding capacities of integrin αV3 and CD47 in osteoarthritic joints. Finally, we carried out multiple in vitro assays to determine how integrin αV3 and CD47 signaling might become activated in osteoarthritis, and what the molecular consequences of such activation might be.

Results: Our transcriptomic and proteomic analyses revealed the involvement of dysregulated integrin αV3 and CD47 signaling in osteoarthritis. Data from investigations of genetically deficient mice and pharmacological modulations showed that αV3, CD47, Fyn, and FAK are crucial to the pathogenesis of arthritis. We detected elevated ligand-binding capacities of integrin αV3 and CD47 in osteoarthritic joints by microPET/CT imaging of mice subjected to DMM. Our in vitro studies demonstrated that chondrocyte breakdown products, derived from the articular cartilage of individuals with osteoarthritis, induced αV3/CD47-dependent expression of inflammatory and degradative mediators, and revealed that the signaling network involved the Ras-CRAF-MEK-ERK pathways.

Conclusions: Our findings identify a central role of deregulated αV3 and CD47 signaling in the pathogenesis of osteoarthritis, and provide a rationale for targeting these signaling pathways as a disease-modifying therapy.

References:

Acknowledgements: We thank Taimen M. Lindstrom for her scientific input. Our research is supported by VA 1018X002345, 101RX005934, and 101RX005858.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7024

SAT0542 SUBCLINICAL CRYSTAL ARTHROPATHY MIGHT INFLUENCE FUNCTIONAL DISABILITY IN PATIENTS WITH KNEE OSTEOARTHRITIS? AN EGYPTIAN CROSS SECTIONAL STUDY
R. H. A. Mohammed, Department of Rheumatology and Rehabilitation, MD, FRCP, FACR, School OF MEDICINE, Cairo University Hospitals, Cairo, Egypt

Background: Osteoarthritis is a complex slowly progressive degenerative disease that affects joint components. Concomitant articular crystal deposits are able to stimulate an inflammatory response in OA through stimulation of the innate immune system.

Objectives: Assess the contribution of sonographically detected crystal deposits to pain severity and functional disability in patients with knee OA (WOMAC score)

Methods: Single-center cross sectional study. Adult patients diagnosed with knee OA diagnosed in accordance with ACR criteria from the Department of Rheumatology and Rehabilitation, Kasr Alainy School of Medicine, Cairo University were recruited. Clinical assessment of pain and functional status in patients with knee OA was measured using Western Ontario and McMaster Universities Arthritis Index score. The Logic p5 ultrasound machine (GE) with linear array probe (8–13 MHz). Examination of the articular and periarticular structures was performed by a trained rheumatologist according to the standard EULAR guidelines for exam of the knee. Serum uric acid was investigated, and plain radiography was done for comparison.

Results: 53 patients (44 females 83% & 9 males 17%) were included, aged mean 53.5 years ± 8.3 SD, disease duration 42.5 months ± 49.5 SD, body mass index mean 34.9±3.3 SD. Crystal deposits were sono-graphically diagnosed in 73 knees (68.9%). Monosodium urate deposits found in 33 knees (31.1%) and Calcium Pyrophosphate Dihydrate deposits were diagnosed in 67 knees (63.2%). Pain, stiffness and disability scores were significantly higher in OA knees with crystal deposition as compared to those without (p<0.05) that in fact resistant to conventional analgesics, chondro-protectives and physiotherapy demanding the ongoing use of NSAIDs.

Table 1. WOMAC pain, stiffness and disability scores in the studied Patients with knee OA showing sonographic evidences of CDDs versus those without

<table>
<thead>
<tr>
<th>Description</th>
<th>OA with CDDs (Mean ± SD)</th>
<th>OA without CDD (Mean ± SD)</th>
<th>Mann-Whitney-U test</th>
<th>r (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC pain score</td>
<td>15.6±3.6 (9–20)</td>
<td>12.0±3.8 (5–20)</td>
<td>596</td>
<td>0.00*</td>
</tr>
<tr>
<td>WOMAC stiffness score</td>
<td>5.5±2.0 (0–8)</td>
<td>3.8±1.8 (0–8)</td>
<td>643</td>
<td>0.00*</td>
</tr>
<tr>
<td>WOMAC disability score</td>
<td>53.4±11.6 (25–67)</td>
<td>41.5±12.8 (14–67)</td>
<td>606</td>
<td>0.00</td>
</tr>
</tbody>
</table>

WOMAC = Western Ontario and McMaster Universities Arthritis Index score. “Significant difference (p<0.05).”

Conclusions: Crystal deposition was associated with significantly increased pain intensity, knee joint stiffness and functional disability as measured by WOMAC in patients with knee OA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1145

SAT0543 CLINICAL PREDICTORS AND RADILOGIC EVIDENCES OF OCCULT CRYSTAL DEPOSITION DISEASE WITH KNEE OSTEOARTHRITIS
R. H. A. Mohammed. Department of Rheumatology, Rehabilitation and Clinical Immunology, MD, FRCP, FACR, School of Medicine, Cairo University Hospitals, Cairo, Egypt

Background: Osteoarthritis is a slowly progressive degenerative disorder that affects joint components. Concomitant articular crystal deposits are able to stimulate an inflammatory response in OA through stimulation of the innate immune system.

Objectives: Assess the contribution of sonographically detected crystal deposits to pain severity and functional disability in patients with knee OA (WOMAC score)

Methods: Single-center cross sectional study. Adult patients diagnosed with knee OA diagnosed in accordance with ACR criteria from the Department of Rheumatology and Rehabilitation, Kasr Alainy School of Medicine, Cairo University were recruited. Clinical assessment of pain and functional status in patients with knee OA was measured using Western Ontario and McMaster Universities Arthritis Index score. The Logic p5 ultrasound machine (GE) with linear array probe (8–13 MHz). Examination of the articular and periarticular structures was performed by a trained rheumatologist according to the standard EULAR guidelines for exam of the knee. Serum uric acid was investigated, and plain radiography was done for comparison.

Results: 53 patients (44 females 83% & 9 males 17%) were included, aged mean 53.5 years ± 8.3 SD, disease duration 42.5 months ± 49.5 SD, body mass index mean 34.9±3.3 SD. Crystal deposits were sono-graphically diagnosed in 73 knees (68.9%). Monosodium urate deposits found in 33 knees (31.1%) and Calcium Pyrophosphate Dihydrate deposits were diagnosed in 67 knees (63.2%). Pain, stiffness and disability scores were significantly higher in OA knees with crystal deposition as compared to those without (p<0.05) that in fact resistant to conventional analgesics, chondro-protectives and physiotherapy demanding the ongoing use of NSAIDs.

Table 1. WOMAC pain, stiffness and disability scores in the studied Patients with knee OA showing sonographic evidences of CDDs versus those without

<table>
<thead>
<tr>
<th>Description</th>
<th>OA with CDDs (Mean ± SD)</th>
<th>OA without CDD (Mean ± SD)</th>
<th>Mann-Whitney-U test</th>
<th>r (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC pain score</td>
<td>15.6±3.6 (9–20)</td>
<td>12.0±3.8 (5–20)</td>
<td>596</td>
<td>0.00*</td>
</tr>
<tr>
<td>WOMAC stiffness score</td>
<td>5.5±2.0 (0–8)</td>
<td>3.8±1.8 (0–8)</td>
<td>643</td>
<td>0.00*</td>
</tr>
<tr>
<td>WOMAC disability score</td>
<td>53.4±11.6 (25–67)</td>
<td>41.5±12.8 (14–67)</td>
<td>606</td>
<td>0.00</td>
</tr>
</tbody>
</table>

WOMAC = Western Ontario and McMaster Universities Arthritis Index score. “Significant difference (p<0.05).”

Conclusions: Crystal deposition was associated with significantly increased pain intensity, knee joint stiffness and functional disability as measured by WOMAC in patients with knee OA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1145
53.5 years ± 8.3 SD, disease duration 42.5 months ± 49.5 SD. Crystal deposits were sono-graphically diagnosed in 73 knees with normal serum uric acid values (68.9%—MSU in 31.1%, CPPD in 63.7%), a picture of mixed deposits in 5.7%). Plain radiography revealed chondrocalcinosis in 3 patients only. Regression analysis models and Forest Plot test revealed a 4.1 fold incidence of crystal deposition in patients with sonographic bursitis than those without (OR=4.13, Cl=1.5–11.2, p=0.01) and a 3.2 fold incidence of crystal deposition in patients with sonographic effusion than those without (OR=3.16, Cl=1.34–7.44, p=0.01).

Conclusions: The study concluded a number of clinical as well as radiographic associates that might be considered as predictors of silent CDD in patients with knee OA as diagnosed by ultrasonography, the most commonly reported clinical associates were bursitis and effusion.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annonhemuds-2017-eular.2376

SAT0544 | SUBGROUPS IN RADIOGRAPHIC FEATURES IN PATIENTS WITH HIP OSTEOARTHRITIS: RESULTS OF THE AMS-OA COHORT

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Background: Radiographic features are important in diagnosing hip osteoarthritis (OA). In daily practice, only the anterior-posterior view is visualized but not the false profile view. Since we assessed radiographic features in both types of radiographic hip images in the AMS-OA cohort, we were able to examine the differences in radiographic features in two regions of the hip (superior-lateral and central-axial region).

Objectives: (i) To describe the presence of radiographic features in patients with hip OA; and (ii) to determine whether radiographic features differ between the superior-lateral and central-axial region of the hip.

Methods: Data from 97 patients with bilateral hip pain and a Kellgren and Lawrence score of >1 of the Amsterdam Osteoarthritis (AMS-OA) cohort of patients with knee and/or hip OA were used. Standard radiographic images were examined of patients in an erect position, both with an anterior-posterior view and with a false profile view, which is an oblique lateral view of the hip. Radiographic images were scored by an experienced radiologist (DR) and an independent researcher (ME). Consensus between two raters was achieved for each score. Four radiographic features were scored: presence of joint space narrowing, osteophytes, sclerosis and cysts. All joint features were scored separately for the superior-lateral and the central-axial region of the hip. A Fisher’s exact test was performed for testing the significance of the differences between the two regions of the hip.

Results: Table 1 shows the frequencies of radiographic features (joint space narrowing, osteophytes, sclerosis and cysts) in the superior-lateral and the central-axial region of the left and right hip joint of patients with hip OA. Significant differences between the two regions were found for osteophytes, sclerosis and cysts with the highest frequency of these features in the superior-lateral region of the hip.

Conclusions: In our cohort we found as expected, that joint space narrowing of the hips was the most frequent feature (>-80% in both the superior-lateral and central-axial region). Moreover, osteophytes, sclerosis and cysts were more frequently present in the superior-lateral region. Our findings indicate that hip OA may exist of two subgroups with differences in radiographic features (i.e., superior-lateral and central-axial). Future research should confirm these results and focus on possible associations with biomechanical and physical function variables.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annonhemuds-2017-eular.2132

SAT0545 | PREDICTIVE FACTORS FOR RESPONSE TO ULTRASOUND-GUIDED INTRA-ARTICULAR GLUCOCORTICOIDS IN KNEE OSTEOARTHRITIS

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Objectives: To investigate predictive factors for good outcome of ultrasound-intra-articular glucocorticoids in knee osteoarthritis (OA).

Methods: We conducted a prospective monocenter cohort study including 116 patients with knee OA, after failure to standard treatments, with pain >4 (numerical rating scale NRS 0–10). Patients received an ultrasound-guided injection of 40 mg triamcinolone acetonide in their most painful knee. We exhaustively collected demographic and clinical data at inclusion, as well as lab, radiographs and ultrasound parameters of the included knees. WOMAC score was calculated at inclusion and after 4 weeks. Responders were defined as patients with at least 40% improvement of their WOMAC score. Univariate analysis was performed in order to select possible predictive factors, and stepwise multiple logistic regression analyses were conducted to identify predictors of response.

Results: Among the 116 patients, 101 were females. Median age was 64 years (40–85) and mean duration of the disease was 14.1±14.8 years. Mean BMI was 29.9±3.8 Kg/m2. Mean NRS of pain was 8.4±1.2 and mean WOMAC was 73.3±11.8 at inclusion. 70.0% of the knees were grade 3 or 4 of Kellgren-Lawrence. 98% of patients expressed ultrasound synovial effusion and/or hypertrophy at inclusion. After 4 weeks, 61.2% of patients were responders. Regression analysis showed that patients with a BMI <30 Kg/m2 (OR=0.38, 95% CI 0.16–0.89) and an ESR <20 mm (OR=0.27, 95% CI 0.08–0.90) were more likely to respond to ultrasound-guided glucocorticoids injection. Having both predictive factors of good response increases the response rate to 72.5%, whereas having no predictive factor decreases the response rate to 25.0%.

Conclusions: Our study is the largest study evaluating predictive factors of response for intra-articular glucocorticoids injections in knee OA. Also, it is the first study of predictive factors for ultrasound-guided injections. Patients with high BMIs and high ESR seem less likely to respond to intra-articular injections.

Disclosure of Interest: None declared

DOI: 10.1136/annonhemuds-2017-eular.1362
TOTAL OSTEOPHYTE SCORE IS A BIOMARKER OF CURRENT AND PERSISTENT PAIN IN KNEE OSTEOARTHRITIS SUBJECTS

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Background: X-ray and magnetic resonance imaging (MRI) demonstrated associations between osteophyte severity and current pain in knee osteoarthritis (OA) patients. Persistent pain over 5 years was also associated with x-ray osteophyte severity. A biomarker to identify knee OA subjects with persistent pain may reduce placebo response rates in clinical trials.

Objectives: To determine whether the total knee osteophyte score (TKOS), as measured by MRI Osteoarthritis Knee Score (MOAKS), is a biomarker of current and persistent pain severity in knee OA subjects.

Methods: Knee OA subjects from the Foundation for the National Institutes of Health Biomarker Consortium were longitudinally assessed over 4 years and categorized as pain and x-ray progressors (n=194), x-ray-only progressors (n=103), pain-only progressors (n=103), and non-progressors (n=200). Knee osteophyte severity was scored at baseline by MOAKS at 12 positions across the knee and summed to obtain the TKOS. TKOS was summarized as means and SDs in the 4 progression groups; each progression group TKOS was compared with the non-progression group using Wilcoxon rank sum tests (Table 1). The longitudinal Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores were plotted and tested with a linear mixed model, by high and low TKOS status, defined as above and below the TKOS median of 6 (Figure 1). Subjects with persistent pain were defined based on WOMAC pain scores at 4 out of 5 time points higher than the thresholds listed in Table 2; at each threshold, mean differences in TKOS were tested using analysis of variance among those with and without persistent pain.

Results: The distribution of baseline TKOS differed by progression group, with the highest TKOS among pain and x-ray progressors (Table 1). In all 4 progression groups, baseline WOMAC pain scores were higher in subjects with high (>6) versus low (<6) baseline TKOS status (p=0.0001, 0.0383, 0.0035, and 0.0466, respectively). The difference in WOMAC pain scores between TKOS high and low subgroups was constant over time (Figure 1; solid curves above and parallel to dashed curves with TKOS effect always significant [P<0.01] in all 4 progression groups), but the TKOS-Time interaction term in the longitudinal mixed model was not statistically significant, indicating that the pain difference between the TKOS high and low subgroups did not change over time. TKOS was highly associated with persistent pain, with TKOS high at all thresholds (Table 2).

Table 1. Distribution Parameters of TKOS at Baseline by OA Progression Type

<table>
<thead>
<tr>
<th>Progression Type</th>
<th>TKOS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray and pain</td>
<td>194</td>
<td>10.43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>X-ray only</td>
<td>103</td>
<td>8.79</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Pain only</td>
<td>103</td>
<td>8.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.91</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.22</td>
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<tr>
<td>None</td>
<td>200</td>
<td>7.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.07</td>
</tr>
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<td></td>
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</tbody>
</table>

Table 2. Group Sizes and TKOS Mean Differences for Different WOMAC Pain Thresholds for Persistent Pain

<table>
<thead>
<tr>
<th>WOMAC Pain Threshold</th>
<th>Subjects With Persistent Pain, n</th>
<th>TKOS Difference for Subjects With Persistent Pain vs Those Without, SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>211</td>
<td>2.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>2.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>112</td>
<td>2.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>6</td>
<td>52</td>
<td>3.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>8</td>
<td>21</td>
<td>2.5</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Conclusions: TKOS is a candidate biomarker for current and persistent pain in knee OA patients and may be a predictive biomarker for reduced placebo response rates in clinical trials.


DOI: 10.1136/annrheumdis-2017-eular.5095

THE INFLUENCE OF OSTEOARTHRITIS ON CLINICAL, LABORATORY AND ULTRASOUND PARAMETERS OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Osteoarthritis (OA) and rheumatoid arthritis (RA) are not infrequent in the general population. The two pathologic entities can overlap and the presence of OA can interfere with the evaluation of patients with RA.

Objectives: This study aims to evaluate the possible impact of OA on the clinical, laboratory and ultrasound parameters currently evaluated in patients with early RA (ERA).

Methods: We have evaluated the data obtained from patients with ERA referred to our Early Arthritis Research Center (EARC). Only data from patients who fulfilled EULAR/ACR 2010 criteria for RA (1) and had a symptom duration of less than 12 months were analyzed. 43 patients were diagnosed with ERA in the EARC between 2012 and 2016 and were enrolled in this study. Patients were evaluated at baseline and after 12 months. All patients underwent clinical examination, laboratory tests and ultrasound (US) examination. For the US examination we have calculated the score proposed by Naredo et al. considering that this simplified US score includes the evaluation of the hand and knee. (2) Results: There was a clear predominance of women (62.8%). The mean age was 55.47±13.71 years. At baseline, 21 patients (48.8%) were diagnosed with OA. 15 patients (34.9%) presented hand OA and 9 patients (20.9%) presented knee OA. Hand OA didn't influence the values of DAS28, SDAI, patient's and physician's visual analogue scale (VAS) or ultrasound scores (p>0.05). For patients with knee OA, significantly higher values for DAS28 were observed at baseline (p=0.018) and were maintained significantly higher after 12 months of observation (p=0.031). All the other parameters were not influenced by the presence of knee OA (p>0.05). The median value and interquartile range for lab tests and for disease activity indices are shown in Table 1.

Table 1. Values for disease activity indices, laboratory tests and US scores for patients with ERA with/without OA

<table>
<thead>
<tr>
<th>Lab test</th>
<th>Median (Interquartile range)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28</td>
<td>5.07 (4.62–5.73)</td>
<td>0.280</td>
</tr>
<tr>
<td>SDAI</td>
<td>29.02 (24.95–56.59)</td>
<td>0.644</td>
</tr>
<tr>
<td>VAS patient (mm)</td>
<td>72.00 (55.00–81.00)</td>
<td>0.018</td>
</tr>
<tr>
<td>VAS physician (mm)</td>
<td>62.50 (50.79–72.25)</td>
<td>0.144</td>
</tr>
<tr>
<td>Naredo score - GS</td>
<td>8.00 (5.50–12.00)</td>
<td>0.932</td>
</tr>
<tr>
<td>Naredo score - PD</td>
<td>4.00 (0.00–6.50)</td>
<td>0.700</td>
</tr>
</tbody>
</table>

Conclusions: Significantly higher values of DAS28 were observed in patients with ERA who associated knee OA, while the values of SDAI were not influenced, suggesting that SDAI may be superior to DAS28 in evaluating patients with ERA and knee OA. Not the same tendency was observed in patients with ERA who associated knee OA, while the values of SDAI were not influenced, not the values of ultrasound scores were not influenced by the presence of OA.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.4592

PLASMA CGRP CONCENTRATIONS WERE NOT ASSOCIATED WITH PATIENT OA SYMPTOMS OR RESPONSE TO GALCANEZUMAB, A MONOCLONAL ANTIbody AGAINST CGRP


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Background: The safety and efficacy of galcanezumab, a monoclonal antibody against calcitonin gene-related peptide (CGRP), currently in phase 3 clinical trials for the prevention of episodic cluster headache, is supported by evidence in patients with chronic primary headache and experimental headache models.2 Subsequently, there has been significant interest in the potential role of CGRP in the pathogenesis of patients with OA.3,4 Previous studies have demonstrated the association between OA and CGRP expression,5,6 which suggests that CGRP may be involved in the pathogenesis of OA.

Objectives: To compare plasma CGRP levels in patients with OA who had OA symptoms or responded to galcanezumab treatment with those who did not.

Methods: This was a post-hoc analysis of all patients with OA who participated in phase 2 and 3 clinical trials of galcanezumab. Plasmatic CGRP was measured at baseline in 249 patients with OA who underwent clinical trials at 5 academic centers in the United States. The patients were divided into two groups: responders and non-responders. Response was defined as a ≥50% reduction in pain scores at the end of the treatment period. CGRP levels were compared with repeated measures ANOVA with Bonferroni post-hoc testing.

Results: The mean change in plasma CGRP concentrations from baseline did not differ significantly between responders and non-responders (−0.0001 versus −0.0015, respectively, p=0.82). The mean change in plasma CGRP concentrations did not differ significantly between patients with OA symptoms and those without OA symptoms (−0.0002 versus −0.0014, respectively, p=0.34).

Conclusions: These findings suggest that plasma CGRP concentrations are not associated with OA symptoms or response to galcanezumab, a monoclonal antibody against CGRP.
directed against CGRP were assessed in a phase 2 clinical trial NCT02192190 in patients with moderate to severe osteoarthritis (OA) knee pain. Patients were randomized to placebo, galcanezumab (5, 25, 120 and 300 mg subcutaneously every 4 weeks, at weeks 0 and 4) or celecoxib (200 mg once daily) for 16 weeks in a 2:1:1:1:1:1 ratio. The study was terminated after an interim analysis due to ineffectiveness for pain outcomes.

**Objectives:** This study assessed the correlation of baseline plasma CGRP concentrations with signs, symptoms and radiographic severity of OA, and response to galcanezumab and celecoxib treatments.

**Methods:** Plasma samples were collected at baseline and weeks 4, 8, 12 and 16 and analyzed for CGRP. CGRP concentrations were determined by a validated high sensitivity (HS) assay. Correlation of baseline CGRP levels to WOMAC scores, PGA and radiographic Kellgren-Lawrence (K-L) grades were assessed using Spearman’s correlation and Wilcoxon test. Patients were stratified into high vs low baseline by baseline CGRP concentrations and post-treatment changes from baseline WOMAC scores evaluated by mixed effect model repeated measures for each subset.

**Results:** At the interim analysis, baseline plasma CGRP samples were available for 262 patients with 54 patients providing samples at study termination through the week 8 visit. The median CGRP concentration at baseline was 1.07 pg/ml, range <0.78 to 33.91, and 31% of patients were below the level of quantitation (BLQ, <0.78 pg/ml). Median baseline CGRP levels were 1.0 pg/ml for K-L grade 2 (N=178), and 1.2 pg/ml for K-L grade 3 (N=84) (p=0.06). Correlations of WOMAC or PGA scores with baseline CGRP levels were all <0.01 (no significant correlations). In OA patients receiving galcanezumab 300mg SC at week 0 and week 4, those with high baseline CGRP levels demonstrated a 14mm improvement in WOMAC Pain response at week 12 (95% CI 0, 29mm). The pain response to galcanezumab 300mg did not reach the magnitude of celecoxib response and no effects were seen at 5–120mg doses. Celecoxib treatment had larger pain reduction among patients with high baseline CGRP compared to low baseline CGRP levels. Treatment with celecoxib did not alter plasma CGRP concentrations.

**Conclusions:** At baseline, CGRP levels in OA patients were not associated with WOMAC or PGA scores. There was a modest association to radiographic K-L grade. Subgroup analyses of patients with high (<median) CGRP levels at baseline suggested a potential response to galcanezumab for the highest dose, 300mg, but not lower doses. Celecoxib response was greater in those with higher CGRP levels. However, interpretation was limited by small sample sizes at the latter time points. Further studies may determine if enriching the OA population for higher CGRP levels at baseline, or if increased or longer dosing of galcanezumab would improve pain responses or if CGRP blockade is relevant in relieving OA knee pain.


**DOI:** 10.1136/annrheumdis-2017-eular.2155
75.0±13.8, WOMAC pain score was 16.±3.6. Eighty-two patients of 161 (50.9%) had neuropathic pain. When diabetics were excluded (n=58), the proportion of patients with neuropathic pain reduced to 45.6%. The most frequently described pain characteristic was sensation of electric shock (58.4%). Mean total WOMAC and physical function subscale was significantly higher in neuropathic pain group compared to non-neuropathic pain group (Table 1). In KOA patients, the serum and SF concentrations of midkine significantly correlated with the baseline thickness of the cartilage on the medial condyle (r=0.41, p<0.05) but not on the lateral condyle of the femur (r=0.12 and 0.15 respectively, p>0.05). Patients with elevated serum and SF midkine (defined as midkine level more than the mean±2 standard deviation of healthy controls’ level) had a twofold increased risk of radiological progression with MSUS (age, sex and BMI adjusted RR 2.4 and 2.6, 95% CI respectively). With elevated serum and SF midkine levels, there was no increased risk of radiological progression detected with plain radiography in KOA Patients (age, sex and BMI adjusted RR 1.3 and 1.6, 95% CI respectively).

Conclusions: Osteoarthritis patients who have significantly elevated serum and synovial levels of midkine that were obviously associated with radiological progression of knee osteoarthritis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6192

SAT0551 INCREASED SERUM AND SYNOVIAL LEVELS OF MIDKINE ARE ASSOCIATED WITH RADILOGICAL PROGRESSION IN KNEE OSTEOARTHRITIS PATIENTS

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Background: Midkine is a heparin-binding growth factor that plays an important role in mesoderm remodeling as in chondrogenesis and adipocyte formation. There is an increased expression of midkine in damaged tissues and it is believed to have functional antagonism, as it helps in tissue repair and survival while, on the other hand it can enhance inflammatory reactions resulting in more tissue injury [1].

Objectives: This study aimed to determine serum and synovial fluid (SF) levels of midkine in patients with primary knee osteoarthritis (KOA) and to examine the relationship between these levels with the clinical and functional parameters as well as radiological progression of KOA.

Methods: We measured midkine in the serum (n=52) and SF samples (n=23) from 52 KOA patients as well as in the serum from 20 healthy control (n=20). In the patients, numerical rating scale of pain (NRPSP), body mass index (BMI) and The Western Ontario Mc Master scale (WOMAC) were recorded. Graded plain radiographs using Thomas score, and musculoskeletal ultrasound examination (MSUS) of both knees were performed at baseline and after 24 months to assess radiological progression [2,3]. Radiological progression was considered if there is an increase in the Thomas grading score or MSUS transition to a higher grade at the 24 months follow up period compared to baseline evaluation.

Results: Serum and SF midkine levels were significantly increased in KOA patients (mean ± SD 80.79±31.8 pg/mL and 216.31±94.93 pg/mL respectively) compared to serum level in the healthy controls (mean ± SD 65.1±47.6 pg/mL, p<0.05 and p=0.001 respectively). In KOA patients, the serum and SF midkine levels were significantly increased in KOA patients (mean ± SD 80.79±31.8 pg/mL and 216.31±94.93 pg/mL respectively) compared to serum level in the healthy controls (mean ± SD 65.1±47.6 pg/mL, p<0.05 and p=0.001 respectively). In KOA patients, the serum and SF midkine levels were significantly increased in KOA patients (mean ± SD 80.79±31.8 pg/mL and 216.31±94.93 pg/mL respectively) compared to serum level in the healthy controls (mean ± SD 65.1±47.6 pg/mL, p<0.05 and p=0.001 respectively). In KOA patients, the serum and SF midkine levels were significantly increased in KOA patients (mean ± SD 80.79±31.8 pg/mL and 216.31±94.93 pg/mL respectively) compared to serum level in the healthy controls (mean ± SD 65.1±47.6 pg/mL, p<0.05 and p=0.001 respectively).

Conclusions: Osteoarthritis patients who have significantly elevated serum and synovial levels of midkine that were obviously associated with radiological progression of knee osteoarthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6192
improvements over placebo were seen in 0.03 mg and 0.07 mg treatment arms, achieving statistical significance for PTGA and MDGA. Further studies to identify relevant sub-populations and evaluate the safety and efficacy of SM04690 are ongoing.


DOI: 10.1136/annrheumdis-2017-eular.6382

**SAT0553 DETECTION OF SERUM LEVEL CHANGES OF MATRIX METALLOPROTEINASE-13 AND INTER LEUKIN-1 BETA DURING REMISSION AND FLARE-UPS OF PRIMARY OSTEOARTHRITIS OF THE KNEES**

Y. Hussein Gazar, H. Bassioumi. Alazhar University Hospital, Cairo, Egypt

**Background:** The diagnosis of osteoarthritis is currently based on radiographic criteria (eg, joint space width) and clinical symptoms (eg, pain and loss of function). The evaluation of new disease-modifying osteoarthritis drugs (DMOADs) is performed on the same basis, since the regulatory bodies currently require evidence for an impact on radiographic joint space narrowing (JSN) and an impact on symptoms. However, the limitations of radiography have led to the research into alternative parameters for monitoring osteoarthritis that could serve as biomarkers in drug development.

**Objectives:** Detection the serum level of MMP-13 and IL-1 beta in OA of the knee during remission and exacerbation and if these Biomarkers can be validated as gold biomarkers in assessing OA progression and drug development in OA treatment.

**Methods:** This study was performed on 60 patients with knee osteoarthritis, 18 males (30%) and 42 females (70%), all diagnosed as osteoarthritis of one or both knees. Their ages ranged from (40-65) years. The duration of their disease ranged from one to 15 years. The control groups were 8 males (32%) and 17 females (68%). Their ages ranged from (40-65) years. The patients were allowed to continue on the medications that they have been on during the study.

**Results:** Among 50 patients with knee OA, 32 patients had flare-ups (during one year follow-up) showing the statistically significantly highest mean IL-1 beta & MMP13 level.

**Conclusions:**

- There is a potential role for IL1 beta and MMP 13 biomarkers in assessing the development in osteoarthritis.
- IL 1 beta and MMP 13 were found to be correlated positively in patients with knee OA this correlation sounded right as the expression of MMP 13 depends on the presence of IL 1 beta.
- Although most medications groups failed to lower the level of IL 1 beta and MMP 13 yet there was a numerical difference in favor of Diacerein and NSAID.
- Patients on both Diacerein and NSAID had the lowerest rate of flare ups.
- It is recommended that the early measurement of biomarkers may detect cases to progress and thus stronger treatment may be given for these groups.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1134

**SAT0554 INVESTIGATION OF SELECTED BIOCHEMICAL MARKERS IN KNEE OSTEOARTHRITIS COHORT**

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**Background:** Osteoarthritis (OA) is a major cause of functional impairment and disability among the elderly. There is an unmet need for the development of biomarkers for identifying patients with high risk for OA and for monitoring drug efficacy. Specific and sensitive biochemical markers revealing the turnover of bone, cartilage, and synovial tissue may be useful for investigation and monitoring of OA.

**Objectives:** To investigate a targeted set of five biochemical markers, which reflect cartilage turnover, for their ability to evaluate the prevalence of radiographic and symptomatic knee osteoarthrosis (OA) in a study from the cross-sectional Framingham OA cohort (FOA).

**Methods:** The subjects from the community-based FOA cohort were divided up based on a terminology proposed by the FNIH-OAI consortium. Two main groups were defined: subjects with radiographic knee OA (ROKA, n=80) and a group with no radiographic OA (NROKA, n=136). The presence of ROA as any Kellgren-Lawrence (KL) grade ≥3 or the ROKA group were further divided into two groups; those with persistent symptoms of a joint (ROKA+S, n=30) and those without (ROKA-, n=50).

- IL-1 beta was negatively associated with the level of Roa and persisted in the ROKA+ group. It is recommended that the early measurement of biomarkers may detect cases to progress and thus stronger treatment may be given for these groups.

- The subjects of this study provide two major findings: 1) aggrecan degradation is not just aggrecan degradation and different neo-epitopes have distinct clinical relevance; 2) CRPM is a candidate biomarker of disease activity and for patient profiling. This data suggest a reference for interpretation of OA subject biomarker data in future human studies.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1744

**SAT0555 MRI-DETECTED KNEE OSTEOARTHRY: NATURAL HISTORY AND STRUCTURAL RISK FACTORS AFFECTING CHANGE**

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**Background:** Although magnetic resonance imaging (MRI) has been proved to be far more sensitive than conventional radiographs to detect OP, the natural history of MRI-detected OP in older adults has not yet been described, and it is unclear whether knee structural abnormalities, including cartilage defects, cartilage volume, bone marrow lesions (BMLs), meniscal extrusion, infrapatellar fat pad (IPFP), and effusion-synovitis, can predict osteoarthritis change.

**Objectives:** To describe the natural history of knee MRI-detected OP, and to determine if knee structural risk factors are associated with change of MRI-detected OP in a longitudinal study of older adults.

**Table 1. Subject characteristics of substudy**

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>CRP</th>
<th>CRPM</th>
<th>hgsAGNx-1</th>
<th>WOAMAC</th>
<th>huARGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio (95% CI)</td>
<td>1.25 (1.12-1.39)</td>
<td>1.17 (1.06-1.29)</td>
<td>1.20 (1.07-1.35)</td>
<td>0.87 (0.72-1.06)</td>
<td>0.82 (0.68-0.98)</td>
</tr>
</tbody>
</table>

**Table 2. Odds ratios of OA in the substudy. Values in bold represent associations p < 0.05.**
Methods: A total of 1000 patients with severe infection were included, 75% of whom were biologic-naïve. The baseline characteristics of both groups were compared. The outcome measure was the rate of serious infections during repeat cycles of RTX. Results: The rate of serious infections was 9.5% in RTX-naïve patients and 12.5% in repeat cycles. Conclusions: Repeat cycles are effective for maintenance but may lead to hypogammaglobulinaemia. Low IgG autoimmunity is not associated with increased OPs over time.

Results: 550 patients were female, median age (IQR) at RTX initiation 58 (46–68) years and median disease duration (IQR) 7.9 (3.4–15.0) years. 506 (72%) had RA, 94 (13%) SLE, 49 (7%) AAV, 14 (2%) DM, 5 (1%) APS, 6 (1%) SSc and 26 (4%) other CTD. 364 (52%) were biologic-naïve and 515 (74%) were on concomitant DMARDs. Total follow-up: 2940 patient-years (PY), 284 serious infections were recorded in 179 patients (9.7/100 PY); 88 cases within 12 months of cycle 1 (C1). In MVA, previous severe infection (OR 10.7, 95% CI 5.8–19.5), low IgG (OR 3.6, 95% CI 1.5–8.6), previous cancer (OR 2.9, 95% CI 1.2–6.6) and chronic lung disease (OR 1.7, 95% CI 0.9–3.1) increased the odds of a severe infection within 12 months of C1. A diagnosis of CTD was associated with lower risk (OR 0.5, 95% CI 0.2–0.9). Low IgG at RTX initiation was predicted by older age, previous cancer, RA diagnosis, previous severe infection and previous treatment with cyclophosphamide. In C1-C3, higher rate of change in IgA and IgG levels were associated with serious infections (Figure 1). Overall, only 7% of the patients required Ig replacement in this cohort.

Conclusions: Knee MRI-detected OP in adults is common and, in contrast to radiographs, is likely to progress over a relatively short period. Progression can be predicted by structural risk factors suggesting they are a consequence of these abnormalities.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1161

SAT16, SATURDAY, 17 JUNE 2017

Infection-related rheumatic diseases

SAT0556

RISK FACTORS FOR SEVERE INFECTION AND RATIONALE FOR IMMUNOGLOBULIN MONITORING DURING RITUXIMAB TREATMENT IN AUTOIMMUNE RHEUMATIC DISEASES

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Background: Rituximab (RTX) has been used in the treatment of various autoimmune rheumatic diseases (AIRDs) for over a decade. Repeat cycles are effective for maintenance but may lead to hypogammaglobulinemia. Low IgG at baseline has been associated with post-treatment infection rate but may be confounded by other clinical variables and fully adjusted models with method for handling missing data have not been presented. Importance of post-treatment infection and IgG subclasses being associated with increased risk of post-treatment infection. Further analysis including predictors of serious infections in repeat cycles is in progress and will be used to develop guidelines for safety monitoring of rituximab.

Acknowledgements: This research was funded/supported by the National Institute for Health Research (NIHR) and NIHR Leeds Musculoskeletal Biomedical Research Unit based at Leeds Teaching Hospitals NHS Trust [DRF-2014–07–155]. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6896

SAT0557

CHIKUNGUNYA OUTBREAK IN BRAZIL: DEMOGRAPHIC AND CLINICAL CHARACTERIZATION OF 732 PATIENTS – CHIKBRASIL COHORT

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Background: Chikungunya Fever (CF) is a disease characterized by acute febrile arthritis and caused by a mosquito-transmitted alphavirus. Considering the wide distribution of the vector, the presence of imported cases from 2010 and Brazilian population’s susceptibility, there was a dispersal and establishment of Chikungunya virus (CHIKV) throughout the country. Since 2014, the CF has achieved a large proportion of the Brazilian population and has been responsible for the development of chronic joint symptoms in thousands of people.

Objectives: To describe the demographic, clinical and serological characteristics of patients from specialized Rheumatology services from northeastern Brazil, in a large, multicenter cohort.

Methods: Data from 732 patients in a prospective, multicenter, observational cohort conducted in six research rheumatology centers were analyzed. Patients
18 years or older who fulfilled the clinical and epidemiological Health Ministry criteria for case definition of CF were included in the study, from April to December 2016.

Results: From 732 patients included, 83.1% were women. The mean age was 54.1 (± 13.4) years; 92.4% lived in urban area and 58.6% had only primary education. The most common comorbidities were hypertension (43.8%), hyperlipidemia (25.3%) and diabetes mellitus (13.7%). Prior rheumatologic disease was observed in 16.4% patients, being the most frequent rheumatoid arthritis (32.5%), osteoarthritis (32.5%) and spondyloarthritis (11.7%). Arthritis was the most frequent symptom referred by all patients; fever and fatigue were also common manifestations, being referred by 95.3% and 97.1% of patients, respectively. Arthritis occurred in 84.3%. The most frequent joint pattern involvement was polyarticular (67.8%) and the additive (84.0%). At the first appointment with the rheumatologist, 75.9% had been or were under corticosteroids, frequently with an average dose of prednisone (8.8 mg) or equivalent; was observed an median of 8 painful joints (IQR 4–21) and arthritis was found in 73.6% patients, with an median of 2 swollen joints (IQR 0–5). The median score of patient global assessment at the time of the initial evaluation was 6 (IQR 4–6) using a 10 points visual analogue scale. After resting stiffness was referred by 86.0%, with 56.8% of these longer than 30 minutes. The most commonly prescribed medications were corticosteroids (58.3%) and hydroxychloroquine (59.1%). The serological tests for CHIKV were positive for IgM in 97.1% and for IgG in 71.7% of patients.

Conclusions: This is the first descriptive study of a cohort Brazilian patients with CF, as an expression of care of patients when compared to those described in the literature. Most of the features of patients in our cohort were similar to the results described in studies/cohorts published.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4537

SAT0558 Concordance between Clinical-Epidemiological Criteria and Chikungunya Fever Serology


Background: The first autochthonous reports of Chikungunya fever (CF) in Brasil was confirmed in 2014, and by December 2016, there were 263,980 probable cases of CF; 55.03% confirmed. According to recommendations of the Ministry of Health (MH) of Brasil, in an established epidemic situation, the diagnosis of CF should be made by applying clinical and epidemiological criteria. There is no indication for the serology for Chikungunya virus (CHIKV) in the acute phase, except in atypical or complicated clinical situations, which may generate doubts in clinical practice about the correct diagnosis of these patients.

Objectives: The objective of this study was to evaluate the concordance of the clinical and epidemiological criteria with the serology results for CF in a cohort of patients with CF.

Methods: The multicenter cohort CHIKBRASIL from the Northeast of Brasil has enrolled CF patients with joint manifestations since April 2016, using as inclusion criteria the presence of fever and arthralgia/arthritus in a patient residing or who had visited an endemic or epidemic area within 15 days prior to the onset of symptoms. In the present study, we evaluated patients in which IgM and/or IgG serology was performed, regardless of the results. For the analysis of agreement with the criteria, the most characteristic symptoms of CF were used individually (fever, arthralgia/arthritus or exanthema) and three models of association of symptoms were created: fever and arthralgia (2) fever and arthritis (3) fever and arthritis/arthritus, and exanthema. The sensitivity (SENS), specificity (SPEC), positive predictive value (PPV) and negative predictive value (NPV) of the criteria were also assessed, with the serology result considered the gold standard.

Results: A total of 143 patients were evaluated, 119 (83.2%) of which were female, with a mean age of 53.89 years (± 13.5); 52.4% of the cases were in the subordinate phase of the disease (15 days to 3 months) and 42.7% were in the chronic phase (over 3 months). The IgM positivity was observed in 95.1% of cases and IgG in 71.67%. The concordance rate between the IgM serology of CHIKV and the clinical criteria (fever and arthralgia) was over 80% for any of the symptoms/symptoms model analyzed, as well as the SENS and PPV of the symptoms/symptoms model, which was over 95% in all situations evaluated. The concordance rate for IgG serology ranged from 51.9 to 72.1%. Model 1 presented the highest agreement with the result of positive combined serology.

Conclusions: During an epidemic situation, the criteria and epidemiological criteria shows high agreement with the serology result, regardless of the combination of symptoms presented, with high sensitivity and positive predictive value.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6431

SAT0559 Septic Arthritis in Coventry in the UK: 5 Year Data

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Background: Septic arthritis (SA) is a serious condition associated with significant morbidity and prolonged hospital stay, posing a large economic burden to healthcare systems. It affects 2–10 people per 100,000 and there has been a suggestion that the incidence is increasing due to iatrogenic causes [1]. Our local secondary centre, University Hospitals Coventry and Warwickshire NHS Trust (UHCW NHS Trust), provides care to Coventry and Rugby covering an estimated population of 550,000.

Objectives: To investigate the incidence of native joint SA in the adult population in a secondary care hospital in the UK. To investigate whether immunosuppression contributes significantly to the burden of SA.

Methods: Patients were retrospectively identified on the basis of the International Classification of Diseases (ICD)-10 coding generated following discharge from hospital for all patients between 2007–11. Exclusion criteria included paediatric patients, diabetic foot, prosthesis joint infections and those who on review were not thought to have SA. The data was analysed using Excel. Formal ethical approval was obtained via the research and development department within the UHCV NHS Trust.

Results: A total of 189 admissions were coded as SA. Of these, 103 were excluded (n=74 not thought to have SA on review of the notes, n=26 paediatric patients and n=3 prostatic joints). Therefore, there were 86 adult admissions for 64 patients with SA. The mean age of these patients was 53.4 years, with the majority of them being males (n=43, 67.2%). The majority of patients had co-morbidities (n=44, 65.7%), with hypertension (n=10, 14.9%) and type 2 diabetes (n=10, 14.9%) being the most prevalent. Joint aspirates were performed on 63.2% (n=56) of admissions and blood cultures on 70.8% (n=63) of admissions. Staphylococcus aureus was the most commonly cultured microbe (n=54, 64.2%) and blood and (42.9%, n=3). The knee was the commonest joint involved (n=31, 46.3%). Other commonly affected joints included the small joints of the hands (n=9, 13.4%) and shoulderacroametocavicularternosttloartic joints (n=9, 13.4%). Interestingly, 23 (35.9%) of the patients were immunocompromised. Of these, 4 patients had a diagnosis of rheumatoid arthritis (RA) and were on steroid treatment alone (n=2), or in combination with disease-modifying anti-rheumatic drugs (n=2). A total of 11 patients had a pre-existing rheumatological diagnosis of which RA was the most common condition (n=6). Two of these patients were not on immunosuppressants. The 5-year mortality was significant at 23.7% (n=19).

Conclusions: Our local data showed the incidence of SA to be approximately 3 per 100,000, which is in keeping with proposed figures. Our cohort highlighted that those with pre-existing co-morbidities or those who were immunocompromised were at greatest risk. An ageing population with multiple co-morbidities means the incidence of SA is set to rise. Greater emphasis therefore needs to be placed on improving awareness and optimising treatment.

References:

Acknowledgements: We would like to thank the PPMO team at UHCW NHS Trust.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4372

SAT0560 Coexistence of Septic and Crystal-induced Arthritis: A Diagnostic Challenge


Background: Septic arthritis (SA) is a rheumatologic emergency as joint destruction occurs rapidly and can lead to significant morbidity and mortality. Accurate diagnosis can be particularly challenging in patients with underlying inflammatory joint disease. Crystal-induced arthritis (CA) is a risk factor for its appearance. When both conditions appear simultaneously, CA may mask diagnosis of infection and delay the antibiotic treatment.

Objectives: To describe the characteristics of patients with concurrent septic and CA.

Methods: Retrospective analysis of patients with coexistence of septic and CA attended between 1985 and 2015 in a university hospital with a reference area of 850,000 inhabitants. We collect demographic, clinical, laboratory and imaging data as well as patient medical treatment, complications and evolution records. All patients had positive bacterial culture (blood and/or joint fluid) and crystals in synovial fluid.

Results: A total of 123 patients with SA were identified. 20.3% (n=25) of them had concomitant CA, with mean age of 67 years (SD 14), 17 (68%) males and 8 (32%) females. Risk factors were: diabetes (24%), diuretic drugs (24%), chronic renal failure (16%) -2 of them undergoing hemodialysis and 4 kidney
transplant patients with immunosuppressive treatment. In only 2 cases there was a previous arthrocentesis. The mean diagnostic delay was 14 days (SD 13) (data available in 14 cases). The most commonly affected joint was the knee (48%), followed by the foot (20%) and the hip (12%). In 2 cases several joints were involved at the same time. In synovial fluid cytological studies, the most frequently identified crystals were: urate (60%), calcium pyrophosphate (20%) and hydroxyapatite (8%). In 32% of cases gram staining was positive, but 88% of patients had a positive joint fluid culture, with the most commonly identified germs being methicillin-sensitive S. aureus (48%), methicillin-resistant S. aureus (MRSA) (12%) and M. tuberculosis (12%). 32% of patients presented positive blood cultures (12% with negative synovial fluid culture), although 48% of patients had fever at the time of diagnosis. It should be noted that 48% had radiological baseline damage. Surgical debridement was performed in 32% of patients. Evolution was successful in 56% of patients; although intercurrent complications were present in 40% who required oxygen 8%, one case due to acute pulmonary edema and the other because of septic shock.

Conclusions: Coexistence of infectious and CA represents a diagnostic challenge and requires a high suspicion index. It usually appears in elderly patients with comorbidities. Gout was the most prevalent CA. S. aureus was the most commonly causative pathogen, with a high rate of MRSA infection. If it's treated early the evolution is usually favorable, which makes synovial fluid microbiological study imperative.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6550

**SAT0562** | CHIKUNGUNYA FEVER IN PATIENTS WITH PRIOR RHUematic DISEASES: IS IT MORE SEVERE?

Background: Chikungunya fever (CF) is an infectious disease caused by a RNA virus and its transmission occurs by the inoculation of the virus by the female bite of Aedes aegypti mosquito. In Brazil, where the vector is endemic, the virus rapidly disseminated and there was an epidemic, especially in the Northeast region of the country with 263,980 notified cases in 2016. It is known that CF may have a chronic course with arthritic symptoms, however there is not consistent data in the medical literature on CF evolution in patients with prior rheumatic diseases.

Objectives: To assess whether there is any difference in the characteristics of arthritic manifestations of CF in patients with prior inflammatory rheumatic diseases (IRD), non-inflammatory rheumatic diseases (NIRD) and controls (patients with no diagnosed prior rheumatic diseases).

Methods: Cross-sectional study using a database from CHIKBRASIL cohort. Patients enrolled had clinical and epidemiological characteristics of CF and were classified in three groups: IRD (rheumatoid arthritis, axial spondyloarthritis and systemic lupus erythematosus), NIRD (fibromyalgia and osteoarthritis) and controls (no prior rheumatic diseases).

Results: In a total of 150 patients were enrolled. There were 55 patients with IRD, 40 patients with NIRD and 55 controls, paired by age and sex. There were no differences in acute phase symptoms in the groups. There was a more frequent occurrence of arthritis in patients with IRD compared to NIRD (p=0.001) and to controls (p=0.002). In 89.1% of the patients with IRD there was an underlying disease exacerbation and 74% described an expressive worsening of symptoms compared to the period prior to infection. Patients with IRD had an increase in the current dose of corticosteroids (median 10mg, IQR 10–20) compared to previous dose used (median 8mg, IQR 5–10) after the onset of CF (p=0.0007). Importantly, there was more methotrexate prescription (23.5%) in IRD group, compared to NIRD group (0, p=0.001) and to controls (3.7%, p=0.003).

Conclusions: Patients with IRD and CF presented significantly more arthritis compared to NIRD or to controls. CF seems to induce underlying rheumatologic disease exacerbation in patients with inflammatory disease and a more aggressive therapeutic approach might be necessary in this group of patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6582

**SAT0561** | USEFULNESS OF POLYMERASE CHAIN REACTION FOR DIAGNOSING WHIPPLE'S DISEASE IN RHUMATOLOGY

Background: No consensus exists about the combination of clinical, laboratory, and radiological findings that warrant tests for Whipple's disease.

Objectives: The primary aim of this multicentre retrospective study was to determine when patients evaluated for rheumatological symptoms should undergo T. whipplei PCR testing. Secondary aims were to describe the clinical patterns and treatments used, to determine the diagnostic yield of PCR testing, and to assess whether centres with higher numbers of tests also had a larger number of Whipple's disease diagnoses.

Methods: In a retrospective observational study done in five hospitals, we assessed the clinical and radiological signs that prompted T. whipplei PCR testing between 2010 and 2014, the proportion of patients diagnosed with Whipple's disease, the number of tests performed and the number of diagnoses according to the number of tests, the patterns of Whipple's disease, and the treatments used.

Results: At least one PCR test was performed in each of 267 patients. Rheumatic signs were peripheral arthralgia (n=239, 89%), peripheral arthritis (n=173, 65%), and inflammatory back pain (n=65, 25%). The main extra-articular signs were constitutional symptoms (n=41, 11, 41%), diarrheaoa (n=70, 26, 5%), fever (n=53, 20%), lymphadenopathy (n=14, 5, 3%), and neurological signs (n=11, 4, 2%). Whipple's disease was diagnosed in 13 patients (4,9%). The main samples tested and the more frequently positive tests in the centres with diagnoses of Whipple's disease were saliva and stool. In the centres with no diagnoses of Whipple's disease, arthritis was less common, whereas constitutional symptoms, fever, and lymphadenopathy were more common. 11 patients with Whipple's disease had the annual incidence ranged across centres from 0 to 36.1/100000 inhabitants. The group patients with Whipple's disease had a higher proportion of males, older age, and greater frequency of arthritids.

Conclusions: Males aged 40–75 years with unexplained intermittent seronegative peripheral polyarthritis, including those without constitutional symptoms, should have T. whipplei PCR tests on saliva, stool and, if possible, joint fluid.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4993
SAT0564 SUBLINGUAL VACCINE: NEW CHALLENGE IN THE PREVENTION OF RECURRENT INFECTIONS IN AUTOIMMUNE DISEASES

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Background: Disease-modifying antirheumatic drugs (DMARDs) and new biologicals have improved the prognosis of systemic autoimmune diseases (SAD), but recurrences increase the risk of recurrence with tetracyclic antidepressants (RRTI) and urinary tract (RUTI) infections. Given the rising of antibiotic resistance, the search for new strategies for the prevention of recurrent infections is a priority.

Objectives: The purpose of this study was to evaluate the clinical benefit of the sublingual polybacterial vaccines on infections’ rates in SAD patients.

Methods: A retrospective observational study on a cohort of SAD patients on active immunosuppression with RRTI and RUTI was conducted. Patients were treated with multibacterial sublingual vaccine formulations either for RRTI (Staphylococcus spp., S. pneumoniae, K. pneumoniae, M. catarrhalis, H. influenzae), or/and RUTI (K. pneumoniae, E. coli, E. faecalis, P. vulgaris) (Bactek/Uromune® ImmuneL. SL Madrid, Spain) for 3-months period and clinical follow-up at 6- and 12-months. We monitored the frequency of infections, the intensity and severity of infections during follow-up. Immunological evaluation was performed, including: Serum immunoglobulin levels, IgG subclasses, specific antibodies’ production: anti-pneumococcal, anti-Typhi polysaccharide and anti-tetanus toxoid antibodies, and B and T cell phenotype.

Results: A total of 50 patients were evaluated, and 34 were eligible at 12-months. The mean age of the patients was 58±13 years, 31 women (91.7%) and 9 men (8.3%). All patients were positive for at least one of the following: 21 (67.6%) with systemic lupus erythematosus (SLE), 8.2% (n=5) mixed connective tissue disease, 2.94% (n=1) ankylosing spondylitis, 2.94% (n=1) psoriatic arthritis, 2.94% (n=1) SLE/RA, 2.94% (n=1) discoid LE/Sjogren, 2.94% (n=1) adult onset Still disease, 2.94% (n=1) sarcoidosis, 2.94% (n=1) SLE-like. All patients showed a significant decrease in RRTI (3.15±2.66 vs 0.46±1.07, p<0.01) and RUTI (1.85±2.49 vs 0.35±1.06, p<0.01) frequency and use of antibiotics at 6-months of vaccine, except one with sarcoidosis. 23 of 34 patients (67.6%) disclosed defects on specific antibody production to polysaccharide and protein immunization. Three patients with antibody production deficit and protein immunization. Three patients with antibody production deficit and protein immunization. Three patients with antibody production deficit and protein immunization.

Conclusions: Mucosal vaccination in immunosuppressed patients due to SAD with recurrent infections resulted in lower rates of RRTIs and RUTIs with subsequent improvement in their quality of life. Our preliminary results need to be validated in controlled trials.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4802

SAT0565 THE FREQUENCY OF SEPTIC ARTHRITIS AFTER ARTHROCENTESIS AND INTRA ARTICULAR GLUCOCORTICOID INJECTION IS LOW

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Background: Intraarticular (IA) procedures have both diagnostic and therapeutic purposes in patients with arthritis. The therapeutic benefit of IA glucocorticoids (GC) injection in patients with rheumatoid arthritis (RA) 23.52% (n=8) with systemic lupus erythematosus (SLE), 8.2% (n=5) mixed connective tissue disease, 2.94% (n=1) ankylosing spondylitis, 2.94% (n=1) psoriatic arthritis, 2.94% (n=1) SLE/RA, 2.94% (n=1) discoid LE/Sjogren, 2.94% (n=1) adult onset Still disease, 2.94% (n=1) sarcoidosis, 2.94% (n=1) SLE-like. All patients showed a significant decrease in RRTI (3.15±2.66 vs 0.46±1.07, p<0.01) and RUTI (1.85±2.49 vs 0.35±1.06, p<0.01) frequency and use of antibiotics at 6-months of vaccine, except one with sarcoidosis. 23 of 34 patients (67.6%) disclosed defects on specific antibody production to polysaccharide and protein immunization. Three patients with antibody production deficit and protein immunization. Three patients with antibody production deficit and protein immunization.

Conclusions: Mucosal vaccination in immunosuppressed patients due to SAD with recurrent infections resulted in lower rates of RRTIs and RUTIs with subsequent improvement in their quality of life. Our preliminary results need to be validated in controlled trials.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4802

SAT0566 ELECTRONEUROGRAPHIC FINDINGS IN PATIENTS WITH SUBACUTE/CHRONIC ARTICULAR SYMPTOMS OF CHIKUNGUYA FEVER AND NEUROPATHIC COMPLAINTS – PRELIMINARY RESULTS

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Background: The mechanisms of nonarticular pain associated with Chikungunya virus (CHIKV) infection are still poorly understood. Many patients that progress to Subacute/Chronic phases have neuropathic pain (NP) besides the articular symptoms. The NP is associated with a less favorable outcome, with greater impact on quality of life and lower efficacy of treatment. The NP can reflect a dysfunction of the nervous system, rather than a neurological lesion induced by CHIKV, but the pathophysiology of the neural dysfunction is not completely understood. There are no studies evaluating the electroneurographic findings in patients with CHIKV infection and neuropathic symptoms.

Objectives: To evaluate the results of electroneuography (ENoG) of patients with Chikunguya Fever (CF) and neuropathic symptoms.

Methods: Patients with diagnosis of CF (clinical and epidemiological) and symptoms of paresthesias underwent EMG of upper and lower limbs. The electrodiagnostic evaluation consisted of nerve conduction study of median, ulnar, tibial, fibular, sural and plantar nerves. Clinical and epidemiological data were also recorded.

Results: The sample was composed by 18 patients (82.3% females) with mean age of 56 (±9.8) years. The mean duration of symptoms of CF at the time of the ENoG was 23.8 (±10.8) weeks and the average of tender and swollen joints (including ankle and foot) was 29.6 (±21.5) and 9 (±9.9), respectively. The mean score of visual analogic scale (VAS) for pain was 4.4 (±2.4) and for fatigue was 5.9 (±2.3). Nine patients (50%) had pain in 10. No patient presented axial pain and the number of painful joints was higher in upper (19.4±13.9) compared to lower limbs (10.2±8.4). Only 3 patients reported unspecific paresthesias prior to the onset of arbovirus and worsening after CF. However, these 3 patients had normal ENoG. Six patients had diabetes. Mononeuropathy was the most frequent result occurring in 12 subjects (67%). Bilateral mononeuropathy of median nerve (at carpal tunnel) was found in 11 patients and one subject had median neuropathy just on the left hand. Other mononeuropathies were also present: bilateral tibial nerve in 4, bilateral plantar nerve in 2 and bilateral fibular nerve in 1 patient. Distal axonal polyneuropathy was present in 8 cases (6 sensory and 2 sensorimotor); 5 of these were diabetic. The ENoG was normal in 4 cases. Ten patients were in use of prednisone (mean dose 11.4mg/d) and just 6 were using antineuropathic agents.

Conclusions: Our preliminary results indicate that the ENoG is altered in most patients with chronic articular manifestations of CF and associated paresthesias. Mononeuropathy is the most frequent finding, even in the chronic phase of the disease when the nonarticular edema is not common. Further clinical studies with a larger number of patients and follow-up tests will be needed to confirm our data.

References:
[1] Andrade DC, Jean S, Clavelou P et al. Chronic pain associated with the...

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5554

SAT0567 IMPACT OF CHIKUNGUNYA FEVER ON FUNCTIONAL STATUS AND QUALITY OF LIFE – A PROSPECTIVE COHORT STUDY OF BRAZILIAN PATIENTS

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Background: An epidemic of Chikungunya Fever (CF) spread throughout South America in 2014. The acute manifestation of CF typically consists of febrile arthritis. The burden of the chronic articular manifestations remains a public health issue affecting activities of daily life. There is a very important impact on quality of life in patients affected by CF, even at chronic phase. The long-term functional status may also be affected by CF.

Objectives: To evaluate longitudinality the disability, Health Related Quality of Life (HRQOL) and functional status of patients with CF and analyze the clinical and epidemiological factors associated with different outcomes.

Methods: Patients with clinical and demographic diagnosis of CF and persistent articular symptoms were evaluated in a cohort study between May 2016 and December 2016. HRQOL was rated by Short Form-12 (SF-12) and the Global Functional Status (GFS). Data were divided per weeks after disease onset and were analysed (Spearmans’s correlation coefficient and Mann-Whitney test).

Results: Sixty-five patients (58 females), mean age of 51.3 (±13.3) years were assessed. As expected, a significant correlation between pain related scores and Physical Health Component Score (PCS), HAQ and GFS was found (p<0.05). Edema and morning stiffness correlated with PCS, HAQ and GFS status from 4 to 20 weeks after disease onset (p<0.05). There was improvement in scores of all instruments used from 4–8 weeks of disease to 12–16 weeks of disease (table 1). The worst indices of PCS, Mental Health Composite Scale Score (MCS) and GFS were scored in the first month, mean scores of 30.07±7.77, 38.13±8.54 and 3.15±1.07 respectively. Higher HAQ values were demonstrated between 4 and 8 weeks after disease onset (mean score 1.87±0.82).

Conclusions: We demonstrated the impact of CF on HRQOL and Functional Status of patients. The SF-12 Health Survey, HAQ and GFS are influenced mostly by patients pain and worsening of this status are more prominent in the first 8 weeks of disease. Further clinical studies of the impact of CF on quality of life and functional studies are needed.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5604

SAT0568 RHEUMATOLOGICAL MANIFESTATIONS IN A SERIES OF PATIENTS WITH CHIKUNGUNYA FEVER

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Background: Chikungunya fever is characterised by a high probability of persistent rheumatological manifestations, producing a negative impact in the work, social and economic fields.

Objectives: To determine the frequency and type of rheumatologic involvement in the subacute and chronic phase of Chikungunya fever.

Methods: Descriptive, cross-sectional study. We included patients ≥ 16 years old with Chikungunya infection (real time PCR, IgM or IgG for Chikungunya) who consulted consecutively for rheumatic symptoms/signs from March 2015 to March 2016. According to the time of evolution, the disease was divided in 2 Phases: acute (<10 days of duration) and subacute/chronic (>11 days).

Results: Two hundred and two patients were evaluated, 80 were excluded due to negative serology for Chikungunya. 122 were included: 107 (88%) female, mean age 52.52±13.19 years, and time of evolution of 116.66±91.61 days. Acute phase, 122 patients: fever 85 (69.67%), rash and pruritus 54 (44.26%), tenosynovitis 23 (18.8%), polyarthralgies 100 (82%) and arthritis 56 (45.90%). Chronic phase. 122 patients: 71 (58%) patients had a chronic persistent rheumatologic manifestations and 51 (42%) presented remission of symptoms but all of them presented subsequent recurrence in an 91±40 days. NARC in 33 patients (27%) and AR in 89 (73%), with no significant differences in age and time of evolution was observed.

NARC: 14 (42.4%) exacerbation of previous osteoarthritis pain, 9 (27.3%) developed fibromyalgia and 10 (30.3%) had localized soft tissue pain.

Conclusions: The frequency of rheumatological manifestations post Chikungunya fever in our sample was high, and can trigger ARC. Patients presenting new immunological manifestations in an endemic area for Chikungunya fever should have a serologic test performed. This series of patients must be evaluated with long-term studies to define their evolution, under the possibility of developing definite autoimmune disease or remission.

References:

Disclosure of Interest: None declared

SAT0569 OUTCOME OF PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES ADMITTED IN INTENSIVE CARE UNIT: A PROGNOSTIC STUDY OF 98 PATIENTS

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Background: Systemic rheumatic diseases (SRD) are a rare and heterogeneous group of diseases, associated with a high mortality rate due to the natural evolution of the disease and/or consequences of their specific treatments (infections, toxicity).

Objectives: To describe the clinical features, outcomes and prognostic factors for patients with SRD admitted to the intensive care unit (ICU).


Results: Ninety-eight patients (57% women; median age, 57 years [19–81years]) accounted for 108 admissions. Connective tissue disease (primarily systemic lupus erythematosus) and systemic vasculitides (mainly ANCA-associated vasculitides) represented respectively 55% and 30% of SRD. For nineteen patients, diagnosis of SRD was made at admission. Reasons for admission were: SRD exacerbations (43%), isolated infections (34%), SRD exacerbations associated with infections (12%) or other (11%). Respiratory failure was the most common organ dysfunction. Mechanical ventilation was necessary for 43 patients (44%), vasoactive drugs for 47 (48%) and extra-renal replacement therapy for 38 (39%). The ICU mortality rate was 30% and 37% one year after admission. Infection was the main cause of death (69%). The factors significantly associated with mortality in the ICU were (multivariate analysis): diabetes, cardiovascular diseases and immunosuppressive treatments on admission. At 1 year of follow-up, additional risk factors were: number of organ dysfunction at ICU admission and mechanical ventilation. It is to be noted that at 1 year of follow-up, diabetes was not anymore a prognostic factor.

Conclusions: Patients with SRD admitted to the ICU have a severe prognosis. Causes of mortality are mainly infections. Our study points out the importance of vaccination and developing new therapeutic strategies. Diagnosis of SRD in the ICU is not rare and should be systematically considered on admission. Prognostic factors of mortality in the ICU were patient comorbidities and immunosuppressive treatments on admission.

Disclosure of Interest: None declared

Acute Fase n 122 (%) Chronic Fase n 122 (%) p

| Fever | 85 (69.7) | 0 | 0.01 |
| Rash and pruritus | 54 (44.2) | 0 | 0.01 |
| Tenosynovitis | 23 (18.8) | 41 (33.61) | NS |
| Polyarthralgies | 100 (82) | 83 (68.03) | NS |
| Arthritis | 56 (45.9) | 81 (66.39) | 0.0005 |

Conclusions: The frequency of rheumatological manifestations post Chikungunya fever in our sample was high, and can trigger ARC. Patients presenting new immunological manifestations in an endemic area for Chikungunya fever should have a serologic test performed. This series of patients must be evaluated with long-term studies to define their evolution, under the possibility of developing definite autoimmune disease or remission.

References:
therapy at admission. In addition, mechanical ventilation and multiple organ failure were risk factors for mortality at 1 year.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3078

SAT0570  | AN IGNORED DISEASE IN ADULTS: ACUTE RHEUMATIC FEVER
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Background: Acute rheumatic fever (ARF) is a delayed, inflammatory sequela of pharyngitis secondary to Group A Streptococcus infection. ARF remains one of the important causes of cardiovascular morbidity and mortality in developing countries. Although it is mainly known as a childhood disease, it is also encountered in adult clinics in developing countries.

Objectives: To investigate the clinical and laboratory characteristics of patients who were diagnosed with ARF in two rheumatology outpatient clinics from June 2015 to January 2017.

Methods: The data of 20 patients (12 female; median age 29.5 (21–40) years) were evaluated. The diagnosis of ARF was based on the 2015 Jones criteria. The data collected included patient age, gender, arthralgia, arthritis, erythema marginatum (EM), subcutaneous nodules (SN), ECG/ Doppler transthoracic echocardiography/TH, and other rare findings. The erythrocyte sedimentation rate (ESR), antistreptolysin O (ASO) and CRP levels of the patients and the drugs initiated were also recorded. Anti-streptolysin O (ASO) test or throat culture were used for the evidence of preceding Streptococcal infection. Patients with post-streptococcal reactive arthritis were differentiated and excluded by clinically. Patients with positive rheumatoid factor or anti-CCP were also excluded. Joint fluid examination was done to exclude septic arthritis in patients with monarthrosis.

Results: All patients were referred to rheumatology for arthralgia or arthritis. Patients were taking some sort of nonsteroidal antiinflammatory (NSAI) drugs before evaluation. The median follow-up time was 9 months (6–18). Sixteen out of 20 patients had mono-, oligo- or polyarthritis (25%, 25% and 30%, respectively). Knees and ankles were the most common involved joints. The median duration of arthritis was 1 week (1–50 weeks). Six out 20 patients had subclinical carditis (30%). Nine out 20 patients had a history of ARF attack previously. Three patients had chronic rheumatic mitral valve thickening without any severe insufficiency. EM and SN were observed in 15% and 60% of patients, respectively. Chorea was diagnosed in one patient. NSAI drugs were given to all patients with maximum dosages. High dose salicylate therapy were not given to patients due to intolerance or side effects. Nine patients were given prednisolone therapy (5–20 mg/d). The median duration of prednisolone therapy was 2 weeks (0–6 weeks). Sulfasalazine was given to two patients for the prolonged arthritis. All patients received secondary prophylaxis with penicillin.

Conclusions: ARF should be considered in the differential diagnosis of arthritides in young adults in developing countries. ARF in adults seems to be resistant to classical NSAI drugs. Our data show that steroid therapy can be given safely instead of salicylates in carditis or arthritis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4944

SAT0571  | PERFORMING SEPTIC ARTHRITIS DIAGNOSIS IN SCENARIOS WHERE SYNOVIAL FLUID IS NOT AVAILABLE: MULTIVARIATE LOGISTIC REGRESSION ANALYSIS
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Background: In order to establish the diagnosis of septic arthritis (SA) it is necessary to demonstrate the presence of bacteria into the synovial fluid. However, clinicians should act according to its suspicious when the differential diagnosis included this possibility even when the microbiologic study of the synovial fluid in unavailable by any cause (small joints, lack of training or logistic deficiencies).

Objectives: The purpose of our study is to determine the relative weight of other clinical or analytical variables that should be useful in these scenarios.

Methods: A retrospective multivariate logistic regression analysis about the registries of monarthrosis assessed in our unit between 2013 and 2016. There were included only registries with cases of synovial joints with all parameters of interest available. The binary response variable was the microbiological demonstration of septic arthritis (culture/Gram stain of synovial fluid or tissue).

Explanatory variables were age (stratified in < 30, 30–39, 40–49, 50–59, 60–69 and > 70 years old), gender, temperature above of 37.9°C, recount of neutrophils in peripheral blood sample, measure of procalcitonin (PCT), and measure of C reactive protein (CRP). Synovial fluid study, although was available in almost all cases was deliberately omitted for purpose of this study. The logistic regression analysis variables were selected from the forward model strategy.

Results: There were included 449 registries. One hundred an sixteen of them were SA. The fixed model showed a Chi-square=226.64 with 5 degrees of freedom and a P<0.0001. Explanatory variable gender was excluded from the forward model strategy due to its lack of impact on the binary response variable. The Odds Ratio for PCT, PCT >1.3 ng/dL, age, neutrophils recount and body temperature were 1.0175, 8.1588, 0.5135, 1.0001 and 3.4147, respectively. The model showed a sensitivity of 68.1%, specificity of 94.8%, PPV of 82.2% and NPV of 89.5%. The following table shows the full results of the logistic regression analysis: Standard error, Wald index, p value and R coefficients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>E. E.</th>
<th>Cmk.</th>
<th>Wald</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR</td>
<td>0.0174</td>
<td>0.0004</td>
<td>52.0052</td>
<td>1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCT</td>
<td>2.0991</td>
<td>0.5407</td>
<td>37.9640</td>
<td>1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>-0.6955</td>
<td>0.1090</td>
<td>25.9793</td>
<td>1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>0.0001</td>
<td>0.0001</td>
<td>14.9560</td>
<td>1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Temperature</td>
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<td>1.2561</td>
<td>0.5326</td>
<td>13.9784</td>
<td>1</td>
</tr>
<tr>
<td>Constant</td>
<td>-3.7227</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>N.A</td>
</tr>
</tbody>
</table>

Conclusions: Previous studies have demonstrated the usefulness of PCT measure for the diagnosis of SA however all of them have been based on joints which synovial fluid is quite easy to obtain for further analysis. Present study allows laying the ground for creation of future diagnostic models based on five clinical variables that could be useful on scenarios where the assessment by joint puncture is not available.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4240

SAT0572  | LEVELS OF SERUM PROCALCITONINE AS DIAGNOSIS DISCERNING TOOL BETWEEN GOUT AND SEPTIC ARTHRITIS
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Background: In a previous study we demonstrated the potential usefulness of the procalcitonine serum measure in order to diagnose septic arthritis. This utility is quite important on the differential diagnosis of knee arthritis in patients with known gout or other inflammatory joint disease which can express as a monarthrosis.

Objectives: Due to that, this study aims to determine sensibility, specificity, positive predictor value and negative predictor value of procalcitonine serum measure (PCT) in patients with knee arthritis for the diagnosis of septic arthritis.

Methods: We reviewed the registries of patients who consulted due to knee acute monoarthrosis between 2013 and 2015 in which a PCT was obtained. Registries were grouped according to the final diagnosis (gouty arthritis only (group I) and septic arthritis with or without gout (group II). Based on a previous study, PCT value of 1.47 ng/mL was considered the cut point. Validation tests were applied fixed to demographic and clinical specific scenarios.

Results: Registries of 121 patients with gout and 47 patients with septic arthritis (SA) were included. From the 47 patients with SA, 9 were previously diagnosed by gout. All diagnosed were based on guidelines and clinical recommendations for SA and gout (Coakley et al. Rheumatology, 2006 and Zhang et al. Ann Rheum Dis, 2006).

Using the cut point of 1.47 ng/mL, test validation results were as follows: sensibility of 87.2%, specificity of 92.5%, PPV of 82.0% and NPV of 94.9%. Excluding patients with less than 48 hours of onset, there were 44 registries of patients with SA and 83 with gout. In this scenario the results of the validation tests were as follows: Sensibility of 93.1%, specificity of 96.3%, PPV of 93.1% and NPV of 96.38%. Excluding all patients with body temperature above 37.5°C there remained 11 with SA and 61 with gout. In this scenario the results of the validation tests were as follows: Sensibility of 72.7%, specificity of 95.1%, PPV of 66.6% and NPV of 96.2%.

Conclusions: This is the first study aimed to validate previous observations about the usefulness of PCT determination in patients with acute knee monoarthrosis. Although the global results in the validation test are a bit inferior that our original observations in a shorter pilot study in terms of sensibility, the NPV remains over 95% in scenarios where the differential diagnosis could be harder to establish such as recent onset flares or cases without an associated febrile syndrome.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4289
**SAT0573** SOCIODEMOGRAPHIC, CLINICAL CHARACTERISTICS AND JOINT INVOLVEMENT OF A CHIKUNGUNYA EPIDEMIC IN COLOMBIA

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**Background:** During 2014 and 2015 a chikungunya epidemic took place in Colombia concurrently with a COPCORD study across the country.

**Objectives:** To describe the clinical characteristics of CHIKV infection in 6 different cities in Colombia and determine the most frequently associated clinical picture with CHIKV.

**Methods:** World Health Organization criteria was used to identify CHIKV patients. A complete characterization and confirmation was established with CHIKV immunoglobulin G and IgM serology. Four possible scenarios were established: patients who met or not the criteria for probable case, and patients who met or not the criteria for confirmed case. 

**Results:** A total of 604 patients with MSK symptoms were evaluated in 6 different cities. The sociodemographic, clinical characteristics and joint involvement of the studied population is depicted in tables 1 and 2. Sensibility and specificity of the WHO criteria were 56.2% and 91.1% respectively (PPV: 83.3%, NPV: 74.4%).

**Conclusions:** Our study revealed a good performance of IgG and regular performance of IgM for the diagnosis of CHIKV in a cohort of CHIKV patients from Colombia’s epidemic. Cut off points for both IgG and IgM were measured for future reference.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1886

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**SAT0574** PERFORMANCE OF IMMUNOglobulin M AND G (IgM AND IgG) ANTIBODIES AGAINST CHIKUNGUNYA VIRUS (CHIKV) BY ENZYME-LINKED IMMUNOSORBENT (ELISA) TECHNIQUE

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**Background:** CHIKV is suspected based on epidemiological and clinical criteria, however confirmation of the disease is only achieved by laboratory tests.

**Methods:** IgM and IgG antibodies against CHIKV were measured by ELISA (Abcam® ab177835 and ab177835 anti-chikungunya virus IgM and IgG human ELISA kit, Cambridge, UK) technique in 604 patients with CHIKV suspicion. A typical case of CHIKV with high sensitivity and specificity obtained from a previous study was used as gold standard for diagnosis of CHIKV. Since CHIKV epidemic of 2014–2015 was the first to be reported in our country (Colombia), no second measurements of IgG were needed to confirmed infection.

**Results:** Cut off point for IgG was 14.3 SU and for IgM was 11.2 SU. Mean values for IgG was 36.7 SU (±22.7) in patients with CHIKV and 8.6 SU (SD: 6.3) for IgM. Statistical significance was obtained for both IgG and IgM (p<0.0001) when comparing patients with and without CHIKV. Receiver operating characteristic (ROC) curves showed and area under the curve (AUC) of 0.81 for IgG and 0.65 for IgM (figure 1).

**Conclusions:** Our study reviewed a good performance of IgG and regular performance of IgM for the diagnosis of CHIKV in a cohort of CHIKV patients from Colombia’s epidemic. Cut off points for both IgG and IgM were measured for future reference.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1879
mg/L; SD±8.4). Association alleles of HLA-A, and DR are depicted in table 1. No association was found with HLA-B alleles.

Table 1. Associated Alleles with CHIKV

<table>
<thead>
<tr>
<th>Resistance</th>
<th>Control</th>
<th>Odds Ratio</th>
<th>CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>A*28</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.040</td>
</tr>
<tr>
<td>A*27</td>
<td>6</td>
<td>0.0</td>
<td>0.0</td>
<td>0.048</td>
</tr>
</tbody>
</table>

CHIKV: chikungunya virus infection; CI: confidence interval 95%; Cp: Bonferroni corrected p value.

Conclusions: Our study demonstrated the alleles A*28 and A*27 were associated with resistance to CHIKV, and alleles A*68, DRB1*01, DRB1*04 and DRB1*13 were to be associated with susceptibility to CHIKV. No association was found in any HLA-B alleles.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1887

**SAT0576** IMPROVED CLINICAL SCENARIO FOR CHIKUNGUNYA DIAGNOSIS


Background: The World Health Organization (WHO) criteria for chikungunya virus (CHIKV) infection are a diagnostic possibility, and the criteria are considered highly sensitive and specific. In order to test the performance of the new criteria and improve sensitivity in diagnosing and treating CHIKV patients, a new clinical scenario was developed with the agreement of CHIKV criteria according to WHO). Patients from outpatient and inpatient departments were recruited irrespective of the duration of anti-tuberculosis therapy.

Methods: We included patients who had active tuberculosis as per World Health Organization (WHO) 2010 criteria. Patients with chronic illnesses were excluded. A detailed history, examination, and appropriate investigations (blood, urine, serological and radiological) of the 100 consecutive patients fulfilling the inclusion criteria were recorded.

Results: Mean age of patients was 32.16±12.93 years. Male to female ratio was 43.57. Mean duration of disease was 6.85±8.33 months. Of the 100 patients, 60 (60%) had pulmonary tuberculosis. Pleural tuberculosis presenting as pleural effusion was seen in 17 (17%) patients. Abdominal tuberculosis was seen in 9 (9%), tuberculous lymphadenopathy in 8 (8%) and pott's spine in 4 (4%). Eye tuberculosis and tubercular breast lump were seen in 1 patient each. 83 (83%) patients had first episode of tuberculosis while the other 17 (17%) patients had second episode of tuberculosis. 74 (74%) patients were on category 1 antituberculosis treatment (ATT), while 23 (23%) were on category 2 ATT and 3 (3%) were on modified ATT. Mean duration of ATT was 1.79±1.34 months. Fibromyalgia was classified in 21 (21%) patients, polyarthralgia was seen in 9 (9%), pott's spine in 7 (7%), osteomyelitis in 4 (4%) and scleritis in 2 (2%) patients. Uveitis, tenosynovitis, erythema induratum, subcutaneous abscess and dactylitis was seen in 1 (1%) each. Rheumatological manifestations as septic arthritis, DILE, poncer's arthritis, tendinopathy, amyloidosis, gout, erythema nodosum and myositis were not seen in any patient. In 21 patients who had fibromyalgia, 11 patients developed fibromyalgia with 2nd episode of tuberculosis amounting to 60.75% patients.

Conclusions: This is the first prospective study to look at the musculoskeletal manifestations of tuberculosis. Patients with active tuberculosis were found to have various rheumatological manifestations.

Acknowledgements: I acknowledge Dr Sushil Gupta, director of the Rajan Babu TB Hospital for allowing me to conduct this study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1357

**SAT0577** LEFLUNOMIDE INHIBITS THE APOTOPSIS OF HUMAN EBRYONIC LUNG FIBROBLASTS INFECTED BY HUMAN CYTOMEGALOVIRUS

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Background: The immunomodulatory drug leflunomide (LEF) is frequently used for treating human cytomegalovirus (HCMV), but its antiviral mechanism is still unclear.

Objectives: In this study, we investigated the effects of the active LEF metabolite AT71726 on the HCMV lifecycle in human embryonic lung fibroblasts. We clarified the mechanism of LEF antiviral infection, and provide a new way to treat immune dysfunction patients with HCMV infection.

Methods: The experiment was divided into four groups: the control group, the HCMV group, the ganciclovir + HCMV group as well as the LEF + HCMV group. The treated cell line was infected with HCMV, and was then treated by staining with fluorescein isothiocyanate (FITC) and propidium iodide. Statistical significance was determined by paired t-test using SPSS software.

Results: The results of the study showed that cell proliferation was significantly inhibited by HCMV at 24 hours and 48 hours. With increasing HCMV concentration, the value-added inhibition of the cells was significantly decreased compared with the control group, and was statistically significant (P<0.01). Ganciclovir can increase proliferation of cell-sorted into HCMV: compared with the control group it was statistically significant (P<0.05). Meanwhile, with LEF treatment cell proliferation was significantly improved at 24 hours and 48 hours, with statistical significance (P<0.05). The apoptosis rate of human embryonic lung fibroblasts infected with HCMV increased significantly at 24 hours, 48 hours and 72 hours, and as time goes on the apoptosis rate increases statistically significantly (P<0.01) compared with the control group. The apoptosis rate of the HCMV infection group decreased by adding LEF and was statistically significant (P<0.05).

Conclusions: This study shows that LEF is an exciting new drug for cytomegalovirus infection. LEF significantly inhibited HCMV infection-induced apoptosis and proliferation, playing an important role in the treatment of patients infected by HCMV. In this study we explored the potential usefulness of LEF for...
cytomegalovirus infection and found it to be a cost-effective new treatment for cytomegalovirus infection that deserves further study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2128

**SAT0579** LOW DOSE IL-2 RESTORES IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH CONNECTIVE DISEASE COMBINED EBV/CMV VIREMIA

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Background: DMARDs are the most important medicine in treatment of autoimmune disease. However, excessive using DMARDs lead to decrease immune function, which increasing opportunistic infection, such as EBV, CMV viremia. Recent study show the imbalance between T help cell 17 (Th17) and regulatory T cell (Treg cell) is a pivotal cause of autoimmune disease and correction of this imbalance to be a potential therapy. So whether low dose IL-2 restores the balance of Th17/Treg and improve immune function?

Objectives: To investigate the effect of low-dose IL-2 on Treg and effector lymphocyte subsets in patients with connective tissue disease (CTD) combined EBV or CMV viremia.

Methods: Clinical records of 70 CTD patients combined EBV or CMV viremia, hospitalized from May 2012 to January 2017 in the second Hospital of Shanxi medical university (Group infection), were analyzed. The group includes 21 patients who received rhl-2 after infected CMV or EBV, and 12 continue receiving DMARDs. As control, we selected 70 health persons (Group health) whose age matched with group infection, 70 naïve CTD patients with no treatment (Group treatment-naïve), and 70 CTD without viremia patients having glucocorticoid and DMARDs medical history (Group Treatment-DMARDs). The two groups’ underlying diseases are matched with the Group infection. The absolute numbers and proportions of peripheral lymphocytes (T cells, B cells, NK cells, the total number of the three cells, CD4+ T cells, CD8+ T cells), and CD4+ T cell subsets (CD4+Th1, CD4+Th2, Th17, Treg cells and Th17/Th2, Th17/Treg) were examined by flow cytometry.

Results: 1. The absolute count of Treg cells in the Group treatment-naïve was significantly low and Th17/Treg was notably increase compared with the Group health (P<0.05). The peripheral lymphocytes and Treg cells are notable low (P<0.05) and Th17/Treg was significantly increase (P<0.05) in the Group treatment-DMARDs compared with the Group treatment-naïve.
2. The peripheral lymphocytes, CD4+ T cells subsets except Treg cells and Th1Th2, Th17/Treg were significantly decrease in the Group infection compared with the Group treatment-DMARDs (P<0.05). While the absolute count of Treg cell was no different between the two groups.
3. After the course of rhl-2 treatment, there were significantly increase of the peripheral lymphocytes and CD4+ T cells subsets (P<0.01). Th17/Treg was significantly low after treatment. Compared with the patients who continue receiving DMARDs, all lymphocyte subsets had a rising trend in patients receiving rhl-2 treatment.

Conclusions: The decrease of Treg cell number and imbalance of Th17/Treg may contribute to the pathogenesis of CTD. Excessive using glucocorticoid and DMARDs may aggravate the imbalance on the other hand, these medicines decrease immune function, which leads to EBV and CMV viremia. Over the treatment of rhl-2, immune function was improved and there was a more significant increase in the absolute count of T reg cells than Th17, and a consequently restore the balance of Th17/Treg.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6247

**SAT0580** OSTEARTICULAR TUBERCULOSIS: A RETROSPECTIVE STUDY OF 119 CASES

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Background: Bone and joint involvement in tuberculosis is uncommon. While osteoarticular tuberculosis most commonly occurs in the vertebral column, less frequently affected sites are the hip, knee and sacroiliac joints. The multiform form of skeletal tuberculosis is exceptional.

Objectives: To evaluate the clinical and diagnostic features of osteoarticular tuberculosis.

Methods: We reviewed the files of all patients admitted to our department from 2000 to 2016 to search for diagnosis of osteoarticular tuberculosis.

Results: We identified 119 patients (52 men, 67 female), having osteoarticular tuberculosis lesions. Mean age was 43 years [21–82]. Diagnosis delay was 4 months. Pain, low-grade fever and loss of weight were the most common presenting symptoms. All the patients consulted because of pain. The spine was involved in 81 patients. Peripheral osteoarticular tuberculosis was diagnostic in 38 cases, mainly in the knee (21 cases). Five patients have a multifocal involvement of the osteoarticular tuberculosis. The tuberculin skin test was positive in 75% of the cases. The diagnosis of spondylodiscitis was provided by CT-scan and/or magnetic resonance imaging. Paraspinal and epidural abscesses has been reported in 11 cases. Bacteriological and/or pathological diagnosis was made in 72 cases (60.5%). The QuantiFeron test was done in 7 cases and was positive. The antibiotic treatment led to recovery in all cases. Tree patients have presented neurological signs.

Conclusions: Our results were similar to those of the literature. Elderly population was, as expected, at risk. The diagnosis can be delayed especially in negative investigations. Therefore it is recommendable to do a very large screening tests especially in endemic areas.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6357

**SAT0582** CHAGAS’ DISEASE IN PATIENTS WITH AUTOIMMUNE DISEASES RECEIVING IMMUNOSUPPRESSIVE THERAPY.

ANALYSIS OF 48 CASES

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Background: DMARDs are the most important medicine in treatment of autoimmune disease. However, excessive using DMARDs lead to decrease immune function, which increasing opportunistic infection, such as EBV, CMV viremia. Recent study show the imbalance between T help cell 17 (Th17) and regulatory T cell (Treg cell) is a pivotal cause of autoimmune disease and correction of this imbalance to be a potential therapy. So whether low dose IL-2 restores the balance of Th17/Treg and improve immune function?

Objectives: To identify the risk factors of the development and exacerbation of NTM infection in patients with rheumatic diseases.

Methods: Among 7013 patients with rheumatic diseases visiting Toho University Ohashi Medical Center and Tokyo Medical Center, 20 patients were enrolled in this study by fulfilling the diagnostic criteria of NTM infection by The Japanese Society for Tuberculosis and The Japanese Respiratory Society, and being followed-up for more than 1 year. The medical records of enrolled patients were retrospectively reviewed.

Results: Eleven patients with rheumatoid arthritis, 4 patients with vasculitis, 3 patients with SJögren's syndrome and 1 patient with dermatomyositis and systemic lupus erythematosus for each were enrolled in this study. Mycobacterium avium complex (MAC) was detected in 13 patients, M. chelonae in 2 patients, M. abscessus and M.Kansasii in 1 patient each, and undetermined mycobacterium in 5 patients. Notably, bronchiectasis was the predominant pulmonary complication observed in 13 patients, and intestinal lung disease was observed in 5 patients. Although 7 patients experienced the exacerbation of NTM during the observation period, immunological state on NTM diagnosis including peripheral blood leucocyte (median 5.8×10³ versus 7.0×10³/μL; p=0.72), lymphocyte (median 1.3×10³ versus 1.1×10³/μL; p=0.10) and the serum IgG level (median 1379 mg/dL versus 1207 mg/dL; p=0.20) were within normal ranges and comparable between ever and never exacerbation patients, respectively, as well as the treatments for rheumatic diseases such as glucocorticoids and biological agents.

Conclusions: NTM infection in patients with rheumatic diseases develops based on the dysfunction of pulmonary barrier rather than the systemic immunosuppression.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6911

**SAT0581** NON-TUBERCULOUS MYCOBACTERIAL (NTM) INFECTION IN PATIENTS WITH RHEUMATIC DISEASES: POSSIBLE IMPORTANCE OF PULMONARY BARRIER FUNCTION RATHER THAN SYSTEMIC IMMUNE STATE IN THE DEVELOPMENT AND EXACERBATION OF NTM INFECTION

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Objectives: To identify the risk factors of the development and exacerbation of NTM infection in patients with rheumatic diseases.

Methods: Among 7013 patients with rheumatic diseases visiting Toho University Ohashi Medical Center and Tokyo Medical Center, 20 patients were enrolled in this study by fulfilling the diagnostic criteria of NTM infection. We identified the patients who were receiving DMARDs [DMARDs] and biological drugs [BD]; 2) had confirmed or were positive for NTM infection in patients with rheumatic diseases.

Results: We identified 13 patients (from our Units and 35 from the literature search) fulfilled the inclusion criteria. There were 41 (85.4%) women, mean age of 57±15 years. The decrease of Treg cell number and imbalance of Th17/Treg was significantly increased in patients receiving DMARDs and biological drugs compared with patients not receiving DMARDs.

Conclusions: The decrease of Treg cell number and imbalance of Th17/Treg may contribute to the pathogenesis of CTD. Excessive using glucocorticoid and DMARDs may aggravate the imbalance on the other hand, these medicines decrease immune function, which leads to EBV and CMV viremia. Over the treatment of rhl-2, immune function was improved and there was a more significant increase in the absolute count of Treg cells than Th17, and a consequently restore the balance of Th17/Treg.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6911
SAT0583 | LATERAL EPICONDYLITIS: WHAT IS NEW? DIAGNOSTIC, IMAGING AND TREATMENT. A SYSTEMATIC LITERATURE REVIEW

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Background: Lateral epicondylitis or tennis elbow is an extremely frequent disease, secondary to intratendinous degeneration of the common carp extensor tendon. However, diagnosis and therapeutic management are still a challenge for the rheumatologist.

Objectives: To determine the available evidence regarding the diagnostic, imaging and treatment of epicondylitis.

Methods: A systematic review literature was performed using PUBMED. Only controlled trials, systematic literature reviews and meta-analysis were selected (Jan 1990 to May 2016). The MESH search words were “tennis elbow”, “lateral epicondylitis” or “tennis elbow tendinopathy”. Diagnostic imaging” and “therapeutics.

Results: 1314 potential articles were screened; 7 articles of clinical diagnosis, 21 of imaging and 18 of treatment were finally selected.

Diagnostic: No controlled trials were found about the diagnosis of the epicondylitis. The clinical tests employed in the retrieved clinical trials were based upon the experts’ recommendations: lateral epicondyle palpation, resisted extension of the carpe and resisted extension of the 3rd and 4th fingers.

Imaging: Among the 21 articles identified, 1 article concerning plain Xray, 1 about scintigraphy, 10 of US and 10 of MRI were selected. One clinical trial, found plain Xrays were not helpful for the initial diagnosis. Ultrasound was found to be sensitive (84–100%) and specific (38–100%) tool for the diagnosis, in one meta-analysis. Ten studies, within a systematic review, showed MRI was reported to be as sensitive (90–100%) as the ultrasound, with a greater specificity (83–100%). In addition, MRI showed better reliability (0.41–0.53 vs 0.73–1.00). An MRI was therefore considered as a good complementary tool between the observed physical and symptoms, severity and involvement of other structures. On the contrary, no data was found to support the use of imaging tests for follow-up.

Treatment: Among the 18 articles, 9 articles (within 4 systematic review and 5 randomized clinical trials) about pharmacological treatment, 10 about the non-pharmacologic approach and 1 about surgery were selected. Corticoids injections were found to be effective in one meta-analysis at short-term and preferably for acute epicondylitis (Pain reduction at 1–3 weeks +1.18 (95% CI 0.27–2.09), 4–8 +1.30 (95% CI 0.55–2.04), 12–24 +0.38 (95% CI 0.85–0.08). Similar results were found for NSAIDs. Five prospective randomized clinical trials showed braces and carpal extension splints were reported to improve pain at rest and during exercise, in short term. Physical therapy was reported to be efficacious in pain and function too, in a systematic review. Therapies like rich platelet plasma show braces and carpal extension splints were reported to improve pain at rest and during exercise, in short term. Physical therapy was reported to be efficacious in pain and function too, in a systematic review. Therapies like rich platelet plasma showed a good agreement between for subscapular tendinosis (accu-

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4484

SAT0584 | THE ROLE OF MRI INTERPRETATION IN PATIENTS WITH ROTATOR CUFF DISEASE

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Background: Shoulder pain is a common musculoskeletal complaint, roughly equal in incidence to neck pain (1). The shoulder pain syndrome has a prevalence to 47% in general population (2) and an incidence to 87–100,000 persons per 100,000 people per year (3,4). The identification of the cause of shoulder pain is very important because of the variability of the treatment. Patients with rotator cuff injuries should be managed with the appropriate pain relief and physical therapy (5). MRI is the imaging modality of choice for evaluating rotator cuff abnormalities. We aimed to determine whether there was agreement among radiologists in the diagnosis and treatment of rotator cuff disorders.

Objectives: To determine whether there was agreement among radiologists in the diagnosis and treatment of rotator cuff disorders. To assess the concordance between two radiologists in the diagnosis and treatment of rotator cuff disorders.

Methods: A systematic review of the literature was performed using PUBMED. Only controlled trials, systematic literature reviews and meta-analysis were selected (Jan 1990 to May 2016). The MESH search words were “infiltration”, “arthrocentesis” or “joint puncture” and “shoulder” or “knee” or “dabigatran” or its brand names.

Results: 12 articles (including 4 systematic reviews and 8 individual clinical studies) were included in the analysis. Among the 18 articles, 9 articles (within 4 systematic review and 5 randomized clinical trials) showed a good agreement between for subscapular tendinosis (accuracy=98%, Kappa=0.79, p=0.000) and perfect compatibility (accuracy=100%, Kappa=1, p=0.000) for terrs minor tendinosis. The poorest concordance between readers was in impingement syndrome (comparing=55%, Kappa=0.11, p=0.05).

Conclusions: The MRI examination is significant in rotator cuff disease only when the radiologist is overtrained for shoulder, otherwise the technique is unsusal and doubtful in clinical practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2301

SAT0585 | IS IT SAFE TO PERFORM JOINT PUNCTURES IN PATIENTS TREATED WITH DABIGATRAN?

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Background: The introduction of new oral anticoagulants provides us with a new therapeutic intervention and secondary prevention opportunity in stroke patients previously not well controlled with acenocoumarol due to not compliance or other issues.

As with other anticoagulants or even antiplatelet agents, the attending doctor may hesitate to perform a joint puncture in patients receiving such treatments. The purpose of this study is to describe the four-year cumulative experience of joint and peri-articular punctures in patients receiving dabigatran, a new oral anticoagulant recently introduced in our country.

Methods: We performed a systematic review of the records of patients who underwent a knee joint aspiration or periaricular joint puncture for diagnostic or therapeutic purposes and who were under treatment with dabigatran between the years 2012 and 2016.

For this purpose we conducted an search for electronic records within that period, using the search terms: "infiltration", "arthrocentesis" or "joint puncture" and "shoulder" or "knee" and "dabigatran" or it's brand names.
Follow up visits in either primary care (HORUS® Application) or emergency settings (CAJAL® Application) were analyzed, regardless of the main complain at admission, and the data was collected from this records.

**Results:** Between 2012 and 2016, 68 joint knee punctures and 49 periaricular shoulder punctures were performed in dabigatran patients. Of the 117 procedures, 73 (66.6%) were performed by attending physicians in Traumatology, 9 (7.8%) in Rheumatology, 10 (8.5%) in Neurology or Physical Medicine and Rehabilitation, and the rest by internal medicine residents. Of the 68 knee arthrocentesis, in 48 (70.5%) of the cases synovial fluid collection and infiltration were performed, while in the rest only infiltration was needed. Of the 49 shoulder punctures, in 12 (24.4%) a bursocentesis was performed while in the rest only an infiltration was done. 16 knee and 17 shoulder punctures (23.5% and 34.6%) were ultrasound assisted procedures. Among the patients with knee puncture, 11 (16.1%) came back before 15 days due to procedure related symptoms. Of these, 9 did so because of persistence of the main symptom or persistent pain and 2 because of increased pain. These two patients were studied sonographically and one of them had a hematoma that was treated conservatively. In the group of patients with shoulder puncture, 7 (14.2%) came back before the first 15 days and in all of them the cause was persistence of the main symptom. None of the patients required admission at the hospital. None of the patients with ecography-assisted procedures came back before the first 15 days. No patient consulted due to bleeding after the first fifteen days. (There were no hemorrhagic cases which lasted 15 days). The outcome of the procedure was not influenced by the person performing it (attending vs resident), however, all the ecdochiagnostic procedures were performed by an attending.

**Conclusions:** Although it is a small population, this is to the best of our knowledge the first published series of dabigatran anticoagulated patients who underwent a large joint or periarticular puncture. We can conclude that this type of punctures are safe in patients with this characteristics. On the other hand, there is evidence that ecography-assisted procedures are more effective in this group of patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6640

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**SAT0587**

**SCHOOL BAGS WEIGHT ARE NOT ASSOCIATED WITH LOW BACK PAIN IN SCHOOLCHILDREN IN CAMEROON**  
F. Kemta Legloa, M.S. Doualla, H. Namme Luma. Service de Médecine Interne, Douala General Hospital, Douala, Cameroon

**Background:** Data are mixed on the role of school bags in the occurrence of low back pain in pupils.

**Objectives:** Thus, we carried out this study with the aim to determine if the school bags were a factor associated with low back pain in Cameroon schoolchildren.

**Methods:** We performed a cross-sectional study between December 2015 and April 2016 in 10 primary schools of the city of Douala, Cameroon. A questionnaire was submitted to the students of these different schools. Informed and signed consent of their parents were obtained. Sociodemographic and clinical data were collected, as well as the weight of each school bags. A p < 0.05 was significant.

**Results:** We included 1070 pupils (543 boys, 532 girls). The mean age was 11.1 years (8–16 years). BMI was normal in 928 children (86.5%). The prevalence of low back pain was 12.3% (132 children: 81 girls and 51 boys). Sixteen children had already met a physician for low back pain. The mean weight of the school bag was 4.9±1.9 kg, with 369 children (57.7%) with a school bags weight > 15% of their body weight in private schools compared with 56 (12.9%) in public schools. We had 99 children with low back pain with a school bag weight >10% of their body weight (Table 1). We didn’t find any relationship between low back pain and the weight of the school bag, regardless of gender, BMI, age of pain, type of school, distance from home to school, way of transportation, and age (p > 0.05). However, the exception was found in girls aged from 8 to 10 years with a school bag weight > 15% of their body weight (p < 0.05). Furthermore, in univariate analysis, factors associated with low back pain were (p < 0.05): age, history of low back pain in at least one parent, competitive sport, a bad seated position on school benches. In multivariate analysis, factors associated with low back pain were female, competitive sport, and low back pain in at least one parent (Table 2).

**Table 1. Relationship between weight of school bag and body weight of pupils with low back pain (n=132)**

<table>
<thead>
<tr>
<th>Weight of the school bag in relation to the weight of the child</th>
<th>Number of pupils, n (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5%</td>
<td>3 (5.5)</td>
<td></td>
</tr>
<tr>
<td>5–10%</td>
<td>30 (11.7)</td>
<td>0.09</td>
</tr>
<tr>
<td>10–15%</td>
<td>46 (13.6)</td>
<td>0.10</td>
</tr>
<tr>
<td>&gt;15%</td>
<td>53 (15.2)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

**Table 2. Factors associated with low back pain in children**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.93</td>
<td>0.81–1.06</td>
<td>0.25</td>
</tr>
<tr>
<td>Sex</td>
<td>1.73</td>
<td>1.19–2.52</td>
<td>0.004</td>
</tr>
<tr>
<td>Competitive sport</td>
<td>1.61</td>
<td>1.03–2.53</td>
<td>0.038</td>
</tr>
<tr>
<td>Low back pain in parents</td>
<td>1.88</td>
<td>1.23–2.89</td>
<td>0.004</td>
</tr>
</tbody>
</table>

**Conclusions:** The weight of the school bags was not associated with low back pain in Cameroon schoolchildren (except for girls aged from 8 to 10). However, female, competitive sport and low back pain in at least one parent were associated to low back pain.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6693

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**SAT0588**

**HEALTHCARE WORKERS ARE NOT MORE AT RISK TO LOW BACK PAIN THAN OTHER OCCUPATIONS**  
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**Background:** Low back pain is common among healthcare workers but is it more frequent than in other occupations?

**Objectives:** In order to answer this question, we carried out this study with the aim to determine if healthcare workers was more at risk for low back pain than other occupations.

**Methods:** We performed a survey on all permanent workers (n=584) of the Douala General Hospital in Cameroon from January to May 2016. Socio-demographic characteristics of workers (distinction with different occupations – healthcare workers, administrative workers, technical workers) and the main features of low back pain were collected. A p < 0.05 was significant.

**Results:** Of the 584 questionnaires distributed, 474 responses were obtained (81.1%). We excluded 27 for incomplete data. 447 were retained for the final analysis: 296 healthcare workers, 79 administrative workers, and 72 technical workers. The mean age was 40±10 years (22–66 years) and 258 (57.7%) were female. Mean BMI was 27±4.9 kg/m² with 103 (23%) obese.

At the end of the study, 252 (56.4%) workers described low back pain, including 170 (57.4%) healthcare workers, 44 (55.7) administrative workers and 38 (52.7) technical workers. There was no significant difference between the different groups (p > 0.05). Same for sex (p=0.9). The overall independent risk factors associated with low back pain were: seniority in their current position (OR 4.97, 95% CI 1.80–13.68, p=0.002), office chair quality (OR 3.06, 95% CI 1.29–7.26,
The aim of this study is to examine the effect of therapeutic education on fears and beliefs in chronic low back pain.

Methods: A prospective, comparative study was conducted with two groups of 50 patients each one having chronic low back pain. Both groups had benefited from the same physical rehabilitation program. The second group concurrently attended therapeutic education sessions.

Objectives: To assess the effectiveness of therapeutic education in reducing fears and beliefs among chronic low back pain patients.

Results: The initial evaluation of apprehension-avoidance showed a high FABQ score in both groups. Despite differences in initial scores, the intervention group showed a significant decrease in FABQ scores compared to the control group.

Conclusions: Therapeutic education significantly reduces fears and beliefs in chronic low back pain patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4385
EFFECT OF INTERFERENTIAL CURRENT THERAPY IN PATIENTS WITH SUBACROMIAL IMPINGEMENT SYNDROME: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: Shoulder pain is one of the most common types of musculoskeletal pain in the adult population. Subacromial impingement syndrome (SIS) has been reported to be the most frequent etiologic factor for shoulder pain (1). A conservative approach using non-steroid anti-inflammatory drugs (NSAID), subacromial injections, exercise, and several physical therapy agents is recommended as the first step treatment for SIS (2). Although interferential current (IFC) is a common electrotherapeutic modality used to treat musculoskeletal pain, there isn’t any randomized controlled trial investigating its clinical efficacy on SIS (3).

Objectives: To investigate the effectiveness of IFC treatment in patients with SIS.

Methods: In this double blind, placebo controlled study, patients with shoulder pain, who had been diagnosed SIS according to clinical evaluation and subacromial injection test were randomly assigned to the IFC or placebo groups. Exercise, cryotherapy, and NSAID were applied to all the groups. Daily 20 min per session, 5 days per week, for 2 weeks. 10 sessions IFC with alternative method were applied to the IFC group while sham IFC therapy were applied to the placebo group with the same protocol. Visual analog scale (VAS), Constant Murley Scale (CMS) and Shoulder Disability Questionnaire (SDQ) were used for evaluation at baseline, post-treatment and 1 month post-treatment.

Results: A total of 60 patients were completed the study; 26 (43.3%) were male and mean age was 50.02±9.10 years. There was not a significant difference in demographic and clinical data of the patients between the IFC (n=30) and placebo (n=30) groups (p>0.05). Significant improvement in all parameters was observed on post-treatment and 1 month post-treatment evaluations compared to baseline evaluations in both groups (p<0.01). Comparison of the VAS, CMS and SDQ scores between the two groups did not show significant difference either pre-treatment or post-treatment (p>0.05).

Conclusions: This study showed that IFC treatment does not provide additional benefit to NSAID, cryotherapy and exercise program in the treatment of SIS. Further studies are needed to investigate the long-term effects of IFC therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2773

GENDER-SPECIFIC ASSOCIATIONS BETWEEN FAT MASS AND MUSCULOSKELETAL PAIN IN COMMUNITY RESIDENTS: A 3-YEAR LONGITUDINAL STUDY

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Background: Increase in fat mass is correlated with musculoskeletal pain in general population.

Objectives: In this study, we sought to delineate the prospective relationship between body mass parameters and the musculoskeletal pain in Korean community residents.

Methods: In the Korean Health and Genome Study, 1,325 participants (mean age 60.2 years, 56.2% women) who completed pain questionnaires and underwent dual x-ray absorptiometry to calculate body composition had 3 year follow-up data on pain. Pain was categorized according to number of pain regions. After 3 years of follow-up, subjects were classified into the following: 1) no pain both at baseline and at 3 years (no pain), 2) any pain (one, two or more, or widespread regions) at baseline and no pain at 3 years (transient pain), 3) no pain at baseline and any pain at 3 years (new pain) 4) any pain both at baseline and at 3 years (persistent pain), 1) and 2) were grouped as no/persistent pain group (no pain) and 3) and 4) as new/persistent pain group (pain).

Results: Female gender and obesity were significant factors associated with the persistence or development of pain. Total fat mass and fat: muscle mass ratio were significantly correlated with development of pain. Odds ratios for persistent pain were significantly increased in subjects in the highest quartile of fat mass ratio after adjustment among female subjects only. Among normal weight subjects, those without metabolic syndrome were less likely to belong to the pain group, especially among women.

Conclusions: The association of fat mass and pain was only significant among females.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2247
musculoskeletal system disorders. Local inflammation could be the major cause of night pain, and using a deep diathermic modality might be contradictory.

Objectives: Investigation of the effectiveness of short wave diathermy SWD treatment in patient with SIS and to emphasize the significance of night pain (NP) status on treatment response.

Methods: In this double-blind, randomized placebo controlled trial, 57 patients aged between 35 to 65 years, diagnosed as SIS were classified into two groups as night pain positive NP(+) (n=28) and night pain negative NP(-) (n=29). Both groups were randomly assigned to SWD treatment NP(+) n=14, NP(-) n=14 and sham NP(+) n=15, NP(-) n=14 subgroups. Exercise, cold pack application and a moderate anti-inflammatory drug treatment were applied to all groups. 27.12 MHz continuous SWD (daily 20 min per session, 5 days per week, for 2 weeks, 10 sessions) was applied to the treatment groups while sham SWD was applied to the sham groups with the same protocol. Rest, activity and night visual analog scale (VAS), Constant (Murley) Score (CS) and Shoulder Disability Questionnaire (SDQ) were used for evaluation of patients at 2 weeks before the treatment, 1 month and 2 months after the treatment.

Results: There were no statistical differences between the SWD treatment and sham groups in all outcome parameters except for the Constant pain scores in NP(+) group. In NP(-) group, SWD treatment improved the parameters of pain strength, total scores of CS, and SDQ compared to sham group at 1 month. SWD treatment was superior to sham for all parameters except for the Constant daily living activity scores at 2 months.

Conclusions: In conclusion, addition of 27.12 MHz continuous SWD treatment to chronic treatment improves long term benefits when compared to sham SWD in terms of rest and activity VAS scores, Constant-Murley scores, and SDQ scores in SIS patients without night pain. However, there was no convincing evidence that SWD treatment is of additional benefit in SIS patients with NP. Therefore, night pain as a symptom should be regarded in the selection of treatment modalities in order to use the deep heat effectively in the management of SIS.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1297

SAT0596 EFFICACY OF EPIDURAL STEROID INJECTION IN LUMBAR SPINAL STENOSIS IS NOT RELATED TO THE DEGREE OF SEVERITY BY MRI
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Background: Lumbar spinal stenosis (LSS) is a common degenerative disease. Treatment modalities for LSS vary and include medication, exercise, interventional techniques, and surgical intervention. The lumbar epidural steroid injection has been used for the treatment of LSS with variable results. The relationship between severity of lumbar spinal stenosis and efficacy of lumbar epidural steroid injection is still undetermined.

Objectives: The aim of our study was to determine the relationship between the severity of LSS using MRI grading system and the response to lumbar epidural steroid injection.

Methods: Thirty patients with degenerative LSS were enrolled in this prospective study. All subjects underwent lumbar spine MRI (T2-weighted axial images). LSS was graded using MRI grading system (grade 1 - mild stenosis with separation of at least 2 – moderate stenosis with some cauda equina aggregated; grade 3 – severe stenosis with none of the cauda equina separated). All fluoroscopy guided transforaminal epidural steroid injections (FG- TFESI) were performed in the procedure room. Outcome measures were obtained using the visual analogue scale (VAS) for both back and leg pain, Oswestry disability index (ODI), Roland 5-point pain scale, walking tolerance and patient’s satisfaction scale at 2 and 8 weeks post-treatment.

Results: Thirty LSS patients treated with FG- TFESI, who were completely followed up, were included in this study, the injection rate was one injection per patient. The patients were followed at 2 weeks and 8 weeks. Fifty-six percent of patients at 2 weeks and 70% at 8 weeks had a successful outcome, reporting at least a 50% reduction between pre-injection and post-injection visual analogue pain scores.Roland 5 point pain scale showed pain reduction in 50% of patients by (25%) at 2 weeks and in 70% of patients by50% pain reduction at 8 weeks. Oswestry low back pain disability questionnaire (ODI) scores showed statistically significant improvement from initial scores to 2 weeks and from 2 weeks in 70% of patients. Walking tolerance showed improvement at 2 weeks in 50% of patients and at 8 weeks in 70% of patients. The outcome was statistically significant even in severe stenotic patients when comparing initial scores of moderate and severe stenosis at 2 weeks and 8 weeks scores in walking tolerance (P<0.006), Back VAS (P=0.717), Leg VAS (P=0.139), ODI (P=0.139), and Roland (P=0.001).

Conclusions: FG-LESI may reduce pain and improve walking tolerance in the short term for the treatment of patients with LSS for a period of 8 weeks. The outcome does not seem to correlate with the degree of lumbar spinal stenosis. Patients with severe LSS may have the same chance to get benefits from FG-LESI as patients with moderate LSS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2233

SAT0597 RELATIONSHIP BETWEEN LUMBAR DISC HERNIATION AND BENIGN JOINT HYPERMOBILITY SYNDROME
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Background: Benign joint hypermobility syndrome (BJHS) can present with a wide variety of musculoskeletal problems. Benign joint hypermobility syndrome (BJHS) is a hereditary disorder characterized by the presence of musculoskeletal symptoms in persons with generalized joint laxity in the absence of systemic rheumatologic disease (1–3). Lumbar disc herniation (LDH) is a common cause of low back pain. On the other hand, low back pain may be a presenting symptom in patients with BJHS.

Objectives: to evaluate relationship between Lumbar disc herniation and BJHS.

Methods: The study included 100 patients diagnosed with LDH depending on history, clinical examination and MRI findings and another 100 healthy control participants. All, patients and healthy controls were assessed for BJHS using the revised (Brighton 1998) criteria.

Results: The mean age was (35.4±8.9) year and (33.72±8.3) for patients and controls respectively, there were 43 males and 57 females in each group. The mean BMI was (27.6±4.6) kg/m2 in patients and (28.3±4.6) in controls. No significant differences found between the groups regarding the age, sex and BMI in all comparisons (Pvalue<0.05). The mean Beighton score was significantly higher among patients in comparison to controls; t(23.1±6.2) versus (1.2±1.3) in controls group; on the other hand major and minor criteria were significantly more prevalent among patients rather than controls, in all comparisons (Pvalue<0.05). BJHS was more prevalent among patients rather than controls, 55% of the patients had BJHS compared to 21% of controls, the odds ratio was (4.6) and (Pvalue<0.05). BJHS was more prevalent among females compared to males, from the total number of all participants, BJHS was present in 76 participants, and of them 47 were females versus 29 males, (Pvalue<0.05).

It had been significantly found that subjects with BJHS in both groups (patients and controls) were relatively shorter than those without BJHS, Pvalue<0.05. The correlation analysis of BJHS with the MRI findings of LDH in patients group showed no significant differences among patients with and without BJHS, in all comparisons Pvalue>0.05.

Conclusions: BJHS is more prevalent among patients with LDH. There is no significant relationship between presence of BJHS in LDH patients and MRI findings.

References:

Disclosure of Interest: None declared


SAT0598 EVALUATION OF THE QUALITY OF SEXUAL LIFE DURING CHRONIC LOW BACK PAIN
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Background: Sexual life has an important role in preserving the good quality of life of patients and their partners. Chronic low back pain (CLBP) as well as other musculoskeletal diseases, can affect all life activities including sexual function.

Objectives: The aim of this study is to assess the impact of chronic low back pain on sexual life and to identify the associated factors.

Methods: It’s a study of 144 patients suffering from chronic low back pain, during a period of nine months (from February to October 2016).We have specifically studied the relationship between chronic low back pain and sexual quality of life, using the Sexual Quotient (QS) (a validated questionnaire), which consists in 10 questions, each of them from 0 to 10, to have a final score rated from 0 to 100.

Results: The average age of our patients was 53.8±10.7 years (23–79 years), with a female predominance in 64% of cases. The mean visual analogue scale for pain was 4.72 (1–9).

The average duration of low back pain was 6.5 years. The average score of the mean Dallas score, the segmental results were as follows: 53.1% of impact on daily activities, 47.6% of impact on work/leisure ratio, 45% of impact on anxiety/depression ratio and 33.4% of impact on sociability.

In our study, 57.2% of cases were under analgesic treatment, 85.5% were under...
non-steroidal anti-inflammatory drugs, 20% had at least one local corticosteroid infiltration, 34% had functional rehabilitation and 4% had surgical treatment. Regarding sexual dysfunction, 34.5% of our patients didn’t have any sexual activity. 2.1% had a catastrophic sexual life (score < 20), 9% had a disappointing sexual life (score between 20 and 40), 20% had an average sexual life (score between 40 and 60), 17.9% had a satisfying sexual life (score between 60 and 80), while only 13.1% had a very fulfilling sexual life (score between 80 and 100. We showed that the alteration of the sexual quotient in our patients is more marked when the age of the patients is more advanced. But we didn’t found a significant correlation with the duration of the disease, the mean visual analogue scale for pain and the functional scores of Quebec and Dallas.

**Conclusions:** Our study suggests that sexuality is profoundly disrupted in chronic low back pain. The advanced age is proved to be correlated with the deterioration of the sexual life. So, sexuality must be taken into account in the management of patients with chronic low back pain.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5339

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**SAT0599**  
**LOW BACK PAIN IN MEDICAL STUDENTS LINKED TO POOR SLEEP QUALITY: RESULTS FROM THE PAX-I STUDY**

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**Background:** Low Back Pain (LBP) is a major public health problem and is classified by the Global Burden of Disease Study among the ten diseases most responsible for Disability-Adjusted Life Years worldwide. All ages may be affected, mostly young adults, with a prevalence going up to 50%. Medical students may be particularly vulnerable due to sedentary lifestyle and high stress levels.

**Objectives:** The primary objective is to evaluate the prevalence of LBP in Lebanese medical students. The secondary objective is to identify predictive factors associated with LBP and to identify prevalence and components of inflammatory back pain (IBP).

**Methods:** PAX-I is a cross-sectional study, completed at the St-Joseph University of Beirut from April to June 2016. All students from the first to the sixth year of medicine were invited to fill a questionnaire about their demographic data, lifestyle habits, Patient Health Questionnaire for Depression and Anxiety (PHQ24) and LBP characteristics, including components of IBP as per ASAS criteria. Student test and ANOVA were used for quantitative variables, chi-square test was used for qualitative variables and logistic regression was used to identify predictive factors for low back pain. Analysis were performed on IBM SPSS Statistics 23.

**Results:** Response rate was 51.3% (258/502). Mean age was 20.86 years (SD 1.92). 54.3% were women. 76.7% drank caffeine. 66.3% had a regular sports activity and 9.7% were smokers. 38% had the habit of walking while studying. 46% were satisfied with their quality of sleep. Mean PHQ24 score was 7.17 and increased with the years of studies (p 0.045). 55.8% of students reported a LBP event during the past year, with a mean number of 3.6 episodes per year. 91% of these students had LBP while studying, with high reported intensity (5.18±10). 62.5% reported LBP after exercise. 80% had episodes of less than one month and 7% of more than three months duration. 12% had IBP according to the ASAS criteria (Details of IBP in Figure 1).

**Predictive factors for LBP in univariate analysis were:** smoking (p 0.040), alcohol consumption (p 0.005), caffeine consumption (p 0.041), telewaching (p 0.042) –positive association-, and number of hours of sleep (p 0.011) and satisfaction with sleep quality–negative association– (p 0.017). Satisfaction with sleep quality remained the only significant association in multivariate analysis (p 0.014).

**Conclusions:** LBP is a frequent problem among medical students with high intensity, especially when studying, and a high recurrence rate. The main predictive factor was poor satisfaction with sleep quality. A significant percentage fulfills IBP criteria by auto-questionnaire and should benefit from further investigation.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5325

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**SAT0600**  
**USEFULNESS OF VERTEBROPLASTY IN VERTEBRAL FRACTURES WITH PERSISTANT BACK PAIN. A REPORT OF 64 VERTEBRAL AUGMENTATION FROM A UNIVERSITY HOSPITAL**

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**Background:** Management options for patients with persistent back pain after a vertebral fracture include vertebral augmentation, but its use is controversial.

**Objectives:** Our aim was to evaluate the clinical efficacy and complications of consecutive vertebroplasties performed in our Hospital in a 12 years period.

**Methods:** Retrospective study of vertebroplasties performed at a University Hospital in the last 12 years (April 2004 to April 2016). The duration of follow-up was more than 12 months. Epidemiological variables, indications, time elapsed, efficacy and complications of the procedure were collected. The indication of vertebroplasties in fractures was pain refractory to usual symptomatic treatment in these pathologies: osteoporosis, trauma, leukemia/lymphoma, metastasis and hemangioma. Efficacy was assessed at 6 and 12 months with a simple verbal scale according to the pain response (improvement/non-improvement). Patients who died before 12 months period were excluded for the that parameter. A comparative study of the efficacy between a)cause of fracture, b)location, c)time elapsed, d)access route and e)complication was performed. For the descriptive analysis we used frequencies and percentages in the case of qualitative variables, and mean and standard deviation (SD) or median and interquartile range for quantitative variables. Chi-square test or Fisher's exact test was used in for qualitative variables, and Wilcoxon's non-parametric test for evolution time.

**Results:** Efficacy and complications of the procedure were collected. Indication of vertebroplasties in fractures was pain refractory to usual symptomatic treatment in these pathologies: osteoporosis, trauma, leukemia/lymphoma, metastasis and hemangioma. Efficacy was assessed at 6 and 12 months with a simple verbal scale according to the pain response (improvement/non-improvement). Patients who died before 12 months period were excluded for the that parameter. A comparative study of the efficacy between a)cause of fracture, b)location, c)time elapsed, d)access route and e)complication was performed. For the descriptive analysis we used frequencies and percentages in the case of qualitative variables, and mean and standard deviation (SD) or median and interquartile range for quantitative variables. Chi-square test or Fisher's exact test was used in for qualitative variables, and Wilcoxon's non-parametric test for evolution time.

**Statistical analysis was performed with the SAS System for Windows V 9.2.**

**Results:** 66 vertebroplasties were performed in 44 patients (75% female/25% male). 80% were satisfied with their quality of sleep. Mean PHQ24 score was 7.17 and increased with the years of studies (p 0.045). 55.8% of students reported a LBP event during the past year, with a mean number of 3.6 episodes per year. 91% of these students had LBP while studying, with high reported intensity (5.18±10). 62.5% reported LBP after exercise. 80% had episodes of less than one month and 7% of more than three months duration. 12% had IBP according to the ASAS criteria (Details of IBP in Figure 1).

**Predictive factors for LBP in univariate analysis were:** smoking (p 0.040), alcohol consumption (p 0.005), caffeine consumption (p 0.041), television watching (p 0.042) –positive association-, and number of hours of sleep (p 0.011) and satisfaction with sleep quality–negative association– (p 0.017). Satisfaction with sleep quality remained the only significant association in multivariate analysis (p 0.014).

**Conclusions:** LBP is a frequent problem among medical students with high intensity, especially when studying, and a high recurrence rate. The main predictive factor was poor satisfaction with sleep quality. A significant percentage fulfills IBP criteria by auto-questionnaire and should benefit from further investigation.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5325
TREATMENT OF CARPAL TUNNEL SYNDROME (CTS) WITH ESWT: A SHAM CONTROLLED DOUBLE BLINDED RANDOMISED STUDY

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Objectives: The aim of this study was to investigate the efficacy of extracorporeal shock wave therapy (ESWT) in the treatment of CTS.

Methods: 49 hand with the diagnosis of CTS were included in the study. Patients were randomised in ESWT (n=29 hands) and sham (n=20 hands) groups. Patients were randomly allocated to receive 1 session per week for 3 weeks of either sham or active ESWT. All patients were prescribed with tendon and nerve gliding exercises and hand-wrist splint which used night. Patients were evaluated before the treatment, and at the end of the first week, first month and third month after the last ESWT treatment session with Boston Scale (symptom severity and functional capacity), Visual Analogue Scale (VAS) for pain and paresthesia assessment, for muscle strength: hand gross grasp and electromyographic variables (P<0.05). In both groups, there was no statistically significant difference between groups in all clinical and electrophysiological parameters.

Conclusions: Although ESWT was effective in symptoms in CTS but this efficacy isn’t superior to placebo. Our results indicated that ESWT was effective in pain and clinical variables in CTS. Wider and high-quality studies are needed to further demonstrate the effectiveness of ESWT in treatment of CTS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5363

MANAGEMENT OF EPICONDYLITIS WITH SINGLE LOCAL INJECTION OF SODIUM HYALURONATE

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Background: Lateral elbow epicondylitis, also known as tennis elbow, is a common musculoskeletal condition causing pain and functional impairment in daily activities.1 It affects between 40–50% of recreational tennis players at some time during their career.2 Hyaluronate (SH) is a natural biological substance which has proven to be effective to improve pain and function in osteoarthritic patients with low incidence of side effects.3 Similarly, the administration of periarticular injections of SH can be an alternative approach to treat chronic epicondylitis.4

Objectives: To evaluate the efficacy and safety of a single percutaneous injection with SH in the treatment of chronic epicondylitis.

Methods: A single-site, and placebo-controlled trial was conducted in patients with chronic epicondylitis. Patients’ condition was assessed at baseline and afterwards they were randomized 1:1 to receive a single 2.5ml injection of SH (manufactured by Tedec Meiji Farma SA) or placebo (saline) at the point of maximal pain at the lateral epicondyle. Additionally, standard of care (RICE: Rest, Ice, Compression and Elevation) was prescribed to both groups. Efficacy assessments were done at days 30 and 90 and included VAS (0–10cm) pain at rest and assessment of grip strength, patient global satisfaction, patient assessment of normal function and physician global assessment of elbow injury (all measured using 5-point categorical scale). Adverse events were recorded for safety purposes.

Results: A total of 60 patients were included and completed the study procedures. Both groups were homogeneous at baseline. A statistically significant reduction from baseline in VAS pain at rest and after grip testing was observed at 30 and 90 days in both treatment groups (p<0.05). Besides, inter-group comparison showed statistically significant differences in favour of SH group at 30 and 90 days (p<0.05). This was associated with significantly greater grip strength, patient global satisfaction and assessment of normal elbow function in SH group vs placebo (p<0.05). Improvement of elbow injury assessed by the physician was also statistically greater in patients treated with SH compared to placebo (p<0.05). No adverse events were recorded.

Conclusions: A single local injection of SH administered to patients with epicondylitis was significantly superior to placebo improving pain at rest and after grip testing, through all the study follow up period. The treatment was highly satisfactory for both physicians and patients and there were no safety concerns.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2586

AN INNOVATIVE TREATMENT MODALITY FOR ACUTE ILIO-TIBIAL BAND SYNDROME IN RUNNERS: LOCAL HYALURONATE + BOTULINUM TOXIN IN A PROSPECTIVE COHORT OF 45 ATHLETES

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Background: Iliotibial band syndrome (ITBS) is the most common cause of lateral knee pain in runners.5 It is an overuse injury that results from repetitive friction of the iliotibial band (ITB) over the lateral femoral condyle. Initial treatment includes activity modification, nonsteroidal anti-inflammatory medication, taping, stretching exercise and in severe cases, a corticosteroid injection.6 Treatment of symptoms and return to activity are variable and can be intractable.

Objectives: To evaluate the efficacy and safety on pain and return to activity of a single injection of ITBS with combination hyaluronate and Botulinum toxin in 45 runners.

Methods: 45 runners with at least grade 2 ITBS underwent baseline investigations including pain following symptom-limited treadmill running test during which pain was recorded on a visual analogue scale (VAS 0–100) every minute. Runners then had injection in the area where the iliotibial band crosses the lateral femoral condyle with 2.5 ml combination hyaluronate (750–1300 kDa) with 40 U Botulinum toxin. Additionally, standard of care (RICE: Rest, Ice, Compression and Elevation) and stretching was prescribed but participants were instructed not to use NSAIDS or taping. The same pain VAS measures as well as peak exercise time, patient global satisfaction and patient assessment of normal running function (all measured using 5-point categorical scale) were repeated after 2, 7, 14 and 30 days. The primary outcome was peak pain during symptom-limited treadmill running.

Adverse events were recorded for safety purposes.

Results: 45 consecutive runners with acute (within 7 days) ITBS were included and completed the study procedures. A statistically significant reduction from baseline in VAS peak treadmill exercise was observed at all time points (p<0.05). This was associated with significantly longer exercise time at 7, 14 and 30 days. Patient global satisfaction was increased progressively after 7, 14 and 30 days and assessment of normal running function was described in >75% at 14 days. No serious adverse were reported. 3 subjects described transient (~24 hours) weakness in knee extension and 2 subjects described mild pain at the time and location of injection.

Conclusions: A single local injection of combination hyaluronate + Botulinum toxin for ITBS in runners improved pain and exercise time with treadmill running by 7 days post treatment and continued to 30 days. This treatment was satisfactory to runners and resulted in few, limited adverse events.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3552

**SAT0604** AUTOLOGOUS BLOOD AND CORTICOSTEROID LOCAL INJECTION IN TREATMENT OF PLANTAR FASCIITIS (RANDOMIZED, CONTROLLED MULTICENTER CLINICAL TRIAL)

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Background: Plantar fasciitis is the most common cause of heel pain. Local injection modalities are among treatment options in patients with resistant pain.

Objectives: The aim of the present study was to evaluate the effect of local autologous blood compared with corticosteroid local injection in treatment of plantar fasciitis.

Methods: In this randomized controlled multicenter study, 36 patients with chronic plantar fasciitis were recruited. Patients were allocated randomly into 3 treatment groups: local autologous blood, local corticosteroid injection and control groups receiving no injection. Patients were assessed with Visual Analogue Scale (VAS), Pressure Pain Threshold (PPT) and Plantar Fasciitis Pain/Disability Scale (PFPS) before treatment, 4 and 12 weeks post therapy.

Results: Variables of pain and function improved significantly in both corticosteroid and autologous blood groups compared to control group. At 4 weeks following treatment, patients in corticosteroid group had significantly lower levels of pain than patients in autologous blood and control groups (higher PPT level, lower PFPS and VAS). After 12 weeks of treatment both corticosteroid and autologous blood groups had lower average levels of pain than control group. The corticosteroid group showed an early sharp and then more gradual improvement in pain scores but autologous blood group had steady gradual drop in pain.

Conclusions: Autologous blood and corticosteroid local injection both can be considered as effective methods in the treatment of chronic plantar fasciitis. These treatments decrease pain and improve function significantly compared to control group.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1771

**SAT0605** LOCAL PROGESTERONE INJECTION: NEW OPTION FOR MANAGEMENT OF CARPAL TUNNEL SYNDROME

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Background: A number of studies, have demonstrated the neuroprotective effects of progesterone and its influence on the recovery after neural injury. Few studies investigated the efficacy of local progesterone in Carpal Tunnel Syndrome.

Objectives: The objective of this study was to compare the long term effects of progesterone versus corticosteroid local injections in patients with mild and moderate carpal tunnel syndrome.

Methods: In this randomized clinical trial, 78 hands with Carpal Tunnel Syndrome were assigned to two groups. Patients were treated with a single local injection of triamcinolone acetonide in one group and single local injection of hydroxyprogesterone in the other group. Variables including pain (based on Visual Analogue Scale), symptom severity and functional status (based on Bostone/Levine symptom severity and functional status scale) and nerve conduction study were evaluated before and 6 months after the treatments.

Results: All outcome measures including pain, functional scales and electrophysiologic findings improved in both corticosteroid and progesterone groups and there were no meaningful differences between two groups regarding mentioned variables. However, functional outcome was significantly better in progesterone compared to corticosteroid group at 6 month follow up (P<0.04).

Conclusions: The study demonstrated the efficacy of progesterone local injection in mild and moderate CTS at long term follow up. Furthermore, local progesterone can be superior to corticosteroid injection for relieving symptoms and improving functional and electrophysiologic findings at long term follow up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1774

**SAT0606** IS THE LEVEL OF PHYSICAL ACTIVITY AN IMPORTANT FACTOR FOR LOW BACK PAIN AMONG STUDENTS OF UNIVERSITY?

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Background: Back pain is a major global health problem, causing greater disability worldwide than any other condition. Regular physical activity is widely believed to have important health benefits, such as improving quality of life and mobility, and reducing disabilities. Conversely, lack of physical activity is considered a risk factor for increasing chronic diseases, functional dependence and mortality. Patients with low back pain (LBP) often report disability to perform daily activities. Also, decreased physical activity level can lead to low back pain.

Objectives: The aim of the study was to determine whether increasing the level of physical activity affects the low back pain or not in the population of university students.

Methods: The cross-sectional study included 350 students (181 females and 169 males) with a mean age of 19.8±1.9 years. LBP was determined using the validated Oswestry Disability Index (ODI). ODI consist of ten items and are completed in reference to the patient’s functional status “today”. Physical activity level was evaluated by the short form of the International Physical Activity Questionnaire (IPAQ). IPAQ is a scale to be recorded at different levels of physical activity time in the last week. IPAQ is a scale to be recorded at different levels of physical activity time in the last week. Individuals whose score is lower than 600 MET are described as inactive (IPAQ 1), between 600–1500 MET (IPAQ 2) are described as moderately active and higher than 3000 MET (IPAQ 3) as described as active. For the statistical analyzing we used spearman correlation test.

Results: According to the short form of IPAQ, 14.8% percent of students were found inactive, 48.1% percent of students were found minimal inactive and 37.1 percent of students were found active. The total score of Oswestry disability index was found 6.2±5.0. There was a significant difference between the Oswestry disability index score of inactive, minimally active and active groups (p=0.02). In addition to this, between the Oswestry disability index and total score of IPAQ was found a weak correlation in the negative direction (p<0.01; r=-0.184). Between the IPAQ3 and Oswestry disability index and total score of IPAQ was found a weak correlation in the negative direction (p<0.05; r=-0.190). And also between IPAQ3, which means moderate intensity activity, and Oswestry disability index was found a significant but weak correlation in the negative direction (p=0.01; r=-0.157). Between Oswestry disability index and sedentary activity and walking was not found any significant correlation (p<0.05).

Conclusions: According to our study, increasing the level of physical activity may reduce low back pain. Especially vigorous and moderate intensity activity can be effective in prevention from low back pain. For reducing of low back pain, sedentary activity and walking did not have any significant effect in our study. Therefore, the level of physical activity should be increased at the young age to prevent of low back pain which is a major health problem.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4953

**SAT0607** DISCOVERY OF A SMALL MOLECULE INHIBITOR OF THE WNT PATHWAY (SM04755) AS A POTENTIAL TOPICAL TREATMENT FOR TENDINOPATHY

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Background: Tendinopathy is an inflammatory and degenerative disorder caused by injuries or overuse. It can progress to a chronic condition with failed healing, tendon fibrosis and micro-tears that lead to pain and sometimes rupture. Current therapeutic options focus mainly on pain relief rather than treatment of underlying disease. The Wnt/β-catenin pathway is upregulated in tendinopathy and has an important role in inflammation, fibrosis and tenocyte differentiation.

Objectives: SM04755, a novel, topical Wnt pathway inhibitor, was evaluated in preclinical studies to determine its potential to inhibit inflammation, reduce fibrosis and increase tenocyte differentiation, thereby promoting tendon healing.

Methods: Anti-inflammatory activity was measured by the reducing activity of ELISA in lipopolysaccharides (LPS) and anti-CD3/anti-CD28 stimulated peripheral blood mononuclear cells (PBMCs). Differentiation of human mesenchymal stem cells (mMSCs) and rat tendon derived stem cells (rTDSCs) into tenocytes was measured by high-throughput qPCR for tenocyte markers scleraxis A (SCXA), tenomodulin and tenasin C. Pharmacokinetics were evaluated following topical application in rats. In vivo efficacy of SM04755 was evaluated in a single injection, collagenase-induced acute rodent tendinopathy model and a chronic, multiple injection, failed healing model, by scoring histological indicators of tendon health. Inflammation was measured by chemokine ligand 1 (CCL1) levels in plasma by ELISA and pro-inflammatory markers (IL-6, TNF-α, IL-1β, IFN-γ, IL-8) in the tendon by qPCR. Tendon regeneration and healing were evaluated by qPCR based gene expression of tenocyte differentiation markers SCXα, tenomodulin and tenasin C. Type V/VI collagen ratio and polarized light microscopy using Sirius Red staining. Pain in the rodent model was measured by force distribution with an incapacitance meter.

Results: SM04755 potentely inhibited cytokine secretion in LPS and anti-CD3/anti-CD28 stimulated PBMCs (EC50<500nM). SM04755 induced expression of tenocyte markers in differentiated mMSCs and rTDSCs (EC50<200nM). A single topical application of SM04755 resulted in tendon concentrations >EC50 for up to 24hrs, with minimal systemic exposure or toxicity. In both the acute and failed healing tendinopathy models, SM04755 (10mg/ml) treatment improved tendon morphology (Figure A), significantly increased mean tendon health
score (p < 0.01), decreased plasma levels of CXCL1 (p < 0.05) and reduced gene expression of pro-inflammatory markers (IL-6, TNF-a, IL-1β, INF-g, IL-8; p < 0.05) compared to vehicle. SM04755 treatment promoted tendon regeneration measured as increased expression of tenocyte markers (p < 0.05), increased Type I/Type III collagen ratio (Figure B; p < 0.01) and Sirus Red stained collagen fibers in tendon compared to vehicle. SM04755 treatment increased wet weight, weight bearing on the affected limb (p < 0.01), at multiple time points (Figure C), indicating reduced pain in the rodent model.

Figure. SM04755 inhibited inflammation, promoted tendon healing and reduced pain in a rat collagenase-induced tendinopathy model

Conclusions: Topical SM04755, a Wnt pathway inhibitor, reduced inflammation, promoted tendon regeneration and healing, and reduced pain compared to vehicle in rodent tendinopathy models. SM04755 is a potential treatment for tendinopathy.

Clinical studies are in progress.


SAT0608 RELATION BETWEEN SCAPULAR MUSCLE ENDURANCE, MUSCLE STRENGTH, PAIN AND FUNCTION IN PATIENTS WITH ROTATOR CUFF LESION

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Background: Rotator cuff lesion (RCL) is an term that encompasses a spectrum of shoulder conditions including: subacromial impingement syndrome (SIS), partial and full thickness rotator cuff tears (RCT) and calcific tendinitis. Symptoms include pain, limited motion, muscle weakness and functional disability.

Objectives: To investigate the relationship between scapular muscle endurance (SME), muscle strength, pain and function in patients with shoulder RCL.

Methods: This study was conducted on 53 patients in shoulder RCL and 23 healthy controls. SME was measured as isometric based on the exercise developed by Sahrmann. Strength was measured as dynamometer. Activity, night and rest pain levels were evaluated by visual analog scale. Functional activity status was assessed by the Functional Impairment Test-Head, and Neck/Shoulder/Arm (FIT-HaNSA).

Results: Consecutive non selected patients, ≥50 years-old with high vascular risk according to European Guidelines on Cardiovascular Disease Prevention, and without signs or symptoms of GCA, were included. Ultrasonography of carotid artery: Carotid ultrasound examinations were performed on a Mylab Seven (Esaote Medical Systems, Italy) with a 4–13 MHz linear-array. The system employed dedicated software radiofrequency-tracking technology to obtain IMT (QIMTM).

Ultrasonography of temporal superficial artery: A color Doppler ultrasound (CDU) and grey scale measure of the IMT/halo sign in the branches of both TA was performed by a second experienced sonographer. A Mylab Twice equipment (Esaote, Geneve, Italy) was used, with a 22 MHz frequency for grey scale and a 12.5 MHz for CDU, with a color gain of 51 and a PRF of 2 kHz. The sonographer was blind to the clinical data and carotid ultrasound IMT measurements. Examination videos were stored for reliability and an intra-reader was performed months after the examination.

Statistical analysis: Descriptive frequencies, Student’s t-test, Cronbach’s alpha and Spearman correlations was used.

Results: Forty patients were studied, 28 men (70%), with a mean age of 70.6 ± 9 years. Three patients were active smoker and 27 ex-smokers, Arterial hypertension was present in 39 (97.5%), dyslipidemia in 34 (85%) and diabetes in 19 (47.5%). The mean erythrocyte sedimentation rate was 13.6 ± 11.0. Eighty carotids were studied, 50 had plaques and 30 did not with an IMT ranged from 0.526 to 1.480 mm. The mean values of TA related with the carotid IMT was presented in the table: the increase in the carotid IMT is associated with an increase in the IMT of the TA with a weak Spearman correlation (p<0.012 and frontal branches 0.228 p=0.048).

Patients with a final GCA diagnosis (n=22)

<table>
<thead>
<tr>
<th>Carotid IMT mm</th>
<th>Branches of Temporal arteries parastial and frontal</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean Halo/IMT mm</td>
</tr>
<tr>
<td>≤ 0.7</td>
<td>12</td>
</tr>
<tr>
<td>≤ 0.9</td>
<td>46</td>
</tr>
<tr>
<td>≤ 1</td>
<td>42</td>
</tr>
<tr>
<td>≤ 1.2</td>
<td>50</td>
</tr>
<tr>
<td>&lt; 1.2</td>
<td>10</td>
</tr>
</tbody>
</table>

From reliability a Cronbach’s alpha of 0.900 and 0.876 were achieved for parietal and frontal branches respectively. Some patients had a TA IMT that can be interpreted as halo sign: 18 (45%) patients and 32 (26.6%) TA branches if we choose a cutoff ≥ 0.30 mm of IMT/halo sign; 4 (10%) patients and 7 (4.4%) TA branches if the cutoff were > 0.34 mm.

Conclusions: The atherosclerotic disease can produce false-positive GCA diagnosis. Carotid IMT > 0.9 mm is associated with halo sign in TA. The IMT cutoff value for the diagnosis of GCA should be established.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6310

SATURDAY, 17 JUNE 2017

Diagnoses and imaging procedures
SAT0610 | TEMPORAL ARTERY ULTRASOUND IN THE DIAGNOSIS OF GIANT CELL ARTERITIS IN A COHORT WITH ELEVATED CLINICAL IMPRESSION

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Background: Giant cell arteritis (GCA) is the most frequent vasculitis in adulthood. The delay in diagnosis sets back treatment and can lead to serious consequences. Diagnosis is complex, and is followed by the classification criteria according to the American College of Rheumatology (ACR). This is an increasing interest on the utility of temporal artery ultrasound (TAUS) as a tool to evaluate inflammation on the vessel wall.

Objectives: to evaluate the utility of TAUS in GCA.

Methods: During 2016, 120 TAUS were carried out in 60 patients with clinical suspicion for GCA. The TAUS was carried to completion by rheumatologist with experience. The symptoms that lead to a TAUS was either one or more of these clinical scenarios: 1) cranial symptoms (recent onset headache, mandibular claudication, visual disturbances) 2) polyarticular syndrome 3) toxic or febrile unspecific syndrome 4) vertebrobasilar (VB) stroke. Demographic and laboratory data were collected, and a follow-up was done to learn the final diagnosis. As for TAUS, the “halo” sign was considered positive if an anechoic image surrounded the vessel was present, and measured >0.30 mm in both, longitudinal and transverse cuts. Other more unspecific signs as stenosis or occlusion were also registered. A temporal artery biopsy was performed whenever the physicians considered necessary, based on clinical criteria, every case in no more than 30 days.

Results: Fifty-two percent were women, mean age 76±7.8 years old. Mean laboratory parameters: eritrosedimentation rate 85±41.9 mm/h, C-reactive protein 77±80 mg/L, Haemoglobin 11.4±2.2 g/L, white blood count 10,228±3,520, platelet count 310,603±123,918. The symptoms that motivated requesting the TAUS were: cranial symptoms (62.2%), toxic, unspecific, febrile syndrome (44%), polyarticular syndrome (30%), VB stroke (5%). A temporal artery biopsy was carried out in 45% of patients (N=27); it was positive in 40.7%, negative in 40.7% and unspecific (given it reported an inflammatory histologic pattern, but without the characteristic giant cells) in 18.5%. From all 60 patients in whom a TAUS was performed, 36% were diagnosed with GCA, based on ACR criteria.

Patients with a final GCA diagnosis (n=22)

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>40.7%</td>
</tr>
<tr>
<td>Positive</td>
<td>22.7%</td>
</tr>
<tr>
<td>Positive</td>
<td>9%</td>
</tr>
<tr>
<td>Negative</td>
<td>9%</td>
</tr>
<tr>
<td>Non-conclusive</td>
<td>9%</td>
</tr>
<tr>
<td>negative</td>
<td>9%</td>
</tr>
</tbody>
</table>

The sensitivity and specificity for TAUS was 80% and 94% respectively, with a positive predictive value of 88.9% and a negative predictive value of 89.2%.

Conclusions: TAUS is a useful, non-invasive, fast, accessible tool for evaluating temporal arteries with a great diagnostic value.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6810

SAT0611 | INTIMA-MEDIA THICKNESS REFERENCE RANGES DEPICTING HALO SIGN FOR THE DIAGNOSIS OF LARGE VESSEL GIANT CELL ARTERITIS BY ULTRASOUND

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Background: Color duplex ultrasonography (CDU) is most promising tool for the assessment of large vessel giant cell arteritis (LV-GCA). There is a need to define ultrasound findings consistent with the diagnosis of GCA.

Objectives: We aimed to score intima-media thickness (IMT) reference ranges for LV-GCA in polish patients.

Methods: 214 patients suspected for GCA and evaluated with CDU were included in the study and followed up for min 9 months. Large vessel CDU, together with arthritis/non-arthritis categorization, were performed before or within 1 week after treatment initiation by a single physician. Vasculitis was defined as hypoechogenic homogenous, increase of IMT with distorted wall structure resulting in no clear intima-media structure, over long distance (not limited only to the place of arterial bifurcations). ROC curves were calculated.

Results: GCA was diagnosed in 81 patients, polymyalgia rheumatica (PMR) in 131 (characteristics – Table 1). Extracranial LV-GCA was diagnosed in 43 patients: axillary vasculitis in 23 patients, common carotid artery (CCA) — 24, subclavian — 18, superficial femoral — 11, brachial (all spreading per continuum from axillary artery) — 8. In 93 remaining patients other diagnosis was confirmed, and they served as non-GCA/PMR controls. Mean IMT in LV-GCA was significantly higher versus controls and isolated PMR (Fig. 1). IMT in GCA was not significantly influenced by gender, hypertension and smoking in contrast with IMT in controls. Proposed cut off values for IMT depicting vasculitis in GCA patients are presented in Table 2. 100% specificity for vasculitis (vs GCA without large vessel vasculitis) was reached with axillary IMT of 1.06 mm (62% sens.), subclavian — 1.35 mm (38% sens.), superficial femoral — 1.55 mm (60% sens.), CCA — 1.27 mm (22% sens.).

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Artery</th>
<th>Group</th>
<th>(N=81)</th>
<th>(N=50)</th>
<th>(N=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td></td>
<td>53 (65%)</td>
<td>37 (74%)</td>
<td>54 (65%)</td>
</tr>
<tr>
<td>Age (mean ± SD; min-max)</td>
<td></td>
<td>73 ± 9; 55-95</td>
<td>69 ± 9.5; 52-87</td>
<td>65±10; 44-89</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>53 (65%)</td>
<td>31 (62%)</td>
<td>44 (53%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td>36 (44%)</td>
<td>14 (28%)</td>
<td>29 (35%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>13 (16%)</td>
<td>6 (12%)</td>
<td>15 (18%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td>25 (31%)</td>
<td>12 (24%)</td>
<td>19 (23%)</td>
</tr>
<tr>
<td>Arterial calcifications</td>
<td></td>
<td>34 (42%)</td>
<td>11 (22%)</td>
<td>33 (40%)</td>
</tr>
<tr>
<td>Upper limbs claudication</td>
<td>4 (9.4%)</td>
<td>0 (0%)</td>
<td>1 (1.2%)</td>
<td>0.131</td>
</tr>
</tbody>
</table>

The sensitivity and specificity for TAUS was 80% and 94% respectively, with a positive predictive value of 88.9% and a negative predictive value of 89.2%.

Conclusions: We demonstrated that cut off values may discriminate between GCA and its mimics as well as between presence and lack of vasculitis in different arteries in GCA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4139

SAT0612 | THE USE OF 18F-FDG-PET IN THE DIAGNOSIS OF POLYMYALGIA RHEUMATICA (PMR) – A PROSPECTIVE STUDY OF 99 PATIENTS SUSPECTED OF PMR

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Background: Previous studies have shown that the majority of patients with polymyalgia rheumatica (PMR) have increased fluorodeoxyglucose (FDG)-uptake around the shoulders, hips and processes of the cervical and lumbar spine on positron emission tomography (PET) (1). The specificity of these findings for PMR is not known.

Objectives: To determine the specificity and sensitivity of FDG-PET findings for the diagnosis of PMR.

Methods: A prospective monocentric study in a tertiary care centre. All patients underwent FDG-PET scanning before treatment with glucocorticoids was started. The clinical suspicion of PMR was quantified by the treating physician on a scale from 1 to 5. FDG-uptake was scored visually in 12 articular regions (cervical spine, processes, lumbar spinous processes, left and right sternoclavicular joint, left and right ischial tuberosity, left and right greater trochanter, left and right hip and left and right shoulder) (score 0–2) and a total skeletal score was calculated reflecting the FDG-uptake in these 12 articular regions. ROC analysis was performed to determine the optimal clinical and total skeletal score for diagnosing PMR. The golden standard for a diagnosis of PMR was the judgment of an experienced clinician after at least six months of follow-up.

Results: 99 consecutive patients with a possible clinical diagnosis of PMR were included in this study. Sixty-seven patients were finally diagnosed with PMR while 32 patients got another diagnosis. A clinical score of 4 or more had a sensitivity
Conclusions: Our results demonstrate that patients with gout and aHU without clinically evident cardiovascular disease have a high prevalence of subclinical atherosclerosis. Disease duration and levels of uric acid are independent factors related with increased cIMT in gout and aHU respectively. These results support the importance of screening for CV risk and to include carotid ultrasound in CV prevention strategies in these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6363

SAT0613 HIGH PREVALENCE OF SUBCLINICAL ATHEROSCLEROSIS IN GOUT AND ASYMPTOMATIC HYPERURICEMIA: A STUDY BASED ON CAROTID ULTRASOUND


1 Division of Neuroscience; 2 Division of Musculoskeletal and Rheumatic Diseases; 3 Rheumatology Department, Instituto Nacional de Rehabilitación; 4 Rheumatology Department, Instituto Nacional de Cardiología Ignacio Chavez; 5 Epidemiology and Social Medicine Department, Instituto Nacional de Rehabilitación, Ciudad de México, Mexico

Background: Accelerated atherosclerosis is known in gout. Hyperuricemia is considered an independent risk factor for cardiovascular (CV) disease. Evidence supporting both proatherogenic and prothrombotic states in HU is also published

Conclusions: To determine the prevalence of increased cIMT, as sign of subclinical atherosclerosis, by an automated US method, and the associated risk factors in patients with gout and asymptomatic hyperuricemia (aHU)

Methods: 138 patients with gout, 105 with aHU and 99 age and sex matched healthy controls were enrolled. For all patients were recorded: clinical history, disease duration, smoking, ischemic heart disease, comorbidities (diabetes mellitus, high blood pressure, dyslipidemia, renal insufficiency, obesity), and current therapy. ESR and serum CRP, total and HDL cholesterol, triglycerides, glucose, creatinine and uric acid were recorded. Patients with history of CV and cerebrovascular events or autoimmune diseases were excluded.

Results: A total of 684 common carotids were assessed. The prevalence of increased cIMT was 47.1%, 47.6% and 1% in patients with gout, aHU, and control group, respectively. The final adjusted logistic regression for patients with gout showed that time of disease progression (OR =0.79, 95% CI 0.66–0.95) and previous smoking (OR =0.32, 95% CI, 0.10–0.97) were associated with cIMT detected abnormalities in aHU. No significant correlation was found with the other variables. No differences in US findings were found between gout and aHU (p=0.936). There was a significant difference in cIMT in gout versus control (p=0.0001) and aHU versus control (p=0.0001).

Conclusions: To compare the ultrasound-detected abnormalities namely double contour sign (DCS) and hyperechoic aggregates (HAGs) at knee and first metatarsophalangeal (1st MTP) joint verses six sites (knee joint, 1st MTP joint, radiocarpal joint, patellar tendon and triceps tendon) in patients of gout.

Methods: Forty seven gout and fifty controls (serum uric acid >7mg/dl) with age more than 18 years were included in this study. DCS was looked for at three articular cartilage sites (first metatarsal, tibiotalar and femoral condyle) whereas HAGs were looked for at one joint site (radiocarpal joint) and two tendon sites (patellar tendon and triceps tendon).

Results: We found sensitivity, specificity, positive predictive value, negative predictive value and positive likelihood ratio of two joint areas (knee and 1st MTP) ultrasound findings for gout were 87.2%, 84%, 83.7%, 85.6% and 5.5 respectively. Similar sensitivity, specificity, positive predictive value, negative predictive value and positive likelihood ratio were observed with 6 sites ultrasound findings. Amongst controls 17.5% were found to have these abnormal ultrasound findings by both two joint area and 6 sites exams.

Conclusions: Screening of two joint areas (knee and 1st MTP) has similar sensitivity, specificity and positive likelihood ratio as compared to six sites in diagnosing gout. While utilizing lesser time in examination.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1680
Background: Articular involvement is a frequent and invalidating manifestation in patients also affected by Systemic Lupus Erythematosus (SLE) ranging from arthralgia to erosive arthritis. Bone erosions are far less common in SLE but require a different management and may display a distinct pathogenesis. Musculoskeletal ultrasonography (MSUS) has proven useful in the assessment of inflammatory arthritis [1] and it is now known that MSUS is more sensitive than radiography in detecting bone erosions.

Objectives: We aimed at analyzing, in a large monocentric cohort of SLE patients who suffered from arthritis, the relationship between 31 polymorphisms in 18 genes previously associated with SLE or other autoimmune/inflammatory arthritis [1] and the presence of bone erosions detected by MSUS.

Methods: Consecutive SLE patients who complained arthritic involvement (defined by 1997 ACR criteria, i.e., ≥ 2 joints with tenderness, swelling or effusion) were enrolled. Patients RF+ve and/or anti-CFP+ve were excluded. Thirty-one SNPs (AID; myositis: n=20; SjS: n=21; rheumatoid arthritis RA n=36; systemic sclerosis SSC n=39; and 77 healthy control samples). Prototype MSUS Erosions (yes/no) 15/80 15.8

Results: Clinical and laboratory features of the 95 enrolled patients are described in table.

The presence of MSUS-detected erosions was demonstrated in 15/95 (15.8%) patients, with a mean±SD of 0.44±1.34. Bone erosions were more frequently observed at iliac metacarpophalangeal joint of the hands (29.4%), followed by the V metatarsophalangeal joint of the feet (16.1%). An association was found between anti-dsDNA and the presence of bone erosions (P=0.009, Fisher’s exact test); indeed, all the 15 patients (100%) with bone erosions were anti-dsDNA positive vs 54/80 (67.5%) of those without erosions. After Bonferroni correction, IL-23R rs11803505 was found to be associated with the presence of MSUS-detected bone erosions both at genotypic (P<0.045) and at the allelic level [P<0.022, OR=8.27 (95% CI 1.02–66.90)]. The association of bone erosions with anti-dsDNA and the presence of bone erosions (P=0.009, Fisher’s exact test); indeed, all the 15 patients (100%) with bone erosions were anti-dsDNA positive vs 54/80 (67.5%) of those without erosions. After Bonferroni correction, IL-23R rs11803505 was found to be associated with the presence of MSUS-detected bone erosions both at genotypic (P<0.045) and at the allelic level [P<0.022, OR=8.27 (95% CI 1.02–66.90)]. The association of bone erosions with anti-dsDNA and the presence of bone erosions (P=0.009, Fisher’s exact test); indeed, all the 15 patients (100%) with bone erosions were anti-dsDNA positive vs 54/80 (67.5%) of those without erosions. After Bonferroni correction, IL-23R rs11803505 was found to be associated with the presence of MSUS-detected bone erosions both at genotypic (P<0.045) and at the allelic level [P<0.022, OR=8.27 (95% CI 1.02–66.90)]. The association of bone erosions with anti-dsDNA and the presence of bone erosions (P=0.009, Fisher’s exact test); indeed, all the 15 patients (100%) with bone erosions were anti-dsDNA positive vs 54/80 (67.5%) of those without erosions. After Bonferroni correction, IL-23R rs11803505 was found to be associated with the presence of MSUS-detected bone erosions both at genotypic (P<0.045) and at the allelic level [P<0.022, OR=8.27 (95% CI 1.02–66.90)].

Conclusions: Our study is the first reporting a contribution of IL-23R gene to detecting bone erosions. As none of the traditional AABs has sufficient sensitivity to achieve diagnosis of SLE, current testing is based on measuring multiple AAB assays either in parallel or serial. We have recently identified novel AABs in SLE, which hold promise for improving diagnostic testing of SLE [1]. We have developed quantitative ELISA-prototypes for five new AABs, which were tested in combination with traditional AABs.

Objectives: The objectives of this study were to evaluate the diagnostic value of novel AABs and to screen for an optimized combination of novel and traditional AABs using logistic regression to increase the diagnostic accuracy of SLE testing.

Methods: Serum samples were obtained from 156 SLE patients with European ancestry at the rheumatology department of the Heinrich-Heine University (Düsseldorf, Germany), and Hannover Medical School (Hannover, Germany). SLE samples were compared against 126 samples from autoimmune diseases (AID; myositis: n=20; Sjögren’s syndrome (SjS): n=31; rheumatoid arthritis (RA) n=36; systemic sclerosis (SSc) n=39); and 77 healthy control samples. Prototype AID was based on five novel antibodies described in [1]. Traditional diagnostic AABs were measured using IVD ELISAs and included: SSA/Ro60, SSA/Ro52, La/SSB, Sm, RNP, dsDNA, Sc70, CENPB, Jo-1, CCP, phospholipid and dsDNA. Optimized marker combinations of new and traditional markers were tested using logistic regression and receiver operating curve analysis (ROC).

Results: When comparing 156 SLE patients with 203 control samples, the area under the curve (AUC) of the five novel SEL ELISAs ranged from 0.63 to 0.75. A cut-off was set at a specificity of 95% and yielded a sensitivity ranging from 13.5% to 21.2% for the five novel AABs. Sensitivity and specificity of novel ELISAs was comparable to traditional ELISAs, which was in this cohort for anti-dsDNA 35% and 97%, anti-Sm 15% and 97%, and anti-RiboP 26% and 97%. A logistic regression model was used to combine the results of multiple tests. Compared to a logistic regression with traditional assays, a logistic regression with novel assays achieved higher sensitivity by pertaining high specificity. The logistic regression model based on a multivariable IVD assay with ten extracted nuclear antigens (ENA) yielded an AUC of 0.87 and a sensitivity of 58% at a specificity of 95%. By contrast, the optimal combination of traditional and novel ELISAs achieved an AUC of 0.92 and a sensitivity of 75% at a specificity of 95%.

Conclusions: This study demonstrates the feasibility of test results of novel and traditional AABs using logistic regression to increase the diagnostic accuracy for SLE. Further studies are required to assess the impact of different ethnicities on marker selection and algorithm performance.

References:


specificity of 85%, positive predictive value of 86%, negative predictive value of 89% and diagnostic odds ratio of 51. UTS was positive in 2 patients with HIV infection and one patient with sarcoidosis. Patients with pSS had significantly higher UTS than patients with systemic diseases (median UTS 27 vs. 10, p<0.001) and patients of the various subgroups (p<0.05; Fig).

Figure: UTS in patient (sub)groups. *p<0.001, **p<0.05. Black horizontal lines indicate median values. The intermittent horizontal line shows the cut-off point. The intermittent black vertical line separates the two major patient groups (pSS vs. systemic diseases) from the subgroups of patients with sarcoidosis, amyloidosis, HIV and HCV infection.

Conclusions: This pilot study indicates that SGUS has a high diagnostic accuracy to discriminate pSS from associated systemic diseases with salivary gland involvement. A minority of HIV and sarcoidosis patients, however, may show SGUS findings mimicking pSS.

References:

Disclosure of Interest:
None declared

SAT0619 ANKLE EVALUATION IN ACTIVE RHEUMATOID ARTHRITIS BY ULTRASOUND: A CROSS SECTIONAL STUDY

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1Rheumatology, Sohag University Faculty of Medicine; 2Rheumatology, Qena faculty of medicine, Sohag, Egypt

Background: Ankle joint evaluation is underestimated in many clinical and sonographic scores used for evaluation and follow-up of rheumatoid arthritis (RA) patients. Moreover, sonographic scores which included the ankle joint had no agreement on examination parameters. More effort is needed to detect the value of the ankle joint examination in RA and also a description of the earliest and the most frequent ultrasonographic signs that should be considered in ankle assessment (1).

Objectives: detection of ankle affection by ultrasound (US) in active RA and correlated findings with disease duration, DAS28-ESR 28 score and rheumatoid factor (RF).

Methods: 126 ankle joints and tendons of 63 active RA patients, aged above 18 years old were included in the study. US examination was done to the tibiotalar and talonavicular joints for synovitis and/or effusion on Greyscale (GS) mode and power doppler (PD). The anterior, lateral and posterior ankle tendons were examined for tenosynovitis and tendinosis.

Results: The mean age and ± standard deviation were 35.1±8.3 with the female-to-male ratio 2:1. The mean disease duration was 22.7±6.6 months. The mean DAS28-ESR 28 score was 3.05±0.66. The most frequent pathologies detected were tenosynovitis of the flexor, extensor or peroneal tendons (found in 30.2% of the affected ankles); followed by synovitis of the tibiotalar and talonavicular joints (18.3%); next was erosion (8.7%) and lastly tendinosis (4%). The earliest sonographic signs were tenosynovitis, followed by synovitis, erosion, and lastly tendinosis.

Conclusions: It can be stated that ankle evaluation should be considered more in RA assessment. The tibial anterior and posterior tendons, the tibiotalar and talonavicular joints were the commonest and most frequent sites to be involved in the ankle. Tenosynovitis appears earlier than synovitis. DAS28-ESR score was correlated to synovitis and tenosynovitis but not to erosion. Bilaterality and erosion were correlated with disease duration. RF positivity has a positive correlation with positive US findings in the ankle region.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4597

SAT0620 POTENTIAL ROLE OF METACARPOPHALANGEAL JOINTS ULTRASOUND IN THE DIFFERENTIAL DIAGNOSIS BETWEEN EARLY RHEUMATOID ARTHRITIS AND EARLY SPONDYLOARTHITIS

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Background: Several studies have demonstrated that musculoskeletal ultrasound (MSUS) is more sensitive in diagnosing arthritis when compared to clinical examination; although, as underlined in a recent review, still remains controversial whether it can improve substantial discriminatory value in an early arthritis (EA) setting. (1) in 2011 Gutierrez M. et al. published preliminary data on high frequency of perionen extension tendon inflammation in Psoriatic arthritis (PsA) patients, suggesting a relevant potential role for US in differential diagnosis between Rheumatoid Arthritis (RA) and PsA at metacarpophalangeal (MCP) joints level and recommending additional research in order to confirm these data (2).

Objectives: To compare MSUS findings between early RA and early Spondyloarthritis (SpA) patients at MCP joints level.

Methods: From a consenting cohort of EA patients presenting to our Rheuma-
VASCULARIZATION IN RHEUMATOID ARTHRITIS

QUANTITATIVE DOPPLER SCORING SYSTEMS FOR THE ASSESSMENT OF SYNOVIAL PATHOLOGICAL VASCULARIZATION IN RHEUMATOID ARTHRITIS

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Objectives: To compare power Doppler (PD) vs colour Doppler (CD) semiquantitative and quantitative scoring of synovial vascularization (RA) and to evaluate the relationship between semiquantitative and quantitative scores in patients with rheumatoid arthritis (RA).

Methods: One hundred RA patients underwent B-mode, PD, and CD assessments of 12 joints at two European centres. Each joint with synovial hypertrophy detected on B-mode was semiquantitatively scored (0–3) for PD (SPD score) and CD (SCD score) synovial signal. PD and CD synovial signal were also quantitatively scored (0–100%) (PDQ and QCD scores, respectively) using a software for counting the colour fraction.

Results: We found SH in 184 joints. SPD and SCD agreed in 92.3% (95% CI: 88.4–96.2%) of paired scores, with Kendall rank correlation coefficient tau=0.95. Significant differences were between marginal distributions of SPD and SCD were not found (p=0.565). PDQ and QCD scores were highly correlated (Pearson’s coefficient=0.70) but Bland-Altman plot showed insufficient agreement, being the QCD scores systematically slightly higher than the QPD scores. The distribution of QPD and QCD values between SPD and SCD scores, respectively, showed significant differences between grade 0 and grade 1 (p<0.001), and grade 2 and grade 3 (p=0.042 and p=0.007, respectively) but not between grade 1 and 2 (p=0.154 and p=0.150, respectively). Significance: SPD and SCD scores were concordant and QPD and QCD scores highly correlated although were not concordant. There was consistency between SPD and SCD moderate and severe scores and QPD and QCD scores. There was an overlapping between SPD and SCD mild and moderate scores regarding PDQ and QCD scores.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5658

SAT0623

CORRELATIONS BETWEEN CLINICAL, ULTRASOUND AND DISEASE ACTIVITY SCORES OF PERIPHERAL ENHESITIS IN SPONDYLOARTHRITIS (SPA)

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Objectives: To look for correlations between clinical, ultrasound (US) and disease activity scores of peripheral enthesitis in an SPA cohort.

Methods: A prospective study of all SpA patients seen at EHS Ben Aoun, over a period from January 2015 to April 2016. Seventeen enthesal sites were assessed bilaterally: insertions of supra-spinatus, infra-spinatus, sub-scapular, medial and lateral epicondylar, triceps brachialis, gluteus minimus and midius, quadriapital, proximal and distal insertion (patellar ligament, medial and lateral collateral ligament), Achilles tendon and plantar aponeurosis. Peripheral enthesitis was assessed by the following clinical scores: Enthesitis Peripheral Score (PES= Sum of symptomatic peripheral entheses sites on clinical examination), Visual Analog Scale of peripheral enthesitis (VAS), Spondylarthritides Research Consortium of Canada score (SPARCC) as well as the following US enthesitis scores: Acute Enthesitis score (Sum of acute enthesitis US scores for each site), Global Enthesitis score (Sum of acute and chronic US scores of entheses), Doppler signal Enthesitis score (Sum of Doppler signal scores less than 2mm from cortical bone for each site), Madrid Sonography Enthesitis Index (MASEI), Simplified Echographic Score (SES) with assesss only the Achilles
tendon and the plantar aponeurosis. Correlations between clinical, activity and US scores were investigated by SSPSS software.

**Results:** A total of 208 patients were included. At examination 88.9% had an active disease and 64.4% of SpA were taking NSAIDs. 62.40 entheses were assessed clinically and with US. A positive correlation was found between activity scores and two clinical scores (RAMRIS and SPARCC). A good correlation was found between Activity scores and all US scores on one hand and with SPARCC scores and PES scores on the other hand. For US and clinical correlations, only Doppler scores was positively correlated with 2 clinical scores (SPARCC and PES scores), Acute Enthesitis score was correlated with the PES scores. No correlation was found between clinical scores and MASEI or SES scores. No correlation was found with the mean enthesitis VAS scores.

### Table 1. Correlations between clinical scores and activity scores with ultrasound scores

<table>
<thead>
<tr>
<th>Scores</th>
<th>PES</th>
<th>VASm Enthesis</th>
<th>SPARCC</th>
<th>ASDAS-vs</th>
<th>ASDAS-crp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Enthesitis</td>
<td>r: 0.14</td>
<td>r: -0.03</td>
<td>r: 0.16</td>
<td>r: 0.43</td>
<td>r: 0.52</td>
</tr>
<tr>
<td>Chronic Enthesitis</td>
<td>r: 0.04</td>
<td>r: 0.72</td>
<td>r: 0.07</td>
<td>p: &lt;0.001</td>
<td>p: 0.001</td>
</tr>
<tr>
<td>Doppler Enthesitis</td>
<td>r: 0.01</td>
<td>r: 0.15</td>
<td>r: 0.06</td>
<td>r: 0.19</td>
<td>r: 0.22</td>
</tr>
<tr>
<td>Global Enthesitis</td>
<td>r: 0.15</td>
<td>r: -0.08</td>
<td>r: 0.13</td>
<td>r: 0.43</td>
<td>r: 0.52</td>
</tr>
<tr>
<td>MASEI</td>
<td>r: 0.03</td>
<td>r: 0.24</td>
<td>r: 0.07</td>
<td>p: &lt;0.001</td>
<td>p: 0.001</td>
</tr>
<tr>
<td>SES</td>
<td>r: 0.02</td>
<td>r: 0.09</td>
<td>r: 0.01</td>
<td>p: &lt;0.001</td>
<td>p: 0.001</td>
</tr>
</tbody>
</table>

### Table 2. Correlations between clinical scores and activity scores

<table>
<thead>
<tr>
<th>Scores</th>
<th>PES</th>
<th>VASm Enthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASDAS-vs</td>
<td>p: &lt;0.001</td>
<td>r: 0.27</td>
</tr>
<tr>
<td>ASDAS-crp</td>
<td>p: &lt;0.001</td>
<td>r: 0.03</td>
</tr>
</tbody>
</table>

**Conclusions:** All US enthesitis scores were correlated with disease activity scores but those correlated with the clinical symptoms and not with its intensity were: Acute Enthesitis Scores, Global Enthesitis Scores and especially Doppler signal Enthesis Scores.

**Disclosure of Interest:** None declared

**DOi:** 10.1136/annrheumdis-2017-eular.1968
showed that joint inflammation is common in ochronotic patients, associated in some cases with peripheral enthesis involvement confirming previously published data (1). The prevalence and the characteristics of the inflammatory manifestations should be further studied in larger cohorts of patients as they could play an important role in the joint damage process in these patients and provide a rationale for the use of new drugs.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6678

SAT0526 METACARPOPHALANGEAL JOINT SWELLING IN PSORIATIC ARTHRITIS: WHAT DOES IT MEAN?

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Background: Clinical metacarpophalangeal joint (MCPj) swelling is a frequent finding in psoriatic arthritis (PsA). It is assumed to be caused by intra-articular synovitis (IAS). However, ultrasound (US) have also demonstrated in PsA peritenon inflammation of the extensor digitorum tendon (PTI). To date the data about the significance of this two lesions (IAS and PTI) in MCPj swelling are sparse.

Objectives: Our objective was to explore PTI and IAS as the cause of clinical MCPj swelling in PsA patients.

Methods: 27 consecutive non selected PsA patients, fulfilling CASPAR criteria, with clinical involvement of at least one 2nd to 5th MCPj were included. A MyLab 70 XVG machine, Easote, Genova, Italy, with a greyscale (GS) 13 MHz probe, and a 7.1 MHz power Doppler (PD) frequency (PRF 750 Hz, Gain 60) was used. Videos (3–5 sec) of each MCPj 2nd to 5th of both hands in transversal and longitudinal views were obtained for central reader analysis, scoring US as presence or absence in GS and PD of: 1) PTI (defined as an hypoechoic swelling of the soft tissue surrounding the extensor tendon at MCPj level with or without PD) and 2) IAS (OMERACT definition). US pathology for each joint and lesion was defined as at least three of five central readers having the same score. SPSS analysis was performed for frequencies, percentage of agreement and Cohen's Kappa test.

Results: 27 PsA patients with a mean (SD) age of 56 (11) years and disease duration 10% (17) months were included. Isolated peripheral involvement was present in 21 patients (78%) and 6 (22%) had both axial and peripheral affection. Mean (SD) CRP level was 8.3 (8.2) mg/l and ESR 21.9 (19.3) mm. The mean DAS28 ESR was 3.88 (1.23). Psoriasis involvement included skin and nails in 15 (55.5%) of the patients.

Table 1. US findings versus Clinical joint swelling

<table>
<thead>
<tr>
<th>Agreement n (%)</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any US lesion (vs. clinical swelling)</td>
<td>16/216 (77.3%)</td>
</tr>
<tr>
<td>Any grey scale lesion (vs. clinical swelling)</td>
<td>16/216 (73.8%)</td>
</tr>
<tr>
<td>Any power Doppler lesion (vs. clinical swelling)</td>
<td>16/216 (78.2%)</td>
</tr>
<tr>
<td>Grey scale IAS (vs. clinical swelling)</td>
<td>16/216 (78.8%)</td>
</tr>
<tr>
<td>Power Doppler IAS (vs. clinical swelling)</td>
<td>17/216 (81.9%)</td>
</tr>
<tr>
<td>Grey scale PTI (vs. clinical swelling)</td>
<td>17/216 (81.0%)</td>
</tr>
<tr>
<td>Power Doppler PTI (vs. clinical swelling)</td>
<td>17/216 (81.5%)</td>
</tr>
</tbody>
</table>

Conclusions: Our study identifies two different US lesions (IAS and PTI) causing clinical joint swelling. PTI is near as frequent as IAS as a cause of MCPj swelling, and future studies are necessary to explore the added value of assessing PTI for prognosis or treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1437

SAT0627 MUSCLE BIOPSY: MASTER ROLE IN DIFFERENTIAL DIAGNOSIS IN PATIENTS WITH SUSPECTED MYOPATHY


Background: The muscle biopsy may be a fundamental technique in the suspicion of myopathy, with high specificity to distinguish between normal or abnormal muscle tissue. It is associated with clinical and laboratory findings, the muscle biopsy has an important role to a more accurate diagnosis.

Objectives: To evaluate the usefulness and safety of muscle biopsies performed in a Rheumatology Unit in patients with suspected myopathy.

Methods: Retrospective analysis of the clinical charts of patients submitted to muscle biopsy between January 2010 and December 2016 at our Rheumatology Unit. Demographic, clinical, laboratory, electromyographic and histological data were collected. The histological study was performed in a Neuropathology Specialized Unit.

Results: A total of 46 patients, 19 men and 27 women, with a mean age of 53.3±11 years, were evaluated. Clinical manifestations included muscle weakness, myalgia and decreased muscle strength. Most patients also had increased muscle enzymes, particularly creatine kinase, but in a patient with generalized muscle atrophy, muscle enzymes were overall diminished. Of the 46 biopsies, 12 (26.1%) did not show alterations, 8 (17.4%) showed nonspecific alterations and only 1 biopsy was not conclusive because the sample was inadequate. In 4 patients, the histological features did not present specific characteristics of a myopathy, but revealed a preferential atrophy of type 2 fibbers, usually associated with prolonged corticosteroïd therapy. Among the others, 9 (19.6%) were compatible with inflammatory myopathies, namely polymyositis (6), dermatomyositis (1), inclusion body myopathy (1), and localized nodular myositis (1). In the latter case, the patient had a different clinical presentation, with intermittent episodes of pain, oedema and flushing of different muscle groups. In addition, 5 metabolic myopathies (2 McArdle’s diseases and 3 non-specific metabolic disorders), 2 muscular dystrophies (1 Becker’s muscular dystrophy and 1 dystrophinopathy), 1 suspected case of myotonic dystrophy and 1 myopathy associated with statins use were diagnosed. In a patient with muscle weakness and prior diagnosis of systemic vasculitis, the histology showed a chronic inflammatory process with no specific alterations. In the patient with overall decrease in muscle enzymes, the biopsy revealed neurogenic atrophy, without inflammatory infiltrates. Overall, the results of electromyography (EMG) did not correlate with the histological findings, because EMG identified alterations both in cases with histologically compatible inflammatory myopathies and in cases without histological pathology. On the other hand, EMG did not reveal any changes in some of the metabolic myopathies. Muscle biopsies were performed mainly in the deltoid muscle. There were no relevant immediate or late complications with this technique.

Conclusions: Although muscle biopsy is an invasive technique, it is a safe technique and allows the differential diagnosis between the various myopathies, which is fundamental to an appropriate treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5069

SAT0628 INCREASE OF CORTICAL MICRO-CHANNELS (COMICS) AS A NEW FEATURE OF STRUCTURAL DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Bone damage in rheumatoid arthritis (RA) typically emerges at certain anatomical hotspots corresponding to the so-called "bare area", an intra-articular region between the cartilage and the insertion site of the joint capsule (1,2). We hypothesized that this region exhibits certain micro-anatomical properties, which facilitates the emergence of bone erosions.

Conclusions: Our study identifies two different US lesions (IAS and PTI) causing clinical joint swelling. PTI is near as frequent as IAS as a cause of MCPj swelling, and future studies are necessary to explore the added value of assessing PTI for prognosis or treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.05069
OBJECTIVES: To find the micro-structural correlate of the origin of bone erosions in the bare area of the human joint

METHODS: Bare areas of human joints were analyzed for early microstructural changes by in-vivo high-resolution peripheral computed tomography (HR-pQCT). First, bare areas were exactly defined by scanning 6 cadaveric hands for localization of the bone lesions found in the cadaveric hand by HR-pQCT were additionally by super-resolution ex vivo micro-CT (μCT40). Then, number and distribution of the type of bare area bone loss found in cadaveric study were analyzed in a cohort of 105 healthy individuals and 107 anti-citrullinated peptide (ACPA) positive RA patients with similar sex and age distribution.

RESULTS: HR-pQCT combined with adaptive thresholding allowed the definition of a new type of bone lesions in the bare areas of the human joint termed ‘COMIC’ standing for ‘cortical micro-channel’. Their existence in the bare area was additionally validated by micro-CT (μCT40) in 1 RA patients. RA patients showed significantly (p<0.001) more CoMiCs (112.9±54.7/joint) than healthy individuals (75.2±41.9/joint) with 20-49 years old RA patients exhibiting similar CoMiC numbers as observed in over 65 years old healthy individuals. Importantly, CoMiCs were found in RA patients already very early in their disease course with enrichment in the erosion-prone radial side of the joint.

Conclusions: CoMiCs represent a new structural feature of the joint, which is characteristic for the bone of the bare area. COMICs at low level are found in young healthy individuals but then they significantly increase with age, and particularly with RA. COMICs develop much earlier and much more pronounced in RA patients than in healthy individuals and therefore represent an interesting new early indicator for erosion development in ACPA positive RA patients.

REFERENCES:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3730

SAT0629
ELECTRODIAGNOSTIC VS ULTRASONOGRAPHY: WHICH ONE IS BETTER TO CONFIRM DIAGNOSIS OF ULNAR NEUROPATHY AT ELBOW?

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Background: Ulnar neuropathy at the elbow is the second most common compression neuropathy preceded by carpal tunnel syndrome. Although this diagnosis has been traditionally confirmed by electrodiagnosis (EDX), ultrasonography (US) is a re-emerging alternative method which can also evaluate the cubital zone anatomy. This study determines the maximum amount of US sensitivity and specificity by assessing different sonographic parameters and evaluates consistency and diagnostic value of the best US method in compare with EDX.

Methods: We included 66 participants (32 elbows of patient and 34 normal elbows) and performed physical exam, US and EDX for both groups. Patients were classified into four severity grades using EDX criteria. The parameters of US were cross sectional area (CSA) of ulnar nerve at three levels: medial epicondyle (CSA med), 2cm distal (CSA dist) and 2cm proximal (CSA prox) to the motor in young healthy individuals would be able to evaluate consistency between CSA med and severity grade (p-value=0.034) and the second correlation was between CSA med and CSA dist with a cross-elbow nerve conduction velocity (NCV) (p-value=0.01 and 0.02, respectively). Finally we assessed US diagnostic value as it showed AU-ROC =0.871, that means a very good coverage for an alternative diagnostic method. Also our results showed specificity of 80% and sensitivity of 84% for US in the CSA med cut-off point <9mm² for diagnosis of ulnar nerve entrapment at elbow.

Conclusions: Based on these results we can conclude that US is a highly sensitive and specific method to diagnose ulnar neuropathy at elbow and can be used as an alternative and complementary method in diagnosis of ulnar neuropathy at elbow in particular when EDX is not available. However it could not be still a definitive and substitute mutually exclusive method to EDX in diagnosis of ulnar neuropathy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1694

SAT0630 EXTRACARTILAGEOUS MUSCULOSKELETAL INVOLVEMENT IN JUVENILE IDIOPATHIC ARTHRITIS: CLINICAL AND ULTRASONOGRAPHIC FINDINGS

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Background: In Juvenile Idiopathic arthritis (JIA), musculoskeletal ultrasound (USUS) has been proven to be more sensitive than clinical evaluation in detecting articular synovitis. Nevertheless, many studies report a variable percentage of clinically active joints, that are judged normal by ultrasound examination. In absence of a feasible and reliable gold standard for pediatric synovitis (histology or MRI), this point may weaken the confidence in ultrasound, that is nevertheless perceived as an interesting tool, in the management of JIA.

Objectives: This preliminary study investigates the possibility that sometimes the clinically detected synovitis could be missed by ultrasound, because of its extra-articular localization.

Methods: 43 consecutive children affected by JIA underwent separated clinical and USUS assessment, in the same day. Patients were followed up in a pediatric Rheumatology Unit. The following clinical data were collected: age, sex, disease duration, subset of JIA, ongoing therapy, previous therapy, disease activity. By USUS, the synovitis was investigated bilaterally, both in gray scale and power Doppler, in the MCP and subtalar joints, wrists, knees, ankles, in the flexor and extensor tendons of the wrist and hand, in the anterior, medial and lateral tendons of the ankle, in the synovial bursae of knee and ankle. The possible involvement of the entheses was also investigated. The definition of ultrasonographic synovitis was based on the preliminary OMERACT definitions of synovitis in children. The inter and intra observer reproducibility of the MSUS examination was tested, independently, both between two operators and through a second assessment of the stored images.

Results: 43 children affected by JIA were recruited, in the outpatient clinic of the Regina Margherita Pediatric Hospital of Torino, Italy. They were 9 boys and 34 girls, median age 7.7 (IQR 5.5–10.1), 27 oligoarticular, 11 polyarticular, 4 psoriatic arthritis, 1 undifferentiated arthritis. The median disease duration was 44 months (IQR: 20.5–61.5), 20 patients in remission, 23 with active disease. 774 joints, 1548 synovial sheaths, 430 entheses and 258 synovial bursae were assessed. The physical examination detected inflammation in 54 joints, 33 tendons, 0 entheses,
0 bursae. Ultrasound abnormalities were found in 62 joints, 73 tendons, 8 bursae, 0 entheses. Overall physical examination and US showed good concordance even if MSUS was more sensitive especially in detecting extra-articular locations.

**Conclusions:** If the extra-articular locations of synovitis are taken in consideration during the ultrasound examination, there is a good sensitivity of MSUS and a better diagnostic clinical skill than the clinical examination. Between clinical and MSUS assessment of JIA, MSUS seems more accurate than physical assessment in detecting the exact position of the inflamed synovial membrane in each anatomical location (joint, synovial sheath, synovial bursa). It could be helpful not only for better addressing the injective procedures, but also for a global quantification of the synovitis (both intra and extra-articular), even if the exact clinical meaning of these ultrasound findings is still unknown, in terms of response to treatments and prognosis.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6900

### SAT0632

#### IMPACT OF LUMBAR SPINE MORPHOLOGY (SCOLIOSIS) ON EARLY Spondylodiscitis Pattern (THE IMPALA-DESIR STUDY)

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**Objectives:** To evaluate the impact of scoliosis on both clinical presentation and lumbar imaging of early inflammatory back pain suggestive of spondyloarthritis.

**Methods:** The DESIR cohort is a prospective longitudinal cohort study of adults aged 18–50 with inflammatory back pain (IBP) >3 months, <3 years. Baseline lumbar X-Rays of patients included in DESIR cohort were read by two central blinded reader (and a rheumatologist spine specialist in case of discrepancy) for presence or not of scoliosis (defined as a Cobb angle >10° and a Nash Moe grade >1). Associations between scoliosis and baseline clinical variables, presence of X-Rays (New York) and MRI (ASAS and MORPHO proposal definition) sacroiliitis, presence of spinal signs of spondylarthropathy (mSASSS, BASRI-total, SPARCC scores), presence of spinal degenerative MRI signs on X-rays (yes or no) and MRI (presence of Modic abnormalities, Pfirrmann score, Canal stenosis, Extrusion, High intensity zone Facet osteoarthritis) according to central reading (two readers) and axSpA diagnostic confidence (according to local clinician’s confidence on a 0–10 visual analogical scale) were assessed by univariate analysis using the chi-square test (or Fisher’s exact test where appropriate) and the Mann-Whitney test. Adjustment for multiple testing was performed according to Bonferroni method.

**Results:** 675 patients (47.1% men, mean age of 33.6 years, 89.6% had lumbar pain, 63% fulfilling ASAS criteria) were studied. The mean Cobb angle was 3.2° (± 4.8) and 49/675 (7.3%) patients had lumbar scoliosis. The only significant difference was the lumberosal sagittal balance. Indeed, scoliotic patients had greater lumbar lordosis (57.8° versus 50.9°; p < 0.001) than non-scoliotic. About MRI findings, spinal degenerative manifestations were very scarce in both groups. The major part of degenerative changes was in the two last lumbar discs and vertebrae, without significant difference between scoliotic and non-scoliotic patients.

**Conclusions:** Scoliotic patients with inflammatory back pain suggestive of spondyloarthropathy do not have more lumbar degenerative lesions than non-scoliotic patients, nor difference of clinical presentation, but they have greater lumbar lordosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3515

### SAT0631

#### INTER-OBSERVER AND INTRA-OBSERVER RELIABILITY OF THE OMERACT ULTRASONOGRAPHIC (US) CRITERIA FOR THE DIAGNOSIS OF CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD) AT THE METACARPAL, PHALANGEAL, CARPAL, WRIST, ACROMION-CLAVICULAR (AC) AND HIP JOINTS

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**Background:** The OMERACT US subtask force “US in CPPD” recently created the definitions for US identification of crystal deposits in joints and tests the reliability at the knee [1].

**Objectives:** To assess the inter/intra-observer reliability of US on detecting CPPD using the OMERACT criteria at the AC joint, hip labrum (HL), hyaline cartilage (HC) of the acetabulum (MC) and femoral head.

**Methods:** The OMERACT criteria for CPPD were used for the exercise [1] using a 2 steps approach. First, the panel of experts gave a dichotomous score (presence/absence of CPPD) of 120 images of the sites included, using a web probes were used.

**Results:** Reliability values of static exercise were high for all sites, demonstrating that definitions were clear. The results of the second step are presented in table 1. On live scanning, the TFCC resulted the most reliable site for CPPD assessment, followed by AC. Other sites demonstrated lower kappa values and thus are not reliable for CPPD assessment.

**Conclusions:** TFCC of the wrist is the most reliable site for CPPD. By adding these results to the previous [2], we confirm that the OMERACT definitions for CPPD can be applied reliably at the knee (meniscus and HC), TFCC and AC, usually the most involved sites in CPPD. In the next step of the OMERACT subtask force will be to test these findings in a longitudinal observational study.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5168

### SAT0633

#### NOT A REPLACEMENT BUT A POSSIBLE SUBSTITUTION: DETECTION OF SACROILIITIS ON MAGNETIC RESONANCE ENTEROGRAPHY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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**Background:** MR Enterography (MRE), a part of the diagnosis in patients with inflammatory bowel disease (IBD), is increasingly used to exclude Crohn’s Disease (CD) in SpA patients with diarrhea. Two important retrospective studies 1,2, on IBD
suggest that acute and structural findings of sacroilitis can be evaluated on MRE. But, it needs to be verified whether it really correlates with sacroiliac MRI.

**Objectives:** We aimed to determine whether assessment of sacroilitis on MRE correlates with magnetic resonance imaging (MRI) of sacroiliac (SI) joint.

**Methods:** MREs used for screening of IBD in Axial SpA patients with chronic diarrhoea and routine semi-coronal SI joint MR images were screened for the presence of acute inflammatory lesions and structural changes of the SI joint by the same radiologist in a blinded fashion to time and diagnosis. Firstly, MRE images and then MR images were evaluated on two separate occasions. Only patients with two imaging modalities with a maximum time distance of a month were evaluated.

**Results:** Forty-four patients with MRE imaging were included. Two MRE studies were excluded because of low resolution. Of those 11 patients (26%) had active inflammatory lesions involving mostly both SI joints and 3 had accompanying chronic structural changes. Ten patients (24%) in the MRE group had chronic structural changes, only. In the remaining 20 (47%) MRE evaluated patients SI joint were not affected. Twenty-five axSpA patients had both MRE and SI joint MRI performed within a month. In 19 cases, out of 25 with both modalities the finding “no sacroilitis” overlapped. An additional four patients had acute inflammatory lesions on both investigations. In only two patients either MRE or SI joint MRI had acute inflammatory lesions. In general, chronic structural changes overlapped in both modalities as well; Fourteen out of 25 patients with no changes and eight with chronic changes overlapped in both examinations. Both modalities differ in only three patients; Chronic changes was present in two patients in SI joint MRI and one patient in MRE only.

<table>
<thead>
<tr>
<th>MRE (Sacroilitis)</th>
<th>(+)</th>
<th>(-)</th>
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<tbody>
<tr>
<td>SI joint MRI</td>
<td></td>
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<tr>
<td>(+)</td>
<td>4</td>
<td>1</td>
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<tr>
<td>(-)</td>
<td>1</td>
<td>19</td>
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</tbody>
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<table>
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<tr>
<th>MRE (Structural Findings)</th>
<th>(+)</th>
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<tbody>
<tr>
<td>SI joint MRI</td>
<td></td>
<td></td>
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<tr>
<td>(+)</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>(-)</td>
<td>1</td>
<td>14</td>
</tr>
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</table>

**Conclusions:** In SpA patients with chronic diarrhoea a present MRE may substitute a conventional semi-coronal MRI of the SI joints and may hence decrease diagnostic expenses. Evaluation of MRE for the acute inflammatory and chronic structural changes of the SI joints may also have a place in the diagnostic flow in IBD patients referred by the gastroenterology clinics, as well.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6114

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MUSCULOSKELETAL ULTRASOUND IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM POST-CHIKUNGUNYA

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**Background:** Since 2013, Chikungunya fever (CHIK) has become a re-emerging disease, with an important number of cases imported in Europe, mainly from South America. At chronic stage (after third month) it can develop a chronic inflammatory rheumatism (CIR), in some cases indistinguishable from rheumatoid arthritis (RA) or spondyloarthropathy (SpA)

**Objectives:** The aim of this study was to investigate the ultrasound (US) alteration in patients with persistent arthralgia at chronic stage of CHIK.

**Methods:** Observational study of patients with persistent arthralgias at the chronic stage of CHIK. We designed a protocol of derivation patients from the Tropical Diseases Unit to the Rheumatology Department which included patients had persistent arthritis after 6 weeks who did not respond to steroids, presence of bone erosion or any diagnosis doubt. In the basic rheumatological visit, we made the clinical history, physical examination, blood analysis, X-ray and US examination. A Mylab Twice equipment (Esaote, Genova, Italy) was used, with a 5–13 MHz frequency for grey scale and 5–12.5 MHz for Power Doppler (PD). Wrist, metacarpophalangeal (MCP), interphalangeal (IP), knee, ankle and metatarsophalangeal joint were assessed and also enthesis if symptomatic. Three patterns of post-CHIK CIR were defined: 1) Post-CHIK RA (if meet RA ACR/EULAR 2010 criteria), 2) post-CHIK Spondylosis (SpA criteria) and 3) post-CHIK undifferentiated arthritis (arthritis without meeting the previous criteria). Post-CHIK musculoskeletal disorders were defined as chronic polyarthritis without objective physical signs of inflammation (without arthritis, tenosynovitis or enthesis).

**Results:** 93 patients were included. 78,3% women, mean age of 46.0±13.65 years. 6 patients (10.2%) were derived to the Rheumatology Department, 5 women and 1 man. In one rheumatoid factor and anti-cyclic citrullinated peptide antibodies were detected. HLA B27 and antinuclear antibodies were negative in all patients. The physical and US data of these patients are shown in the table. 5 of these patients were diagnosed with post-CHIK CIR: 1) post-CHIK RA, 1 non-radiographic axial SpA with peripheral affection (arthritis and enthesis) and 3 patients with post-CHIK undifferentiated arthritis. The other patient was diagnosed with post-CHIK musculoskeletal disorder. All 59 patients received NSAIDs and steroids. In addition, post-CHIK CIR received methotrexate (2 patients) and sulfasalazine (1 patient), all with improvement. In the full cohort, only 5.9% of patients had arthralgias prior to CHIK infection, vs. 33.3% in the post-CHIK CIR (p=0.081). 3 patients (5.08%) had a family history of arthritis, all in the post-CHIK CIR.

**Conclusions:** Arthralgias are a frequent symptom even at chronic stage of CHIK. Sometimes it is true arthritis and in others cases edema. For this reason US is very useful in doubtful cases. In our cohort, patients that developed post-CHIK CIR were more frequently women, with a higher percentage of family history of arthritis. To the best of our knowledge, this is the first US study in patients with post-CHIK CIR.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6702

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DESCRIPTIVE ANALYSIS OF THE QUANTICAP STUDY: A MULTICENTRIC PROSPECTIVE STUDY FOR THE VALIDATION OF QUANTITATIVE AND QUALITATIVE PARAMETERS OF NAILFOLD CAPILLAROSCOPY

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**Background:** Nailfold capillaroscopy (NC) is a useful tool to study Raynaud’s phenomenon (RP) and other diseases. Different findings and patterns has been described however there is currently no work that validates the qualitative and quantitative NC findings.

**Objectives:** To describe the morphological and metrological findings of NC in patients with RP and autoimmune diseases.

2-Describe the morphological and metrological findings of CP in patients with RP and autoimmune diseases.

3) Describe the morphological and metrological findings of NC in patients with RP and other autoimmune diseases.

4) Describe the morphological and metrological findings of CP in patients with RP and autoimmune diseases.

**Methods:** Observational study performed in 10 hospitals by rheumatologists with experience in NC. Patients with diffuse systemic sclerosis (dSSc), limited systemic sclerosis (SSc), dermatomyositis (DM), polymyositis (PM), systemic lupus erythematosus (SLE) Primary Sjögren’s syndrome (PSS), rheumatoid arthritis (RA), primary RP and a control group without RP or rheumatological condition were collected.A video NC 200x magnification were made in all patients. 8 Fingers in each hand were analyzed to find: megacapillary and thrombosis, haemorrhages, tortuosity, dermatoangiitis, haemorrhages, thrombosis and destructuration. Also we analyzed the diameter of the afferent and efferent loop, the capillary apex, the capillary diameter and density/mm. The following variables were also collected: sex, age, years of evolution of the disease and RP, history of digital ulcers or medication for
RP, smoking and presence of hypertension or diabetes. To compare qualitative variables, the test used was Chi-square or Fisher’s test. To compare quantitative vs qualitative variables Student’s T test was used. Significance was considered for those values with p-value <0.05.

Results: Between May 2014 to December 2016 images of 406 patients were collected: 24 dSSc, 41 sSSc, 19 DM, 14 PM, 40 SLE, 39 PSS, 37 RA, 44 PRP and 145 controls. C 84.5% were women, the age of the sample were 51.32±15.21 years. 28.9% had a history of smoking and 21.1% and 5.5% of hypertension or diabetes, respectively. Excluding the cases of dSSc, ISSc, PRP and the 145 controls, the presence of RP was observed in 18/152 (11.84%). The inter-observer reliability exercise study in JIA patients as the final 3rd phase of the process. The definitions were tested in four joints (wrist, 2nd MCP, knee and ankle) of JIA patients divided in four age groups following standardized image acquisition and machine setting protocol. Statistics program R (version 3.3.0) was used for the statistical analyses. For intra-rater agreement Cohen kappa values and for inter-rater agreement prevalence and bias adjusted kappa (PABAK) were calculated if needed.

Results: Reliability exercise included 20 JIA patients (distributed in equal numbers by age groups), 14 observers, 4 joints/observer, 3 observers/joint, 360 intra- and 360 inter-observer tests. A 0–3 semi-quantitative B-mode and color power/Doppler US definitions for synovial components and grading were agreed (presented in Figure 1).

Conclusions: The proposed synovitis grading for children showed to be reliable why the next step should be to test sensitivity to change in order to possibly be used as an outcome tool in clinical trials.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6199

SAT0637 ULTRASOUND ASSESSMENT OF SKIN THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS: CORRELATION WITH CLINICAL FEATURES

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Background: Although modified Rodnan skin score (mRSS) is the most widely used measure for assessment of skin involvement in Systemic Sclerosis (SSc), ultrasound (US) of skin thickness seems to be a promising complementary tool.

Objectives: To compare skin thickness measured by US of a defined anatomical point between SSc patients and age and sex matched controls. To compare, among patients, US measurements of skin thickness with local and total mRSS and other specific clinical variables.

Methods: Forty-eight SSc patients and 45 age and sex matched controls were evaluated in a cross-sectional study at our Rheumatology Unit. SSc patients had a mean age of 56.98±12.73 years and mean disease duration of 9.77±6.12 years; 42 patients had limited cutaneous disease. For comparison between groups, mean skin thickness (mST) of combined right side was used. Patients' local and total mRSS were also assessed.

Conclusions: mST was found to have face and content validity for detecting synovitis in juvenile idiopathic arthritis (JIA) with higher sensitivity than clinical examination. In order to test validity and improve the applicability of US in JIA, the OMERACT US pediatric subtask force recently published preliminary definitions for the sonographic features of synovitis in children.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4408

SAT0636 ULTRASONOGRAPHY DEFINITIONS FOR SYNOVITIS GRADING IN CHILDREN: THE OMERACT PEDIATRIC ULTRASOUND TASK FORCE

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Background: Ultrasound (US) was found to have face and content validity for detecting synovitis in juvenile idiopathic arthritis (JIA) with higher sensitivity than clinical examination. In order to test validity and improve the applicability of US in JIA, the OMERACT US pediatric subtask force recently published preliminary definitions for the sonographic features of synovitis in children.

Objectives: Aim of this study was to confirm and improve B-mode and color power/Doppler (PD) US definitions for synovial components and grading in children, by using an image and patient based exercise.

Methods: The definitions were confirmed and modified in a multi-step process. In the 1st step, definitions were developed in multi-round Delphi web based consensus process were performed. Participants would need to reach >80% of agreement on a Likert scale from 1–5 (1 strongly disagree, 2 disagree, 3 neutral, 4 agree, 5 strongly agree). In the 2nd step, in a face to face meeting, a subgroup of these experts revised the definitions for final wording and performed intra- and inter-observer reliability exercise study in JIA patients as the final 3rd phase of the process. The definitions were tested in four joints (wrist, 2nd MCP, knee and ankle) of JIA patients divided in four age groups following standardized image acquisition and machine setting protocol. Statistics program R (version 3.3.0) was used for the statistical analyses. For intra-rater agreement Cohen kappa values and for inter-rater agreement prevalence and bias adjusted kappa (PABAK) were calculated if needed.

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Conclusions: The proposed synovitis grading for children showed to be reliable why the next step should be to test sensitivity to change in order to possibly be used as an outcome tool in clinical trials.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6199

Figure 1. Synovitis grading definitions in children and inter- and intra-observer reliability in B-mode (GS) and color power/Doppler (PD).
**Clinical Activity, Ultrasound Assessment and Drug Monitoring in Rheumatoid Arthritis Patients Receiving Anti-TNFα Therapy with Extended Interval of Administration**

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**Rheumatology; Laboratory, Hospital Marina Baixa, Villajoyosa (Alicante); 2Rheumatology, Hospital Dr. Negrín, Las Palmas de Gran Canaria; 3Centro de Investigación Operativa, Universidad Miguel Hernández, Elche, Spain.**

**Objectives:** To assess clinical activity, ultrasound synovitis and drug levels in rheumatoid arthritis (RA) patients receiving anti-TNFα therapy with extended interval of administration (EIA).

**Methods:** Prospective observational study. Population: RA patients, in clinical remission, receiving adalimumab (ADL) or etanercept (ETN) with EIA. Clinical activity was assessed by DAS28-ESR, DAS28-CRP, DASAI and SDAI scores at each visit. Twelve-joint ultrasound assessment (elbows, wrists, 2nd and 3rd metacarpophalangeal joints, knees and ankles) was performed evaluating synovitis through B-mode (BM) and Color Doppler signal (CD). A BM and CD score was calculated summing the highest score from each joint to a maximum of 36 points. We consider positive score ≥1 point. Serum drug levels were measured using Promonitor® ELISA kits (Progenika Biopharma, Spain).

**Results:** A total of 39 patients less than or equal to 62 years of age were included since February 2011 to December 2016. One patient was excluded due to blindness violation and 2 patients never received anti-TNFα due to low drug levels. 31 patients were women (82%) and the mean age was 61 (39–81) years. Most patients were RF positive (87%) and ACPA positive (74%). 22 patients were with ADL treatment and 16 with ETN. 32 patients reduced anti-TNFα: 20 (62%) and CDAD (5%) and 7 patients were with low-dose CS (18%). Mean time to response to ETN 4,61 (2,74 3,59 (2,9) 3,03 (0,84) and to rituximab 12 (20.3%) tocilizumab (74.7%) of whom 47 (79.7%) on combination with csDMARD therapy, 4 (5.7%) were biologic naive. 42 (63.6%) of bioprepared patients had a DAS28 >3.2 and were eligible for a change in their biologic however, only 17 of these patients had US-confirmed synovitis, 21 had evidence of osteoarthritis (OA), 1 tenosynovitis and 3 had no abnormalities. All biologic naive patients had a DAS28-CRP >5.1 before US however, 3 had US-confirmed synovitis and 1 had OA. Of bioprepared, 13/66 (19.4%) patients, including 4 with DAS-28 >3.2 but US-confirmed synovitis, had a new biologic started. 3 rituximab patients (including one with re-treatment) had a new biologic (tacrolimus) treatment. Concomitant treatment was needed in 13 (24.2%) patients. Metabolic (35.3%) and US scan findings 4 with US synovitis/tenosynovitis, had no change in their treatment. 2 (3.0%) patients self-discontinued treatment.

**Conclusions:** By identifying lack of inflammatory synovitis in biologic eligible patients US reduced the unnecessary and costly change of biologics. US also detected subclinical synovitis warranting modification of their treatment.

**References:**

**Disclosure of Interest:** None declared. DOI: 10.1136/annrheumdis-2017-eular.5633

**Diagnosis and Imaging in Spondyloarthritis**

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**Objectives:** To evaluate the diagnostic utility of detecting enthesitis by ultrasound in patients with peripheral spondyloarthritis (SpA).

**Methods:** A single-center cohort study was performed in patients with symptoms suggestive of peripheral SpA (inflammatory back pain, arthritis of the lower limbs, tenderness of the entheses and dactylitis). Patients with only axial symptoms in the absence of peripheral symptoms were excluded. Fourteen sites of entheses (both sides of lateral epicondyle, quadriceps tendon insertion into the patella, patellar ligament insertion into the patella and tibial tuberosity, medial and lateral femoral condyles, and Achilles tendon) were assessed at baseline by ultrasound. Ultrasound assessment was made by Japan College of Rheumatology (JCR)-registered sonographers. Furthermore, articular synovitis and tenosynovitis of both hands were scored by two experienced rheumatologists using Clinical, laboratory, CRP, HLA typing, radiological (X-ray and MRI of sacroiliac joint) findings and SpA classification criteria (Amor's, ESSG and ASAS) were also evaluated. The gold standard was the diagnosis made by the JCR-certified rheumatologists during a six-month follow-up period.

**Results:** Between April 2014 and November 2016, one hundred-thirty six patients were consecutively enrolled. A definite diagnosis was obtained in 112 patients (72 SpA and 40 non-SpA). Diagnosis was not made in the remaining 24 patients. Seventy-two SpA patients (62 with undifferentiated SpA, 6 with psoriatic arthritis, 2 with reactive arthritis, 1 with spondyloarthropathy associated with another disease) and 40 non-SpA patients were investigated in this study. In ultrasound findings, SpA patients showed power Doppler (PD) signals of the articular synovitis (57%), tendon sheath synovium (71%) and enthesis (94%). A PD signal for at least one enthesis sites was the most useful finding for differentiation of SpA from non-SpA (sensitivity 96.1%, specificity 78.6%; positive likelihood ratio 6.3) regarding ultrasound findings. In logistic regression analysis, fulfillment of peripheral ASAS criteria, that of Amor’s criteria, and presence of PD signals at least one enthesis sites were independent variables to the contribution of diagnosis of SpA (Figure 1).

**Diagnosis Utility of Detecting Enthesitis by Ultrasound in Peripheral Spondyloarthritis**

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**Objectives:** To evaluate the diagnostic utility of detecting enthesitis by ultrasound in patients with peripheral spondyloarthritis (SpA).

**Methods:** A single-center cohort study was performed in patients with symptoms suggestive of peripheral SpA (inflammatory back pain, arthritis of the lower limbs, tenderness of the entheses and dactylitis). Patients with only axial symptoms in the absence of peripheral symptoms were excluded. Fourteen sites of entheses (both sides of lateral epicondyle, quadriceps tendon insertion into the patella, patellar ligament insertion into the patella and tibial tuberosity, medial and lateral femoral condyles, and Achilles tendon) were assessed at baseline by ultrasound. Ultrasound assessment was made by Japan College of Rheumatology (JCR)-registered sonographers. Furthermore, articular synovitis and tenosynovitis of both hands were scored by two experienced rheumatologists using Clinical, laboratory, CRP, HLA typing, radiological (X-ray and MRI of sacroiliac joint) findings and SpA classification criteria (Amor’s, ESSG and ASAS) were also evaluated. The gold standard was the diagnosis made by the JCR-certified rheumatologists during a six-month follow-up period.

**Results:** Between April 2014 and November 2016, one hundred-thirty six patients were consecutively enrolled. A definite diagnosis was obtained in 112 patients (72 SpA and 40 non-SpA). Diagnosis was not made in the remaining 24 patients. Seventy-two SpA patients (62 with undifferentiated SpA, 6 with psoriatic arthritis, 2 with reactive arthritis, 1 with spondyloarthropathy associated with another disease) and 40 non-SpA patients were investigated in this study. In ultrasound findings, SpA patients showed power Doppler (PD) signals of the articular synovitis (57%), tendon sheath synovium (71%) and enthesis (94%). A PD signal for at least one enthesis sites was the most useful finding for differentiation of SpA from non-SpA (sensitivity 96.1%, specificity 78.6%; positive likelihood ratio 6.3) regarding ultrasound findings. In logistic regression analysis, fulfillment of peripheral ASAS criteria, that of Amor’s criteria, and presence of PD signals at least one enthesis sites were independent variables to the contribution of diagnosis of SpA (Figure 1).
**SAT0642**

**ULTRASONOGRAPHY AND INTRA-ARTICULAR INJECTION THERAPY IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE RANDOMISED ARCTIC TRIAL**

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**Background:** Intra-articular (i.a.) corticosteroid injections are in many countries an integral part of rheumatoid arthritis (RA) treatment. Ultrasonography (US) is increasingly used in the management of RA as a tool to select joints for i.a. injections. How selection of joints based on US information affects distribution of injections has not been previously studied. US can detect joints with subclinical inflammation, however, it is unknown whether there is any added value of injecting these joints.

**Objectives:** We aimed to explore how US information influences the selection of joints for corticosteroid injection therapy. Additionally, we wanted to examine the efficacy of injecting joints with subclinical inflammation detected by US in terms of reduction of subclinical inflammation and prevention of clinical synovitis.

**Methods:** In the ARCTIC trial, DMARD-naive RA patients fulfilling the 2010 ACR/EULAR criteria were randomised 1:1 to follow-up with or without US.[1] In both arms the same DMARD treatment strategy was applied, and clinically swollen joints were treated with i.a. steroids when indicated. In the US arm, clinicians could also inject non-swollen joints with PD activity. Patients were assessed at 13 visits during the first 2 years of follow-up and injections could be performed at all visits. Distribution of injections in patients followed with and without US was assessed. The proportion of patients with any injection was compared between arms using logistic regression, adjusted for gender. In addition, we examined the effect of injections in clinically non-swollen joints with PD ≥ 0.3 by injecting (PD ≥ 0.3) vs non-injection (PD < 0.3) comparing clinical joint swelling and estimated mean change in PD activity at the next visit in injected versus non-injected joints. We used logistic and linear mixed model with random intercept by patient in order to adjust for within-patient dependencies.

**Results:** 230 patients were included (US arm 118, conventional arm 112). Mean (SD) age was 50.6 (13.3)/52.3 (14.1) years, 71/51% were females and mean (SD) baseline DAS was 3.5 (1.2)/3.4 (1.2) in the US/conventional arms. [1] More injections occurred in the US arm than in the conventional arm (770 vs 548), especially in intercarpal (58 vs 5) and MTP joints (200 vs 104) (Table 1). In the US arm, 193 joints were clinically non-swollen, but had PD score ≥2. Of these, 77 joints were injected. 72/77 injected joints (93.5%) remained non-swollen at next visit compared to 88/116 non-injected joints (75.9%), with an odds ratio of 3.97 (CI: 1.25–12.57, p=0.019, NNT:6). Estimated mean (SE) reduction of PD activity was 2.3 (0.1) compared to 2.0 (0.1) versus non-injected joints (p<0.001).

**Conclusions:** Our study shows that follow-up with US may lead to an increased number of joint injections with a different distribution of injected joints compared to follow-up without US. Joints with subclinical inflammation were more likely to remain non-swollen at next visit if injected. However, as the number of joints needed to treat one swollen joint was six, the clinical relevance of injecting joints with subclinical inflammation may be questionable.

**References:**


**Disclosure of Interest:** L. Nordberg: None declared, S. Lillegraven: None declared, A.-B. Aga: None declared, I.C. Olsen: None declared, E. Lie: None declared, H. Hammer Consultant for: Consultant for AbbVie, Pfizer, BMS, Roche, UCB, T. Uhlig: None declared, D. van der Heijde: None declared, T. Kvien: None declared, E. Haavardsholm Grant/research support from: Pfizer, MSD, UCB, AbbVie, Roche

**DOI:** 10.1136/annrheumdis-2017-eular.2505
VALUE OF POWER DOPPLER ULTRASOUNDOGRAPHY FOR PREDICTION OF TREATMENT FOR RHEUMATOID ARTHRITIS (RA) IN EARLY ARTHRITIS DURING THE FIRST 12 MONTHS OF FOLLOW-UP

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Background: There is a short window of opportunity for early diagnosis and treatment of rheumatoid arthritis, that may be critical for achieving remission and a low rate of radiographic progression. High resolution power doppler ultrasonography (PDUS) is helpful in early detection of synovitis and may help to select patients that will need early establishment of treatment for RA.

Objectives: To study whether the presence of basal power doppler signal in patients with early arthritis in a clinical basis treatment decision could predict the risk of receive treatment for AR at 3 and 12 months of follow-up.

Methods: We studied the presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, knees) and 44 joints (28 joints and in addition hips, Tarsus, ankles and MTPs), with a mid-range equipment GE L5, in 70 patients with suspected early arthritis. The patients were included with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with <12 months duration of the symptoms. Clinical treatment decision was not offered to basal power doppler results. Statistical study: Chi-square, Fisher exact test, p univariate and Odds Ratio calculation.

Results: The presence of basal power doppler signal in ≥1 joints of 44 (PD44) at baseline shows statistically significant association with treatment with oral steroids (p=0.001, OR 6.6 (1.9–22.1), but not sulfasalazine (SSZ) (p=0.145) at 3 months. The presence of basal power doppler signal in 28 joints (PD28) was significantly associated to esteroids (p=0.003, OR 10.3 (2.2–49.9), at 12 months. The presence of at least one joint with power doppler signal in 12 months duration of the symptoms. Clinical treatment decision was not offered to basal power doppler results. Statistical study: Chi-square, Fisher exact test, p univariate and Odds Ratio calculation.

Conclusions: Power doppler ultrasonography in at least one joint of 44 (PD44) may predict the patients that will need esteroids, any DMARD, MTX and SSZ teraphy in early arthritis at 3 and 12 months of follow-up. PD28 may predict the patients that will need esteroids, any DMARD, MTX and SSZ teraphy in early arthritis at 12 months, but may only predict the need of esteroids and MTX at three months.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6910

IS ANKLE INVOLVEMENT IMPORTANT IN RHEUMATOID ARTHRITIS?

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Background: The ankles may be affected by rheumatoid ankles (RA). In daily evaluation of RA patients, the ankles are often neglected by clinical examinations, while composite activity scores do not include them.

Objectives: The aim of the study is to assess the inflammatory lesions in RA ankles, regarding frequency and possible correlation with activity disease.

Methods: The study included 76 RA patients fulfilling the 2010 ACR/EULAR classification criteria. In every patient we recorded clinical ankle involvement (ankle swelling and/or tenderness on physical examination); both ankles were evaluated by gray scale (GS) and Power Doppler (PD) ultrasound examination, signal (PD28). In each ankle we assessed: tibial anterior joint (TT); tibialis anterior (TA) tendon; extensor halluc (EH) and extensor digitorum (ED) tendons; talo-navicular joint (TN); bimalis posterior (TP) tendon; flexor digitorum (FD) and flexor halluc (FH) tendons; peroneus brevis (PB) and longus (PL) tendons; Achilles tendon (AT); subtalar joints (ST); posterior, lateral, medial recesses; planatar fascia (PL). We recorded the following abnormalities: synovitis, tenosynovitis, bursitis, entesopathy and rupture. Activity scores (DAS28, DAS44, SDAI), inflammatory markers (ESR, CRP), serology (FR, ACPR) and HAQ were also assessed.

Results: The mean age was 57.2±14.2 years; 88% were women; mean disease duration was 12.2±9.2 years; 56.6% had symptomatic ankles; 61.6% had undergone ankle arthroscopy. The most frequent ultrasound pathology encountered was ST synovitis (56.6%), followed by TT synovitis (48.7%), TN synovitis (38.2%), TP tenosynovitis (30.3%), PL tenosynovitis (15.8%). Ultrasound abnormalities were recorded in 93% of the symptomatic ankle patients and in 56% of the asymptomatic ankle patients (p=0.008). Overall, 43% had positive PD signals, but the prevalence of positive PD signals was significantly higher in symptomatic ankle patients than in asymptomatic ankle patients (60.5% compared to 21.2%, p=0.011). Statistically significant correlations were found between ultrasound inflammatory pathology (synovitis and tenosynovitis), activity disease markers and quality of life (Table 1).

Conclusions: Musculoskeletal ultrasound detected a high prevalence of inflammatory abnormalities in rheumatoid ankles, both in symptomatic and asymptomatic patients, while power Doppler signal was present mostly in symptomatic patients. The ultrasound pathology was highly correlated with activity disease markers and quality of life.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.6217

MAGNETIC RESONANCE IMAGING AND HISTOPATHOLOGICAL CORRELATION IN DERMATOMYOSITIS

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Background: Dermatomyositis represents one of the major forms among the inflammatory myopathies (IM). Although the muscle biopsy remains the definitive test, MRI has been used to detect unique patterns of muscle involvement. To date, no studies have compared MRI with muscle pathology in naïve DM.

Objectives: To compare the patterns of muscle MRI with muscle pathology.

Methods: All the patients enrolled in the Hospital Clinic de Barcelona (HCB) from January 2009 to December 2016 with an available MRI, performed just before muscle biopsy were included. The HCB ethics committee approved this study, and written informed consent was obtained from each participant.

MRI findings were classified according to the classical clinical and histologic features. Patients were prospectively collected.

Conclusions: Magnetic resonance imaging and histopathological correlation in dermatomyositis.
COMPARISON OF US, CT, X-RAY AND MRI EFFICACY FOR LASER DOPPLER IMAGING: AN OBJECTIVE OUTCOME

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Background: Moscow, Russian Federation

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Objectives: of disease regression in pts receiving urate-lowering therapy is not sufficiently to identify affected joints and surrounding tissues (tophi, erosions and synovitis) computed tomography (CT), and X-ray are the alternative diagnostic modalities used. Dose of allopurinol administered in all pts was adjusted by titration starting from 300–600 mg/day, 9 (45%) pts had to take 600 mg/day and more. At baseline US examination detected periarticular tophi in 3 (14%) pts, MRI - in 6 (28%) pts, CT in 3 (14%), X-ray - 1 (5%) pts, after one year - by US in 4 (9%) pts and MRI - 3 (14%) pts, CT in 2 (9%), X-ray - 1 (5%) pts. At baseline intraosseous tophi were detected only by CT and X-ray in 18 (81%) and 2 (9%) pts respectively, and in 17 (77%) and 3 (14%) pts respectively. At baseline erosions were detected in 19 (86%) pts by MRI, in 11 (50%) pts - by US, in 14 (65%) pts - by CT, and in 9 pts (41%) - by X-ray, after one year in 14 (64%) pts by MRI, 10 (45%) pts by US, 12 (54%) pts by CT, 8 (36%) pts by X-ray. At baseline synovitis was reliably diagnosed by MRI and US: in 15 (68%) pts and 7 (33%) pts, after one year in 2 (9%) pts and 3 (14%) pts respectively.

Conclusions: MRI and US, as for synovitis, erosions and tophi dynamics, are comparable, at that for erosions MRI is more accurate. CT is the most informative approach to monitor intraosseous tophi regression. X-ray is low- informative modality for sequential assessment of gout.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3722

SAT0647 | LASER DOPPLER IMAGING: AN OBJECTIVE OUTCOME MEASURE FOR ASSESSMENT OF CUTANEOUS LUPUS ERYTHEMATOUS

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Background: Cutaneous lupus erythematosus (CLE) is the most common manifestation of SLE and may occur without systemic features. Skin disease is particularly heterogeneous, rendering assessment of activity difficult. Laser Doppler imaging (LDI) is a non-invasive imaging tool that monitors blood perfusion in dermal tissue. It has been shown to correlate with inflammation in psoriasis but no study has been undertaken in CLE.

Objectives: To evaluate validity of LDI against the gold standard of histology from skin biopsy as well as other clinical tools including the Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI) and Visual Analogue Scale (VAS) scoring of photographs.

Methods: A prospective observational study was conducted in consecutive patients with CLE flare at a single centre. Disease activity was assessed using RCLASI and measured using a high resolution LDI system (Morin Instruments) by JB and YY, both blinded to clinical assessment. Relative difference to the non-lesion area was calculated and expressed in perfusion unit (PU). Skin biopsy was obtained in those who consented and scored as 0=non-active, 1=mild activity and 2=active. Photographs were taken on the same day and were later assessed by a dermatologist and a rheumatologist who were blinded to LDI results using a 100mm VAS. The agreement of VAS between both clinicians was analysed using Bland-Altman limits of agreement (LOA) and the correlation between histology and LDI, RCLASI and VAS were analysed using Kendall’s Tau-a.

Results: 20 patients were studied (19 female, median age 47.2 (range 21–62) years, 6 smokers, 2 CLE only, 14 (70%) ANA positive at the time of the scan). The distribution of CLE type were: acute CLE=7, subacute CLE=6 and chronic CLE=7. The agreement between the VAS scores of the two clinicians was fair; mean difference 7.8 (95% CI LOA -26 to 41) mm versus average. In 10 patients with skin biopsy, the correlation with histology was better for LDI (τ=0.56) than RCLASI [0.09; difference (90% CI) 0.64 (0.10, 1.19)] or VAS [0.16; 0.71 (0.13, 1.29)] (figure 1). One patient who was deemed to have a subacute CLE flare based on clinical assessment indeed had a negative histology and a low PU. Conclusions: In this preliminary analysis, assessment of blood perfusion to dermal tissue using LDI provides a valid quantitative and objective measure of inflammation in cutaneous lupus. The findings from LDI also had a better correlation with histology than skin biopsy compared to currently used clinical tools. Further validation and longitudinal analysis including assessment of responsiveness to therapy will provide further evidence on the usefulness of LDI in clinical practice and trials.

Acknowledgements: The authors would like to acknowledge Lorraine Green for substantial contribution in the acquisition of data and NIHR for funding the Laser Doppler Imaging.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3746

SA6046 | COMPARISON OF US, CT, X-RAY AND MRI EFFICACY FOR SEQUENTIAL ASSESSMENT OF CHRONIC GOUT MANIFESTATIONS


Background: Ultrasonography (US), magnetic resonance imaging (MRI), computed tomography (CT), and X-ray are the alternative diagnostic modalities used to identify affected joints and surrounding tissues (tophi, erosions and synovitis) in gout patients, but the potential of each method for sequential assessment of disease regresses in pts receiving urate-lowering therapy is not sufficiently studied. One patient who was deemed to have a subacute CLE flare based on clinical assessment indeed had a negative histology and a low PU. Conclusions: In this preliminary analysis, assessment of blood perfusion to dermal tissue using LDI provides a valid quantitative and objective measure of inflammation in cutaneous lupus. The findings from LDI also had a better correlation with histology than skin biopsy compared to currently used clinical tools. Further validation and longitudinal analysis including assessment of responsiveness to therapy will provide further evidence on the usefulness of LDI in clinical practice and trials.

Acknowledgements: The authors would like to acknowledge Lorraine Green for substantial contribution in the acquisition of data and NIHR for funding the Laser Doppler Imaging.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3746
Disclosure of Interest: None declared

SAT0648

ULTRASOUND FINDINGS IN SYMPTOMATIC AND ASYMPTOMATIC JOINTS IN PATIENTS WITH GOUT

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Objectives: To determine sensitivity and specificity of ultrasound (US) findings for gout, “double contours” (DC) and hyperechogenic aggregates (HAGs) of symptomatic and asymptomatic joints in patients with gout.

Methods: This prospective study included 69 persons (34 patients with primary gout and 35 healthy subjects). Including criteria for patients with gout were: age ≥18 years; diagnosis of primary gout; absence of acute gout attacks during the study tests; the absence of any other inflammatory and infectious joint disease, and secondary gout. The research included: demography and medical history, Physical and US examination covered following structures: 138 radiocarpal joint, 276 patellar and triceps tendon and 414 articular cartilages (first metatarsal, talar and femoral condyle).

Results: Both groups were compatible for age and gender. In the gout group 124 (30%) symptomatic and 284 (70%) asymptomatic joints were found and in healthy group all joints was asymptomatic. The sensitivity of the DC for symptomatic joint was 56 to 84% and specificity also was very high 91% to 94% as well as positive and negative predictive value (69 - 86% and 38 - 71%). Sensitivity of DC finding for the asymptomatic joints was 42 to 73% and specificity was 91 to 94%, with also high positive and negative predictive value (69 - 89% and 44 - 62%). The specificity of the HAGs for both symptomatic and asymptomatic joints was very high 99% but sensitivity of HAGs symptomatic structures was moderate (41 do 56%), while its sensitivity for asymptomatic structures was low (18 to 34%), table 1.

Table 1

<table>
<thead>
<tr>
<th>Structure</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>“Cut-off”</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic DC</td>
<td>56-84</td>
<td>91-94</td>
<td>0.50</td>
<td>69-86</td>
<td>38-71</td>
</tr>
<tr>
<td>HAGs</td>
<td>41-56</td>
<td>98-99</td>
<td>0.50</td>
<td>69-89</td>
<td>44-62</td>
</tr>
<tr>
<td>Asymptomatic DC</td>
<td>42-73</td>
<td>91-94</td>
<td>0.50</td>
<td>58-86</td>
<td>38-71</td>
</tr>
<tr>
<td>HAGs</td>
<td>18-34</td>
<td>98-99</td>
<td>0.50</td>
<td>49-75</td>
<td>31-60</td>
</tr>
</tbody>
</table>

DC - “double contours”; HAGs - hyperechogenic aggregates; PPV - positive predictive values; NPV - negative predictive values.

Conclusions: Ultrasound examination of symptomatic and asymptomatic joints in patients with gout equally observed structural changes characteristic of gout. The finding of “double contours” in the symptomatic and asymptomatic joints has a very high sensitivity and specificity. Consequently, future research should be focused on the ultrasound examination of asymptomatic joints in patients with gout.

Disclosure of Interest: None declared

SAT0649

CHANGES IN CARTILAGE QUALITY (dGEMRIC) FOLLOWING KNEE JOINT DISTRACTION OR HIGH Tibial OSTEOTOMY: A TWO-YEAR FOLLOW-UP

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Background: Since abnormal loading can cause onset and progression of OA, unloading the affected compartment of an osteoarthritic knee, should slow down OA progression, or even enable joint repair. High tibial osteotomy (HTO) is a well-known unloading approach for treating unilateral compartment osteoarthritis (OA) with mechanical axis deviation. Transient unloading using knee joint distraction (KJD) has demonstrated a progressive decrease in pain, normalization of function, and an increase in walking distance. 1 Although both treatments show indications of joint repair, there is limited information about the actual quality of the regenerated tissue.

Objectives: To evaluate the change in quality of the repaired cartilaginous tissue using dGEMRIC after KJD or HTO treatment.

Methods: 40 patients (20 with KJD, and 20 with HTO), treated for medial tibiofemoral OA, are included in this study. Radiographic changes, clinical changes, and changes in cartilage quality are evaluated after one and two years follow-up. Joint space width (JSW) is evaluated on weight-bearing radiographs. Clinical improvement is evaluated by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analogue Scale (VAS) pain score. In order to evaluate the quality of the (newly formed) cartilaginous tissue, quantitative MRI analysis, in the form of Delayed gadolinium enhance Magnetic Resonance Imaging of cartilage (dGEMRIC) is performed.

Results: A significantly increased medial (± 1.15 mm, p < 0.000), minimal (± 0.93 mm, p < 0.000) and mean (± 0.79 mm, p < 0.000) JSW one year after KJD, sustaining up until 2 years, was demonstrated (medial (± 0.99 mm, p < 0.000), minimal (± 0.04 mm, p < 0.000), mean JSW (± 0.68 mm, p < 0.027)). Similarly, medial (± 0.69 mm, p < 0.017) and minimal (± 0.32 mm, p < 0.023) JSW were significantly increased one year after HTO, sustaining up until 2 years (medial: ± 1.03 mm, p < 0.000, minimal: ± 0.72 mm, p < 0.015), after which mean JSW (± 0.46 mm, p < 0.030) is also significantly increased. Both interventions led to clinical improvement, observed as an increase in WOMAC after one year (KJD: ± 33.89. p < 0.000, HTO: ± 33.74. p < 0.000) and two years (KJD: ± 32.52. p < 0.000, HTO: ± 24.15. p < 0.002), and a decrease in VAS Pain, after one year (KJD: ± 30.79. p < 0.001, HTO: ± 41.89. p < 0.000) and two years (KJD: ± 30.50. p < 0.004, HTO: ± 34.64. p < 0.000). However, no statistically significant changes in cartilage quality were found after KJD or HTO, not in the medial and lateral compartments of the tibiofemoral joint, nor in the separate ROIs (see figure 1).

Conclusions: Treatment of medial compartmental OA by either HTO or KJD leads to alleviation of pain and recovery of function, achieved one year after either intervention, and maintained for another year. Within the first year after treatment, KJD shows a statistically significantly higher increase in WOMAC as compared to HTO. Both treatments led to a statistically significant increase in JSW after one and two years, postponing the natural osteoarthritis progression rate. No statistically significant change in the quality of newly formed cartilaginous tissue could be detected by dGEMRIC.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3400

SAT0650

18F]-FLUORO-PEG-FOLATE PET: A NOVEL IMAGING TECHNIQUE TO VISUALIZE RHEUMATOID ARTHRITIS

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Background: Imaging arthritis activity in rheumatoid arthritis (RA) patients using PET macrophage tracers holds promise for both early diagnostics and monitoring response to therapy (1,2). Previously, (R)-[18F]CPK11195 has been used, but this macrophage tracer is limited due to high background uptake, especially in bone and bone marrow. Recently, a novel macrophage tracer, [18F]fluoro-PEG-folate,
was developed, which showed excellent targeting of the folate receptor beta on activated macrophages in synovial tissue in a preclinical arthritis rat model (3).

Objectives: To assess the value of [18F]fluoro-PEG-folate PET-CT for imaging inflamed joints in patients with clinically active RA.

Methods: Nine RA patients with at least two clinically inflamed hand joints were included. PET-CT scans (120 min after injection with 370 MBq of [18F]fluoro-PEG-folate) were acquired at 2 time points: baseline (T0) and 3 months (T3) after initiation of methotrexate (MTX) or infliximab (IFX) treatment. PEM PET images were analyzed semi-quantitatively using a region of interest (ROI) analysis approach. Outcome parameters were calculated based on visually marked uptake and SUVs were calculated. The area under the curve (AUC) was calculated for each ROI.

Results: No side effects were observed, and the high uptake in inflamed joints was confirmed in all patients. The AUC was significantly higher in inflamed joints compared to non-inflamed joints.

Conclusions: PEM PET with [18F]fluoro-PEG-folate PET-CT provides a promising imaging approach to assess early arthritis inflammation.

References:
SAT0653 | QUANTITATIVE ASSESSMENT OF INTERSTITIAL LUNG DISEASE IN SJÖGREN SYNDROME: A PILOT STUDY


Background: The interstitial lung disease (ILD) is the most frequent form of lung damage in Sjögren’s syndrome (SS). The diagnosis is still nowadays challenging: the absence of a specific functional test, the presence of non-specific radiological images, the chest CT is the gold standard. Semiquantitative (SQCT) assessment (such Taouli or Goh visual scores) could estimate ILD severity or burdened by relevant inter-rater variability. Quantitative chest CT (QCT) is a promising method to assess primary or secondary ILD, but there are not studies focused on SS-ILD.

Objectives: Herein we designed a study to evaluate if QCT indexes may assess differences in SS-ILD.

Methods: We conducted a multicenter, cross-sectional, and retrospective study, identifying subjects affected of SS (per modified American-European consensus criteria) with a thorax CT ordered by local physician by any reason. We enrolled 52 cases, divided in two cohorts according to the presence/absence of ILD on CT. A centralized SQCT assessment was carried out to calculate both Goh and Taouli scores. A DICOM-viewer open-source software (Horos) was used to analyse, blindly and anonymously, all CT images and to calculate QCT indexes (pulmonary function tests; total lung volume; functional, standard deviation, mean total lung attenuation). QCT indexes and SQCT scores were compared using the Spearman rank and Mann-Whitney tests. ROC curves were calculated to assess the sensibility and specificity of the QCT indexes to detect ILD.

Results: Median age was 50.5 (95% CI 51.6–51.7) years, 52.2% were female, 9 cases had ILD, and 41 were not affected - patients not assessable. The disease duration (tilt CT thorax) have a median of 21 (95% CI 6 – 42.4) months. 42.3% have secondary SS and 57.7% a primary SS. All QCT scores, except pSdev (105.6 (IQR 101.4 - 122.95) vs 96.4 (IQR 92.38 to 104.94), p=0.006; pSdev (149.4 (IQR 149.0 - 194.2) vs 146.0 (IQR 144.0 to 196.0), p=0.101), TurkT 7.62, IQR 7.09 to 9.01 vs 6.45, IQR 6.04 to 8.71, p<0.001; sensitivity 88.89% (95% CI 51.8–99.7), specificity 65.85% (95% CI 49.4–79.9), p<0.001. The correlation coefficients for QCT and Goh and Taouli’s score ranges around 0.4.

Conclusions: QCT indexes identify some differences between SS-ILD and those not. These parameters could be useful both to improve imaging diagnosis and also the decision to treat those cases. This innovative tool might open up a potential research area to be developed in SS. Moreover, the operator independence of QCT makes it a time-saving method extremely suitable for multi-centre trials. Our pilot study have some handicaps: small sample, low number of events, different reasons for CT performance, no smoking identification, and biological differences between primary and secondary SS. However, it could be point out that GTC could be a useful tool to identify and quantify ILD in SS, and further data are needed to ascertain this hypothesis.

Disclosure of Interest: None declared


SAT0655 | EARLY ENDOTHELIAL DAMAGE IN PATIENTS WITH RAYNAUD’S PHENOMENON

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Background: Endothelial dysfunction is highly prevalent in Raynaud’s phenomenon (RP). Among Raynaud’s phenotypes, patients with capillaroscopic abnormal pattern (CPA) are at higher risk of cardiovascular and cerebrovascular events. However, the role of endothelial dysfunction in early phase of Raynaud’s disease is unknown.

Objectives: To evaluate the difference of plasma levels of tissue-type plasminogen activator (t-PA) and von Willebrand factor (vWF) in primary Raynaud’s disease (PRD) and secondary RP divided in CPA and capillaroscopic normal pattern (CNP).

Methods: A cross-sectional study was conducted in the period 2013–2015. PRD and secondary RP patients were included in the study by means of the recruitment of consecutive patients attending the Rheumatology Unit of the University of Parma. Baseline demographic, clinical and laboratory characteristics were evaluated. Plasma levels of t-PA and vWF were evaluated by ELISA technique. The differences among the groups were evaluated by means of the non-parametric Mann-Whitney U test and the χ2 test. The normality of the data was evaluated by using the Shapiro-Wilk test and the Q-Q plot. A significance level of p<0.05 was used for all statistical analysis.

Results: A total of 309 patients with primary RP and 80 patients with secondary RP were included in the study. The mean age of the patients was 43 ± 13 years and 75% were female. The most common RP phenotype was PRD (95%). Primary RP included 134 patients with secondary RP included 175 patients. The mean age of the patients with CPA was 40 ± 13 years and 73% were female. The differences in age and sex between the CPA group and the CNP group were not statistically significant. The serum levels of t-PA and vWF were statistically significantly higher in the CPA group than in the CNP group (p=0.005 and p=0.004, respectively). The differences between the CPA group and the CNP group were statistically significant for both primary RP and secondary RP (p=0.001 and p=0.001, respectively). The serum levels of t-PA and vWF were statistically significantly higher in the CPA group than in the CNP group (p=0.005 and p=0.004, respectively).

Conclusions: Our study demonstrated that the serum levels of t-PA and vWF were higher in CPA than in CNP group. These findings suggest that endothelial damage is present in CPA patients and may be a marker of early vessel damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5047

SAT0654 | THE RECALL SURVEY: DIFFERENCES OF ULTRASOUND EXAMINATION BETWEEN EARLY VS LONG LASTING RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION


Background: Ultrasound (US) examination is able to show subclinical synovitis and bone involvement in patients with RA in clinical remission (CR).

Objectives: To investigate the differences of US examination of US small joints of hands, feet and wrists in pts with very early (ERA, <1y) vs early (ERA, <3y duration) vs long lasting RA (LRA, > 7 y duration) in clinical remission (CR).

Methods: In 2015 an educational event (RECALL survey) focused on the added value of US in RA was held in 22 Italian centers. In each center, the local rheumatologists provided RA pts to be examined by US. Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). Bilateral US examinations of wrists, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, using a Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe.

All US findings were scored using a 4 degree semiquantitative scoring system.

Results: Eighty-eight pts were classified as VERA, 183 as ERA and 165 as LRA. LRA usage was not different among the three groups of pts. LRA pts were older (p<0.001), had longer disease remission before US examination (p<0.001) and had an higher prevalence of female sex (p<0.01). Table 1 reports the differences of US examination between VERA vs ERA vs LRA patients. LRA pts had more erosions at MTP and wrists with no differences at MCP joints. Synovial hyperthrophy and PD signal had the same degree in the two groups of patients. LRA pts had more MTP joints with effusion with lower degree as compared to patients with ERA and VERA (see table 1).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>VERA (A)</th>
<th>VERA+ERA (B)</th>
<th>LRA (C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>88 pts</td>
<td>183 pts</td>
<td>165 pts</td>
</tr>
<tr>
<td>M/F</td>
<td>25-63</td>
<td>58-152</td>
<td>22-143</td>
</tr>
<tr>
<td>% of pts with remission &lt;12 months</td>
<td>85</td>
<td>90</td>
<td>48</td>
</tr>
<tr>
<td>% of pts with &gt;1 eroded joint</td>
<td>39</td>
<td>54</td>
<td>62</td>
</tr>
<tr>
<td>% of pts with &gt;1 joint with synovial hypertrophy</td>
<td>69</td>
<td>71</td>
<td>73</td>
</tr>
<tr>
<td>% of pts with synovial hypertrophy &gt;1</td>
<td>46</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>% of pts with &gt;1 joint positive for PD signal</td>
<td>48</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>% of joints with PD signal &gt;1</td>
<td>32</td>
<td>34</td>
<td>35</td>
</tr>
<tr>
<td>% of pts with effusion at MTP joints</td>
<td>45</td>
<td>49</td>
<td>59</td>
</tr>
<tr>
<td>% of pts with MTP joints effusion &gt;1</td>
<td>25</td>
<td>21</td>
<td>12</td>
</tr>
</tbody>
</table>

Conclusions: At US examination VERA, ERA and LRA pts in CR have the same degree of synovial hyperplasia and PD signal despite the differences of duration of CR. Higher degree of erosive disease (at wrist and MTP joints), lower degree of MTP effusion and higher prevalence of joint effusion at MTP joints were present among LRA vs ERA and VERA pts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6888
SAT0656  OPTICAL IMAGING OF PHAGOCYTE MIGRATION REPRESENTS A NOVEL METHOD TO DETERMINE DISEASE ACTIVITY IN CIA

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Background: Recruitment and migration of phagocytes to the site of inflammation are key events in the onset of inflammation. Albeit crucial for pathogen elimination, tissue repair and restoration of tissue homeostasis, dysregulated phagocyte infiltration can also cause severe inflammatory disorders. Therefore, targeting and modulation of phagocyte infiltration represents a promising new approach to fight inflammatory disorders and diseases, such as rheumatoid arthritis. Additionally, non-invasive tracking of phagocyte migration to the site of inflammation could contribute to scientific knowledge as well as the repertoire of diagnostic strategies in clinical use.

Objectives: The aim of this study was to establish a fluorescence reflectance imaging (FRI) based system to visualize and analyze migration properties of different cell populations in inflammatory disease models, like experimental arthritis, in vivo.

Methods: Immortalized murine myeloid progenitor ER-HoxB8 cells were differentiated to neutrophils or monocytes (1). Cells were labeled with the membrane-selective fluorescent dyes DOR (2) or DID, respectively. We analyzed viability and functionality of stained cells in vitro and investigated their ability to migrate to sites of inflammation in vivo in several mouse models - particularly in a collagen-induced arthritis (CIA) mouse model - via fluorescence reflectance imaging (FRI).

Using CRISPR-Cas9 technology we introduced targeted gene deletions for main adhesion molecules.

Results: Differentiated ER-HoxB8 cells could effectively be labeled with DOR or DID. Labeling of monocytes or neutrophils did not affect cellular viability or functionality in vitro. Subsequent in vivo imaging experiments allowed the visualization of migrated labeled phagocytes in different murine disease models, thereby cells could be detected at sites of inflammation with high sensitivity and specificity. In a leucocyte recruitment during the early stages of arthritis, Correlation of labeled cells could even be associated closely to disease score and disease severity. Thus, the detection of immigration of labeled cells might also give hints about new inflammatory spots that are about to settle up before they can be detected macroscopically. Furthermore, differential cell labeling allowed direct quantitative comparison of differences in migration rates of wildtype and CD18 or CD49d knockout cells in vivo.

Conclusions: Specific and distinguishable labeling of diverse cell types allows in vivo tracking and subsequent quantification of migrated cells within the same animal. Targeted gene deletion allows analysis of molecular mechanisms relevant for leucocyte recruitment during different stages of arthritis. Correlation of the amount of immigrated cells to disease severity offers new opportunities to non-invasively detect and monitor inflammatory sites in vivo.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6151
elasticity was attached to the transducer during the elastostenography. The inlet of the carpal tunnel at the scaphoidprocess level and the proximal portion of the inlet carpal tunnel were scanned in a transverse plane. The cross-sectional area (CSA) and the elasticity of the median nerve, which was measured as the acoustic coupler/median nerve strain ratio, were evaluated. The measurements were Power Doppler (PD) scans of the average strain ratio was used for analysis.

Results: We analyzed 342 hands in 177 RA patients (139 female, mean age: 63.5±11.6 years) and 158 hands in 81 non-RA (68 female, mean age: 71.5±14 years) finally. There were no significant differences in the cross-sectional area of median nerve (left: 8.9 vs 8.7 mm², p=0.91, right: 8.2 vs 8.4 mm², p=0.62) or the circumference of median nerve (left: 13.1 vs 13.4 mm, p=0.41, right: 13.7 vs 13.7 mm, p=0.95) within carpal tunnel between RA group and non-RA group. Strain ratio within carpal tunnel in RA group was higher than that of non-RA group (left: 2.6 vs 2.1, p=0.002, right: 2.7 vs 2.2, p=0.003). There were no significant differences in the cross-sectional area of median nerve (left: 7.5 vs 8.1 mm², p=0.07, right: 8.8 vs 8.3 mm², p=0.6), the circumference of median nerve (left: 13.1 vs 13.5 mm, p=0.3, right: 13.7 vs 13.9 mm, p=0.71) and strain ratio (left: 2.1 vs 2.0, p=0.88, right: 2.3 vs 2.1, p=0.01) at the entrance of the carpal tunnel between RA group and non-RA group.

Conclusions: Real-time Elastosonography showed the stiffness of the median nerve with RA patients without any symptoms of CTS was higher than controls. It suggests that inflammation of flexor tenosynovitis and wrist joint may generate fibrotic change of median nerve in patients with RA.


SAT0659 COMPARISON BETWEEN EIGHT DIFFERENT ULTRASONOGRAPHIC SCORES AND ASSESSMENT IN RHEUMATOID ARTHRITIS - A CROSS-SECTIONAL STUDY

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory condition associated with well-recognised inflammatory joint features, which are amenable to ultrasound (US) examination. The implementation of US scoring systems in addition to clinical examination could help standardise the way RA is monitored; however, due to variation in local availability of US and sonographer expertise, different scoring systems have been used in clinical practice (1). Despite significant research progress in supporting the role of US in RA, there is no consensus as different scoring systems have been used in clinical practice (1). Despite significant research progress in supporting the role of US in RA, there is no consensus as different scoring systems have been used in clinical practice (1).

Methods: We performed a cross-sectional study of 224 RA patients stratified based on their DAS-28 scores and assessed using eight preselected US examination protocols including 22, 18, 16, 14, 10, 8 and two different combinations of 4 joints, respectively. Student T, Mann-Whitney U and Kuskal-Wallis tests were employed for analysis of clinical, laboratory and US parameters in the RA patient groups. (P < 0.05 was considered significant). Spearman’s coefficients were used to correlate permutations of pairs of US scores, and US and DAS-28 scores.

Results: We found a significant difference between different US hand scores and their ability to detect the presence of active and chronic inflammation in RA patients. The DAS-28 scores correlated very well (R=0.89–1, P < 0.05) with the total Power Doppler (PD) scores generated by all US protocols irrespective of patients’ disease activity. Simplified US scores missed information on presence of erosions (P < 0.05), but were equivalent to the extensive 22 joint score in appreciating the amount of chronic and active inflammation compared to the extensive 22 joint score (P=0.15, P=0.11, respectively).

Conclusions: SAT0660 SAFETY, FEASIBILITY AND TOLERABILITY OF PERFORMING CONSECUTIVE MINIMAL INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSY PROCEDURES ON THE SAME WRIST IN A PROSPECTIVE RHEUMATOID ARTHRITIS STUDY

S.A. Just1, C. Nielsen2, E.K. Heibo1, H.D. Schroder3, I.M.J. Hansen4, T. Barrington5, H.M. Lindegaard1, 1Rheumatology; 2Clinical Immunology; 3Clinical Pathology, Odense University Hospital, Odense; 4Medical, Svendborg Hospital, Odense University Hospital, Svendborg, Denmark

Background: Studies on synovial tissue retrieved using the minimal invasive ultrasound-guided synovial biopsy (USG-SB) method have led to major advances in the understanding of Rheumatoid Arthritis (RA). The method is now used in multicenter RA studies and recommended in the phases of RA drug development. Only to biopsy disease active joints at start and end of a study, can lead to biopsies being retrieved from different joints. This can make interpretation of the changes in the synovial tissue and gene-expression profile difficult, as synovial histology patterns can vary between joints. We here present an approach where we biopsy the wrist with disease activity at presentation and the same wrist after six month of disease duration. We use the same biopsy site, as it is the joint most commonly involved in the upper extremity in RA. The joint is easily accessible for USG-SB and therefore ideal to use to follow disease activity/treatment response/biomarker change in prospective RA studies.

Objectives: To assess the safety, tolerability and feasibility to perform repeated synovial biopsies from the same wrist, using a minimally invasive USG-SB technique in patients suffering from RA.

Methods: Patients with newly diagnosed untreated RA or longstanding (>5 years) RA and at least one clinically swollen wrist, underwent x-ray, magnetic resonance imaging (MRI) and ultrasound examination of the affected wrist and hand on the day of the biopsy. This was repeated 6 months later, where the second biopsy from the same wrist was taken. EULAR guidelines for RA treatment were followed in the 6 months between biopsies. Patient-reported outcomes (PRO) included a standard questionnaire given to all patients on the day of the biopsy as well as 2 weeks after the biopsy. Tolerability and the patient-reported willingness to repeat the procedure was assessed using the 5-point Likert scale.

Results: 38 RA patients (22 early, 16 longstanding) underwent USG-SB procedure at inclusion and after 6 months. One patient was excluded and did not have second biopsy due to diagnosis of Osteoporosis. All patients have undergone first biopsy and at present time and 50% second biopsy. At the EULAR congress complete data will be presented. At present time, at both first and second biopsy no worsening in PRO of the biopsied joints was reported 2w after the biopsy, as compared before the biopsy. No infection, hemorrhage, nerve or tendon damage has currently been observed. One patient developed a tenosynovitis after biopsy (the CPPD patient), successfully treated with glucocorticoid injection. 10% of the patients were somewhat or very unlikely to have another biopsy procedure after the first procedure, and 6% after the second. All included RA patients accepted to have a second biopsy. Detailed data on differences in tolerability between early untreated RA patients versus patients with longstanding RA, will be presented at the conference.

Conclusions: To our knowledge, we are the first, to demonstrate that retrieving synovial tissue using the USG-SB method on the same wrist, at start and end of a prospective RA study, is safe and well tolerated.


SAT0661 FINGER JOINT CARTILAGE THICKNESS EVALUATED BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: Joint destruction in RA includes both bone and cartilage lesions. By using the USG-SB method, cartilage thickness is evaluated as a joint space narrowing (JSN). However, joint space narrowing is not a direct evaluation of cartilage.

Objectives: We aimed to examine the finger joint cartilage thickness (CT) by ultrasound (US) imaging and clarify its clinical significance in patients with RA.

Methods: We enrolled 121 RA patients in low disease activity or clinical remission...
EVALUATION OF ANTI-DDOUBLE STRANDED DNA ANTIBODIES IN THE MONITORING OF SYSTEMIC LUPUS ERYTHEMATOSUS

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1 Exagen Diagnostics, Vista, CA; 2 Research and Development, Inova Diagnostics, San Diego, CA, United States

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune rheumatic disease characterized by the production of pathogenic autoantibodies. Amongst these antibodies, those directed to dsDNA are routinely used to monitor disease activity. QUANTA SLEDAI is a scoring index to score severity of SLE disease. Because the predictive value of anti-dsDNA is dependent on the sensitivity and robustness of the assays used, the choice of anti-dsDNA is crucial in the clinical laboratory and clinical research setting.

Objectives: The objective was to compare four anti-dsDNA assays for their performance characteristics of SLE disease activity.

Methods: A cohort of 36 subjects with active SLE presented with classical complement activation were enrolled and followed monthly for 1 year. At each study visit blood was collected, serum isolated and frozen until analysis. A total of 371 specimens were collected. Disease activity was scored on the day of each study visit according to the SELENA-SLEDAI index to score disease activity.

Results: At enrollment the sensitivity of the QUANTA Lite and High Avidity anti-dsDNA both reached 64%; whereas anti-dsDNA positivity was 83% by QUANTA Flash and reached 96% by CLIFT. Study visits with active disease presented with several fold higher anti-dsDNA titers than those with inactive disease status (Table 1). Linear mixed model testing indicated that the decrease in ns-SELENA-SLEDAI scores were associated with significant reduction in titers of all three anti-dsDNA kits (Table 2). QUANTA Flash yielded highest marginal R² in ns-SELENA-SLEDAI scores were associated with significant reduction in titers.

Conclusions: A direct visualization and quantification of finger joint CT, especially MCP joints, by US is valid and useful in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4703

Table 1. Anti-dsDNA antibody and disease activity

<table>
<thead>
<tr>
<th>Anti-dsDNA</th>
<th>Inactive Disease</th>
<th>Active disease</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QUANTA Flash</td>
<td>72 (30-134)</td>
<td>170 (56-813)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High Avidity</td>
<td>72%</td>
<td>86%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QUANTA Lite</td>
<td>32 (12-170)</td>
<td>129 (47-775)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CLIFT</td>
<td>56%</td>
<td>77%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Linear mixed model effects of anti-dsDNA on SELENA-SLEDAI scores

<table>
<thead>
<tr>
<th>Assay</th>
<th>Intercept + Estimate SE</th>
<th>p value</th>
<th>Marginal R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>QUANTA Flash</td>
<td>3.330.0 + 0.0110±0.0001</td>
<td>&lt;0.001</td>
<td>0.112</td>
</tr>
<tr>
<td>High Avidity</td>
<td>2.838.0 + 0.0023±0.0011</td>
<td>0.001</td>
<td>0.082</td>
</tr>
<tr>
<td>CLIFT</td>
<td>3.330.0 + 0.0033±0.0003</td>
<td>0.28</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Conclusions: These preliminary data indicate that anti-dsDNA antibodies determined by QUANTA Flash have value in monitoring SLE disease activity.


DOI: 10.1136/annrheumdis-2017-eular.5317

Table 2. Linear mixed model effects of anti-dsDNA on SELENA-SLEDAI scores

<table>
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<tr>
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<th>Intercept + Estimate SE</th>
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<tr>
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</tbody>
</table>

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Table 2. Linear mixed model effects of anti-dsDNA on SELENA-SLEDAI scores

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</table>

Conclusions: These preliminary data indicate that anti-dsDNA antibodies determined by QUANTA Flash have value in monitoring SLE disease activity.


DOI: 10.1136/annrheumdis-2017-eular.5317
with primary SS, 66% with secondary SS). Frequently inhomogeneity was found in all major SG (33%, 22% left and right submandibular, 77%, 44% left and right parotid glands) in primary SS. Both submandibular glands were symmetrically involved (p < 0.02). Duration of disease was negatively correlated to inhomogeneity of right parotid gland (p < 0.02).

Conclusions: Inhomogeneity in major SG in GS US was found in the majority of patients with primary and secondary SS. The symmetrical involvement of submandibular glands was significant. The inhomogeneity appears in the early period of diagnosis. No major differences were found between two groups.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2104

### SAT0665

**DOES PATIENTS’ OPINION OF REMISSION IN RHEUMATOID ARTHRITIS OVERLAP US “TRUE” REMISSION?**

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Background: Patients describe RA remission as the absence of any symptoms or return to normality. Ultrasound (US) in RA remission patients did not exactly overlap clinical evaluation of remission in previous studies (residual synovitis frequently described). US tenosynovitis evaluation and scoring seemed to better follow clinical remission scores than synovitis in RA [1].

Objectives: To verify with US/clinical evaluations if patients’ reported remission is “true” remission, and if and which clinical and US scores are lowest possible in that cohort.

Methods: Forty-eight RA patients were enrolled in this pilot study between 2015–2017 according to their positive answer to the question “Are you feeling free of symptoms, like before RA started for you?”; the enrollment was regardless of the treatment they were on. Written informed consent was obtained. Clinical evaluation of tendon and swollen joints was performed the same day with US evaluation of 24 joints and 26 tendon sites and with lab CRP evaluation, blinded from one another. DAS28 and SDAI were calculated after, counting VAS1–5, for both physician and patients.

Results: Mean patients age was 58, 35/48 (72.9%) patients were also in remission per DAS28 criteria. Except for CRP value, no other variables (tendon, swollen joints, RF, CCP, remission duration) were significantly different in the group with overlapping DAS28 remission. Considering 1.00 as the “ideal” situation (absolute overlapping of US remission and remission felt by patients), the closest was PD scoring in tenosynovitis of the ankle and feet (100%) and the furthest (absolute overlapping of US remission and remission felt by patients), the closest group with overlapping DAS28 remission. Considering 1.00 as the “ideal” situation (absolute overlapping of US remission and remission felt by patients), the closest was PD scoring in tenosynovitis of the ankle and feet (100%) and the furthest (absolute overlapping of US remission and remission felt by patients), the closest group with overlapping DAS28 remission.

Conclusions: Patients describe RA remission as the absence of any symptoms or return to normality. Ultrasound (US) in RA remission patients did not exactly overlap clinical evaluation of remission in previous studies (residual synovitis frequently described). US tenosynovitis evaluation and scoring seemed to better follow clinical remission scores than synovitis in RA [1].

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4244

### SAT0666

**SAMPLE SIZE FOR RA CLINICAL TRIALS USING ULTRASOUND OUTCOME MEASURES MAY BE REDUCED BY NOVEL JOINT SELECTION METHODS: A PILOT STUDY**

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1Office of Clinical Sciences, Centre for Quantitative Medicine, Duke-NUS Medical School; 2Yong Loo Lin School of Medicine, National University of Singapore; 3Duke-NUS Medical School; 4Department of Rheumatology and Immunology, Singapore General Hospital, Singapore; 5NHRI Leeds Musculoskeletal Biomedical Research Unit; 6Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

Background: Novel outcome measures selecting a reduced joint count for ultrasonography can be highlyresponsive in demonstrating the improvement in joint inflammation seen in rheumatoid arthritis (RA) patients on treatment [1].

Objectives: To determine whether the use of the novel methods can translate into smaller sample sizes for subject recruitment into RA clinical trials. Results from the existing methods are used for comparison.

Methods: 24 RA patients with treatment starts or escalations had clinical and ultrasonar joint assessment at baseline and 3 months. The novel methods select joints based on (A) ultrasound joint findings (i.e. Individualized Ultrasound (IUS) method) or (B) a composite of ultrasound and clinical joint findings (i.e. Individualized Composite Ultrasound (ICUS) method). In contrast, the existing methods select joint sites for ultrasonography. Scores at the relevant joints per patient are summed up to obtain the total inflammatory score (TIS). The effect size (ES) was measured as the mean change of the TIS divided by the standard deviation of the change in the TIS. Sample sizes were calculated from confidence intervals (CIs) on ES that reflect uncertainty in estimating ES. For a given CI on ES sample sizes are computed as the minimum number of patients required to provide >80% power at α = 0.05 for rejecting the null hypothesis (defined as no difference in the 3-month mean change in TIS comparing novel versus existing methods).

Results: Based on the 95% CI analysis, sample sizes using existing joint assessment methods in conjunction with the 12-joint approach ranged from 10 to 234. The corresponding sample sizes using the ICUS method with the 12-joint approach ranged from 7 to 39, and using the IUS method with the 12-joint approach ranged from 6 to 37. The corresponding sample sizes using the ICUS method with the 7-joint approach ranged from 6 to 24, and using the IUS method with the 7-joint approach ranged from 6 to 35.

Conclusions: Our findings strongly suggest that novel ultrasound joint selection methods result in smaller sample size requirements compared to existing methods, and provide justification for larger studies to confirm these observations.

References:

Disclosure of Interest: None declared


### SAT0667

**PRESEPSIN AND PROCALCITONIN ARE OF DIAGNOSTIC VALUE FOR BACTERIAL INFECTION IN PATIENTS WITH CONNECTIVE TISSUE DISEASES**

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Background: Recently, presepsin (soluble CD14-subtype) and procalcitonin are reported as a good diagnostic markers of bacterial infection, especially sepsis. However, their utility in patients with connective tissue diseases (CTDs) has been unknown.

Objectives: To assess the diagnostic value of presepsin and procalcitonin in patients with CTDs.

Methods: We enrolled the consecutive patients with CTDs, who checked the level of procalcitonin and/or presepsin during January to September, 2016, retrospectively. We divided two groups; the infection group and non-infectious group. Infection was diagnosed by symptoms, micro-bacterial methods and the good response to antibiotics. The data analysis were assessed using IBM SPSS statistics 22.

Table 1. Summary statistics for novel versus existing methods on 3-month change in scores

<table>
<thead>
<tr>
<th>Method/Approach</th>
<th>Mean 3-month change in TIS</th>
<th>SD of change in TIS</th>
<th>Effect Size</th>
<th>Post hoc Sample Size</th>
<th>Effect Size</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICUS/7-joint</td>
<td>0.61</td>
<td>0.54</td>
<td>1.13</td>
<td>9</td>
<td>0.61</td>
<td>6.24</td>
</tr>
<tr>
<td>ICUS/12-joint</td>
<td>0.87</td>
<td>0.91</td>
<td>0.96</td>
<td>11</td>
<td>0.46</td>
<td>7.39</td>
</tr>
<tr>
<td>IUS/7-joint</td>
<td>0.66</td>
<td>0.67</td>
<td>0.99</td>
<td>11</td>
<td>0.49</td>
<td>1.67</td>
</tr>
<tr>
<td>IUS/12-joint</td>
<td>0.91</td>
<td>0.94</td>
<td>0.97</td>
<td>11</td>
<td>0.47</td>
<td>6.37</td>
</tr>
<tr>
<td>Existing/7-joint</td>
<td>0.10</td>
<td>0.29</td>
<td>0.34</td>
<td>70</td>
<td>-0.07</td>
<td>16.1</td>
</tr>
<tr>
<td>Existing/12-joint</td>
<td>0.22</td>
<td>0.35</td>
<td>0.63</td>
<td>68</td>
<td>0.18</td>
<td>10.234</td>
</tr>
</tbody>
</table>

Ct: Confidence Interval; SD: Standard Deviation. 3Forest contains zero which corresponds to the null hypothesis, so upper limit cannot be calculated.
Results: Eighty-four patients with CTDs were enrolled, including 42 patients with rheumatoid arthritis (RA). The level of procalcitonin was evaluated in all patients, and the level of presepsin was in 48 patients. Thirty-six patients were classified in infection group; 38 patients in the CRP-positive non-infection group; and 10 patients in CRP-negative non-infection group. The level of procalcitonin was significant higher in infection group than CRP-positive non-infection group (693 +/- 577 pg/mL vs. 250 +/- 101 pg/mL, p < 0.01) (Fig. 1). Among the patients with RA, the level of procalcitonin was significant higher in infection group than non-infection group (809 +/- 637 pg/mL vs. 233 +/- 135 pg/mL, p < 0.01). AUCs of procalcitonin (0.823) and presepsin (0.821) showed similar diagnostic value. The cut-off value of presepsin and procalcitonin were 265 pg/mL and 0.16 ng/mL, respectively (sensitivity: 78.3% and 82.6%, specificity: 76.0% and 76.0%).

Conclusions: Procalcitonin and presepsin may be of diagnostic value for bacterial infection in patients with CTDs, especially may distinguish bacterial infection from active phase in patients with CTDs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4763

SAT0668 ASSESSMENT OF INTRACRANIAL VESSELS AND VASCULAR LESION IN RHEUMATOID ARTHRITIS. A DETAILED TRANSCRANIAL DOPPLER, CAROTID ULTRASOUND AND BRAIN MRI STUDY


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Background: Stroke has been associated with rheumatoid arthritis (RA). Vascular physiology should be assessed in the preclinical vascular state.

Objectives: We assessed RA patients and healthy controls by transcranial Doppler (TCD), carotid ultrasonography and brain MRI. We wished to determine preclinical pathophysiological changes in the cerebral vasculature.

Methods: Altogether 63 female RA patients and 60 age-matched controls underwent TCD assessment of the medium cerebral (MCA), basilar and vertebral arteries. Pulsatility (PI), resistance (RI) indices and circulatory reserve capacity (CRC) were determined. The presence of carotid plaques and intima-media thickness (cIMT) were also determined. Intracerebral vascular lesions were investigated by brain MRI. RA subsets include MTX- and biologic-treated patients.

Results: MCA PI and RI values at rest and after aperine are significantly increased in the total RA population vs controls. MCA PI (r) and RI (r) is also lower in biologic-treated patients. MCA CRC was also impaired and basilar artery PI was decreased (CRC) were determined. The presence of carotid plaques and intima-media thickness (cIMT) were also determined. Intracerebral vascular lesions were investigated by brain MRI. RA subsets include MTX- and biologic-treated patients.

Conclusion: Correlation analysis suggested multiple associations between right and left TCD parameters. There may be an association of TCD and carotid features with cerebral atrophy and age. Disease duration, disease activity and anti-CCP may influence left MCA PI and RI, as well as CRC. Lp(a) may also influence the development of carotid plaques.

Conclusions: This may be the first study to show increased distal MCA and basilar artery occlusion in RA as determined by TCD. RA patients also exert CRC defect. We also confirmed increased carotid plaque formation, increased cIMT. Biologics may beneficially influence some parameters in the intracranial vessels.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2846

SAT0669 HOW DO WE USE BIOLOGICS IN PATIENTS WITH A HISTORY OF MALIGNANCY? AN ASSESSMENT OF TREATMENT PATTERNS USING SCANDINAVIAN REGISTERS


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Background: Immune competence is of importance for the occurrence and outcome of malignancies. Robust data on risk of relapse of previous cancer following treatment with biological immune-modulators are scarce. Most treatment guidelines caution about their use in patients with a history of cancer, leaving rheumatologists with the decision whether a potential treatment benefit may offset any potential risk of cancer relapse.

Objectives: To assess the overall use of biologics and the relative use of different biological drugs in RA patients with a history of cancer.

Methods: As part of a Nordic collaboration, and using data from the ARTIS (Sweden), ROB-FIN (Finland), and ICEBIO (Iceland) biologics registers, we identified all patients with RA who initiated a first ever biological treatment 2010 through 2014. Through linkage to the national cancer registers, we identified those patients who had a history of any invasive malignancy (including squamous cell skin cancer) either within the years preceding start of biological treatment (‘recent history of malignancy’) or more than five years before start of biological treatment (‘non-recent history malignancy’).

Results: The age- and gender distributions were similar across countries and drugs. Initiators of non-TNFα biologics were older than TNFI-initiators; the median age at treatment start was the highest for rituximab. Out of a total of 8065 bio-initiations, 6% occurred in individuals with a history of cancer (2% with a cancer within 5 years, and 4% with a cancer more than 5 years before treatment start). Whereas there was little variation (around 5%) across TNFI initiators, the proportion of patients with a history of cancer at treatment start was higher among rituximab initiators, in part explained by age (Table). There were only small variations across country (not shown).

Conclusions: In Sweden, Finland and Iceland, one out of 20 biologics-initiators (and almost one out of five rituximab initiators) have a history of an invasive cancer, underscoring the need for more data on benefit/risk in this treatment context. The higher proportion in rituximab initiators is partly explained by differences in age at treatment start and reflects the preference for rituximab by clinicians for treatment of patients with history of cancer.

Disclosure of Interest: K. Chatzidionysiou Consultant for: Roche, Pfizer, Abbvie, Elli-Lilly, UCB, K. Aaltonen: None declared, D. Nordström: Speakers bureau: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB; B. Gudbjornsson: Speakers bureau: Actavis, Celgene, MSD, Pfizer, G. Grondal: None declared, A. Geirsson: None declared, L. Steingrimsdottir: None declared, T. Frisell: None declared, J. Askling: Grant/research support from: AbbVie, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Samsung

DOI: 10.1136/annrheumdis-2017-eular.6665
SAT0670 | THE PREVALENCE OF NEUROPATHIC PAIN-LIKE SYMPTOMS AND ASSOCIATED RISK FACTORS IN THE NOTTINGHAM COMMUNITY: A CROSS-SECTIONAL STUDY

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Background: Knee pain (KP) affects 1 in 4 adults over the age of 50. Aside from structural joint changes, person-specific factors influence the KP experience. Increased central sensitisation of neural pathways due to localised joint pain or ineffective descending inhibitory mechanisms can cause an enhanced pain response and neuropathic pain-like (NP) symptoms. Understanding these person-specific factors and how they modulate the pain experience might help profile different KP and NP phenotypes.

Objectives: a) To determine the prevalence of NP in a KP community population b) To identify significant risk factors associated with NP and those with both NP and non-NP KP.

Methods: 9,513 men and women, aged 40+ years, were recruited from the East Midlands region (United Kingdom) via postal questionnaire. The questionnaire included sections on KP severity (numerical rating scale) and type (NP versus nociceptive) using the modified PainDETECT Questionnaire (mPDQ); quality of KP using the intervention Rats constant osteoarthritis pain (IOAP) tool as well as other risk factors including age, body mass index (BMI), injury, pain catastrophizing scale (PCS) and mental wellness (Hospital Anxiety and Depression Scale). KP participants were those who reported “knee pain for most days of the past month” while likely NP was mPDQ scores of ≥13 and NP ≥19. Differences between groups were assessed using t-tests for continuous data and χ² for categorical data. We used multinomial regression analysis to determine the odds ratios (ORs) of risk factors with 95% confidence intervals (CI) and significance set at p<0.05.

Results: The prevalence of definite NP in the Nottingham Community was 366 (13.62%). There were more women (p=0.04) and higher BMI (p<0.001) in KP vs. non-KP responders but no age difference (p=0.05). When comparing the neuropathic-like KP to non-neuropathic KP responders, significant risk factors associated with adjustment for age, BMI, gender and pain severity included: anxiety (OR 3.17 (95% CI 2.38,4.23)); depression (OR 2.99 (95% CI 2.14,4.19)); PCS in highest tertile (OR 5.39 (95% CI 2.94,9.88)); fibromyalgia (OR 4.06 (95% CI 2.48,6.66)) and previous knee injury (OR 1.5 (95% CI 1.12,2.00)). When comparing non-KP responders to non-KP responders, anxiety (OR 1.74 (95% CI 1.31,2.30)), depression (2.05 (95% CI 1.40,3.01)), PCS 3.78 (95% CI 2.57,5.56), fibromyalgia (OR 1.94 (95% CI 1.10,3.40)) and previous injury (OR 1.35 (95% CI 1.05; 1.73)) were significant risk factors after adjustment.

Conclusions: This is the first population based cross-sectional study in the UK to determine prevalence of NP in people with KP. The results suggest that both psychological factors (depression, anxiety, high catastrophising) and peripheral risk factors (injury) associate with NP reporting. These factors can augment pain sensitivity and produce an amplified response via central and peripheral pathways. Phenotypes based on these risk factor profiles may warrant specific management in KP populations.

Acknowledgements: Arthritis Research UK Grant Refs: 20777, 20194

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4930

SAT0671 | THE IMPACT OF OBESITY ON TARGET GOALS AND FUNCTIONAL ABILITY IN THE ERAS/ERAN UK PROSPECTIVE COHORTS

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Background: The links between adipose tissue and inflammation on the one hand and obesity and joint dysfunction on the other, are well established. However, how these translate into clinical disease activity and functional disability in rheumatoid arthritis (RA), remains to be clearly defined.

Objectives: To investigate the association between BMI and 1. The achievement of disease remission or low disease activity and 2. Functional ability. In RA.

Methods: Data from two consecutive UK multi-centre RA inception cohorts with similar design were used: the Early RA Study (ERAS) and Early RA Network (ERAN). Recruitment figures/median follow up for ERAS and ERAN were 1465/10 years (maximum) and 1236/6 years (maximum age 81 yrs), respectively. Standard demographic and clinical variables were recorded at baseline and then annually until loss to follow-up or the end of study follow-up. Multilevel logistic regression analysis was used with either remission (R-DAS) or low disease activity status (L-DAS) and health assessment questionnaire (HAQ, <1 vs ≥1) as the outcome. Independent variables of interest in models adjusting for patient disease-related clinical variables and recruitment year. BMI was examined in separate models as both a continuous and categorical predictor variable according to WHO definitions: underweight (BMI less than 18.5), normal (BMI between 18.5 and 25), overweight (BMI between 25 and 30) and obese (BMI greater than 30).

BMI was included in the models relating to the same time point as the outcome assessed.

Results: Baseline BMI data from 2420 patients (90%) indicated that 40.0% had BMI scores in the normal range, 1.8% were overweight, 37.2% were overweight and 21.3% were obese. Mean BMI increased slightly over time from 26.5 at baseline to 26.8 at 2 years and then 27.1 at 5 years. In multilevel logistic models adjusting for age, sex, smoking status, antibody status, haemoglobin, erosions and year of recruitment, higher BMI was associated with reduced odds of achieving R-DAS (OR 0.97;95% CI 0.95, 0.99) (table) and L-DAS, although the latter did not reach statistical significance (OR 0.98;95% CI 0.90, 1.06). Obesity was related to a significantly lower chance of R-DAS by 29% (OR 0.71;95% CI 0.55, 0.93) and L-DAS by 31% (OR 0.69;95% CI 0.55,0.87). Higher BMI was predictive of higher disability (OR 1.04;95% CI 1.01,1.06). More specifically, obesity increased the odds of higher disability by 63% (OR 1.63;95% CI 1.20,2.23) and in the same models, higher BMI was also strongly predictive of higher disability (OR 3.67;95% CI 3.41,3.95).

Table. Impact of BMI category on disease activity and functional ability in models adjusting for patient demographic, clinical & disease variables.

Conclusions: The findings support a link between high BMI and worse clinical outcomes, namely lower disease activity and functional ability. Obesity was associated with lower levels of both remission and low disease activity states, and of higher disability. The findings highlight the importance of monitoring the patients’ weight, screening and targeting obesity as part of routine clinical practice, in order to improve disease outcomes. This work provides clinical insights into the role of BMI on disease outcomes in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5510

SAT0672 | RISK OF FRACTURE FragILE FrACTURE AMong PATIENTS WITH PSORIASIS: A POPULATION BASED MATCHED COHORT STUDY FROM THE UNITED KINGDOM

Z. Paskins1,2, R. Whittle1, A. Abdul Sultan1, S. Muller1, M. Blagojevic-Bucknall1, T. Helliwell1, S. Hider1,2, E. Roddy1,2, M. Callen1.

1Research Institute for Primary Care and Health Sciences, Keele University, Keele; 2Haywood Rheumatology Centre, Haywood Hospital, Burslem, Stoke-on-Trent, United Kingdom

Background: Psoriasis is a common inflammatory skin disease affecting 2–4% of the population and of these a subset will develop an associated inflammatory arthritis (psoriatic arthritis - PsA). An increased risk of osteoporosis has previously been reported in psoriasis patients but the risk of fracture in patients with both psoriasis and PsA has not been established.

Objectives: To estimate the effect of psoriasis, and PsA, on the risk of fracture using a large electronic primary care health database.

Methods: A matched cohort study was conducted utilizing data from the Clinical Practice Research Datalink, a large UK database of primary care medical records. The exposed population was defined as psoriasis patients aged over 40 years with an incident diagnosis between 1990–2004, who were followed up until 2015. Four unmatched patients were matched to each exposed based on age, sex and general practice. The incidence rate of fracture were calculated as the number of incident diagnoses per 10,000 person-years, stratified by sex. Hazard ratio (HR) and 95% confidence intervals were estimated using a Cox proportional hazards model to compare the hazard rate between the exposed and unexposed, adjusting for BMI, alcohol consumption, smoking status, Charlson comorbidity index and steroid use. Fracture risk was estimated for patients with both psoriasis and PsA, identified as patients with an incident diagnosis of psoriasis between 1990–2004.

Results: 24,219 patients with psoriasis and 94,820 controls were included in the study. The mean age was 59 years at study entry and just over half (51%) of the patients were female. The incidence rate of fracture was 4.8 (95% CI 4.55–6.13) and 53.1 (51.7–54.5) per 10,000 person-years for the exposed and unexposed, respectively. After adjusting for confounding factors, patients with psoriasis had 12% increased risk of fracture (HR: 1.12; 95% CI 1.06–1.19) compared to the matched unexposed group. The risk was slightly higher in males (1.22 (1.09–
1.36) than females (1.09 (1.03–1.17)). Among those with psoriasis, 4.1% were also diagnosed with PsA. An increased risk of 45% was found in those exposed to both psoriasis and PsA compared to the unexposed group (1.45 (1.09–1.94)).

**Conclusions:** This study reports for the first time, an increase in fracture risk in patients with psoriasis. A higher risk was found in males than females and the risk was further increased if the patient also had PsA. These findings suggest that fracture risk assessment needs to be considered for individuals with psoriasis and PsA.

**Acknowledgements:** This study was funded by the National Institute for Health Research School for Primary Care Research (NIHR SPCR). CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and a NIHR Research Professorship in General Practice (NIHR-2014-04-026). TH is funded by an NIHR Clinical Lectureship in Genetic Epidemiology. AAS is funded by an NIHR Postdoctoral Fellowship. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2856

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**SAT0673** **RISK AGE AND RELATIVE RISK OF CVD IN INFLAMMATORY JOINT DISEASES**

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**Background:** Individuals with inflammatory joint diseases (IJD) [rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA)] have increased risk of cardiovascular disease (CVD). In the European guidelines for CVD prevention, calculation of relative risk and risk age is advised in patients with low absolute risk of fatal CVD events the next 10 years estimated by the systematic coronary risk evaluation [SCORe] algorithm; the rational being that low absolute risk may conceal high relative risk and risk ages far beyond chronological age. Thus, more patients needing intensive CVD prevention may be identified. Relative risk is a ratio comparing absolute CVD risk in a specific patient to the risk given optimal CVD risk factor levels (CVDRFs). Risk age denotes the age with similar CVD risk and optimal CVDRFs. At this date, no studies have evaluated relative risk and risk age across IJD entities, neither has the agreement between different risk age models been investigated.

**Objectives:** 1) Estimate relative risk and risk age across IJD entities. 2) Investigate agreement between different risk age models.

**Methods:** RA/axSpA/PsA patients aged ≤65 years with moderate 10-year risk of fatal CVD were included from a nationwide quality assurance project implementing CVD risk assessment. Relative risk and cardiovascular risk age was calculated in accordance with risk charts published by the European Society of Cardiology (2016) and Cooney et al (2012). Vascular age was calculated by matching SCORE to estimated risk ages in accordance with Cuyedi et al (2010). Four different vascular age estimations were calculated, depending on whether the EULAR 1.5 multiplicative factor in RA was applied (mSCORE) and if SCORE version with HDL-c (SCORE-HDL-c) was used: SCORE, SCORE-HDL-c, mSCORE and mSCORE-HDL-c. Risk years beyond chronological age, were calculated. Linear regression models were used to investigate agreement between risk age estimations.

**Results:** Relative risk was increased in 53% of all patients and 20% had three times the risk or higher compared to individuals with optimal CVDRF levels. In total, 42% and 20% had a risk age ≥5 years higher than their chronological age, according to the cardiovascular risk age model and the vascular age model derived from SCORE, respectively. There were minor differences between RA, axSpA and PsA patients in terms of relative risk and risk age. Agreement between cardiovascular risk age and various vascular age models varied (Figure). Discrepancies ≥5 years in estimated risk age were observed in 14–43% of estimations. The largest observed difference in calculated risk age was 24 years. Similarly, linear regression models yielded a R² of 0.81–0.96. Across all models, median difference between risk age and risk age increased with advancing relative risk. Moreover, several patients had high relative risk despite a risk age close to their chronological age.

**Conclusions:** Relative risk and risk age may identify several patients at high need of intensive CVD preventive efforts despite low estimated absolute risk. However, there are considerable discrepancies between risk age models.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3379

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**SAT0674** **EARLY TREATMENT RESPONSE TO CONVENTIONAL DMARD THERAPY IN RHEUMATOID ARTHRITIS IS A BETTER PREDICTOR OF LOW DISEASE ACTIVITY OR TREATMENT ESCALATION AT 12 AND 24 MONTHS THAN AUTOANTIBODIES OR EROSIONS**

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**Background:** The EULAR guidelines recommend using the presence of seropositivity or erosions to support treatment decisions. The prognostic value of these factors regarding the primary treatment target in rheumatoid arthritis, remission or low disease activity (LDA), is unclear.

**Objectives:** To investigate biomarkers, csDMARD treatments and response to treatment regarding their usefulness to predict LDA or the need to escalate treatment within 24 month.

**Methods:** The control group in RABBIT (Rheumatoid Arthritis: Observation of biologic therapy) comprises N=2,228 patients who were enrolled at treatment start with conventional-synthetic (cs)DMARDs after failure of at least one csDMARD therapy, mostly methotrexate (MTX) monotherapy. We excluded patients with a DAS28-ESR≤3.2 at enrollment and those with ≥2 csDMARD failures (n=618). 102 patients were excluded due to enrollment less than 12 month prior to closure of the data base (April 30th, 2016). The DAS28-ESR, physical function, age, seropositivity (RF+ACPA+), comorbidities (≥3 vs. <3) and the presence of erosions at baseline were evaluated as prognostic factors. Concomitant treatment with glucocorticoids (mgt/d) and csDMARDs, response to treatment (3–6 month after enrollment) were additionally examined. We applied a multinomial generalized-estimating-equation (GEE) model to investigate: 1) achievement of LDA at month 12/24 or (2) treatment escalation (biologic therapy) in year one and thereafter.

**Results:** More than one third of patients (34.2%) were treated with a combination of MTX and leflunomide (LEF), 23.6% with LEF mono, 20.8% with MTX + hydroxychloroquine (HCQ) or sulfasalazine (SSZ), 16.5% with MTX mono, and 4.9% with SSZ mono. We found no major differences across treatment regimens except for patients treated with MTX+HCQ who had a lower DAS28, better physical function and shorter disease duration at treatment start. Significant predictors for achieving LDA were low DAS28 at baseline, improvement in DAS28 within 3–6 month, better physical function and less than 3 comorbidities (table). Escalation to bDMARD therapy was significantly more frequent in younger patients, those with no improvement in DAS28 or concomitant glucocorticoid treatment, and in patients with less than 3 comorbidities. There were no differences between treatments regarding achievement of LDA. However, switching to bDMARDs was
most frequent in patients treated with LEF mono or with LEF+MTX. The presence of erosions or seropositivity were not associated with any of the outcomes (table).

Conclusions: The highest impact on achieving LDA was found in disease activity at baseline and response to treatment within 3–6 month. The relevance of erosions, and/or seropositivity regarding the prediction of a poorer outcome is disputable.

Acknowledgements: RABBIT is supported by a joint, unconditional grant from Abbvie, Bristol-Myers Squibb, Celtrion, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis and UCB.

Disclosure of Interest: A. Richter Consultant for: Pfizer, A. Strangfeldt bureau: BMS, MSD, Pfizer, Roche, Sanofi-Aventis, P. Herzer Consultant for: Abbvie, Pfizer, J. Kaufmann: None declared, T. Klopsch: None declared, S. Zinke: None declared, J. Listing Consultant for: Sandzoz, Pfizer, A. Zink Speakers bureau: Abbvie, VAS, MSD, Pfizer, Roche, UCB

DOI: 10.1136/annrheumdis-2017-eular.4979

SAT0675 | THE ROLE OF EROSIONS TYPICAL OF RHEUMATOID ARTHRITIS IN THE 2010 ACR/EULAR RHEUMATOID CLASSIFICATION CRITERIA: RESULTS FROM A VERY EARLY ARTHRITIS COHORT

G.H. Brinkmann 1, 2, E.S. Norli 2, 3, P. Bøyesen 2, D. van der Heijde 4, L. Grøvle 1, (SERONEGATIVE) MALES SHOW BETTER EULAR G.H. Brinkmann 2, E. Lie 2.

Background: A EULAR task force has proposed that in addition to the 2010 ACR/EULAR rheumatoid arthritis (RA) classification criteria (2010 RA criteria), patients can still be classified as having RA with less than 6 criteria points on the ACR/EULAR rheumatoid arthritis (RA) classification criteria (2010 RA criteria), i.e. ≥3 erosive joints (1). We calculated the additional number of patients being classified as RA based on the erosion criterion at baseline and during follow-up. Other cut-offs and the distribution of erosive joints was also examined.

Methods: Patients with arthritis of ≥16 weeks duration and a clinical diagnosis of RA or undifferentiated arthritis (UA) with available hand and feet radiographs were included from the Norwegian Very Early Arthritis Clinic (NOR-VEAC) study. Erosive disease was defined according to the EULAR definition accompanying the 2010 RA criteria. The current study included 289 patients (mean (SD) age 48 (14.7) years, 54.3% females, median (25, 75 perc) duration of joint swelling 46 (19.5, 79.0) days). At baseline, 120 patients (41.5%) fulfilled the 2010 RA criteria. Of the remaining 169 not fulfilling the 2010 RA criteria, 55 patients had ≥1 erosive joint (40 with hand erosions, 28 with feet erosions and 13 with hand and feet erosions) and 15 (5.2%) patients fulfilled the erosion criterion (Figure 1). The distribution of erosive joints in the 169 patients not fulfilling the 2010 RA criteria at baseline is shown in the table.

Results: The current study included 289 patients (mean (SD) age 48 (14.7) years, 54.3% females, median (25, 75 perc) duration of joint swelling 46 (19.5, 79.0) days). At baseline, 120 patients (41.5%) fulfilled the 2010 RA criteria. Of the remaining 169 not fulfilling the 2010 RA criteria, 55 patients had ≥1 erosive joint (40 with hand erosions, 28 with feet erosions and 13 with hand and feet erosions) and 15 (5.2%) patients fulfilled the erosion criterion (Figure 1). The distribution of erosive joints in the 169 patients not fulfilling the 2010 RA criteria at baseline is shown in the table.

> 1 erosive joint (n=55) 23 17 12 8 22 12
> 2 erosive joints (n=27) 11 13 10 8 12 8
> 3 erosive joints (n=15) 6 8 9 6 8 7

118 patients had radiographic follow-up at 2 years, of whom only 1 additional patient solely fulfilled the erosion criterion during follow-up (7 additional patients fulfilled both the 2010 criteria and the erosion criterion). Among patients with no erosions at baseline (N=74), 13 (17.6%) developed erosions during follow-up (PIP joints n=3, MCP n=4, wrist n=3, CMC joint n=1, MTP joints n=9 and IP1 joint in 2 fingers). Of the 118 patients with erosions at baseline (N=74), 13 (17.6%) developed erosions during follow-up (PIP MCP Wrist CMC + os trapezium MTP IP1 feet). Other cut-offs and the distribution of erosive joints was also examined.

Erosive joints at baseline

1 erosive joint (n=55) 23 17 12 8 22 12
2 erosive joints (n=27) 11 13 10 8 12 8
3 erosive joints (n=15) 6 8 9 6 8 7

Conclusions: Among this cohort of patients with very early arthritis, 5.2% were classified as RA at baseline based solely on the erosion criterion. Of the 118 patients with 2-year follow-up data, only 1 additional patient was classified based on the erosion criterion alone during follow-up, thus, follow-up radiographs in patients with early RA do not seem to provide additional information in classifying patients with RA.

References:

Disclosure of Interest: G. Brinkmann: None declared, E. Norli: None declared, P. Bøyesen: None declared, D. van der Heide: None declared, L. Grøvle: None declared, A. Haugen: None declared, H. Nygaard: None declared, O. Bjørneboe: None declared, C. Thunem: None declared, T. Kvien Consultant for: Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandzoz and UCB.


SAT0676 | (SERONEGATIVE) MALES SHOW BETTER EULAR TREATMENT RESPONSE THAN FEMALES IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS (RA)

M. Yates 1, J. Galloway 1, A. Rivett 2, S. Norton 1, J.M. Ledingham 3, E.M. Dennison 1, A.J. Macgregor 4, K. Bechman 1, A. Rutherford 1, N. Snowden 1.

Academic Rheumatology, King’s College London; 2The British Society for Rheumatology, London; 3Rheumatology Dept, Portsmouth Hospitals NHS Trust, Portsmouth; 4MRC, Southampton University, Southampton; 5Rheumatology Dept, Norfolk and Norwich University Hospital, Norwich; 6Rheumatology Dept, Pennine MSK Partnership, Oldham, United Kingdom

Background: Gender has been reported to play a role in attainment of RA remission (1), but the data are inconsistent. The impact of gender in early RA therefore warrants further investigation.

Methods: An audit, designed as a national prospective longitudinal observational study, was conducted to assess early RA care. All NHS providers in England were required to participate. Follow up data were captured over 3 months for subjects with a diagnosis of RA. Logistic regression was used to estimate associations between gender and DAS-28 response. Smoking status, baseline disease activity, age, antibody status, symptom duration, referral times, and treatment were considered in multivariate models.

Results: Of 146 eligible trusts submitted data. 11,752 subjects consented, 5,622 were diagnosed with RA. DAS-28 response was available for 2234/5622 (39.7%). Male patients had a similar 3 month improvement in their DAS-28 to females, despite having a lower mean baseline score. Male gender associated with a higher rate of good EULAR response (DAS improvement ≥1.2, follow up DAS <3.3), with an adjusted odds ratio of 1.42 (CI 1.17–1.72). There were no differences between the genders in their treatment use or in other aspects of care including speed of referral (Table 1).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Male N=798</th>
<th>Female N=1432</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean (SD)</td>
<td>61.8 (13.2)</td>
<td>58.1 (15.1)</td>
<td>0.0</td>
</tr>
<tr>
<td>Smoker %</td>
<td>28</td>
<td>21</td>
<td>0.0**</td>
</tr>
<tr>
<td>Social deprivation decile mean (SD)</td>
<td>5.4 (2.9)</td>
<td>5.5 (2.9)</td>
<td>0.6**</td>
</tr>
<tr>
<td>Seropositive %</td>
<td>66</td>
<td>70</td>
<td>0.05**</td>
</tr>
<tr>
<td>symptom duration days</td>
<td>230</td>
<td>228</td>
<td>0.8*</td>
</tr>
<tr>
<td>Baseline DAS-28 mean (SD)</td>
<td>5.1 (1.4)</td>
<td>5.3 (1.3)</td>
<td>0.03*</td>
</tr>
<tr>
<td>FU DAS-28 mean (SD)</td>
<td>3.3 (1.5)</td>
<td>3.6 (1.5)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Change in DAS-28 mean (SD)</td>
<td>1.8 (1.7)</td>
<td>1.7 (1.6)</td>
<td>0.08*</td>
</tr>
<tr>
<td>EULAR good response %</td>
<td>43.4</td>
<td>36.7</td>
<td>0.002**</td>
</tr>
<tr>
<td>Timely referral %</td>
<td>16</td>
<td>15</td>
<td>0.3**</td>
</tr>
<tr>
<td>Timely rheumatology assessment %</td>
<td>39</td>
<td>39</td>
<td>0.7**</td>
</tr>
<tr>
<td>Steroids commenced at baseline %</td>
<td>87</td>
<td>86</td>
<td>0.7**</td>
</tr>
<tr>
<td>Early DMARD treatment %</td>
<td>28</td>
<td>27</td>
<td>0.9**</td>
</tr>
<tr>
<td>Any DMARD prescribed within 6 weeks %</td>
<td>70</td>
<td>70</td>
<td>0.09*</td>
</tr>
<tr>
<td>DMARD choice; Methotrexate monotherapy %</td>
<td>69</td>
<td>68</td>
<td>0.6**</td>
</tr>
<tr>
<td>DMARD choice; combination therapy %</td>
<td>44</td>
<td>44</td>
<td>0.8**</td>
</tr>
</tbody>
</table>

* t-test ** Chi-squared. Social deprivation decile from deprivation rank calculated via super output area.
The male excess in good EULAR response was more pronounced in seronegative RA (1.98 (CI 1.4–2.8) compared to 1.21 (0.96–1.53)).

Conclusions: The association of male gender with improved outcomes in early RA has not been shown before in a national cohort of this scope. Previous work suggests seronegative individuals achieve greater clinical response (2), here we present this effect amplified in men. To the authors’ knowledge this is a new finding. This is likely multifactorial, with biological effect of gender, greater diagnostic uncertainty and higher reporting of global scores in women all potentially playing a role.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1560

SAT0677 [**THE IMPACT OF DISEASE ACTIVITY DURING PREGNANCY IN WOMEN WITH SLE ON THE OCCURRENCE OF PREECLAMPSIA AND PREMATURE BIRTH**]

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Background: Pregnancy in women with systemic lupus erythematosus (SLE) is associated with an increased risk of complications such as preeclampsia and premature birth. Active disease is considered one of the risk factors.

Objectives: The aim of this study was to explore the impact of disease activity in pregnant women with SLE on preeclampsia and premature birth, and compare the occurrence with pregnancies from the general obstetric population.

Methods: We linked data from RevNatus with data from the Medical Birth Registry of Norway (MBRN). RevNatus is a Norwegian nationwide prospective observational register including women with an inflammatory rheumatic disease when planning pregnancy or after conception. The register was established in 2006 and is administered by the National advisory unit on pregnancy and rheumatic diseases. Women 18 years or older are recruited and followed-up in each trimester of pregnancy and at 6 weeks, 6 months and 12 months after birth. MBRN is a national birth registry. The population constituted all singleton live births recorded in MBRN in the period 2006 – 2014. The births in women diagnosed with SLE in MBRN and included in RevNatus formed the patient group (n=180). The references were all other births (n=498849). We performed logistic regression, and calculated OR for preeclampsia and premature birth in the patient population compared to the references from the general obstetric population. The target population was then split in two groups according to disease activity, assessed in the 2nd trimester, and compared to references.

Results: Women with SLE had a significantly higher risk of preeclampsia and premature birth than references from the general obstetric population. Women with active disease in pregnancy are most prone to these complications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1509

SAT0678 [**SIGNIFICANTLY INCREASED SEROPOSITIVITY, RHEUMATOID FACTOR TITRES AND RHEUMATOID NODULES IN CORNISH KAOLIN WORKERS**]

D. Murphy 1,2, E. Fleeing 2, K. Bellis 1, D. Hutchinson 1,2. 1Rheumatology, Royal Cornwall Hospital; 2University of Exeter Medical School, Cornwall Campus, Truro, United Kingdom.

Background: Kaolin has been mined in Cornwall, UK for over 250 years. With half of the world’s production originating from the area at the turn of the 20th century. Mineral kaolinite does not react as free silica, and is used in heavy metal contamination containment due to its adsorption capabilities.

Objectives: To investigate the prevalence of occupational kaolin dust exposure in male rheumatoid arthritis (RA) patients in Cornwall, UK.

Methods: All males diagnosed with RA under follow up at the Royal Cornwall Hospital, UK, during the study period April 2015-January 2017, were invited to complete an occupational questionnaire, detailing current occupation, last occupation (if retired) and other occupations for >1 year.

Results: 39/720 (5%) cases were included and 329/720 (45%) had a history of kaolin exposure. 1720 (9%) cases died during the study period (22 months), 54/640 (8%) remaining cases had occupational kaolin exposure, approximately 12 times higher than expected based on current census employment rates. 30/54 had long term kaolin dust exposure, living in the post code region PL22-PL26 (total male population 33693). These were matched for age ±2 years, sex and index of multiple deprivation (IMD) ±1 decile, to RA patients with no occupational dust or fume exposure. 40/110 potential controls were successfully matched. Significant more RA kaolin workers were seropositive for RF and ACPR than non-dust exposed RA controls (Table 1). Of RF seropositive patients, mean RF titres were significantly higher in kaolin workers than unexposed controls (p<0.01). No significant differences were seen in ACPR titre. Smoking prevalence rates were not significantly different between kaolin workers and controls. Amongst ever smokers, median pack years smoked showed no difference between cases and controls.

Conclusion: Kaolin exposed never smokers demonstrated significantly higher RF titres than unexposed never smokers (kaolin median RF 109 (IQR 32–193.5), control median RF 24 (IQR 7–61), p<0.04), as did kaolin exposed smokers (kaolin median RF 146.7 (IQR 56–231.5), control median RF 61 (IQR 18.5–70), p<0.03, figure 1). Interestingly, 7/30 (23%) kaolin workers demonstrated nodular disease, compared to 3/40 (7.5%) matched controls, p=0.06, significantly higher than the background nodular rate 79/720 (11%) of male RA patients throughout Cornwall, p<0.04.

Figure 1. Rheumatoid factor titres, RA kaolin workers vs RA controls.

**p<0.04, ***p<0.003

Table 1. Preeclampsia and premature birth in references and in women with SLE

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>References</th>
<th>SLE</th>
<th>Adj OR* (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>15132 (3.0)</td>
<td>14 (7.8)</td>
<td>2.64 (1.53, 4.58)</td>
<td>0.001</td>
</tr>
<tr>
<td>Premature birth</td>
<td>27063 (5.5)</td>
<td>13 (7.5)</td>
<td>4.25 (2.92, 6.19)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Adjusted for maternal age, parity and smoking in pregnancy.

Table 2. Preeclampsia and premature birth in references and in women with SLE according to disease activity status

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>References</th>
<th>No disease activity†</th>
<th>Disease activity‡</th>
<th>Adj OR* (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>15132 (3.0)</td>
<td>14 (4.7)</td>
<td>3.80 (2.90, 5.30)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Premature birth</td>
<td>27063 (5.5)</td>
<td>13 (7.5)</td>
<td>3.71 (1.46, 9.68)</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

†LAI=Po. ‡LAI=P. *Adjusted for maternal age, parity and smoking in pregnancy.

Conclusions: Women with SLE have a higher risk of preeclampsia and premature birth than references from the general obstetric population. Women with active disease in pregnancy are most prone to these complications.

Acknowledgements: Cornwall Arthritis Trust.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1890
**SAT0679** | ARE ADULT TRAJECTORIES OF WEIGHT OVER A LIFETIME LINKED TO FOOT PROBLEMS YEARS LATER?

A.B. Dufour 1, E. Losina 2, H.B. Menz 3, M.P. LaValley 4, M.T. Hannan 1, 1 Institute for Aging Research, Hebrew SeniorLife; 2 Brigham and Women’s Hospital, Boston, United States; 3 School of Allied Health, La Trobe University, Bundoora, Australia; 4 Biostatistics, Boston University, School of Public Health, Boston, United States

**Background:** Obesity and foot problems are common in older adults and associated with many negative health outcomes. Better understanding of the consequences of patterns of weight change may lead to better prediction and dealing with foot pain and foot disorders.

**Objectives:** This study identified longitudinal trajectories of weight in a population-based study and examined the association of these groups with current foot problems.

**Methods:** We used 28 measures of weight over 57 years to identify trajectories of weight in 2445 members of the Framingham Foot Study using k-means longitudinal cluster analysis. Foot examinations (2002-2008) recorded presence of foot pain, hallux valgus, claw toes, hammer toes and overlapping toes on each foot. Associations between weight group membership and foot problems at time of foot exam, adjusted for age and sex, were examined using logistic regression with generalized estimating equation correction for two feet per subject. The reference group used for analysis was the group with the lowest weight trajectory (“E”).

**Results:** We found 5 trajectories of weight, representing relatively constant patterns over time, with weight increasing from groups E to A. Those in group E were more likely to be older, while the youngest were in group “A.” E had the lowest prevalence of foot pain (14%) while group “A” had the highest (22%). Similarly, group “A” had the lowest prevalence of hallux valgus, while group E had the highest (36%) (Table 1).

Compared to group “E,” other groups were more likely to have foot pain (ORs 1.57–3.50, Table 2) and less likely to have hallux valgus (ORs 0.73–0.99). For claw toes, all but one group were more likely to have claw toes compared to group “E.” Groups “A” and “D” were more likely to have hammer toes (ORs 2.40 and 1.35, respectively) compared to group “E.” We found no associations between overlapping toes and group membership.

**Table 1. Participant characteristics by weight trajectory group**

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=201</td>
<td>N=644</td>
<td>N=617</td>
<td>N=506</td>
<td>N=477</td>
</tr>
<tr>
<td>402 feet</td>
<td>1288 feet</td>
<td>1233 feet</td>
<td>1011 feet</td>
<td>954 feet</td>
</tr>
</tbody>
</table>

| Age (years) | 63±9.0 | 69±11.2 | 68±10.5 | 66±9.7 | 71±11.9 |
| Body mass index (kg/m²) | 37±6.3 | 37±6.3 | 27±3.3 | 29±4.0 | 31±4.3 | 23±2.9 |
| Female (%) | 19% | 1036% (80%) | 78% | 16% (14%) | 9% | 8% (9%) |
| Foot pain (%) | 8% (22%) | 24% (19%) | 22% (18%) | 18% | 13% (14%) |
| Hallux Valgus (%) | 57% (14%) | 49% (32%) | 26% (22%) | 16% (17%) | 34% (16%) |
| Claw Toes (%) | 9% (2%) | 29% (2%) | 29% (2%) | 24% (2%) | 18% (2%) |
| Hammer toes (%) | 9% (22%) | 246% (19%) | 197% (16%) | 165% (16%) | 174% (18%) |
| Overlapping toes (%) | 14% (3%) | 99% (8%) | 73% (6%) | 48% (5%) | 90% (9%) |

**Table 2. Association between weight trajectory group membership and foot problems, adjusted for age and sex**

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean birth weight g</td>
<td>3518 (588)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
</tr>
<tr>
<td>Birth weight g</td>
<td>3518 (588)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
</tr>
<tr>
<td>Birth weight g</td>
<td>3518 (588)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
</tr>
<tr>
<td>Birth weight g</td>
<td>3518 (588)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
<td>3091 (691)</td>
</tr>
</tbody>
</table>

**Conclusions:** Trajectories with higher weight over a lifetime had increased odds of foot pain and claw toes, and decreased odds of hallux valgus later in life. These results provide evidence that having lower weight over one’s lifetime can reduce the likelihood of foot problems later in life.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3018

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**SAT0680** | THE IMPACT OF DISEASE ACTIVITY DURING PREGNANCY IN WOMEN WITH SLE ON THE BIRTH WEIGHT OF THE CHILD

A.C.G. Skorpen 1, E. Losina 2, S. Lydersen 3, I.-M. Gilboe 4, K.Å. Salvesen 5, 1 Norwegian University of Science and Technology, Trondheim; 2Department of Neuromedicine and Movement Science; 3Regional Center for Child and Youth Mental health and Child Welfare, Oslo; 4Biostatistics, Boston University, School of Public Health, Boston, United States

**Background:** Mean birthweight is lower in children of SLE-mothers than in reference. Active disease in pregnancy is considered one of the risk factors.

**Objectives:** The aim of this study was to explore the association of disease activity in women with SLE in pregnancy and the birth weight of the child expressed as mean birth weight and mean z-score for birth weight.

**Methods:** We linked data from RevNatus with data from the Medical Birth Registry of Norway (MBRN). RevNatus is a Norwegian nationwide prospective observational register including women with an inflammatory rheumatic disease when planning pregnancy or after conception. The register is administered by the National advisory unit on pregnancy and rheumatic diseases. Women 18 years or older are recruited and followed-up in each trimester of pregnancy and at 6 weeks, 6 months, and 12 months after birth. MBRN includes all singleton live births recorded in MBRN in the period 2006–2014. The women in both groups with diagnosed with SLE in MBRN and included in RevNatus formed the patient group (n=180). The references were all other births (n=498649). Mean birth weight in the patient group was compared to mean birth weight in the general obstetric population. We calculated z-score for birth weight adjusted for gestational age and sex. The target population was then split in two groups according to disease activity assessed in the 2nd trimester, and compared to references. One-way ANOVA was performed to compare SLE-women without active disease, SLE-women with active disease and references from the general obstetric population.

**Results:** The mean birth weight and mean z-score were both significantly lower in women with SLE compared to references.

**Table 1. Mean birth weight and z-score in references and in women with SLE**

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>References n=49795</th>
<th>SLE n=180</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight g</td>
<td>3518 (588)</td>
<td>3091 (691)</td>
<td>3518 (588)</td>
</tr>
<tr>
<td>Birth weight g</td>
<td>3518 (588)</td>
<td>3091 (691)</td>
<td>3518 (588)</td>
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</tbody>
</table>

**DOI:** 10.1136/annrheumdis-2017-eular.5820

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**SAT0681** | RISK OF ACTIVE TUBERCULOSIS IN PATIENTS WITH INFILTRATORY ARTHRITIS RECEIVING TNF-INHIBITORS

A.M. Gheorghi 1,2, A. Garaian 2, A. Radu 1,2, A. Soare 1,2, V. Aramă 2,2, D. Bumbăcea 1,2, D. Roburta 2,2, R. Onetea 1,2, S. Pintilie 1,2, M. Milicescu 1,2, I. Ancuta 1,2, A. Martin 1,2, M. Sasu 1, C. Ciofu 1,2, L. Macovei 1,2, V. Stoica 1,2, M. Bojinca 1,2, M. Boinca 1,2, Internal Medicine and Rheumatology, Cantacuzino Hospital; 2 Carol Davila University of Medicine and Pharmacy; 3 Infectious Diseases 1, Matei Bals National Institute for Infectious Diseases; 4 Dept. of Pneumology, Elias Emergency University Hospital, Bucharest, Romania

**Background:** Tuberculosis (TB) is a major concern in patients receiving TNF inhibitors (TNFi).

**Objectives:** To assess the incidence of active TB and the efficacy of TB prevention measures in a large, single-center cohort of patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and anklylosing spondylitis (AS) receiving TNFi.

**Methods:** Data of all patients in whom treatment with TNFi was initiated in our rheumatology clinic from January 1st 2002 until December 31st 2015 have been retrospectively analysed. The cohort was divided into 2 groups per the mandatory latent TB infection (LTBI) screening method at baseline: tuberculin skin test (group TST), and QuantiFERON®-TB Gold test (group QFT). The incidence of active TB was analysed for each group and compared to TB incidence data in general population.

**Results:** 653 patients were included (344 RA, 52 PsA, 257 AS); 324 patients belonged to the TST and 329 to the QFT group. The number of active TB cases/ time of exposure to TNFi (person-years, PY) was 17/2002.6 and 7/1041.2 respectively. The incidence of active TB was 0.001 and 0.001 respectively. There were no significant differences in disease in women with active as opposed to quiescent disease.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3038
had pulmonary TB, whereas the rest were disseminated TB (8 cases), TB pleurisy and/or pericarditis (4 cases), one mediastinal lymph node TB and one isolated hepatic TB. Using Pearson chi-square test, we found no significant differences between LTBI group and active TB (Table B).

Conclusions: In our cohort, new infection TB exceeds reactivation TB, suggesting the necessity of periodical LTBI re-screening.

Disclosure of Interest: A. M. Gheorghiou: None declared, A. Garaivan: None declared, A. Radu: None declared, A. Soare: None declared, V. Arama: None declared, D. Bumbaca: None declared, R. Dobrota: None declared, R. Oneata: None declared.

SAT0684 | PREVALENCE OF SARCOPENIA IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

A. Tournade 1,2, P. Jaffeux 3, T. Fraysse 1, A. Fan 1, M. Couderc 1, J.J. Dubost 1, A. Elmerri 1,2, P. Arnaud 1,2, C. Mihai 1, A. Sato 1,2, P. Arnaud 1,2.

Background: Evaluation of sarcopenia is of major relevance because of these chronic repercussions on morbidity and mortality. Although the definition should include both low muscle mass and function, a combination of the 2 criteria was not reported in inflammatory rheumatic diseases (IRDs).

Objectives: To determine in a cohort of IRDs the prevalence of sarcopenia using an accepted cut-off and evaluate its associations with clinical characteristics.

Methods: 324 patients with chronic inflammatory arthritis (RA, ankylosing spondylitis (SpA), and psoriatic arthritis (PsA)) without known history of cancer, chronic steroid treatment, or severe comorbidities were enrolled. Lean body mass was measured by dual energy X-ray absorptiometry (DXA) and muscle strength by handgrip strength. The prevalence of sarcopenia was defined based on these cut-off values.

Results: The prevalence of sarcopenia was 28% in RA, compared to 20.5% in SpA and 18% in PsA. The prevalence of sarcopenia was associated with age, duration of disease, smoking, low education level, and morning stiffness.

Conclusions: Sarcopenia is frequently observed in patients with chronic inflammatory rheumatic diseases. Its prevalence is lower in SpA and PsA than in RA. Further studies are needed to determine predictive factors and to assess the impact of sarcopenia on outcomes in these patients.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5835

SAT0685 | PREVALENCE OF OSTEOPEOROSIS IN ALBANIAN POSTMENOPAUSAL WOMEN AND THE ROLE OF RISK FACTORS IN OSTEOPOROSIS

A. Kollcaku, J. Kollcaku, V. Duraj, Rheumatology, University Hospital Center "Nene Tereza", Tirana, Albania

Background: Menopause is the time in woman’s life when production of sex hormones ceases. Sex hormone deficiency leads to increasing bone fragility and, thus, fracture risk. Bone turnover and bone mass could be affected by too many other risk factors. Osteoporosis threatens the health and quality of life of women aged over 70 years-old (2). Reduced muscle mass only was not highly prevalent and lower than that reported in elderly supporting important cofactors such as functional limitations or muscle quality in sarcopenia associated with rheumatic diseases.

Objectives: The aims of this study were to assess the prevalence of osteoporosis in Albanian postmenopausal women and the role of risk factors in osteoporosis.

Methods: A cross-sectional study was conducted in Tirana city in a period 2009–2013, including a population-based sample of 4,789 women. All subjects enrolled in the study were asked for risk factors for osteoporosis by completing a specific questionnaire. Low bone mineral density (osteoporosis defined as a bone mineral density T-score less than -1 and osteoporosis for T-score less than -2.5) was assessed with a bone ultrasound device which is simple and easy to use for screening of bone mineral density in population-based studies. Binary logistic regression was used to determine the relationship of osteoporosis and independent factors in this study population.

Results: The prevalence of osteoporosis in this study population was 6.2% (N=286) and prevalence of osteoporosis was 16.6%; 77.1% of osteoporosis women were in postmenopause. In logistic regression models was seen that menopausal women had 69% more chances than no menopausal women to have osteoporosis (OR=1.69, 95% CI=1.45–1.77, P<0.001). Osteoporosis was positively associated with multiparity (P<0.001) and long treatment with glucocorticoids (OR: 1.52; CI95% 1.46–1.64; p=0.020). In multivariable analysis osteoporosis was positively associated with the rheumatoid arthritis component (OR: 1.83; CI95% 1.62–2.06; P<0.001). In Kendall’s correlation coefficient, osteoporosis was negatively associated with level of education (r=0.101, p<0.001) and body mass index (r<0.003, p<0.009) and positively associated with white color of skin (r<0.003, p<0.027) and treatment with diuretics (r=0.007, p<0.001).

Conclusions: This study offers useful evidence about the osteoporosis and osteopenia prevalence among postmenopausal Albanian women. Caucasian females with early menopause, multiparous, lower body-weight, suffering from rheumatoid arthritis, long treated with glucocorticoids and diuretics and lower education should be followed-up more carefully for development of osteoporosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4495

SAT0686 | DETERMINANTS OF 12-MONTHS PERSISTENCE IN RHEUMATOID ARTHRITIS PATIENTS INITIATING SUBCUTANEOUS TNF-ALPHA INHIBITORS

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Background: Biotherapies such as subcutaneous tumor necrosis factor-alpha

Disclosure of Interest: Biotherapies such as subcutaneous tumor necrosis factor-alpha

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5122

Table 1. LTBI screening results and TB occurrence in the 653 TNFi-treated patients (Pearson χ² test)

<table>
<thead>
<tr>
<th>TST (n=324)</th>
<th>QFT (n=329)</th>
<th>All (n=653)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive immune-diagnostic test at baseline</td>
<td>52 (16.0%)</td>
<td>63 (19.1%)</td>
<td>115 (17.6%)</td>
</tr>
<tr>
<td>Active TB</td>
<td>17 (5.2%)</td>
<td>7 (2.1%)</td>
<td>24 (3.7%)</td>
</tr>
<tr>
<td>Reactivation TB</td>
<td>4 (1.2%)</td>
<td>20 (6.0%)</td>
<td>0.002</td>
</tr>
<tr>
<td>New infection TB</td>
<td>13 (4.0%)</td>
<td>5 (1.5%)</td>
<td>18 (2.8%)</td>
</tr>
<tr>
<td>Total TB incidence (per 10⁵ PY)</td>
<td>848.9</td>
<td>672.3</td>
<td>798.5</td>
</tr>
<tr>
<td>Maximum period of TNFi exposure in group 2002-2016 2011-2016 2002-2016</td>
<td>0.04/0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measurment of sarcopenia in the respective period in 10⁵ PY</td>
<td>102.3</td>
<td>76.7</td>
<td>102.3</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, disease duration.
SAT0685  DETERMINANTS OF 12-MONTHS PERSISTENCE IN PSORIATIC ARTHRITIS PATIENTS INITIATING SUBCUTANEOUS TNF-ALPHA INHIBITORS

B. Fautrel 1, M. Belhassen 2, C. Hudry 3, M.-C. Woronoff 4, N. Gouyette 5, A. Clément 6, E. Van Ganse 6, F. Tubach 7, C. Charles-Schoeman 8

1 APHP, Hôpital Pité-Salpétrière, Délégation de Biostatistiques, Santé publique et Information médico, APHP, Centre de Pharmacopédiologie (Cephei); INSERM, UMR 1123 ECEVE; Université Pierre et Marie Curie Paris 6, Sorbonne Universités, Paris, France

Background: Biotherapies such as subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFis) have transformed the management of inflammatory joint diseases such as psoriatic arthritis (PsA). The assessment of SC- TNFis persistence and its determinants is needed.

Table 1: Determinants of 12-month non-persistence (Cox model)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard Ratio</th>
<th>IC 95%</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC-TNFis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GLM</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CZP</td>
<td>1.642</td>
<td>1.343-2.006</td>
<td>0.0001</td>
</tr>
<tr>
<td>ETA</td>
<td>1.512</td>
<td>1.297-1.763</td>
<td>0.0001</td>
</tr>
<tr>
<td>ADA</td>
<td>1.418</td>
<td>1.258-1.599</td>
<td>0.0001</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Female</td>
<td>1.610</td>
<td>1.367-1.897</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-18</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>&gt;18</td>
<td>0.681</td>
<td>0.578-0.803</td>
<td>0.0001</td>
</tr>
<tr>
<td>Interaction with time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interaction sex * time</td>
<td>1.001</td>
<td>1.000-1.001</td>
<td>0.0025</td>
</tr>
<tr>
<td>Interaction socio-economic status * time</td>
<td>0.999</td>
<td>0.998-0.999</td>
<td>0.0023</td>
</tr>
</tbody>
</table>

Conclusions: Non-persistent patients were more likely female, with multiple comorbid conditions, and more line of biotherapies. Hospital admission for IRMD, and rheumatologist with treatment (COMPARED TO CZP ETA) decreased the risk of non-persistence. Further analyses are needed to better understand behaviours of patients and to assess the impact of non-persistence on clinical and economical outcomes.

Disclosure of Interest: B. Fautrel Grant/research support from: Abbvie, MSD, Pfizer, Consultant for: Abbvie, Biogen, BMS, Celgene, Hospira, Janus, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen Employee of: PELyon, C. Hugy Consultant for: Abbvie, BMS, PFIZER, ROCHE, CELGENE, NOVARTIS, BIOGEN, UCB, SANDOZ, AMGEN, Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, N. Gouyette Employee of: MSD France, A. Clément Employee of: MSD France, E. Van Ganse Consultant for: PELyon, ALK ABELO; AstraZeneca; Bayer; BMS, BIF; GSK; IMS; LASER; MSD, F. Tubach: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5023

SAT0686  MAJOR ADVERSE CARDIOVASCULAR EVENTS: RISK FACTORS IN PATIENTS WITH RA TREATED WITH TOFACITINIB

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Background: Patients (pts) with RA have increased risk of myocardial infarction (MI) and stroke that cannot be completely explained by traditional cardiovascular

Conclusion: Non-persistent patients were more likely female, with deprived socio-economic status, and multiple line of biotherapies. Treatment with GML (compared to CZP and ETA) decreased the risk of non-persistence. Further analyses are needed to assess the impact of non-persistence on clinical and economical outcomes.

Disclosure of Interest: C. Charles-Schoeman Grant/research support from: Abbvie, MSD, Pfizer, Consultant for: Abbvie, Biogen, BMS, Celgene, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, N. Gouyette Employee of: MSD France, A. Clément Employee of: MSD France, E. Van Ganse Consultant for: PELyon, ALK ABELO; AstraZeneca; Bayer; BMS, BIF; GSK; IMS; LASER; MSD, F. Tubach: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5081

Table 1: Determinants of 12-month non-persistence (Cox model)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard Ratio</th>
<th>IC 95%</th>
<th>P-value</th>
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<tbody>
<tr>
<td>SC-TNFis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GLM</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CZP</td>
<td>2.315</td>
<td>1.348-3.726</td>
<td>0.0005</td>
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<tr>
<td>ETA</td>
<td>1.631</td>
<td>1.199-2.217</td>
<td>0.0016</td>
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<tr>
<td>ADA</td>
<td>1.167</td>
<td>0.944-1.443</td>
<td>0.1525</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
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<tr>
<td>Male</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Female</td>
<td>1.480</td>
<td>1.301-1.684</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-18</td>
<td>1.000</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>&gt;18</td>
<td>0.996</td>
<td>0.991-1.001</td>
<td>0.1544</td>
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<tr>
<td>Interaction with time</td>
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<td></td>
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<tr>
<td>Interaction sex * time</td>
<td>1.001</td>
<td>1.000-1.001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Interaction socio-economic status * time</td>
<td>0.999</td>
<td>0.998-0.999</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusions: Non-persistent patients were more likely female, with deprived socio-economic status, and multiple line of biotherapies. Treatment with GML (compared to CZP and ETA) decreased the risk of non-persistence. Further analyses are needed to assess the impact of non-persistence on clinical and economical outcomes.

Disclosure of Interest: C. Charles-Schoeman Grant/research support from: Abbvie, MSD, Pfizer, Consultant for: Abbvie, Biogen, BMS, Celgene, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, N. Gouyette Employee of: MSD France, A. Clément Employee of: MSD France, E. Van Ganse Consultant for: PELyon, ALK ABELO; AstraZeneca; Bayer; BMS, BIF; GSK; IMS; LASER; MSD, F. Tubach: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5081
(CV) risk factors. Tofacitinib is an oral JAK inhibitor for the treatment of RA. Treatment with tofacitinib may increase total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c) and high-density lipoprotein-cholesterol (HDL-c), without affecting TC/HDL-c ratio.

Objectives: To evaluate major adverse CV event (MACE) risk factors in tofacitinib-treated patients with RA in a clinical development programme.

Methods: Data were pooled from pts with moderately to severely active RA receiving ≥1 tofacitinib dose in 6 Phase 3 and 2 long-term extension (LTE) studies (1 LITE study ongoing, data cut-off: April 2015). MACE was any MI, stroke or CV death (coronary, cerebrovascular, cardiac). Cox model regression evaluated associations between baseline (BL) values and time (BL to first tofacitinib dose) to first MACE. Changes (BL to Week [wk] 24) in MACE predictors and time to future MACE (first occurrence after 24 wks) were evaluated after adjusting for age, BL values and time varying tofacitinib dose. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated.

Results: 52 MACE cases occurred over 12,873 pt-years (py) of exposure in 4076 pts (incidence rate: 0.4 pts with events/100 py). At BL, compared with pts without MACE, pts with MACE were older (mean age 60.2 vs 52.7 years) with a higher mean BMI (29.2 vs 27.0 kg/m²) and longer mean RA disease duration (10.1 vs 7.7 years), and were more likely to have a history of diabetes (15.4% vs 7.8%) and hypertension (57.7% vs 33.7%). Pts with MACE had higher mean TC (208.2 vs 198.3 mg/dL), LDL-c (123.3 vs 114.0 mg/dL), TC/HDL-c ratio (4.0 vs 3.5) and triglycerides (152.1 vs 125.3 mg/dL) at BL, and lower HDL-c (53.5 vs 59.4 mg/dL) pts without MACE. In univariate analyses, traditional CV risk factors and use of corticosteroids or statins at BL were associated with MACE risk (Table). BL disease activity and inflammation measures were not associated with MACE risk (Table). In multivariate analysis, BL age, hypertension and the TC/HDL-c ratio were significantly associated with MACE risk. Increases in LDL-c (p<0.001) and decreases increases in TC/HDL-c ratio (p<0.05) after 24 wks of tofacitinib therapy were significantly associated with decreased risk of future MACE (Figure). Increases in erythrocyte sedimentation rate (ESR; p<0.09) may be associated with increased future MACE risk. Changes in TC, LDL-c or other disease activity measures were not associated with future MACE risk.

Conclusions: In pooled analyses of tofacitinib-treated pts (age and BL value adjusted), increases in LDL-c and TC after 24 wks of tofacitinib therapy were not associated with future MACE risk. Increases in HDL-c and decreases in the TC/HDL-c ratio after 24 wks of tofacitinib therapy were associated with reduced future MACE risk. Increases in ESR after 24 wks may be associated with increased future MACE risk. Changes in TC, LDL-c or other disease activity measures were not associated with future MACE risk.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by C Viegelm of CMC and was funded by Pfizer Inc.


DOI: 10.1136/annrheumdis-2017-eular.2434

SAT0687

ADHERENCE OF RHEUMATIC PATIENTS TO INH PROPHYLAXIS PRESCRIBED BEFORE BIOLOGICAL TREATMENT: HUR-BIO SINGLE CENTER REAL LIFE RESULTS

E. Seyho˘glu1, O.A. Uyaro˘glu1, A. Erden2, L. Kılıç2, B. Armaga2, A. Sarı2, M. Baykal2, S. Ak3, Ö. Karada˘g2, A. Akdo˘gan2, S. Apra¸s Bilgen2, S. Kiraz2, I. Ertendi2, U. Kalyoncu2

1Department of Internal Medicine, 2Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey

Background: Isoniazid (INH) prophylaxis is strongly recommended for the patients who have latent tuberculosis (TB) and who are going to be under anti-TNF treatment. INH is usually prescribed for 9 months and patient adherence to INH affects the risk of active TB development.

Objectives: In this study we aimed to assess the levels of patient adherence to INH prophylaxis.

Methods: Patients, who are under biological treatment and who have a quantiferon (QFT) test result, were evaluated with a questionnaire between August 2015-August 2016. Questionnaire included the demographic and clinical characteristics. Besides, patients were asked whether they had been prescribed INH. Patients, who were given INH prophylaxis, were asked to answer those questions: i) Did you take INH daily and regularly for 9 months? ii) If not what was the reason? The reasons are classified into three categories: 1) The patient discontinued INH of his/her own volition before 9 months. 2) Continued INH for 9 months but did not take regularly due to forgetfulness. 3) Treatment stopped by physician due to an adverse effect (elevation of liver enzymes, neuropathy, etc.).

Results: 1. 710 patients were recruited. INH was prescribed to 169 (23.8%) of 710. Demographic characteristics of INH-prescribed patients: 88 (52.1%) of 169 were female, mean age was 46.2 (SD:11.4), 82 (48.5%) of 169 at least graduated from a high school. Diagnosis were followed: RA 65 (38.4%), SpA 85 (50.3%), PsA 13 (7.7%), others 6 (3.6%). Totally 34 (20.1%) of 169 took INH irregularly, 19 (11.2%) of 169 patients discontinued INH of his/her own volition before 9 months. During follow-up of 5 were prescribed INH again after the physician and they completed the 9-months duration. 9 (5.3%) of 169 patients did not take INH regularly due to forgetting. INH was stopped by a physician due to liver enzyme elevation in 6 (3.5%) of 169 patients. There was not a statistically difference in demographical and clinical characteristics between regular and irregular INH takers.

Conclusions: There is an inadherence to INH treatment approximately in one of five patients. Only 35% of INH-recommended patients had a medical reason of inadherence. Among other patients, causes of inadherence were discontinuance of own volition and forgetfulness or perfunctoriness. Physicians should be aware that reminding of INH is one of the question in every outpatient clinic visits. Other reminding methods such as regular calling should be considered in those of high risk population. Further studies were needed for reminding process.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4093

SAT0688

JOINT INVOLVEMENT IN PATIENTS WITH KNEE AND HIP OA SCHEDULED FOR SURGERY: MULTI-JOINT OA, THE RULE NOT THE EXCEPTION?

E. M. Badley1, C. Yip1, J. D. Power2, R. Gandhi1, N. Mahomed2, J. R. Davey2, K. Syed3, T. R. Rampersaud2, C. Veillette2, A. V. Perruccio1,2

1Division of Health Care and Outcomes Research, Krembil Research Institute, 2The Arthritis Program, Toronto Western Hospital, Toronto, Canada

Background: Multijoint involvement in osteoarthritis (OA) has long been documented clinically and in the literature. Even so, the vast majority of OA research is conducted on single joint OA, and the implicit assumption is often that OA is OA, irrespective of whether a single joint or several joints are involved. The implicit assumption is often that OA is OA, irrespective of whether a single joint or several joints are involved.

Objectives: To examine the joint sites involved and investigate whether the extent of joint involvement changes with the presence of knee and hip OA.

Methods: A health questionnaire completed prior to surgery captured demographic and clinical characteristics. Baseline joint involvement was measured using 68 joints (28 joints in each of the left and right knee and hip). Patients were given INH prophylaxis, were asked to answer those questions: i) Did you take INH daily and regularly for 9 months? ii) If not what was the reason? The reasons are classified into three categories: 1) The patient discontinued INH of his/her own volition before 9 months. 2) Continued INH for 9 months but did not take regularly due to forgetfulness. 3) Treatment stopped by physician due to an adverse effect (elevation of liver enzymes, neuropathy, etc.).

Results: 1. 710 patients were recruited. INH was prescribed to 169 (23.8%) of 710. Demographic characteristics of INH-prescribed patients: 88 (52.1%) of 169 were female, mean age was 46.2 (SD:11.4), 82 (48.5%) of 169 at least graduated from a high school. Diagnosis were followed: RA 65 (38.4%), SpA 85 (50.3%), PsA 13 (7.7%), others 6 (3.6%). Totally 34 (20.1%) of 169 took INH irregularly, 19 (11.2%) of 169 patients discontinued INH of his/her own volition before 9 months. During follow-up of 5 were prescribed INH again after the physician and they completed the 9-months duration. 9 (5.3%) of 169 patients did not take INH regularly due to forgetting. INH was stopped by a physician due to liver enzyme elevation in 6 (3.5%) of 169 patients. There was not a statistically difference in demographical and clinical characteristics between regular and irregular INH takers.

Conclusions: There is an inadherence to INH treatment approximately in one of five patients. Only 35% of INH-recommended patients had a medical reason of inadherence. Among other patients, causes of inadherence were discontinuance of own volition and forgetfulness or perfunctoriness. Physicians should be aware that reminding of INH is one of the question in every outpatient clinic visits. Other reminding methods such as regular calling should be considered in those of high risk population. Further studies were needed for reminding process.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4093
characteristics (age, sex), symptomatic joints other than the surgical joint (right and left shoulders, elbows, wrists, hands, hips, knees, feet, ankle, neck and back), body mass index (BMI), comorbidities (hypertension, depression, diabetes, migraine headaches, cancer, respiratory disease, heart disease, stomach/bowel disease, stroke) and WOMAC hip- and knee-specific pain and function.

Results: Study questionnaires were completed by 366 hip and 407 knee patients. The mean age of the sample was 65 years (SD=9.2; range 38–89 years), 57% were female. The most frequently reported symptomatic joints among knee patients were the contralateral knee (53.2%), one or both hands (32.1%), and the upper-, mid- or lower-back (31.0%), and among hip patients were one or both knees (49.4%), the back (36.6%), and the contralateral hip (21.3%). The overall mean number of symptomatic joints other than the surgical joint was 3.0 (SD=3.2; range 0–17). Only 19.0% reported the surgical joint as the only symptomatic joint; 23.0% reported 5 or more additional symptomatic joints. Mean hip/knee-specific pain and function scores were significantly worse with increasing symptomatic joint count (p<0.01). Additional symptomatic joints were significantly more frequent in women than men; mean count 3.6 vs. 2.3 (p<0.01). No significant difference in mean joint count (p=0.64) was observed by age. Similarly, no difference was found by BMI (i.e. overweight/obese vs. normal); p=0.24 for mean count. However, the number of co-occurring conditions increased with increasing joint count: 27.2% reported 2+ co-occurring conditions among those with 1–4 symptomatic joints, and 42.8% among those with 5+ symptomatic joints (p<0.01).

Conclusions: In this clinical OA sample, the “average” patient reported multiple symptomatic joints. Increasing age was not associated with increasing frequency of symptomatic joints. Irrespective of age and obesity, multiple symptomatic joints were the rule, not the exception. It was notable that the frequency of co-occurring conditions increased with increasing symptomatic joint count. This may suggest a need to re-examine how OA is characterized and perhaps its underlying etiology as it relates to single vs. multi-joint involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6432

SAT0689 | PREVALENCE OF AND TEMPORAL TRENDS IN HYPERURICAEMIA AMONG ADULT PATIENTS WITH CHRONIC KIDNEY DISEASE IN IRELAND

F. Adeel1,2, A.A. Udayakumar2,3, D. Ryan2, X. Li2, A.D. Fraser1,2, A.G. Stack2,3

on behalf of Health Research Institute, University of Limerick. 1Department of Rheumatology, University Hospital Limerick; 2Graduate Entry Medical School, University of Limerick; 3Department of Nephrology, University Hospital Limerick, Limerick, Ireland

Background: An increasing body of evidence links hyperuricaemia with the development of several metabolic disorders and major cardiovascular outcomes. A better understanding of the burden and variation of hyperuricaemia within the health system is important in order to identify high-risk groups and facilitate early intervention with effective management strategies.

Objectives: The aim of this study was to describe the prevalence of hyperuricaemia, and period trends within the Irish Health System among patients with chronic kidney disease.

Methods: 136,325 adult CKD patients aged 18 and above with valid measurements of serum uric acid and creatinine levels were identified between 2006 and 2014 from the laboratory systems within the Irish health system. Hyperuricaemia was defined as serum uric acid ≥420μmol/L in men and ≥360μmol/L in women. Estimated glomerular filtration rates were determined using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation and patients were classified by CKD stage according to the Kidney Disease Improving Global Outcomes (KDIGO) staging system. Age- and sex-specific prevalence of hyperuricaemia estimates with 95% confidence intervals were determined for each group and across calendar years. Comparisons among groups and across years were conducted using chi-square and multivariate logistic regression was used to explore associations using adjusted odds ratios (AOR) and 95% Confidence Intervals (CI).

Results: Patients with hyperuricaemia were noted to be older [58.2 (18.5) vs. 50.4 (15.8) years]. The prevalence of hyperuricaemia increased progressively between 2006 and 2014 from 20.3% (19.5, 21.0) to 26.5% (25.8, 27.2%) in men and from 17.9% (17.2, 18.6) to 20.4% (19.8, 21.0) in women, p<0.001. Age-specific prevalence increased significantly over time for all age groups (18–39, 40–59, 60–79, and ≥80 years) for men and women, p<0.001. Prevalence was significantly higher with increasing CKD stage: 18.1% (14.5, 15.6) in Stage 1 CKD compared to 43.0% (34.8, 51.1) in Stage 5 CKD, p<0.001. However, rates fell significantly for those Stage 4 and 5 CKD respectively (Figure 1). In multi-variable models, the adjusted likelihood of hyperuricaemia increased with each successive year (Figure 2).

Conclusions: The prevalence of hyperuricaemia is substantial in the Irish health system and has increased in frequency over the past decade. Although the burden was highest among patients with more advanced CKD, an encouraging decline in prevalence was observed in recent years. Greater management of gout and hyperuricaemia from increasing utilization of urate-lowering therapies may be responsible for this trend.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5556

SAT0690 | RISK OF HOSPITALIZED INFECTION IN CANCER PATIENTS WITH AUTOIMMUNE DISEASES: A SINGLE-CENTER COHORT STUDY

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Background: Whether the risk of hospitalized infection is associated with autoimmune diseases compared with those without autoimmune diseases.

Objectives: To examine the risk of hospitalized infection in incident cancer patients with autoimmune diseases compared with those without autoimmune diseases.

Methods: During 2000–2016, we identified 37,027 incident cancer patients from the Cancer Registry database of Taichung Veterans General Hospital. Autoimmune diseases included rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), psoriasis (PSO)/psoriatic arthritis (PSA), antiphospholipid syndrome, polymyositis, dermatomyositis, systemic sclerosis, Sjögren’s syndrome, mixed connective tissue disease, multiple sclerosis, neuromyelitis optica, palindromic rheumatism, myasthenia gravis, Hashimoto’s thyroids, immune thrombocytopenic purpura, autoimmune hemolytic anemia, juvenile idiopathic arthritis, adult onset Still’s disease, Crohn’s disease, ulcerative colitis, Wegner’s granulomatosis, and uveitis. Of all subjects, 1,334 had autoimmune diseases. The association between autoimmune diseases and hospitalized infection risk was studied using hazard ratios (HRs) with 95% confidence intervals (CIs) using Cox proportional regression analyses after adjusting for baseline age, sex, cancer stage, hemoglobin (Hgb), creatinine (Cr), log(ALT), log(WBC), and use of biologic agents or tofacitinib.

Results: Among all cancer subjects, the mean ± SD age was 60.2±14.7 years, and the proportion of male gender was 55.7%. Of the 1,334 patients with autoimmune diseases, 338 (25.3%) patients had RA, 221 (16.6%) patients had SLE, 61 (4.6%) patients had AS, 151 (11.4%) patients had PSO/PSA, and 563 (46.8%) had other autoimmune diseases. The incidence rates of hospitalized infection were 143.8 per 10,000 years in patients with autoimmune diseases and 118.9 per 10,000 years in patients without autoimmune diseases. The risk of hospitalized infection was higher in patients with RA and SLE, but not in patients with AS, PSO/PSA, or other autoimmune diseases. Prior use of biologic agents or tofacitinib did not increase hospitalized infection risk. HRs for risk factors for hospitalized infection included older age (HR, 1.01; 95% CI, 1.01–1.1), higher cancer stage, CR (HR, 1.04; 95% CI, 1.02–1.06), log(WBC) (HR, 1.21; 95% CI, 1.14–1.28), Female gender (HR, 0.85; 95% CI, 0.62–0.68) and Hgb (HR, 0.89; 95% CI, 0.80–0.90) were associated lower hospitalized infection risk.

Table 1: Univariable and multivariable analyses for the association between autoimmune diseases and hospitalized infection among cancer patients

<table>
<thead>
<tr>
<th>Autoimmune diseases</th>
<th>Univariable analysis*</th>
<th>Multivariable analysis*</th>
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<td>HR (95% CI)</td>
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*Adjusted for age, gender, cancer stage, prior use of biologic agents or tofacitinib, baseline hemoglobin, creatinine, log (ALT) and log (WBC).

Conclusions: Hospitalized infection was associated with a comorbidity of RA or SLE in incident cancer patients.

Acknowledgements: With thanks to Cancer Registry database and Clinical Informatics Research & Development Center of Taichung Veterans General Hospital for the Support of Clinical data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4676
SAT0691 INFLUENCE OF SMOKING IN THE EXPRESSION OF CHRONIC PERIODONTITIS AND ANTI-CITRULLINATED PROTEINS ANTIBODIES IN RHEUMATOID ARTHRITIS

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Background: Environmental, genetic and epigenetic factors can induce citrullination of structural peptides by the enzyme PAD, which induce anti-citrullinated protein antibodies (ACPA) preceding RA. Among the environmental factors are cigarette smoke, infections, such as P. gingivalis in periodontitis (PD) and Pre-votella copit, intestinal microflora, and silica dust. Given the implication of these two exogenous factors, tobacco and PD, in citrullination, and tobacco enhancer factor in PD, we studied:

Objectives: 1. The risk of smoking for developing advanced PD in patients with RA. 2. Possible influence of smoking on the expression of severe PD and ACPA in RA patients.

Methods: Observational, descriptive, cross-sectional study in RA patients older than 18 yrs. (ACR/EULAR 2010), with ≥4 teeth, without tooth cleaning nor antibiotic intake 6 months previously. Socio-demographic and anthropometric variables included smoking status, social indicators such as Grafta scale, stress level, annual dental visits, prophylaxis, and co-morbidities such as diabetes mellitus, dyslipidemia, ischemic cardiovascular disease. Serum ACPA detection: semiquantification Ab IgG against citrullinated peptides (ELISA) with Immunocan CCPiustest kit. Eurodiagnostica: positive →25% ACPA title stratification: Low (25–75), moderate (75–90), high (>90%). Periodontal parameters: plaque index (PI), Bleeding on probing (Bop), probing pocket depth, recession, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti): T level 0 (absence), T1 (mild), T2 (severe), Statistical analysis: 1-student, Kruskal Wallis, Chi-cudarado by Stata program 13.1.

Results: We studied 187 patients, F: 74.8±21.4%, mean age 54.4 yrs. Follow-up time 8.8 y.o. RF: 74.2%, ACPA positive in 114/167 patients (67.8%). Smoking habit: current smoker (29.15%), former smoker (26.4%); low socioeconomic status (36.5%) relative poverty (33.7%), PD was observed in 97.3%. T1 52.4%, T2 19.6%. A “risk gradient” was observed for PD relative to smoking habit. Former smoker OR 1.62 (95% CI 0.81–3.27), p=0.174; smokers, OR 2.27 (95% CI 1.05–4.91), p=0.037. When analyzing the influence of smoking on PD development according to ACPA profile, a gradient effect of developing severe PD was observed for former smokers OR 2.37 (95% CI 0.52–7.64) to current smokers OR 6.99 (95% CI 1.53–32.07) (p=0.029) in ACPA (−) patients. This relationship was not observed in ACPA (+) patients (p=0.383).

Conclusions: 1. There is a “risk gradient” to develop PD in RA in relation to past or current exposure to tobacco, so that, although not significant, former smokers are at greater risk than non-smokers, and current smokers have a significant risk 2.3 times higher. 2. This risk gradient is shown in ACPA (−) patients, but not in ACPA (+) patients, which suggests an independent relationship between PD and ACPA (+) RA.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5201

SAT0692 PREDICTORS AND PERSISTENCE OF UNACCEPTABLE PAIN DURING THE FIRST YEAR OF RHEUMATOID ARTHRITIS IN SWEDEN

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Background: Pain is a dominant symptom in rheumatoid arthritis (RA). Objectives: Investigate unacceptable pain (VAS-pain ≥40) during the first year of the disease and whether it can be predicted from baseline disease characteristics. Methods: The cohort included all incident RA cases from the Swedish population-based case-control Epidemiological Investigation of Rheumatoid Arthritis study (EIRA), who also were in the Swedish Rheumatology Register. Unacceptable pain was defined as scoring 40 mm or above on the pain visual analog scale (VAS) (i.e. not reaching the patient acceptable symptom state (PASS)) (1), and the proportion of patients going in and out of PASS was traced over the first year. Association between baseline parameters, divided into quartiles, and unacceptable pain at one year was assessed using modified Poisson regression and expressed as risk ratios with 95% confidence intervals (95% CI), adjusted for sex and age at diagnosis. Results: A total of 2808 patients were included in the study and 33.8% of the patients remained in PASS (i.e VAS pain below 40) at inclusion. If a patient had PASS at any given visit, there was over 70% chance that the patient remained in PASS at the following visit. The most common PASS pattern (25.6%), was to present with unacceptable pain, reach PASS at the 3 month visit, and then remain in PASS. However, one year after diagnosis, only two thirds of the patients had PASS. Higher disability (measured as HAQ) at baseline was significantly and independently associated with an increased risk for unacceptable pain at one year (for the highest quartile of HAQ: RR=1.97 [95% CI:1.60–2.42]). Also high tender joint count at baseline was associated with an increased risk for unacceptable pain; RR=1.40 [95% CI: 1.18–1.65] for the highest quartile, whereas high swollen joint count at baseline was associated with a decreased risk; RR=0.79 [95% CI: 0.66–0.95] for the highest quartile.

Conclusions: The results highlight the need for efficient pain treatment strategies early in the disease.

therapy group were found to be significantly lower (-0.41±0.29 mg/dL, \( p < 0.001 \)). However, the serum uric acid levels in the estrogen monotherapy and tibolone groups did not differ significantly from the control group level.

**Conclusions:** Serum uric acid levels decreased in response to estrogen-progestogen combination therapy in postmenopausal women. We attribute our findings to the effects of progestogen, rather than estrogen.

**References:**


**Acknowledgements:** No grants or other support were received for this study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular:1950

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**SAT0694**

**SUBLIMING OF EARLY RA-PATIENTS IDENTIFIED CLUSTER OF PATIENTS WITH HIGH LEVELS OF PAIN, FATIGUE AND PSYCHOSOCIAL DISTRESS 3 YEARS AFTER DIAGNOSIS**

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**Background:** The wide range of effective treatment alternatives for rheumatoid arthritis (RA) makes treating the disease to inflammatory remission a feasible goal for a majority of patients. However, earlier studies have reported that symptoms other than inflammatory disease activity causes a substantial burden of illness for RA-patients. These unmet needs include persistent pain, fatigue, impaired physical function and mental health status (1).

**Objectives:** To identify clusters of early RA-patients based on pain, fatigue, sleep, physical function, mental health status and perceptions of quality of life, 3 years after diagnosis. Withal investigate associations between clusters and clinical parameters at the time of diagnosis.

**Methods:** Data was compiled from the Swedish case-control cohort Epidemiological Investigation of Rheumatoid Arthritis (EIRA) and linked to the Swedish Rheumatology Quality Register (SRQ). All patients were diagnosed with RA according to the 1987 ACR criteria. Early RA-patients with clinical data from diagnosis and 3 year follow-up questionnaire data were included (N=618; 74% women, median age at diagnosis 58 years). Measurements of pain, fatigue, sleep problems, physical and mental functioning and quality of life was entered into a hierarchical agglomerative clustering procedure using Ward’s method of squared Euclidian distances. Number of clusters was determined by largest changes in hierarchical agglomerative clustering procedure using Ward’s method of squared Euclidian distances. At the time of diagnosis compared to cluster 3.

**Results:** Through cluster analysis, we could identify a subgroup of almost a third of the RA-patients with high levels of pain, fatigue, sleep problems and poor physical and mental health related quality of life 3 years after RA-diagnosis. These symptoms are found to be predictive of a central sensitization syndrome. Cluster 3 was associated with female sex (p=0.0007) and lower education level (p=0.0003) compared to cluster 3. Cluster 1 was also associated to higher HAQ (p<0.0001), higher patient global assessment of health (p<0.0001), higher pain ratings (p<0.0001) and lower swollen/tender joint count ratio (STR) (p=0.0065) at the time of diagnosis compared to cluster 3.

**Conclusions:** Through cluster analysis, we could identify a subgroup of almost a third of the RA-patients with high levels of pain, fatigue, sleep problems and poor physical and mental health related quality of life 3 years after RA-diagnosis. These symptoms are found to be predictive of a central sensitization syndrome. Cluster 3 was associated with female sex and lower education level compared to cluster 3. Cluster 1 was also associated to higher HAQ, higher patient global assessment of health, higher pain ratings and lower swollen/tender joint count ratio at the time of diagnosis compared to cluster 3.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular:4302

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**SAT0695**

**NO ASSOCIATION BETWEEN VITAMIN D LEVELS AND CARDIOVASCULAR DISEASES IN INFLAMMATORY JOINT DISEASES AND SYSTEMIC AUTOIMMUNE DISEASES – A SYSTEMATIC REVIEW**


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**Background:** In recent years, vitamin D deficiency has been linked to disease activity and pathogenesis of systemic autoimmune diseases (SAD) like systemic lupus erythematosus (SLE) and inflammatory joint diseases (IJD) such as rheumatoid arthritis (RA). In the general population, the association between vitamin D with risk for cardiovascular diseases (CVD) is still debatable. While people with IJD and SAD tend to be vitamin D deficient and suffer from an elevated CVD burden, the effect of vitamin D on their cardiometabolic risk factors is of much interest.

**Objectives:** To provide an overall conclusion on whether vitamin D deficiency contributes to an increased cardiovascular morbidity in these patients, a systematic literature review was done.

**Methods:** A systematic literature search was done in PubMed/MEDLINE and EMBASE to identify all articles that assessed the association of vitamin D with cardiovascular disease and its risk factors in patients with IJD (rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis) and SAD (systemic lupus erythematosus (SLE), Behcet’s disease, vasculitis, Sjogren syndromes, systemic sclerosis). Eligible studies were assessed for quality and risk of bias according to the Cochrane Handbook Chapter 13.5.2.1. (Higgins JPT, GS. Cochrane Handbook for Systematic Review of Interventions The Cochrane Collaboration 2011.)

**Results:** In total 3273 abstracts were identified. After screening, selection and quality assessment, 16 studies were included (6 case-control and 10 cohort studies), which described only RA and SLE except for one study which focused on PsA. Therefore, this study focused on RA and SLE because they are the most frequent IJD and with highest CVD risk respectively. In RA patients (n=812) vitamin D deficiency was associated with presence of (components) of metabolic syndrome (OR =1.8 (95% CI:1.3; 2.5), P<0.001) in RA, especially dyslipidemia (OR 1.7; 95% CI:1.2–2.5; P=0.013) and obesity. No studies with prospective design in RA have assessed CVD risk in relation to vitamin D. In SLE patients (n=1850) the only prospective study observed no association between vitamin D deficiency and CVD, although weak associations with dyslipidemia and obesity were observed in some studies.

**Conclusions:** No clear association between vitamin D deficiency and CVD was found in patients with RA and SLE, probably due to large heterogeneity in terms of sample sizes, designs, analyses and outcome measures. As conclusions were made only on cross-sectional data there is a need for long-term prospective studies to assess if vitamin D levels are associated with cardiovascular outcomes.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular:1795

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**SAT0696**

**ENDOTHELIAL NITRIC OXIDE SYNTHASE T-786C GENOTYPE PROMOTER POLYMORPHISM IS A POTENTIAL PREDICTOR OF LOW RESPONSE TO THE THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS, UKRAINE POPULATION**

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**Background:** Recently endothelial nitric oxide synthase (eNOS) T-786C gene promoter polymorphism was considered to be a factor of a high severity of RA [1,2]. It is possible that the eNOS T-786C gene promoter polymorphism can modify the efficacy and safety of treatment in patients with RA, but there is no information on this. The aim of this study is to find findings indicate that other factors than inflammatory disease activity causes a significant burden of illness also at an early stage of RA and that there is a need for additional intervention strategies for these patients.

**References:**


**Acknowledgements:** All patients and staff involved in EIRA ans SRQ.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular:3740

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**SAT0697**

**ENDOTHELIAL NITRIC OXIDE SYNTHASE T-786C GENOTYPE PROMOTER POLYMORPHISM IS A POTENTIAL PREDICTOR OF LOW RESPONSE TO THE THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS, UKRAINE POPULATION**

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**References:**

“Ethical principles of medical research involving human subjects” (2000), the requirements of GCP, the applicable national legislation.

Results: Among patients with RA frequency of the genotypes was as follows: TT – 37.2%, TC – 42.6%, CC – 20.3%. Age, seropositivity and the duration of the disease were not differing in patients with RA, carriers of the different genotypes of eNOS. Though, CC genotype was associated with high disease activity according to DAS28-ESR < 5.2 (OR = 9.60; 95% CI 2.18–42.2), HAQ > 2 (OR = 2.38; 95% CI: 0.94–6.02) and extrarticular manifestations (OR = 3.26; 95% CI 1.40–7.56).

After 12 weeks treatment we estimated, that among patients with TC genotype there were 58.3; 16.7; and 8.3% responders ACR20; ACR50; ACR70, and among patients with CC genotype - 20.0; 10.0; 0.0% (p < 0.05). TC heterozygotes patients had lower (by 22–25%, p < 0.05) clinical response to the treatment by DAS28 and HAQ than the homozygotes TT.

Conclusions: eNOS T-786C gene promoter polymorphism influence on the efficacy of the treatment, and CC genotype can be considered as a possible predictor of a low response to the treatment in patients with rheumatoid arthritis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3962

SAT0697 PREVALENCE OF HEPATITIS B AND C INFECTION AND REACTIVATION IN PATIENTS RECEIVING BIOLOGIC IV THERAPIES

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Background: With the use of biological therapy, cases of reactivation of hepatitis B (HBV) and C (HCV) have been described, consequently its use has to be carefully evaluated. In some cases these therapies have to be administered together with antiviral treatment. Despite the fact that before the beginning of the biological therapy the screening of HBV and HCV virus is done, during the course of treatment serologies are no longer used to detect serovonversions.

Objectives: To analyze the prevalence of HBV and HCV in patients with rheumatic disease at the beginning of biological therapies. To identify the cases of hepatitis reactivation.

Methods: Retrospective observational analysis of the biological treatments administered to patients with Rhesumatoid Disease of the rheumatology department of La Fe hospital, during the period 2000–2015 who had HBV and/or HCV serology at the beginning of treatment. Demographic data and diagnosis of the patients, months of treatment and the results of the serologies performed at the beginning and in the follow-up of the treatment are specially evaluated. In some cases these therapies have to be administered together with antiviral treatment. Despite the fact that before the beginning of the biological therapy the screening of HBV and HCV virus is done, during the course of treatment serologies are no longer used to detect serovonversions.

Results: A total of 388 patients were selected of which 62.4% were female; the mean age at diagnosis was 38.96±14.46 years. 46.9% of the patients were diagnosed with rheumatoid arthritis (RA), 25.3% of ankylosing spondylitis (AE), 18.6% of psoriatic arthritis (APSO) and 6.7% with other diagnoses. The mean treatment time with patients' biological therapy is 200±118 months (3–464 months), and the mean time between the two serologies is 172±102 months (2–1032 months). Incidence of 10% of cases with HBV infection (39 patients) is observed. The serological pattern was 8 cases with Ac-core (+)/Ac-surface (-)/Ag-surface (+) HBV and 31 HBV/Ac- surface (-). The incidence of HCV at the start of treatment was 1.1% (4 patients). A case of reactivation (12.5%) was detected among the 8 patients with Ac-core (+)/Ac-surface (-)/Ag-surface (-) HBV. The patient had infliximab and methotrexate, and reactivation was observed after 12 years of treatment. No reactivation of HCV has been detected.

Conclusions: In our series of patients the incidence of HBV and HCV has been 10% and 1.1%, respectively. One of the 8 patients with Ac-core (+)/Ac-surface (-)/Ag-surface (-) HBV had reactivation of the virus.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4827

SAT0698 DISEASE ACTIVITY DURING AND AFTER PREGNANCY IN WOMEN WITH AXIAL SPONDYLOARTHRITIS

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Background: Studies on disease activity of ankylosing spondylitis in pregnancy have shown diverging results. A large retrospective study from 1998 without validated disease activity scores found no particular pattern of disease course during pregnancy (1). Later two small studies demonstrated a trend towards lower disease activity in the beginning of pregnancy and deterioration in late pregnancy (2,3). None of these studies included women with non-radiographic axial spondyloarthritis. The only large study was conducted before the widespread use of biological DMARDs.

Objectives: The aim of this project was to prospectively study disease activity in women with axial spondyloarthritis before, during and after pregnancy with BASDAI as disease activity measure.

Methods: RevNatus is a Norwegian nationwide register designed for the follow-up of pregnant women with rheumatic diseases. RevNatus included 181 full term pregnancies in 168 women with axial spondyloarthritis between 2006 and 2016. The women had seven visits at a rheumatology unit; before pregnancy, in each trimester, and six weeks, six months and twelve months postpartum. BASDAI-values from each visit were analyzed in a linear mixed model.

Results: Even though we found a statistically significant relationship between disease activity and time point in the follow-up period, our study demonstrated that women with axial spondyloarthritis had stable, low disease activity during and after pregnancy. Disease activity in second trimester was significantly higher than six weeks after delivery, but the change in estimated mean BASDAI was small (BASDAI 3.97 vs. BASDAI 3.46, p = 0.005). The figure below shows changes in disease activity throughout the study period.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1604

SAT0699 RAPID ASSESSMENT PREDICTS DISEASE ACTIVITY IMPROVEMENT IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS (RA)

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Background: Early intervention in RA is associated with improved outcomes in randomised trials. UK guidelines stipulate that those with suspected RA are assessed by a rheumatologist within 3 weeks of referral. However, there are limited real world data confirming the value of early assessment. Previous work suggests social deprivation predicts severe disease at presentation and a worse
Comprehensive Risk of Respiratory Depression in

Methods: An audit, designed as a prospective longitudinal observational study, was conducted to assess early RA care. All NHS providers in England and Wales were required to participate. Follow up data were captured over 3 months for subjects with a diagnosis of RA. Rheumatologist assessment within 3 weeks of referral was the predictor variable. The primary outcome was good EULAR DAS28 response; the secondary outcome was meaningful improvement in RAID score. Logistic regression was used to estimate for associations. Confounders including age, gender, baseline DAS28 and RAID scores were considered in analyses. The index of multiple deprivation (IMD) rank was calculated for each individual based on super-output geographical areas. The IMD rank was then stratified into quintiles and included as a confounder.

Results: 136 of 146 eligible trusts submitted data. 11,752 subjects consented, 5,622 were diagnosed with RA, 94,562 (1.7%) had incomplete assessment data. DAS28 response was available for 2234/5622 (39.7%), and RAID response for 901/5622 (16%). The table shows baseline characteristics and response for subjects with complete data. Assessment within 3 weeks associated with a significantly greater improvement in DAS28 and RAID scores, with an adjusted odds ratio for a good EULAR response 1.38 (1.15–1.66) and meaningful RAID reduction 1.44 (1.03–2.02).

Conclusions: There are few data on the incidence of RD in opioid users for non-malignant pain and no comparative data between drugs. Fentanyl, oxycodone, morphine monotherapy have a significantly higher risk of RD than codeine, but these are not significantly different from each other. Combination opioids confer the highest risk of RD, compared to both codeine and morphine. The strengths of this study include capture of real time and reported outcomes. Amongst those who were assessed within 3 weeks of referral, an additional 8% achieved a good EULAR response. The association with RA severity was strengthened when social deprivation was included as a confounder. The relationship between IMD and RAID response appears to be non-linear and requires further study.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2462

SAT0701 | COMPARATIVE RISK OF RESPIRATORY DEPRESSION IN PATIENTS TREATED WITH OPIOIDS FOR NON-MALIGNANT PAIN

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Background: Opioid use for non-cancer pain has increased considerably over the last 30 years. The U.S. Food and Drug Administration announced several boxed warnings in 2016 to highlight serious opioid-related risks (1) in an effort to reduce fatal overdoses, 80% of which are unintentional (2). The most serious opioid related adverse event, respiratory depression (RD), which can be potentially fatal. There are few data on the incidence of RD in opioids users for non-malignant pain and no comparative data between drugs.

Objectives: To assess the comparative risk of RD in new users of opioids for non-malignant pain using routinely collected electronic patient records (EPR).

Methods: Opioid users from Salford hospital EPR were identified between 2014–2016. Patients with prior malignancy were excluded on the basis of ICD-10 codes and health issues. Those with prior history of opioid use were excluded using codeine as the referent, patients on fentanyl, morphine, oxycodone and combination treatment had the highest crude rates of RD (table). In the age and gender adjusted Cox-model, using codeine as the referent, patients on fentanyl, morphine, oxycodone and combination opioids had the highest risk of RD (table), adjusted HR (95% CI) for combination opioids: 2.22 (1.56, 3.16). Compared to morphine, combination opioids had an adjusted HR of 1.52 (1.09, 2.13).

Conclusions:• Fentanyl, oxycodone, morphine monotherapy have a significantly higher risk of RD than codeine, but these are not significantly different from each other. Combination opioids confer the highest risk of RD, compared to both codeine and morphine. The strengths of this study include capture of real time and reported outcomes. Amongst those who were assessed within 3 weeks of referral, an additional 8% achieved a good EULAR response. The association with RA severity was strengthened when social deprivation was included as a confounder. The relationship between IMD and RAID response appears to be non-linear and requires further study.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1802

SAT0701 | TOWARDS DIAGNOSIS-SPECIFIC LIFETIME RISKS FOR TOTAL HIP ARTHROPLASTY REVISION SURGERY

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Background: An important aspect regarding optimal timing of primary hip arthroplasty (THA) is to weigh the benefit associated with the primary surgery at a certain point in time against the risk for revision surgery. Revision surgery should be avoided, as outcomes after revision surgery are less favourable than outcomes after primary surgery. Information on lifetime revision risks is needed to guide decision making for individual patients regarding timing of primary surgery.

Objectives: Our aim was to provide the 7 year cumulative percentages for revision surgery stratified for diagnosis, sex, type of fixation and age at which primary THA was performed.

Methods: Data on arthroplasties was available from the Dutch Arthroplasty Register (LR01), a nationwide population-based registry with information on all joint arthroplasties in the Netherlands from 2007 onwards. For the current study, all patients who received a primary THA in the period 2007 to 2015 were included except patients with a metal on metal prosthesis, patients with a hybrid or reversed hybrid fixation type or patients with revision surgery without primary surgery registered. Revision surgery was defined as any change of one or more components of the prosthesis. For the current study age at primary surgery, diagnosis, sex, type of fixation (uncemented, cemented) and survival (alive/dead) and revision of prosthesis (yes/no) were extracted from the LR01 database.
Diagnosis was dichotomized into osteoarthritis (OA) and other diagnoses. Annual revision rates were calculated for each subsequent year after primary arthroplasty by dividing the number of revisions by the total number of patients at risk during that year. The risks were stratified according to the underlying diagnosis, sex, age at primary arthroplasty and fixation type. In addition cumulative annual revision rates were calculated for the full follow-up period. Furthermore we estimated the percentage of avoided OA revisions by assuming that all OA patients received their primary THA 5 years later (in all age groups <85 yrs) and that the revision risks remained the same in all age categories.

Results: In total 134463 primary THA patients were included of whom 68% were female, 89% had OA as underlying indication and 66% of the THAs were uncemented. The 7th year cumulative risk percentage varied between 2.0 and 11.7% (Table 1). Overall cumulative revision percentages were higher in younger age categories (Table 1), with the exception of a 11.7% revision in the group aged 85–90 yrs (uncemented, male, other diagnosis), but this finding is likely due to chance as this group existed of 67 patients. We estimated that by delaying THA for 5 years, a total of 197 revision surgeries (4.4% of all revision surgeries) could be avoided, 48 (14.0%) in the OA male cemented group, 11 (0.9%) in the OA male uncemented group, 69 (3.3%) in the OA female cemented group and 69 (8.6%) in the female uncemented group. This could result in a yearly cost reduction of approximately 4 million euros.

Table 1. Cumulative revision percentages within 7 years after index surgery.

<table>
<thead>
<tr>
<th>Age Categories</th>
<th>Osteoarthritis</th>
<th>OA</th>
<th>Other diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Uncemented</td>
<td>3.4</td>
<td>4.4</td>
<td>2.6</td>
</tr>
<tr>
<td>Female Uncemented</td>
<td>5.7</td>
<td>6.4</td>
<td>2.9</td>
</tr>
<tr>
<td>Male Cemented</td>
<td>6.3</td>
<td>6.5</td>
<td>2.6</td>
</tr>
<tr>
<td>Female Cemented</td>
<td>2.9</td>
<td>2.6</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Conclusions: Cumulative 7th year risk revision percentages decreased by age in all different categories. By delaying the primary THA surgery, revisions might be avoided thereby resulting in cost reduction.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4274

SAT0702 LOCAL AND SYSTEMIC INFLAMMATION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS WITH CHLAMYDIA TRACHOMATIS INFECTION

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Objectives: We had to study local and systemic inflammation in rheumatoid arthritis patients with persistence Chlamydia trachomatis (Ch tr) in the joint Methods: 31 patients with early RA; mean age 54.5 (10.6) years, disease duration 21.5 (14.4) weeks with persistent Ch tr in the joint (mRNP Ch tr had been revealed in synovial fluid by NASBA PCR) were enrolled in this study. The comparison group was with RA (n=42) without mRNP in synovial fluid (Ch tr-). Mean age was 51.7 (15.4) years, disease duration 20.8 (13.3) weeks. All the patients had been received only symptomatic treatment (NSAID). Disease activity had been detected by DAS 28. Systemic inflammation was estimated by levels of erythrocyte sedimentation rate (ESR), hsp C-reactive protein (hspCRP), and OR in synovial fluid of research group (Ch tr+) and comparison group (Ch tr-). Level of hsp CPR and OR in synovial fluid of research group (Ch tr+) were significantly higher than comparison group (4,1±0,3 mg/l versus 2,4±0,2 mg/l, tr-. Level of hsp CPR and OR in synovial fluid of research group (Ch tr+) were significantly higher than comparison group (4,1±0,3 mg/l versus 2,4±0,2 mg/l, tr-). Differences in specific questionnaires mean they should be used together to provide more detailed information.

Aknowledgements: This work was funded by project PI/13/00948, integrated in the Plan Nacional I+D+i and cofounded by ISCIII/Subdirección General de Evaluación and European Regional Development Fund (ERDF).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2180

SAT0704 THE IMPACT OF AUTOIMMUNE DISEASE IN THE MANAGEMENT AND PROGNOSIS OF ACUTE CORONARY SYNDROME

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Background: Patients with autoimmune diseases (AID) have a high burden of cardiovascular disease leading to premature morbidity and mortality. But it is unclear if it is due to a higher prevalence of cardiovascular disease, to a worse case fatality or to a different management after an index event.

Objectives: The primary aim of the study is to assess the prognostic implications of the presence of AID both during the hospitalization and after discharge after an acute coronary syndrome (ACS). The secondary objectives included the assessment of the prevalence of AID in patients with ACS, their clinical profile and the management of this index event.

Methods: The study included consecutive patients admitted after ACS from January 2011 to December 2015 at the University Hospital Virgen de la Arrixaca, Murcia, Spain.

Results: Differences in generic and specific questionnaires mean they should be used together to provide more detailed information.

Aknowledgements: This work was funded by project PI/13/00948, integrated in the Plan Nacional I+D+i and cofounded by ISCIII/Subdirección General de Evaluación and European Regional Development Fund (ERDF).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2180

SAT0703 INFLUENCE OF PHYSICAL ACTIVITY AND SLEEP ON FUNCTIONAL CAPACITY AND PAIN IN PATIENTS WITH KNEE OSTEARTHRITIS

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Background: Knee osteoarthritis (OA) is a degenerative disease in which pain and functional disability progression trend to increase with reducing the health-related quality of life (HRQOL). Factors related to healthy lifestyles, such as physical activity and sleep, are known to have restorative benefits on function and pain in these patients. A previous study found that patients with reparative sleep achieved better WOMAC and SF-36 HROQL questionnaire dimension scores.

Objectives: To investigate the influence of physical activity and sleep on functional capacity and pain in patients with long-term knee OA.

Methods: Cross-sectional study. Sociodemographic and clinical variables, physical activity (PA) (regular physical exercise ≥ 3 times a week >30 minutes per session (PE) and sitting ≤6 hours/day (S)) and sleep quality (RS) were determined using the question: How do you usually sleep? (1=well [RS], 2=regular, 3=badly, 4 =with medication/treatment [NRS]). Functional capacity and pain were evaluated using the WOMAC (specific) and SF-36 (generic) HROQL questionnaire.

Results: 453 patients (84.3% female), mean age 69.73 (8.64), BMI 35.27 [SD 6.3], comorbidities 2.43 (SD 1.5), 78.6% with obesity (BMI 33.68 [SD 6.7]), depression/anxiety in 36.4%, PE 60.5%, S 72.2% and PA 48.6%, were included. 22.5% reported RS. Bivariate analysis showed patients with PA and those with RS had better functional capacity and less pain intensity (< 0.01–0.001, in both WOMAC and SF-36). The four multiple regression showed that patients with PA and SR had better scores, both in functional capacity (dependent variables, WOMAC and SF-36) and pain (dependent variables, WOMAC and SF-36), < 0.006. Age, gender, number of comorbidities and obesity were included in the models as potential confounders. Obesity was associated with worse function and more pain in the four models (p<0.05). Being female and greater comorbidity were associated with poorer functional capacity and pain assessed by the SF-36.

Conclusions: Physical activity and sleep were associated with less pain and better functional capacity. But it is unclear if these variables should be determined systematically in clinical practice due to their significant relationship with HROQL. Obesity was negatively associated with function and pain. There was also a negative relationship between female gender and comorbidity according to the SF-36. Differences in generic and specific questionnaires mean they should be used together to provide more detailed information.

Aknowledgements: This work was funded by the Plan Nacional I+D+i and cofounded by ISCIII/Subdirección General de Evaluación and European Regional Development Fund (ERDF).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6876
higher percentage of atrial fibrillation and chronic obstructive pulmonary disease in AID patients. Compared to non-AID patients, AID patients had similar ACS presentation and no differences were found with respect to revascularization strategies or medical treatment at discharge. With respect to prognosis the two groups had comparable rates of adverse events during hospitalization (10% vs 10%, p=0.920) with no statistically significant differences in any single event studied. However after a follow-up of 397 [375–559] years, AID patients had higher rate of combined adverse events (44% vs 28% p<0.001). After multivariate adjustment the presence of AID was associated with increased total mortality (hazard ratio 2.1, 95% CI 1.2 to 3.7, p=0.008) and it was also a borderline risk factor for higher bleeding complications (hazard ratio 2.2, 95% CI 0.9 to 5.5). The presence of AID was not an independent risk factor for neither stroke or recurrent non-fatal myocardial infarction. 

Conclusions: The presence of AID did not change ACS presentation and clinical management. Although AID is not associated with worse outcomes during hospitalization it is independently linked to higher total mortality and a trend to an increased risk of major bleeding during follow-up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6756

SAT0705 DO DIET CHARACTERISTICS IMPACT EFFECT OF A 12-MONTH VITAMIN D SUPPLEMENTATION ON 25OH-VITAMIN D SERUM LEVEL AMONG OVERWEIGHT ELDERLY? 

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Methods: A randomized clinical trial comparing high (3750 IU/day) versus low (600 IU/day) dose of vitamin D supplementation in ambulatory overweight (BMI exceeding 25) elderly subjects (age ≥65 years), with serum 25OH vitamin D level between 10 and 30 ng/ml at screening. Outcome measure: 25OH-D serum levels at 12 months of follow-up.

Results: One hundred and seventy-five participants out of three centers participated in a randomized clinical trial comparing high (3750 IU/day) versus low (600 IU/day) dose of vitamin D supplementation in ambulatory overweight elderly subjects (age ≥65 years), with serum 25OH vitamin D level between 10 and 30 ng/ml at screening. The high-dose group achieved significantly higher 25OH-vitamin D serum levels (1.21) mcg and 8.53 (1.36) mcg from the 24 h recall, and food frequency baseline BMI, Fok, Bsml and Taq genetic polymorphism, baseline serum vitamin D and dietary intake of vitamin D, calcium, proteins, carbohydrates, fats and total calories assessed by food frequency and 24h recall questionnaires, administered a year after the termination of the trial.

Conclusion: Achieving desirable 25OH vitamin D serum levels with vitamin D supplementation may be influenced by many confounders including lifestyle factors and vitamin D receptor genetic polymorphism.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2206

SAT0707 EFFICACY AND SAFETY OF PROPHYLACTIC TREATMENT ON ACTIVATION OF LATENT TUBERCULOSIS DURING GLUCOCORTICOID THERAPY IN PATIENTS WITH RHEUMATIC DISEASES 

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Background: More than 80% of cases of tuberculosis are the result of reactivated latent infection, and nearly all these cases could be prevented by the administration of a course of antibiotic treatment. Therefore, it is suggested screening and treatment are most beneficial for those patients taking immunosuppressive medications. Although the prevalence of latent tuberculosis infection in China was much higher than the United States on the basis of tuberculin skin testing, In China, so far, no study has been done about prophylactic treatment on prevention of tuberculosis activation during glucocorticoid therapy in patients with rheumatic diseases. It should be recommended that all patients with rheumatic diseases be screened for the presence of active tuberculosis or LTBI before the use of long term glucocorticoid or immunosuppressive medications in China? It is reported only about 5% of immunocompetent persons with a positive test will have progression from latent infection to disease in their lifetime. and decisions about whether to treat latent tuberculosis should take into account the individual patient’s risk for the development of active tuberculosis and the risks of therapy.

Objectives: To evaluate the risk of reactivation of LTBI in patients with rheumatic diseases who were undergoing prednisone use and the efficacy and safety of prophylactic treatment on prevention of tuberculosis reactivation.

Methods: 1000 patients with rheumatic diseases who were treated with prednisone were enrolled since 2012. IGRA test (the T-SPOOT.TB test) were performed for all subjects. 50 patients with a IGRA-positive were administrated with rifampin for 4 months. 2-years follow-up was conducted to evaluate the risk factors of reactivation of LTBI and the efficacy and safety of rifampin treatment on prevention of tuberculosis reactivation.

Disclosure of Interest: None declared
**SAT0708** | SYMPTOMS INDICATIVE OF INFLAMMATORY ARTHRITIS ARE COMMON IN THE PRIMARY CARE POPULATION: FINDINGS FROM THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS SURVEY

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**Background:** Early, accurate diagnosis of RA is critical to improving outcomes. Patients with RA may develop a variety of symptoms including joint pain, swelling and stiffness. The Symptoms in Persons at Risk of Rheumatoid Arthritis (SPARRA) questionnaire was derived to assess the presence, severity and impact of common symptoms in patients at risk of RA (1). However, to date there is little data available on how common these symptoms are in primary care consultants.

**Objectives:** To describe the prevalence of self-reported inflammatory joint symptoms in primary care patients consulting for both musculoskeletal and non-musculoskeletal complaints.

**Methods:** Questionnaires were sent to 10161 individuals, of whom 5050 had consulted primary care for musculoskeletal problems. The remainder were matched to this sample by age, gender and general practice and had consulted for any non-musculoskeletal indication. Respondents provided data on presence of common symptoms such as joint pain, stiffness and swelling. The prevalence of these symptoms, their severity and impact was compared between musculoskeletal and non-musculoskeletal consultation groups.

**Results:** 4549 people responded to the survey (adjusted response 45.8%) of whom 523% were in the musculoskeletal consultation group. The mean (SD) age was 61.6 (14.8) years and 58.9% were female. Symptoms commonly associated to increased risk of mortality in univariable analyses (1).

**Conclusions:** Although symptoms such as joint pain, swelling, and stiffness are predictive of inflammatory arthritis, a large proportion of those consulting primary care for musculoskeletal complaints report these symptoms. The impact of these symptoms is significant and it may be important to consider whether these symptoms are due to inflammatory arthritis or other causes.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3937

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**SAT0709** | MORTALITY PREDICTION IN MIXED CONNECTIVE TISSUE DISEASE

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**Background:** Mixed Connective Tissue Disease (MCTD) is a chronic, immune-mediated disorder defined by the combined presence of serum anti-nuclear antibodies and selected clinical features of Systemic Sclerosis, Systemic Lupus Erythematosus, Rheumatoid Arthritis and Polymyositis. Several clinical manifestations and laboratory findings have been found to be associated with increased risk of mortality in univariable analyses (1).

**Objectives:** Here we present a mortality predicting model in a long-term observational unselected nationwide cohort aiming to enhance the knowledge of long-term prognosis in MCTD.

**Methods:** 135 patients were included from our nationwide MCTD cohort. Abnormal high resolution computed tomography (CT) findings of ground glass attenuation and reticular patterns were defined as Interstitial Lung Disease (ILD) and expressed as percentage of Total Lung Volume (TLV). Pulmonary function tests and laboratory tests were performed within 2 months of the HRCT examination. Pleuritis was defined as typical pleurisy for more than one day, pleural effusions or pleural rub present at or before baseline. Pericarditis was defined as typical pericardial pain for more than one day, pericardial friction, pericardial rub or pericarditis by electrocardiography at or before baseline. Myositis was confirmed by muscle biopsy and/or electromyogram and CK elevation at or before baseline. Cox regression analyses were used to find the predictive factors of mortality. Variables at a significant level of P < 0.05 were considered a candidate in the prediction model by manual backward elimination procedure.

**Results:** 21 patients died after a mean (standard deviation) observation of 9 (2) years. The predictive model is shown in Table 1. According to the Harrell's C index, patient outcomes were accurately predicted by this model 85% of the time.

**Table 1**

<table>
<thead>
<tr>
<th>Univariable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HR</strong></td>
<td><strong>95% CI</strong></td>
</tr>
<tr>
<td>Pericarditis ever</td>
<td>4.0</td>
</tr>
<tr>
<td>Male gender</td>
<td>2.5</td>
</tr>
<tr>
<td>ILD of TLV</td>
<td>1.1</td>
</tr>
<tr>
<td>DLCO &lt; 60%</td>
<td>3.1</td>
</tr>
<tr>
<td>Agegroups* at diagnosis</td>
<td>1.8</td>
</tr>
<tr>
<td>Baseline ESR &gt; 30 mm</td>
<td>3.3</td>
</tr>
<tr>
<td>FVC &lt; 80%</td>
<td>3.6</td>
</tr>
<tr>
<td>Arthritis present at or before baseline</td>
<td>2.1</td>
</tr>
<tr>
<td>Pleuritis ever</td>
<td>2.2</td>
</tr>
<tr>
<td>Baseline Hb &lt; 12 g/dL</td>
<td>2.7</td>
</tr>
<tr>
<td>Myositis</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Patients were divided in 6 age groups at diagnosis (<25 years, 26 to 35 years, 36 to 45 years, 46 to 55 years, 56–65 years and above 65 years). FVC = Forced Vital Capacity % of predicted, DLCO = Diffusing Capacity of the lung for carbon monoxide % of predicted, ESR = erythrocyte sedimentation rate, TLV = total lung volume, Hb = Haemoglobin.

**Conclusions:** The strongest predicting factors of mortality in MCTD is increasing % ILD of TLV, pericarditis, male gender, DLCO less than 60% of predicted and increasing age at diagnosis.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1855

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**SAT0710** | RENAL FUNCTION CONTRIBUTE TO RISK OF CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS

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**Background:** The excess mortality associated with rheumatoid arthritis (RA) is due largely to cardiovascular disease. This highest risk is not related primarily to traditional cardiovascular/atherosclerotic risk factors. The presence of RA independently, as well as high inflammation associated with RA has been reported as a cardiovascular risk factors. Also, subclinical decreased kidney function has been identified as an independent risk factor for CV events in patients with RA. RA-mediated inflammation of impaired kidney function on atherosclerosis in RA requires more elucidation.

**Objectives:** To assess the role of renal parameters, alongside with inflammation and traditional cardiovascular risk factors in predicting cardiovascular disease; as manifested by carotid intima media thickness (cIMT), among RA population.

**Methods:** cIMT measurement was carried out in 68 RA patients, and correlated with renal function parameters with adjustment for traditional CV risk factors and RA associated inflammation. Glomerular filtration rate (GFR) was estimated with the abbreviated Modification of Diet in Renal Disease formula. Linear regression determined the association between renal parameters and the thickness of cIMT.
Results: Carotid intima media thickness was positively associated with 1-demographic characteristics of the participants such as age of the participants (p<0.001), and age at RA symptoms onset (p=0.001). 2-traditional cardiovascular risk factors such as systolic blood pressure (p<0.001), diastolic blood pressure (p=0.016), triglyceride level (p=0.016), and low density lipoprotein (LDL) (p<0.001). 3-Rituximab used as erythrocyte sedimentation rate (ESR) (p=0.020) and C-reactive protein (CRP) (0.020), and 4-renal function parameters such as uric acid level (p=0.006), uric acid microalbumin level (p=0.030), cMTT negatively associated with high density lipoprotein (HDL) (p=0.037), 24 hours uric creatinine level (p=0.020) and glomerular filtration rate (p=0.008).

Conclusions: Subclinical renal function in conjunction with traditional and non-traditional cardiovascular risk factors work synergistically to accelerate atherosclerosis in RA population.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1664

SA07012 SELF-REPORTED SEDENTARY BEHAVIOUR IS ADVERSELY ASSOCIATED WITH MICROVASCULAR ENDOTHELIAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS
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Background: Patients with Rheumatoid Arthritis (RA) are at increased risk for cardiovascular disease (CVD). Research suggests impaired vascular function contributes to this heightened risk. At present, little is known regarding factors associated with vascular function in RA. Epidemiological evidence demonstrates that sedentary behaviour i.e. sitting (7.5 or more hours whilst sitting or lying), to be adversely linked to CVD risk in the general population. Whilst the biological processes underlying this relationship are not understood, vascular dysfunction may play a role (1, 2). However, research is yet to examine the association between sedentary behaviour and vascular function in healthy adults and/or clinical populations. Studies investigating this relationship in RA, will help to determine the extent to which sedentary behaviour may represent a modifiable risk factor for CVD in these patients.

Objectives: To investigate the cross-sectional associations between sedentary behaviour and microvascular and large vessel endothelial function among patients with RA.

Methods: Fifty-three patients with RA participated in the study (M age=52.9±12.8, 72% female). Laser Doppler imaging with iontophoresis was used to assess microvascular endothelium-dependent (acetylcholine, ACh) and endothelium-independent (sodium nitroprusside, SNP) function. Large vessel microvascular-endependent and endothelium-independent functions were measured via flow-mediated dilatation (FMD) and glycyl trinitrate dilatation (GTN), respectively. Sedentary behaviour was self-reported via the International Physical Activity Questionnaire (hours/week sitting). Data were analysed using multiple linear regression adjusting for traditional CVD risk factors.

Results: FMD was negatively associated with self-reported sedentary behaviour (i.e. sitting ≥7.5 hours whilst sitting or lying) (β=−0.568, p<0.01) after adjustment for traditional CVD risk factors. Sitting time accounted for 8% and 12% of the variance in microvascular endothelium-dependent function (ACh) and endothelium-independent function (SNP), respectively (traditional CVD risk factors, R²=0.3). No significant associations were observed between self-reported sitting time and large vessel endothelium-dependent vasodilation (FMD, β=0.16, p=0.29) or endothelium-independent vasodilation (GTN, β=−0.08, p=0.55).

Conclusions: Sedentary behaviour appears to adversely affect microvascular endothelial function, but not large vessel function in patients with RA. It may therefore represent a modifiable risk factor for CVD in this population. Experimental studies employing objective measures of sedentary behaviour are necessary to confirm these findings, and to determine the utility of sedentary behaviour interventions for improving vascular function and reducing CVD risk in RA.

References:

Disclosure of Interest: None declared

SA07013 SURVEY ON PREVALENCE OF RHEUMATOC DISORDERS IN BANGLADESHI ADULTS
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Background: From Community based COPCORD (community oriented program for control of rheumatic diseases) study in Bangladesh about a quarter of people is suffering from musculoskeletal disorders. But the study was conducted over a small number of samples and some specific localities of the country. So further study was required, covering the whole Bangladesh to justify this high prevalence.

Objectives: To determine the prevalence of musculoskeletal symptoms and specific rheumatic disorders in adult population of Bangladesh.

Methods: A cross-sectional survey, a random sample of 1,084 individuals age 15 years or older were selected in twenty clusters (primary sample unit) from the seven divisions of the country. Modified COPCORD (Community Oriented Program for Control of Rheumatic Disorders) questionnaire was used to detect positive responses. Standard criteria were used for diagnosing rheumatic disorders. Clinical judgment was used to solve diagnostic problem.

Results: In total 1,843 individuals were interviewed with a response rate of 92.1%. The point prevalence of musculoskeletal pain was 33.7%. It was higher in women (38.7%) than men (28.4%) and higher in rural (34.5%) than in urban (32.4%) areas. Higher prevalence rates were observed in homemakers (16.0%), labores
Background: The increased risk of opportunistic infections (OIs) in rheumatoid arthritis (RA) patients who start biologic disease modifying anti-rheumatic drugs (DMARDs) has been well known. However, it has not been studied regarding the increased risk of OIs in the early stage of RA.

Objectives: To study the increased risk of incidence rate (IR) of OIs in early RA patients compared with established RA patients, and to evaluate the risk factors for developing the OIs in the early stage of RA.

Methods: Retrospective cohorts of early and established RA patients were conducted independently using the Korean National Healthcare claims database. Established RA patients (n = 226,838) were recruited between 2010 and 2012 with using the ICD10 code of RA and any DMARD use. Follow-up started for 1 year before index date, and receiving continuous treatment for over three years. Established RA patients (n = 226,838) were recruited between 2010 and 2012 with using the ICD10 code of RA and any DMARD use. Follow-up started for 1 year before index date, and receiving continuous treatment for over three years.

Results: The increased risk of opportunistic infections (OIs) in the early stage of RA compared with established RA patients, and to evaluate the risk factors for OIs in the early stage of RA.

Table 1

<table>
<thead>
<tr>
<th>Type of opportunistic infection</th>
<th>IR/100PY</th>
<th>95% CI</th>
<th>IR/100PY</th>
<th>95% CI</th>
<th>SIR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3.67</td>
<td>3.59–3.74</td>
<td>3.81</td>
<td>3.52–4.11</td>
<td>1.14</td>
<td>1.05–1.23</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0.71</td>
<td>0.67–0.75</td>
<td>0.70</td>
<td>0.54–0.87</td>
<td>1.06</td>
<td>0.82–1.33</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>2.79</td>
<td>2.72–2.85</td>
<td>2.89</td>
<td>2.64–3.13</td>
<td>1.12</td>
<td>1.03–1.22</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>0.02</td>
<td>0.02–0.03</td>
<td>0.03</td>
<td>0.00–0.06</td>
<td>0.98</td>
<td>0.20–2.86</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>0.01</td>
<td>0.00–0.01</td>
<td>0.04</td>
<td>0.00–0.07</td>
<td>3.54</td>
<td>0.96–9.06</td>
</tr>
<tr>
<td>Pneumocystis jiroveci pneumonia (PJP)</td>
<td>0.01</td>
<td>0.01–0.02</td>
<td>0.02</td>
<td>0.01–0.04</td>
<td>1.20</td>
<td>0.15–4.34</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>0.10</td>
<td>0.08–0.11</td>
<td>0.11</td>
<td>0.07–0.16</td>
<td>2.40</td>
<td>1.55–3.54</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td>0.02</td>
<td>0.02–0.03</td>
<td>0.03</td>
<td>0.00–0.05</td>
<td>0.84</td>
<td>0.17–4.27</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>0.01</td>
<td>0.00–0.01</td>
<td>0.01</td>
<td>0.00–0.02</td>
<td>1.15</td>
<td>0.03–3.49</td>
</tr>
</tbody>
</table>

RA = rheumatoid arthritis, SIR = standardized incidence ratio, PY = person year, N = number, IR = incidence rate, CI = confidence interval.

Conclusion: The increased risk of OIs in early stage of RA is associated with comorbidities, high corticosteroid use, and disease activity.

Disclosure of Interest: None declared

Results: Hospitalisation rates for comorbidity were 13.9/million/year in SLE patients. SLE patients were similar to controls for age and gender, but more likely to be Indigenous, have renal failure, cardiovascular and thrombotic conditions (Table 1). Independent predictors of mortality risk following hospitalisation for a comorbid condition included: SLE diagnosis (OR 1.6, CI: 1.3–1.9, p < 0.001) (Fig. 1), cerebrovascular events (OR 2.0, CI: 1.2–3.7, p < 0.001), renal disease (OR 1.75, CI: 1.4–2.3, p < 0.001), thrombotic events (OR 1.8 CI: 1.1–2.8, p < 0.001) and reliance on Medicare (OR 1.5, CI: 1.3–1.8, p < 0.001) (Table 2).

Conclusions: SLE patients were more frequently hospitalised than controls for cardiovascular or renal conditions and this increased their mortality risk. These results strengthen the need for close monitoring and interventions to prevent such comorbidity in all SLE patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5902
Genomics, genetic basis of disease and HLA/T cell recognition

AB0001 FIRST DESCRIPTION AND FUNCTIONAL PROTEOMIC ANALYSIS OF A PROTECTIVE FOR RHEUMATOID ARTHRITIS GENE POLYMORPHISM

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Background: Rheumatoid Arthritis (RA) is the most common systemic autoimmune disease, with a respective expanded genetic research. Immunogenetic studies have documented the positive correlation of various gene loci with incidence and/or disease profile. However, the description of gene loci negatively related to the incidence of RA is rarely documented. Apart from an early study involving HLA class II, there has been no reference to any genetic locus associated with a protective role against RA incidence.

Objectives: To identify the sequence of the functional areas of the TRAF1 (TNF receptor associated factor 1 - a protein involved in the intracellular signaling pathway of TNF) gene.

Methods: 172 patients and 95 controls were genetically assessed for the sequence of the seven exons of the gene TRAF1.

Results: On the position 9:120905076 of exon 7, the registered polymorphism G/A (rs143265058) was described in the controls group. The same polymorphism was not confirmed in any of the patients. Further functional proteomic study of the polymorphism with controlling programs (software), revealed that the presence of this polymorphism leads to a differentiation of the quaternary structure of TRAF1 protein, possibly affecting the cohesion of intracellular TNF signaling pathway.

Conclusions: The present reference is one of the extremely rare genetic studies describing a protective gene locus against rheumatoid arthritis, and a pioneer of its kind in the use of Applied Informatics in the depiction of the quaternary structure of the encoded protein. At the same time, it is one of the few immunogenetic studies describing the functional proteomics of the encoded protein, plotting on a molecular level specific interaction modifications affecting the intracellular signaling pathway of TNF.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6818

AB0002 GENETIC STUDY OF THREE-PRIME REPAIR EXONUCLEASE (TREX1) IN THE SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AMONG EGYPTIAN PATIENTS

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Background: Interferon-alpha (IFNs) pathway has a crucial role in the pathogenesis of SLE. Many genes have been encoding with this pathway and their impaired expression have been reported in patients with SLE. TREX1 is a DNA exonuclease involved in the metabolism and clearance of single stranded DNA from apoptotic cells, which is impaired in SLE. TREX1 mutations have been reported in SLE2.

Objectives: Our study was aiming to assess the role of TREX1 in the genetic susceptibility to systemic lupus erythematosus (SLE) among Egyptian patients.

Methods: Fifty SLE Egyptian patients and 50 age & sex matched healthy controls were included in this study. Based on the clinical history and immunological investigations, the 50 SLE patients were divided into two groups according to the presence of positive family history of autoimmune disease: Group I: 28 patients with positive family history & Group II: 22 patients with no family history. Further, the single exon of TREX1 and its flanking sequences were amplified by PCR and sequenced in both directions.

Results: Our work showed a recurrent TREX1 polymorphism rs11797 (c.531C>T) among Egyptian patients (56%) in comparison to control group (36%) (p value of 0.070) especially in cases with NPSLE, seizures and chilblains; with minor allele frequency of 0.28 in cases and 0.18 in controls (p value=0.342). TREX1 polymorphism was present in 57.1% patients (16/28) of SLE patients in group I versus 54.5% patients (12/22) of SLE cases in, group II. The polymorphism was positively associated with neuropsychiatric manifestations (OR=7.000, 95% CI=0.791–61.975) and chilblains (OR=10.532, 95% CI=0.550– 201.679). Furthermore, there was a statistically significant difference in cases with oral ulcers (p value=0.004), photosensitivity (p value=0.047) and seizures (p value=0.029).

Conclusions: We confirm that rs11797 (c.531C>T) could be associated with the susceptibility to neurological manifestations among the studied SLE patients. References:

Genetic determinants of Psoriatic Arthritis: genes involved in the Mestizo Population

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Background: Psoriatic Arthritis (PsA) is a not a regular systemic autoimmune disease, many expert define it as autoinflammatory disease, resulting in chronic inflammation of the synovium and consequent cartilage and bone erosion in approximately 10% of patients with skin psoriasis. It is important to identify novel genomic biomarkers associated with disease susceptibility but also able to detect early those patients with negative prognostic factors who may benefit from a more aggressive therapeutic approach. This paper reports the expression of tumor necrosis factor (TNF)-α, a central element in the pathogenesis of psoriasis and psoriatic arthritis (2). The levels of TNF-alpha are under genetic control. An “A” at position -308 in the TNFA promoter has been shown to be associated with increased level of TNF-alpha expression and “A” at position -238 with a diminished level of TNF-α expression (3,4). Many authors consider that is a disease only of Europeans descendants or Caucasians, however never be studied in mestizo population.

Objectives: We investigate the potential association between the TNFA-238 G/A, TNFA-308 G/A, IL10 -1082 G/A, IL10 -819 C/T and -592 C/A polymorphisms and the Psoriatic Arthritis (PsA) in patients with a history of ancestors, at least back to the third generation.

Methods: The study included 52 PsA patients diagnosed by CASPAR criteria and 52 controls. The polymorphism of TNFA-308 G/A (rs1800629) and TNFA-238 G/A (rs13163525), IL10 -1082 G/A (rs1800886), -819 C/T (rs1800871) and -592 C/A (rs1800872) were genotyped by single specific primers-polymerase chain reaction (SS-PCR). All subjects were from an unrelated Venezuelan-Mestizo population with a history of ancestors, at least back to the third generation.

Results: When comparing allele and genotype frequencies between the groups studied, no significant differences were observed for the TNFA-308 G/A (rs1800629) and IL10 -1082 G/A (rs1800886), -819 C/T (rs1800871) and -592 C/A (rs1800872). However, our results showed a significant decrease in the frequency of the TNF-238A allele among PsA patients compared to healthy individuals (3.8% vs. 10.57%, respectively; OR: 0.31, 95% CI: 0.92–1.05, p=0.02), suggesting that TNF-238A allele may have a protective effect (Table 1).

Table 1: Genotypes and allele frequencies of the 308 G/A (rs1800629) and 238 G/A (rs13163525) variants of the TNFA gene in patients with psoriatic arthritis and healthy controls

<table>
<thead>
<tr>
<th>Genotype</th>
<th>TNFA-238 G/A (rs13163525)</th>
<th>Controls n=52</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td>19.3%</td>
<td>15.6%</td>
<td>1.0</td>
</tr>
<tr>
<td>AA</td>
<td>0%</td>
<td>0%</td>
<td>1.0</td>
</tr>
<tr>
<td>GG</td>
<td>80.6%</td>
<td>84.6%</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Discussion: These results suggest that upregulation of IL23 and TGFβ1 in addition to downregulated Foxp3 expression may contribute to skewing towards Th17 profile in SLE pathogenesis and this was the most markedly manifested at the highest level of disease activity. Our results support indirectly the idea for restoring Th17/Treg balance as a therapeutic target in SLE.

Disclosure of Interest: None declared

Genotyping Assay in blood samples obtained from 47 patients BD diagnosed according to 1990 international criteria for behcet disease and 50 matched healthy controls. Disease activity was done using BD current activity form (BDCAF).

**Results:** Study of miRNA-499 polymorphism, showed that the genotype frequencies of TT, CT, and CC were 21.3%, 63.8%, and 14.9% in BD patients and 18.0%, 52.0%, and 30.0% in the control group respectively. A significant increase in the relative expression of miRNA-499 was found in BD patients compared to control (P < 0.05). There was no significant relation between relative expression of miRNA-499 and activity of BD patients assessed by BDCAF (P > 0.05). In addition there was association between genotypes of miRNA-499 and posterior uveitis (P < 0.05). There was association of the relative expression of miRNA-499 with vascular manifestations and aneurysm.

**Disclose of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4476

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**AB0007**  
**SHARED GENETIC PREDISPOSITION IN RHEUMATOID ARTHRITIS–INTERSTITIAL LUNG DISEASE AND FAMILIAL PULMONARY FIBROSIS**


**Background:** Despite its high prevalence and mortality, little is known about the pathogenesis of RA–associated interstitial lung disease (RA-ILD). Given that familial pulmonary fibrosis (FPF) and RA–ILD frequently share the usual interstitial pneumonia pattern and common environmental risk factors, we hypothesized that the two diseases may share additional risk factors including FPF-linked genes.

**Objectives:** Our aim was to identify coding mutations of FPF-risk genes associated with RA-ILD.

**Methods:** We used whole-exome sequencing (WES) followed by restricted analysis of a discrete number of FPF-linked genes and performed a Burden test to assess the excess number of mutations in RA–ILD patients compared to controls.

**Results:** Among the 101 RA–ILD patients included, 12 (11.9%) had 13 WES-identified heterozygous mutations in the TERT, RTET1, PARN or SFTP C regions. The burden test, based on 81 RA–ILD patients and 1010 controls, did not show evidence of an excess of TERT, RTET1, PARN or SFTP mutations for RA–ILD patients (p=9.45·10^-6), odds ratio [OR] 3.17 95% CI 1.53–6.12). Tomelores were shorter for RA–ILD patients with a TERT, RTET1 or PARN mutation than controls (p=2.67·10^-1).

**Conclusions:** Our results support the contribution of FPF-linked genes to RA–ILD susceptibility.

Disclose of Interest: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5237

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**AB0008**  
**THE ASOCIATION OF THE PTNP22 RS2476610 GENOME POLYMORPHISM WITH JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN FROM RUSSIA**

L.S. Nazarova1, K.V. Danilko1, V.A. Malievsky1, 2, Bashkir State Medical University; 1Institute of Biochemistry and Genetics, Ufa, Russian Federation

**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. The exact cause of the disease is still unknown, but seems to be related to both genetic and environmental factors [1]. The protein tyrosine phosphatase non-receptor type 22 (PTPN22) gene single-nucleotide polymorphism (SNP) rs2476610 was shown to be associated with JIA in different populations, but according to recent reports this association is restricted only to females [2,3].

**Objectives:** The aim of the study was to determine whether the PTNP22 rs2476610 SNP is associated with the development of JIA and its subtypes in children from Russia.

**Methods:** The study included 330 patients with JIA and 346 healthy controls from Russia. Genotyping was performed using real-time PCR method and statistical analysis - using two-tailed Fisher’s exact test (p), odds ratio (OR), 95% confidence interval (95% CI).

**Results:** The frequencies of the genotype AG and the allele A were significantly higher in patients with JIA than controls (p<0.016, OR=1.65, 95% CI 1.10–2.48; p=0.028, OR=1.48, 95% CI 1.05–2.08; p=0.016, OR=0.62, 95% CI 0.43–0.91; p=0.028, OR=0.68, 95% CI 0.48–0.95, correspondingly). The same analysis was then performed separately for patients with two most frequent ILAR subtypes: persistent oligoarthritis (n=106) and RF-negative polyarthritis (n=85). Significant associations similar to those in the whole JIA group were found only for persistent oligoarthritis (p=0.018 for the genotype AG; p=0.037 for the allele A; p=0.022 for the genotype GG; p=0.037 for the allele G). No significant differences were found for patients with RF-negative polyarthritis (p=0.6). Sex-stratified analysis showed that the frequency of the allele G is higher in girls with the genotype AG: p=0.024 and p=0.008; with the allele A: p=0.016 and p=0.0061; correspondingly; for boys: p=0.2 for all comparisons.

**Conclusions:** In this study we revealed the association of the PTNP22 rs2476610 SNP with the development of JIA and its persistent oligoarticular subtype in girls from Russia.

**References:**

**DOI:** 10.1136/annrheumdis-2017-eular.4377

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**AB0009**  
**GENOMIC SIGURATURES MAY BE ASSOCIATED WITH VASCULAR PATHOLOGY ASSOCIATED WITH RHEUMATOID ARTHRITIS**

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**Background:** Accelerated atherosclerosis and cardiovascular (CV) disease have been associated with rheumatoid arthritis (RA). Many genes have been implicated in atherosclerosis, RA or both. However, most of these studies described SNPs in CD40, SMAD3, HLDAR, CTLA4 genes, showing GVR also had good clinical response to biologics. Up-regulation of 99 genes was found in responders and non-responders to biologics, as well as patients that show or do not show improvement of vascular pathology.

**Disclose of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3208
**Adaptive immunity (T cells and B cells) in rheumatic diseases**

**AB0010**

**LILRB3 EXPRESSION ON T CELLS CORRELATES WITH DISEASE ACTIVITY IN RA**

A. Holz, T. Witte, R.E. Schmidt. Department of Clinical Immunology and Rheumatology, Hannover Medical School, Hannover, Germany

**Background:** Leukocyte immunoglobulin-like receptors (LILR) participate in the generation of immunological tolerance (1-2). LILRB3 can be expressed on T cells and is an inhibiting receptor (3).

**Objectives:** We wanted to study LILR expression on T cells in RA compared to SLE and controls.

**Methods:** Heparinised human blood from blood donors was obtained from the Institute of Transfusion Medicine, Medical School Hannover (Germany). Blood samples from RA (DAS28 \( \leq 3.2 \) n=11; DAS28 \( \leq 3.2 \) n=8) and SLE patients (n=9) were obtained from Outpatients’ Clinic of the Department of Rheumatology and Immunology after informed consent. PBMCs were stained with LILRA2 (Biolegend, APC), LILRB3 (Biolegend, PE), CD3 (Biolegend, APC-Cy 7), CD4 (BD, PerCP-Cy5.5), CD8 (Biolegend, V500), CD25 (Biolegend, PE/Cy5), CDS8 (Biolegend, Pacific Blue). Results were compared to isotype controls. Statistical analyses and figures were made with GraphPad Prism, ANOVA and t-test (Biolegend, APC), LILRB3 (Biolegend, PE), CD3 (Biolegend, APC-Cy 7), CD4 (BD, PerCP-Cy5.5), CD8 (Biolegend, V500), CD25 (Biolegend, PE/Cy5), CDS8 (Biolegend, Pacific Blue).

**Results:** The percentage of both CD4+ and CD8+ T cells expressing LILRB3 was significantly higher in both inactive as well as active RA compared to controls or SLE (See Fig. 1) (p=0.0397 ANOVA: RA all vs. SLE vs. controls). Within the group of RA patients, the percentage of LILRB3 expressing T cells was highest in active compared to inactive (DAS28 \( \leq 3.2 \) RA (p=0.0297). LILRA2 was not expressed on T cells.

**Conclusions:** Expression of LILRB3 correlates with disease activity of RA and is decreased after successful treatment with DMARDS or biologicals. Since LILRB3 is an inhibiting receptor the increased expression in active RA may be a counterregulation to reduce disease activity.

**References:**


**Acknowledgements:** We thank the StrucMed program for the support, and Katja Kneisch for technical assistance.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1697

**AB0011**

**KLRG1 AS A MARKER OF CD28 NEGATIVITY IN RHEUMATOID ARTHRITIS, COMPARISON WITH CD57 AND CD45RA**

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**Background:** Our research has shown that patients with RA have higher proportions of peripheral blood CD3+CD8+CD28- Treg cells compared to healthy individuals. CD3+CD8+CD28- Treg cells in patients with RA have lost their ability to suppress lymphocyte proliferation 1. Thus CD28 negativity may mark senescent T cells. CD57+ CD45RA+ and killer-cell lectin like receptor G1 (KLRG1)5 cell surface molecules have been associated with CD8+ T cell activation and senescence. Defining the phenotypic signature of CD8+CD28- Treg cells will help establish their significance in the immunoregulation of RA.

**Objectives:** To use immunofluorescence and flow cytometry to define the phenotype of CD3+CD8+CD28+/- cells in relation to early RA progression.

**Methods:** The effector characteristics of peripheral blood CD8 T cells were evaluated by flow cytometry. RA patients with established (n=21) and early disease (n=20) were recruited, and compared to twenty four healthy controls. The mean age of the subjects was 59 (SD=12.5), 25/38 (66%) were female, 27/38 (71%) were anti-CCP positive and 25/38 (66%) rheumatoid factor positive. The mean age for the controls was 43 (SD=11.6), 14/20 (70%) were female. Among RA patients, the percentage of KLRG1+ T cells was highest in active disease (DAS28 \( \leq 3.2 \)) RA (p=0.0287). LILRA2 was not expressed on T cells.

**Conclusions:** Our research has shown that patients with RA have higher proportions of peripheral blood CD3+CD8+CD28- Treg cells compared to healthy individuals. CD3+CD8+CD28- Treg cells in patients with RA have lost their ability to suppress lymphocyte proliferation 1. Thus CD28 negativity may mark senescent T cells. CD57+ CD45RA+ and killer-cell lectin like receptor G1 (KLRG1)5 cell surface molecules have been associated with CD8+ T cell activation and senescence. Defining the phenotypic signature of CD8+CD28- Treg cells will help establish their significance in the immunoregulation of RA.

**References:**

[1] Boeckstaes D, Monger L, Aajogina S, Ludvigsson F, Svensson B, Toes R, Trows L, Trouv T, Huizinga T, Berenbaum F, Morel J, Rantapää-Dahlgren S, van der Helm-van Mil I, Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; 2Department of Medicine Huddinge, Karolinska Institutet, Stockholm; 3Department of Clinical Sciences, Section of Rheumatology, Lund University and Skåne University Hospital; 4Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund, Sweden; 5Department of Rheumatology, Sophiahemmet University, INSERM UMR s938, DHR U28, Assistance Publique-Hôpitaux de Paris, Saint-Antoine Hospital, Paris; 6Department of Rheumatology, Teaching hospital Lapeyronie and Montpellier University, Montpellier, France; 7Department of Public Health and Clinical Medicine/Rheumatology, University Hospital, Umeå, Sweden

**Background:** Rheumatoid arthritis (RA) consists of two syndromes, one autoantibody-positive and one autoantibody-negative. This multi-cohort study
assessed the age of onset in relation to the presence of autoantibodies. The association with characteristics of the anti-citrullinated protein antibodies (ACPA)-response was also explored.

Objectives: 1) determine the association between age of RA-onset and the presence of ACPA, rheumatoid factor (RF) and anti-citrabamyalted protein (anti-CBP) antibodies, 2) study age of onset was associated with characteristics of the ACPA-response, 3) substantiate previously reported associations between age of onset and clinical characteristics.

Methods: 3,321 1987-positive RA-patients included in the Leiden-EAC, BARFOT, EPOIR, Umea and Lund cohorts were studied at presentation on age of onset and the presence of ACPA, RF and anti-Carb antibodies. Logistic regression analyses were performed; effect sizes were summarized in inverse-weighted meta-analyses. Within ACPA-positive RA, ACPA-level was studied in all cohorts; ACPA-isotypes, ACPA-line-specificity and ACPA-avidity index and clinical characteristics were assessed in the Leiden-EAC.

Results: From the age of fifty onwards, the proportion of ACPA-negative RA-patients increased in Dutch, Swedish and French cohorts. Similar observations were done for RF and anti-Carb. The composition of the ACPA-response did not change with increasing age of onset with respect to titer, isotype distribution, line specificity and avidity index. With increasing age of onset RA-patients smoked less often, had higher acute phase reactants and more often a sub(acute) symptom onset.

Disclosures: None declared Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3781

AB0013 IS THERE IMMUNE DISREGULATION IN NON-SJÖGREN SICCA SYNDROME? A STUDY OF BLOOD LYMPHOCYTE SUBPOPULATIONS


Background: A large number of patients with sicca syndrome not fulfilling Sjögren’s syndrome (SS) classification criteria, present manifestations of autoimmunity, like arthritis, Raynaud’s, rash or hematologic disturbances, and have anti-nuclear antibodies, lacking however more specific antibodies. The designation Undifferentiated Connective Tissue Disease was coined to refer to those patients, and some will eventually progress to a definite disease, of which SS would be a likely candidate. Immune cell disturbances could be progression marker, since diseases like pSS have distinct lymphocyte profiles.

Objectives: We aim to study the circulating lymphocyte subsets in non-Sjögren sicca patients (n-SS), and compare them with pSS and healthy controls.

Methods: Blood samples of n-SS patients, 53 pSS patients (2002 AECG criteria) and 22 healthy controls. Lymphocyte subsets were characterized by flow cytometry and PCR after the treatment (p<0.002), leading to marked decrease of CD4+/CD8+ ratio (p<0.009). Except three patients, overall percentage of neutrophils decreased after the treatment (p<0.01). Although ACPA pulse did not influence the percentage of NK, the percentage of NK cells carrying stimulatory receptor: CD69 increased after ACPA (p<0.037). Similarly, CFA enhanced the percentage of co-stimulatory molecule CD27 on B lymphocytes (p<0.048). Among subsets of monocytes, CFA treatment increased percentage of CD14+CD16+ monocytes (p<0.006) and increased expression (MFI) of Fc fragment CD64 (p<0.04). Moreover, increase of HLA-DR was observed on CD14+CD16+ monocytes (p<0.037). The investigations whether the changes in immune cell subpopulations in treated patients have prognostic potential are ongoing.

Conclusions: Single dose of CFA resulted in increase of percentage of CD6+ T lymphocytes (p=0.002), leading to marked decrease of CD4+/CD8+ ratio (p=0.009). Except three patients, overall percentage of neutrophils decreased after the treatment (p=0.01). Although ACPA pulse did not influence the percentage of NK, the percentage of NK cells carrying stimulatory receptor: CD69 increased after ACPA (p=0.037). Similarly, CFA enhanced the percentage of co-stimulatory molecule CD27 on B lymphocytes (p=0.048). Among subsets of monocytes, CFA treatment increased percentage of CD14+CD16+ monocytes (p=0.006) and increased expression (MFI) of Fc fragment CD64 (p<0.04). Moreover, increase of HLA-DR was observed on CD14+CD16+ monocytes (p<0.037). The investigations whether the changes in immune cell subpopulations in treated patients have prognostic potential are ongoing.

Disclosures: None declared Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4663

AB0015 CAPTURE OF IGA IMMUNE COMPLEXES AND ENRICHMENT IN IGA IG GENE EXPRESSION BOTH SUGGEST A ROLE FOR FCRL4+ B CELLS IN THE LINK BETWEEN MUCOSAL AND JOINT INFLAMMATION

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Background: Recent evidence points to the autoimmune process of rheumatoid arthritis (RA) originating at mucosal surfaces. Previous work from our group described a subset of B cells in the synovium and synovial fluid (SF) of RA patients which can be distinguished by their expression of the Fc-like receptor 4 (FCRL4) and elevated expression of RANKL, indicating a unique pathogenic function. B cells expressing FCRL4 were originally described as a distinct memory B cell subset in human tonsils where they accumulate in the epithelium. We have recently shown that FCRL4+ B cells are enriched in cells recognizing citrullinated autoantigens (Amara, K. et al. under revision). Recent in vitro work suggested that FCRL4 is a low affinity receptor for aggregated IgA.

Objectives: 1) To investigate the interaction of RA synovial fluid FCRL4+ B cells with IgA

Methods: SF mononuclear cells were isolated, labelled for FCRL4, IgA and CD19 and analysed by flow cytometry. In experiments identifying IgA B cell receptors, SF mononuclear cells were briefly incubated in an acidic buffer to remove surface receptor bound antibodies before staining. Heat-aggregated purified human IgA
was added to assess IgA binding to FcRl4+ B cells. Single B cells were sorted from SF of RA patients and their constant region genes probed for identification of their Ig subclass by PCR.

Results: Ex vivo, FcRl4+ B cells in SF of RA patients have a higher load of IgA bound to their surface compared to their FcRl4- counterparts. After in vitro removal of surface bound IgA, they can bind heat-aggregated IgA (p = 0.0313). We also demonstrate that a significantly higher proportion of FcRl4+ B cells use IgA BCRRs (p = 0.0061) by flow cytometry and further more by probing constant region genes by PCR for enrichment for Ig genes coding for the IgA1 isotype (p = 0.009) was found.

Conclusions: Both their ability to capture IgA immune complexes through binding to FcRl4 and their enrichment in IgA Ig gene expression suggest a potential role for synovial fluid FcRl4+ B cells in the mucosal origin of joint inflammation.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6488

AB0016

B-CELL SUBSETS DIFFERENCES IN INFLAMMATORY RHEUMATIC DISEASES

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Background: Targeting humoral immunity has been proved effective in several inflammatory rheumatic diseases (IRD). Though clinical trials have shown some efficacy of B-cell depletion in ankylosing spondylitis (AS), results are less convincing. Other studies have revealed an association between mutations and expression of immune regulatory genes suggesting B-cell dysfunction in the development and progression of AS. Yet, there is still lack of data describing B-cell subsets in AS compared to other inflammatory B-cell compartment homeostasis in the pathophysiology of this disease.

Objectives: To assess and compare the immature, naïve and antigen differentiated subsets of peripheral B-cell compartment in AS with those in healthy controls (HC) and other IRD

Methods: Patients (pts) with AS, RA and SLE according to respective classification criteria were included in this study. Pts under biologic DMARDS were not included. Sociodemographic and clinical variables were recorded. Blood samples were collected for quantification of inflammatory markers (ESR and CRP), immunoglobulins and serum levels and assessment of B-cell immature transitional stages and mature subsets by flow cytometry (figure). Mann-Whitney and Fisher’s exact test were used for comparison of AS with other groups

Results: Overall, 60 pts and 12 HC were included (Table). All patient groups presented similar and rather low levels of inflammation, as measured by CRP, ESR and immunoglobulins, in addition to a decreased lymphocyte count by comparison with HC. There were no differences in the B-cell counts between AS pts and HC, with both groups having higher B-cell counts than RA and SLE pts. Regarding B-cell subsets, the immature transitional compartment of AS pts was found in normal range, but not in the RA and SLE groups. In fact, the latter presented a significant decrease in all transitional maturity stages (T1-T3). The next step in B-cell differentiation is mature naïve cells, also found in normal levels in AS and decreased in RA and in particular in SLE. AS pts presented slightly higher counts of CD27+ IgD- M2-like and class able to switch memory cells with reference to HC and these cell numbers were found to be lower in and even lower in SLE pts. Switched memory CD27+IgD- B-cells were reduced in all patient groups, however, only SLE pts presented highly decreased cell levels.

Conclusions: We found that while a severe dysfunction is present in the homeostasis of the B-cell compartment in RA and in particular SLE pts, which are lymphopenic in both immature and mature B-cell compartments, it appears that AS pts are not affected in the same way. At this stage, functional studies appear to be necessary in order to identify differences in key mechanisms of B cell development and differentiation that may play a role in the etiology and progression of these inflammatory rheumatic diseases. Our first results, however, establish that pathophysiological mechanisms involving B-cells clearly differentiate AS from RA and SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5553

AB0017

THERAPEUTIC EFFECT OF UMBILICAL CORD-DERIVED MESENCHYAL STEM CELLS TRANSPLANTATION IN A MOUSE MODEL OF PRIMARY BILIARY CIRRHOSIS

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Background: Primary biliary cirrhosis (PBC) is a cholestatic liver disease characterized by slow progression of non-suppurative cholangitis with immune mediated destruction of intrahepatic bile ducts. Previous studies have shown beneficial effects of mesenchymal stem cells (MSCs) transplantation in many autoimmune diseases. However, few studies have focused on the effects of MSCs on PBC.

Objectives: In our study, we investigated the therapeutic effect of umbilical cord-derived mesenchymal stem cells (UC-MSCs) transplantation in a well-defined mouse model of PBC and explored the potential mechanism.

Methods: After 2OA-BSA-induced autoimmune cholangitis was created in C57BL/6 mice, cultured human UC-MSCs or a vehicle control was administered. Liver injury severity was assessed by clinical and histologic analysis. The immunity suppression effects and mechanism of UC-MSCs were tested.

Results: UC-MSCs administration alleviated biliary duct damage and intrahepatic inflammatory cell infiltration in C57BL/6 mice that had undergone 2OA-BSA immunization. Serum levels of ALT and ALP were significantly decreased. Also, UC-MSCs reduced the production of anti-mitochondrial autoantibodies (AMA) in PBC mice. UC-MSCs downregulated immunoregulatory cytokine, such as IFN-γ, TNF-α, IL-12 and IL-17A production both in peripheral blood and local liver. Notably, Infusion of UC-MSCs resulted in an increase in regulatory T cells (Tregs) in peripheral blood but a decrease of this kind of cells in liver tissues. Furthermore, UC-MSCs significantly suppressed Th1- and Th17-cell responses and these alternations could be detected in spleen, peripheral blood and liver in PBC mice.

Conclusions: In summary, the current study shows that UC-MSCs based therapy has profound inhibitory effects on inflammatory responses and immunoregulatory effects both in local and systemic abnormalities in PBC. This findings also provide further evidence regarding the role of MSCs in the clinical trials of PBC.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3346
B CELL DISTURBANCE IN RHEUMATOID ARTHRITIS PATIENTS: COMPARATIVE STUDY BETWEEN TREATED AND NON-TREATED PATIENTS

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Background: B cells have been shown to play a key role in the pathogenesis of rheumatoid arthritis (RA). Alterations of B cell homeostasis as well as B cell activation markers, such as B-cell activating factor (BAFF) and A Proliferation-Inducing Ligand (APRIL) have been described in RA patients. Up to our knowledge, no data is currently available on differences between treatment naïve patients and those receiving disease modifying anti-rheumatic drugs (DMARDs), regarding B-cell surface expression as well as levels of circulating BAFF/APRIL.

Objectives: The aim of this study is to investigate disturbance of B cell as well as B cell activation markers namely BAFF and APRIL in patients with rheumatoid arthritis comparing treatment naïve patients with those receiving disease modifying anti-rheumatic drugs.

Methods: Sixty RA patients and 30 healthy controls were enrolled. Thirty patients receiving non biologic DMARDs and had not received prior biological treatment and 30 treatment naïve patients. Absolute number of blood CD19 B cells was determined by flow cytometry using the CD19-PE Kit (Immunotech, France). BAFF and APRIL blood concentration was measured using commercially available ELISA kits (Bosterbio, USA).

Results: There was statistically significant difference (p-value <0.05) between different study groups as regard B cell count with low mean among treated RA patients (137.2±60.5) and high mean among controls (243.7±22.5). The B cell count was diminished in the two groups of RA patients, however it is more pronounced in treated patients. Circulating BAFF levels were increased in RA compared to HC (p-value <0.05) with more increase in patients on treatment. Circulating APRIL levels were significantly lower (p-value <0.05) in treatment naïve rheumatoid arthritis patients (343.9±21.7) than the control group (371.5±24.3). However, there was no statistical significant difference (p-value >0.05) between each of treated rheumatoid arthritis group and controls or with non treated rheumatoid arthritis group.

Conclusions: More decrease in B cell count and more increase in BAFF level were observed in RA patients receiving non-biologic DMARDs. Conversely, APRIL levels were not affected by treatment.

The contribution of B lymphocyte to RA pathogenesis goes beyond autoantibody production. Disturbances in B cell homeostasis in RA are not only due to disease process itself but also closely related to the use of anti-rheumatic drugs.

REFERENCES


Disclosure of Interest: None declared

HDLC PROMOTES A REGULATORY PHENOTYPE OF THE IMMUNE SYSTEM BY INDUCING THE PROLIFERATION OF HUMAN CD4+ T CELLS WHILE INCREASING THE EXPRESSION OF FOXP3 IN REGULATOR T CELLS

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Background: High-density lipoproteins (HDL) are the plasma lipoproteins responsible for reverse cholesterol transport. Its protective effect on cardiovascular disease is attributed to the cholesterol efflux capacity as well as to its anti-oxidant and anti-inflammatory properties. HDL low levels are associated with immune disturbance, including systemic lupus erythematosus and rheumatoid arthritis, implying a potential link between HDL and immunity.

There is few evidence on the effects of HDL on human T cells. Animal studies suggested that HDL inhibits lymphocyte proliferation1, but the only study in humans showed that HDL from young and healthy subjects increases the proliferation of lymphocytes2. Previous studies also showed that HDL levels are positively correlated with the prevalence of regulator T cells in peripheral blood3. Furthermore, it has been shown that one of the main actions of HDL in lymphocytes is the disaggregation of lipid rafts provoked by cholesterol efflux from the membrane, but the final consequences of this effect are not known.

Objectives: To determine the in vitro effects of HDL in human T cell proliferation and in the frequency of FoxP3+ regulator T cells.

Methods: Peripheral blood mononuclear cells from six healthy donors were cultured with and without HDL to measure membrane cholesterol and proliferative rates. CD19+ lymphocyte membrane cholesterol was measured by filipin binding, assessed by flow cytometry. T cell proliferation was studied by Ki-67 expression and cell trace staining for multiple generations. T cell phenotyping and FoxP3 fluorescence were analyzed by flow cytometry.

Results: HDL significantly reduced the amount of membrane cholesterol in CD4+ T cells, after 24 hours in culture. When added in the absence of stimulation, HDL did not induce any proliferation in CD4+ T cells. When added in conjunction with CD3/CD28 stimulation, HDL significantly increased the proliferation of CD4+ T cells. T cell phenotyping showed a significant increase in CD4+CD25+FoxP3+ regulatory T cells, after culture.

Conclusions: This study shows that HDL promotes cholesterol efflux from the membrane of CD4+ T cells in vitro and increases CD4+ T cell proliferation. However, the increase in T cell numbers seem to favor the expression of FoxP3 in regulator in T cells, which is associated with suppression of inflammation. With the development of therapies to increase HDL levels, the knowledge of the HDL effects on T cell subsets is very important for the future management of cardiovascular and rheumatic diseases.

REFERENCES


Disclosure of Interest: None declared

EXPRESS LEVELS OF SIGNALING LYMPHOCYTE ACTIVATION MOLECULE FAMILY 6 (SLAMF5) ON CIRCULATING FOLLICULAR HELPER T CELLS ARE ASSOCIATED WITH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: T follicular helper cells (Tfh) are necessary for B-cell maturation and differentiation in the germinal centers (GC). The signaling lymphocyte activation molecule family (SLAMF) receptors on the cell surface mediate T cell:B cell interaction for formation and maintenance of GC. But it remains to be elucidated whether SLAMF5 is expressed in circulating T follicular helper cells (cTfh).

Objectives: The aim of this study was to investigate the levels of SLAMF3 and SLAMF5 on cTfh and to analyze their association with disease activity in systemic lupus erythematosus (SLE) patients.

Methods: Blood samples were collected from 50 SLE patients, 24 Sjogren’s syndrome (SS) patients and 25 age- and sex-matched healthy controls (HCs). In this study, CXCR5, programmed death protein 1 (PD-1), and CD4 were used as markers to define cTfh in peripheral blood mononuclear cells (PBMCs). The expression levels of SLAMF3 and SLAMF5 on cTfh were compared to that of circulating B cell subsets by flow cytometry. Clinical features including disease activity and laboratory tests were analyzed according to expression of SLAMF3 and SLAMF5.

Results: Surface expression of SLAMF5 on CD4 T cells was significantly increased in SLE patients compared to SS patients (mean fluorescence intensity [MFI], mean ± SD: 1291±319 vs 1098±147, p=0.015) and HCs (1291±319 vs 1098±147, p=0.011). But there was no difference in expression of SLAMF3 on CD4 T cells between SLE patients and SS patients or HCs. SLAMF6 expressions on cTfh cells, identified as CD4+CXCR5+PD-1+, were significantly increased in SLE patients than in SS patients (1500±270 vs 1296±140, p=0.001) and HCs (1500±270 vs 1295±161, p=0.001). SLAMF6 expressions on cTfh cells had correlation with systemic lupus erythematosus disease activity index (SLEDAI) (Spearman’s rho=0.477, p=0.001), proteinuria (rho=0.321, p=0.030) and double strand DNA (rho=0.340, p=0.026) in SLE patients. Moreover, expression levels of SLAMF6 on cTfh cells were correlated with those of several B cell subsets including total B cells (CD19+), naive B cells (CD19+CD27-), and class-
switched memory B cells (CD19+CD27+IgD-). But SLAMF6 expressions of B cell subsets were not correlated with disease activity.

Conclusions: Surface expression of SLAMF6 was increased in cTfh cells in patients of SLE and had correlation with disease activity.

References:

Disclosure of Interest:

HUMAN T CELL LEUKEMIA VIRUS TYPE 1 (HTLV-1) ASSOCIATION BETWEEN MEX-SLEDAI AND INFECTIONS WITH HTLV-1 INFECTED CELLS

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Background: Human T cell leukemia virus type 1 (HTLV-1) positive rheumatoid arthritis (RA) patients show severe inflammatory state and resistance to anti-rheumatic therapy, including biologic agents (1). HTLV-1 infected T cells was increased in the synovial fluid and tissue from an HTLV-1 positive RA patients (2). However, the mechanism of worsening RA by HTLV-1 infection remains unclear. We focused on the role of HTLV-1 infected T cells as a key player in the exacerbation of RA.

Objectives: To clarify the role of HTLV-1 infected T cells in the pathogenesis of RA. We investigate inflammatory mediators derived from HTLV-1 infected cells.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from asymptomatic HTLV-1 carriers (AC) (n=5) and healthy subjects (HS) (n=5). Rheumatoid arthritis synovial fibroblasts (RASFs) were co-cultured with PBMCs for 5 days. Cytokine profiles of supernatants were analyzed by multiplex. Exosomes were isolated and purified from cultured medium of HTLV-1 infected cell line (MT2). RASF was cultured with MT2 derived exosomes with and without IFN-gamma for 24hours. Total RNA was extracted using TRIZOL method. The expression of RIG-I, IL-6, CXCL10, and CCL5 mRNA in RASF was measured using real-time quantitative PCR. The expression of pattern recognition receptor, RIG-I was determined by immune blotting. Silencing of RIG-I in RASF was performed by transfection of siRNA against RIG-I.

Results: The levels of cytokine, including IFN-gamma, IL-2, IL-9, IL-13, IL-6, and CCL20, were higher in supernatants co-cultured with HTLV-1 positive PBMCs than in those of negative PBMC (p<0.05). The expression of CXCL10 and IL-6 mRNA was increased in RASF co-cultured with HTLV-1 positive PBMCs compared to those of negative PBMCs. IFN-gamma expression was increased in the pathogenesis of HTLV-1 associated inflammatory diseases. IFN-gamma induced the expression of IL-6, CCL5, and CXCL10 mRNA in RASF. HTLV-1 infected cell line, MT2, autonomously released a large amount of exosomes which contain nucleic acids such as RNA and DNA. MT2 derived exosomes significantly enhanced the expression of CXCL10 mRNA, but not IL-6 and CCL5, in RASF activated by IFN-gamma. Therefore, we hypothesized that exosomes play the role of ligand for pattern recognition receptors. IFN-gamma increased the expression of RIG-I protein in RASF in a dose-dependent manner. The expression of RIG-I protein also increased in RASF co-cultured with HTLV-1 positive PBMCs compared to those of negative PBMCs. Finally, the silencing of RIG-I suppressed the expression of CXCL10 in RASF induced by co-stimulation of both exosomes and IFN-gamma.

Conclusions: It is possible that HTLV-1 infected T cells exacerbate the inflammatory responses of RASFs. Exosomes derived from HTLV-1 infected cells enhance the expression of CXCL10 in RASF induced by IFN-gamma via pattern recognition receptor, RIG-I.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2036

CYTOTOXIC PROFILE CHARACTERIZATION OF NK AND NKT CELLS IN PATIENTS WITH BEHÇET DISEASE

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Background: Behçet disease (BD) is a rare inflammatory small vessel vasculitis. It is a chronic systemic disorder with multorgan damage and various clinical manifestations such as cutaneous ulcers, genital ulcers, oral ulcers and uveitis. Etiology is still unknown. Some gene polymorphisms have been associated with BD [1]. In addition, a high frequency of circulating Natural Killer T cells (NKT cells) has been found in BD patients compared to patients with other inflammatory uveitis such as Vogt-Koyanagi-Harada disease (VKH) [2].

Objectives: The objective of this study was to characterize the cytotoxic profile of circulating Natural Killer (NK) and NKT cells in BD patients.

Methods: Peripheral Blood Mononuclear Cells (PBMCs) were collected from 23 BD patients (according to 1990 ISG criteria), 7 VKH patients (according to 2001 Revised Diagnostic Criteria) and 9 healthy subjects [3,4]. BD activity was evaluated with BD Current Activity Form 2003. Anti-CD56 and anti-CD3 antibodies were used to identify NK (CD56+CD7+) and NKT (CD56−CD3+) cells by flow-cytometry. Expression of one inhibiting receptor (NKG2A) and five activating receptors (CD16, CD69, NKG2D, Nkp30 and Nkp46) was determined on the surface of NK and NKT cells. Cytotoxic potential of NK and NKT cells was assessed through incubation of PBMCs with K526 cells in presence or absence of IL-15 followed by flow-cytometry detection of the surface marker CD107a on NK and NKT cells [5].

Results: A higher frequency of NKT cells was detected in peripheral blood of BD patients than VKH patients. Compared to healthy subjects, an increased proportion of CD16 positive NKT cells was found in BD patients. Furthermore it was observed a higher percentage of NKG2D positive cells in both NK and NKT lymphocytes. No difference in the inhibitory markers was detected. In BD patients, incubation of PBMCs with K562 cells in absence of IL-15 induced a lower percentage of NKT cells expressing CD107a compared to VKH patients. Frequency of CD107a positive NKT cells was -1% and similar between groups. Finally, no differences were found between BD patients with active and inactive phase of the disease.

Conclusions: Our study confirms previous reports about an increased level of NKT cells in peripheral blood of BD patients, but we additionally identified a cytotoxic profile of NK and NKT cells characteristic of BD patients when compared to healthy subjects and patients with VKH. Our data revealed for the first time a potential involvement of NKG2D in the pathogenesis of BD. We conclude that NK and NKT cells of BD patients are more prone to respond to stress/danger signals when exposed on target cells leading to cyclic auto-inflammation.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3493

ASSOCIATION BETWEEN MEX-SLEDIA AND INFECTIONS WITH MBL STRUCTURAL AND PROMOTER GENOTYPES IN MEXICAN-MESTIZO PATIENTS


Background: The mannose-binding lectin protein (MBL) is a multimeric molecule with a structure that is the analogue to the C1q protein. Deficient and low MBL concentrations in serum are due to the presence of mutations in the structural or promoter region.

Objectives: To investigate the role of alleles and haplotypes of MBL2 gene in the clinical expression of systemic lupus erythematosus (SLE) and its association with infections in Mexican-mestizo patients.

Methods: An observational, cross-sectional, retrospective study. We included 74 SLE patients and 75 matched controls. All > 16-years-old who met at least four 1982 ACR criteria for SLE were included. The association of MBL locus haplotypes with disease activity and past history of infection was studied in those patients. Allele and haplotype determinations in the promoter and structural regions of the MBL2 gene were performed from genomic DNA isolated peripheral blood. Probes were sent to Invitrogen (Carlsbad, California) for synthesis. The disease activity was determined by MEX-SLEDIA. Infections were categorized arbitrarily if patients had >4 events. The associations between the codons, clinical activity, and having >4 infection events were by odds ratio.

Results: There were 13/73 (17.8%) SLE patients with >4 infections. The presence of homozygous C/C codon 57 was observed to be greater risk for SLE activity and

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6078

Innate immunity in rheumatic diseases
present more than 4 infections. The significance of heterozygous HYLX promoter was observed only for the presence of infection. Table 1.

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<td>Median (IQR)</td>
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<td>n (%)</td>
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<td>Codon S52, n=71</td>
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<td>Codon S57, n=73</td>
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Conclusions: MBL2 gene polymorphisms of the homozygous C/C in codon 57 of the structural region and heterozygous HYLX of the promoter region are associated with increased risk of a higher number of infections. Also, we observed that homozygous C/C in codon 57 was associated to a higher MEX-SLEDAI.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3304

**AB0024**

A NOVEL REAL-TIME IMAGING TECHNIQUE TO CHARACTERIZE MECHANISMS OF CELL DEATH IN NEUTROPHILS

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Background: Neutrophils play a key role in the pathogenesis of autoimmune diseases through various mechanisms including the formation of neutrophil extracellular traps (NETs), NETosis, a recently described distinct form of program cell death and quantifies NETosis in a rapid, accurate and reproducible way. This technique may facilitate studies in neutrophil biology.

Objectives: Techniques to assess and quantitate NETosis in an unbiased, reproducible and efficient way are lacking. We developed a new method to automatically quantify the percentage of neutrophils undergoing NETosis using real-time quantitative live-cell analysis with IncuCyte ZOOM™ (Essen BioScience, Inc.) platform and a dual-dye system dependent on membrane integrity to stain DNA, to image neutrophils and characterize their mechanisms of cell death.

Methods: Neutrophils were isolated from healthy controls and differentiated into osteoclasts (OCs). These osteoclast progenitors (OCPs) were differentiated in the cytokine milieu and chemokine mediated trafficking.

Figure 1

Cytokines and inflammatory mediators

**AB0026**

CHEMOKINE SIGNALS ARE CRITICAL FOR HOMING AND ENHANCED DIFFERENTIATION OF CIRCULATING OSTEOCLAST PROGENITOR CELLS

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Background: Peripheral blood (PB) monocyte pool contains cells capable of differentiating into osteoclasts (OCLs). These osteoclast progenitors (OCPs) contribute to osteoresorption in inflammatory arthritides under influence of the cytokine milieu and chemokine mediated trafficking.
Objectives: Our study aimed to define chemokine receptor profile of peripheral OCPs in rheumatoid arthritis (RA), with comparison to psoriatic arthritis (PSA), as well as their susceptibility to chemotactic signals.

Methods: 129 RA, 53 PSA and 110 control patients were enrolled after Ethical approval. PB samples and synovial fluid (SF) samples, with clinical data of disease activity, progression and autoantibody levels were collected. Patients starting anti-TNF therapy were followed up 6 months. TNF-α and CTX serum levels were measured by ELISA. Frequency of OCP-rich subpopulation (CD3–CD19–CD56–CD11b+CD14+) with expression of FN, RANKL, and IL-33 was measured by FACS. OCPs, cultured with M-CSF and RANKL, were stained for TRAP enzyme and mature OCPs counted. Levels of CCL2, CCL3, CCL4, CCL5, CCLX9 and CCLX10 were measured using cytometric bead array, and of CXCL12 by ELISA. Osteoclastogenic effects of CCL2, CCL5 and CCLX10 were measured in cell culture and chemotactic effects on OCPs were studied by cell migration assay using Transwell, with count of number of migrated cells and subsequently differentiated mature osteoclasts.

Results: OCP population was moderately enlarged in PB, further expanded in SF and correlated with TNF-α and rheumatoid factor (RF) levels in patients with RA. However, sorted OCPs generated similar number of mature OCPs as control. RA RNK+ subpopulation was enlarged in SF vs PB and correlated with number of tendon joints. In PSA, the OCP population was not enlarged, and had a higher RF expression. OCPs in RA and PSA had higher expression of CCR1, CCR2, CCR4, CXCR4, CCR6, and all except CCR4 showed positive PB-to-SF gradient. RA had higher expression of CCL2, CCL3, CCL4, CCL5, CCLX9 and CCLX10, with a positive PB-to-SF gradient for all except CCL5 and CCLX9. OCP frequency correlated with levels of CCL2 and CCL5. Subset expressing CXCR4 was associated with TNF-α, CTX and RF levels and was lower in patients treated with DMARD, who at the same time had lower osteoclast formation (CTX). Subset expressing CXCR4 showed significant negative trend during anti-TNF treatment. CCL2, CCL5 and CCLX10 showed significant osteoclastogenic effect. CCL5 showed greatest chemotactic effect, attracting the highest number of cells in the migration assay. At the same time, attracted cells possessed greater osteoclastogenic potential.

Conclusions: Our study provides evidence of the specific importance of certain chemokine signals for stimulation of OCP mobilization, subsequent tissue homing, and maturation, explaining local as well as generalized bone loss seen in RA. Novel insights in regards to migratory behavior and functional properties of PB OCPs in response to chemotactic signals could open way to new therapeutic targets in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2317

AB0027 EXPRESSION DENSITY OF RECEPTORS TO TNF-ALPHA IS ASSOCIATED WITH DAS-28 SCORE IN RHEUMATOID ARTHRITIS

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Background: For a number of cytokines and growth factors density of receptors expression has been shown to be important in regulation of action intensity and variation. Although TNF-alpha is actively involved in the development and progression of chronic inflammation in rheumatoid arthritis (RA) role of membrane receptors and their regulatory function in RA remains unclear.

Objectives: To assess associations of membrane-bound receptors expression and cytokine content with disease activity score in patients with rheumatoid arthritis.

Methods: To reveal linear relationships among integrated score DAS-28 and studied parameters of intact T-cells, B-cells and monocytes (evaluated by flow cytometry) and parameters of mediators soluble content (evaluated by ELISA) building of multiple linear regression model (MLRM) with a standard assessment of the regression coefficients by least squares method were used. To determine receptor number on the cells QuantibritePE Beads (BD) were used.

Results: For the group of patients with acute stage of RA MLRMs with best statistical quality characteristics revealed that for lymphocytes both TNFR1 and TNFR2 number had significant associations with DAS-28; for monocytes only number of TNFR2 was significant. Lower DAS-28 index is associated with higher number of TNFR2 per cell and lower number of TNFR1. Comparison of models with different combinations of studied TNFR-parameters revealed that percentages of cells expressing receptors for TNFα validated not more than 20% of DAS-28 variation, while the number of receptors indicators on cells validated 40–50% of DAS-28 variation. Full MLRM with all 15 studied parameters validated about 70% of DAS-28 variation.

Conclusions: Number of receptors to TNF-alpha is more associated with RA activity score as compared with soluble receptors or cytokine. Number of receptors type 1 and type 2 to TNF-alpha per cell have opposite influence on disease activity score. Our findings indicate the involvement of receptors expression density changes in the pathological process in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2643

AB0028 FIBROBLAST-LIKE SYNOVIOCYTOMES MAY NOT BE THE TARGET OF IL-33 IN THE JOINT PHISIOPATHOLOGY

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Background: Rheumatoid arthritis (RA) and osteoarthritis (OA) are chronic joint diseases in which fibroblast-like synoviocytes (FLS) actively participate in the synovitis- damage cycle, trough production of cytokines such as IL-8 and metalloproteinases (MMPs). FLS. It has already been showed that serum IL-33 levels correlated with disease activity in RA. IL-33 is capable to enhance TNF-α effects in FLS. In the collagen-induced arthritis (CIA) model, the injection of IL-33 exacerbated the disease. Since ST2 receptor is expressed in FLS, it is hypothesized that IL-33 could activate FLS and increase downstream production of inflammatory cytokines.

Objectives: To evaluate the production of IL-6, MMP-1, and MMP-3 by FLS stimulated with IL-33, TNF-α, and IL-1β.

Methods: FLS were cultured from synovial fluid and tissue of OA patients (OAFLS n=8), RA patients (RAFLS n=3), and patients without rheumatic disease (health) (HFLS n=4). FLS were stimulated with TNF-α at concentrations of 1; 5; 10 and 50 ng/ml, IL-1β at concentrations of 0.1; 0.2; 0.3; 0.5 and 1 ng/ml and IL-33 at concentrations of 1; 3; 10; 30; 100 ng/ml, soon after, IL-6, MMP-1, and MMP-3 levels were evaluated by ELISA, in the cell supernatant.

Results: MMP-1, MMP-3 and IL-6 were constitutively expressed by FLS at baseline in all groups. Both TNF-α and IL-1β stimulated the production of IL-6 and MMP-1 with statistical significance in a dose-dependent manner in all three groups. Only IL-1β increased the production of MMP-3. TNF-α stimulated the production of MMP-3 only on FLS. There was no difference between the concentration of MMP-1, MMP-3 and IL6 in the supernatant of OAFLS, RAFLS and HFLS when IL-33 stimulated and non-stimulated were compared.

Conclusions: This study demonstrated that IL-33 failed to induce the production of IL-6, MMP-1 and MMP-3 by FLS of different diseases sources, suggesting that must be another cell type that plays the role of target to IL-33 in physiopathology of joint inflammation. The absence MMP-3 in response to TNF-α stimulus in RAFLS and OAFLS could be explain by saturation of this cytokine in synovial cells from these diseases.

References:

Acknowledgements: Capes, Fapemig and Fundo de Apoio a Pesquisa e Ensino da Sociedade Brasileira de Reumatologia - FAPE-SBR.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6673
ANTI INFLAMMATORY EFFECT OF PDE5 INHIBITION: SCOPE FOR A NEW POTENTIAL INDICATION IN SSC ASSOCIATED MYOSITIS

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Background: Skeletal muscle damage can occur as clinical manifestation of Systemic Sclerosis (SSc) [1], and it is known to be associated to type I IFN pathway activation [2]. The type I IFN-induced chemokine CXCL10 is associated with the severe SSc prognosis and skeletal muscle disease [3,4], and it has been reported to play a role in inflammatory myopathy (IM) and in diabetic cardiomyopathy (DCM) [5,6]. In DCM the phosphorysederase type 5 inhibitor (PDE5i) sildenafil significantly decreased CXCL10 systemic and cellular release [7]. In SSc, sildenafil is used to treat pulmonary artery hypertension (PAH) and digital ulcer diseases.

Objectives: To determine the serum levels of CXCL10 in SSc patients with or without muscle involvement and treated or not with sildenafil. To determine the role of sildenafil on IFNγ+TNFα-induced CXCL10 release in human skeletal muscle (Hfsmc).

Methods: Sera from 109 patients fulfilling ACR/EULAR 2013 classification criteria for SSc and 34 age and gender matched healthy controls (HC) were analysed by multiplexed, bead-based immunoassay. Hfsmc were cultured and analysed as previously described [5].

Results: CXCL10 serum level was significantly higher in SSC vs. HC (602 ±155.1 pg/ml vs. 197.5±14.9 pg/ml, P <0.001) independently of diffuse or limited clinical subset (p <0.05); the presence of sildenafil in therapeutic regimen was associated with lower serum CXCL10 (455.2±211.8 pg/ml vs. 633.±183.02 pg/ml, P <0.05). CXCL10 was significantly higher in patients with increased Creatine Kinase (CK) (r=0.52, p=0.017) and Protein Kinase C (r=0.445, P <0.001) and its concentration strongly correlate with the levels of CK (r=0.986, P <0.001) and with Medsger Muscle severity score (r=0.445, P <0.001). In vitro, sildenafil suppressed IFNγ+TNFα-induced CXCL10 release by Hfsmc in a dose dependent manner, down to 50% secretion at 10 μM (P <0.05). The inhibition of CXCL10 secretion was associated with significant reduction in cytokine-induced STAT1, NFkB and JNK phosphorylation (P <0.01).

Conclusions: High CXCL10 level is associated with SSc independently from local or diffuse clinical subset and is lower in patients assuming sildenafil independently of other therapies. The strong correlation of CXCL10 and severity of muscle damage as assessed by serum CK and Medsger Muscle severity score, strongly indicate/confirm the involvement of IFN-1 pathway activation during myositis in SSc. The direct inhibitory effect of PDE5 inhibitor Sildenafil on proinflammatory induced CXCL10 secretion warrant further research on the potential role of PDE5 inhibitors as disease modifying agents in SSc.

References:
[5] Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6233

THE EFFECT OF SILDENAFIL AND ILOPROST ON CXCL10 LEVEL IN SYSTEMIC SCLEROSIS: IN VIVO AND IN VITRO COMPARISON

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Background: Th1 cell/cytokine repertoire contributes to systemic sclerosis (SSc) pathogenesis from early autoimmune/vascular stages while Th2 dominance pathogenesis from early autoimmune/vascular stages while Th2 dominance indicates/confirm the involvement of IFN-I pathway activation during myositis in SSc. The direct inhibitory effect of PDE5 inhibitor Sildenafil on proinflammatory induced CXCL10 secretion warrant further research on the potential role of PDE5 inhibitors as disease modifying agents in SSc.

Objectives: To determine the serum levels of CXCL10 in SSc patients with or without muscle involvement and treated or not with sildenafil. To determine the role of sildenafil on IFNγ+TNFα-induced CXCL10 release in human skeletal muscle (Hfsmc).

Methods: Sera from 109 patients fulfilling ACR/EULAR 2013 classification criteria for SSc and 34 age and gender matched healthy controls (HC) were analysed by multiplexed, bead-based immunoassay. Hfsmc were cultured and analysed as previously described [5].

Results: CXCL10 serum level was significantly higher in SSC vs. HC (602 ±155.1 pg/ml vs. 197.5±14.9 pg/ml, P <0.001) independently of diffuse or limited clinical subset (p <0.05); the presence of sildenafil in therapeutic regimen was associated with lower serum CXCL10 (455.2±211.8 pg/ml vs. 633.±183.02 pg/ml, P <0.05). CXCL10 was significantly higher in patients with increased Creatine Kinase (CK) (r=0.52, p=0.017) and Protein Kinase C (r=0.445, P <0.001) and its concentration strongly correlate with the levels of CK (r=0.986, P <0.001) and with Medsger Muscle severity score (r=0.445, P <0.001). In vitro, sildenafil suppressed IFNγ+TNFα-induced CXCL10 release by Hfsmc in a dose dependent manner, down to 50% secretion at 10 μM (P <0.05). The inhibition of CXCL10 secretion was associated with significant reduction in cytokine-induced STAT1, NFkB and JNK phosphorylation (P <0.01).

Conclusions: High CXCL10 level is associated with SSc independently from local or diffuse clinical subset and is lower in patients assuming sildenafil independently of other therapies. The strong correlation of CXCL10 and severity of muscle damage as assessed by serum CK and Medsger Muscle severity score, strongly indicate/confirm the involvement of IFN-1 pathway activation during myositis in SSc. The direct inhibitory effect of PDE5 inhibitor Sildenafil on proinflammatory induced CXCL10 secretion warrant further research on the potential role of PDE5 inhibitors as disease modifying agents in SSc.

References:
[5] Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6233

IL37 INHIBITS GAG RELEASE FROM HUMAN OA CARTILAGE EXPLANTS

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Background: In healthy cartilage, there is a balance between anabolic and catabolic activities of chondrocytes that maintains the functional integrity of the extracellular matrix. However, during osteoarthritis (OA), chondrocytes become more catabolically active and express increased levels of matrix degrading enzymes, such as MMPs and ADAMTSS. Increased MMP and ADAMTS activity results in a net loss of the extracellular matrix and therefore leads to cartilage damage. Previously, we found that the anti-inflammatory cytokine Interleukin 37 (IL37) is able to counter-regulate the catabolic status of chondrocytes by reducing the IL1α-driven expression of pro-inflammatory cytokines and catabolic enzymes.

Objectives: The goal of this study was to investigate, in human OA cartilage explants, the effect of IL37 on the release of matrix degrading enzymes and on the synthesis of extracellular matrix molecules and cartilage degrading enzymes to investigate its therapeutic potential in OA.

Methods: Human cartilage was obtained from eighteen OA patients undergoing total knee or hip arthroplasty. Bopsy punches of 4 mm in diameter were made to equalize sample size. After culturing overnight, explants were incubated for 48 h with three doses (1, 10 or 100 ng/ml) of recombinant-human IL37 (rIL37). In the supernatant of the explant cultures, GAG release was measured with the DMB assay and levels of the ARGS neoepitope, which is one of the products of aggrecan degradation by ADAMTS5, were detected using Western Blot. Furthermore, gene and protein expression of extracellular matrix molecules and cartilage degrading enzymes were measured. Nitric oxide (NO), an important effector molecule that may suppress cartilage matrix synthesis, levels were measured in the supernatant using Griess reagents.

Results: Adding rIL37 (100 ng/ml) to OA cartilage explants caused a highly significant reduction in GAG release to the supernatant of, on average, 32% in eighteen donors (Figure 1). Gene expression of the matrix molecules aggrecan and collagen type II was not affected, indicating that this effect of rIL37 was not due to a loss of aggrecan synthesis. Another mechanism to prevent GAG release in cartilage is via inhibition of NO synthesis, but NO levels in the supernatant were comparable between rIL37 treated groups and the control group. In contrast, after addition of rIL37, ARGS neopeptide levels, which reflect ADAMTS activity, did not change, therefore indicating that the inhibition of GAG release by rIL37 in cartilage is via inhibition of NO synthesis, but not inhibition of aggrecan degradation. Further, protein analysis of the explants showed that rIL37 reduced ADAMTS 5 levels. These data indicate that IL37 interferes with the matrix active degradation enzymes in the cartilage matrix. However, gene expression of ADAMTS 5 was not affected by rIL37, indicating that the effect of IL37 on ADAMTS 5 is post translational.

Conclusions: rIL37 reduces GAG release by OA cartilage explants. The mechanism behind this protective effect of IL37 probably runs via a reduction in ADAMTS 5 abundance in the cartilage matrix, which is the main aggrecanase involved in OA. This effect of rIL37 on ADAMTS 5 is probably post translational. Our data indicate that IL37 can maintain cartilage matrix integrity.
UPREGULATION OF CD64 EXPRESSION ON MONOCYTES IN PATIENTS WITH ACTIVE ADULT-ONSET STILL’S DISEASE: A POSSIBLE BIOMARKER FOR ASSESSING DISEASE ACTIVITY
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Background: Adult-onset Still’s disease (AOSD) is a systemic inflammatory disease of unknown etiology. Overproduction of multiple inflammatory cytokines and subsequent hyperactivation of monocytes/macrophages are prominent characteristics of AOSD. However, there are no convenient and precise methods for evaluating monocyte/macrophage activation in AOSD. We previously reported that monocyte CD64 (mCD64) expression could be quantitatively measured by flow cytometry and its expression was tightly correlated with the activity of systemic lupus erythematosus.

Objectives: We examined the association between mCD64 expression and AOSD disease activity.

Methods: This was a prospective, single-center, observational study conducted between January 2013 and December 2016. Eleven active AOSD patients who fulfilled the Yamaguchi criteria for AOSD and had the modified Pouchot score of ≥2 were enrolled. The mCD64 expression levels were quantitatively measured by flow cytometry and individually assessed both before (Pouchot score ≥2) and after treatment (score <2). Other disease-related laboratory data, such as C-reactive protein, ferritin, and white blood cell count, were simultaneously measured. As a control, 16 active systemic lupus erythematosus (SLE) patients (SLE disease activity index ≥6), 22 active rheumatoid arthritis (RA) patients (disease activity score 28 with 28-joint counts >10) and 10 healthy individuals (both Biolegend), NK cells (CD15-CD16+), neutrophils (CD15+CD16+), monocytes (CD33+CD14+CD16+-/+), mast cells (CD117+FcER1α+) and eosinophils (CD15+FcER1α+) were used. Different lymphoid and myeloid cell types were IL-17A positive in PsA blood of first diagnosed PsA patients such as CD3+, TCR αβ+, γδ T cells, NK cells, neutrophils, eosinophils, mast cells, and monocytes in PsA blood and on neutrophils, monocytes, mast cells and eosinophils in PsA SF.

Conclusions: These preliminary data show that not only lymphoid cells but also specific myeloid cell types may be sources of IL-17A in PsA. Furthermore, not lymphoid cells but IL-17A/IL-17RC positive myeloid cells such as monocytes, neutrophils, eosinophils and mast cells may be potential IL-17A producers in PsA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5916

PARAMETERS OF TOTAL BLOOD COUNT; MIGHT THEY BE INDICATORS OF INFLAMMATION IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS?
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Background: Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are launched as recent markers of inflammation in chronic inflammatory diseases. However, it is not clear which cell types in PsA patients are responsible for the production of IL-17A. In addition, the expression of IL-17RA and IL-17RC on different cell types is not well defined.

Objectives: To identify IL-17A, IL-17RA and IL-17RC positive cells in blood of first diagnosed PsA patients with arthritis and in synovial fluid of established PsA patients with active disease.

Methods: Fresh blood was taken from first diagnosed DMARD and steroid naïve PsA patients (n=10), having arthritis in 1 or more joints (PsA blood). The diagnosis was made by a rheumatologist according to the CASPAR-criteria. In addition, fresh synovial fluid was obtained from established PsA patients (PsA SF) with arthritis in 1 or more joints (n=3) or NSAIDs (n=4). Multicolor flow cytometric analysis was performed on PsA blood and PsA SF. For the detection of IL-17A, IL-17RA or IL-17RC the following antibodies were used: IL-17A-PE (eBioscience), IL-17RA or isotype control IgG1k (both Boleigen), IL-17RC or isotype control IgG2b (both R&D systems). The following markers were used to discriminate between different cell populations: T cell subsets (CD3, CD4, CD8, CD45RO, CCR6, TCRγδ), B cells (CD19), NK cells (CD15-CD16+), neutrophils (CD15+CD16+), monocytes (CD33+CD14+CD16-/+), mast cells (CD117+FcER1α+) and eosinophils (CD15+FcER1α+). Different lymphoid and myeloid cell types were IL-17A positive in PsA blood of first diagnosed PsA patients such as CD3+, TCRγδ+, CD4+, CD8+ lymphoid cells, CD14+ monocytes and eosinophils. In PsA SF of established PsA patients TCRγδ+ T cells, neutrophils, NK cells and eosinophils were IL-17A positive.

Conclusions: These preliminary data show that not only lymphoid cells but also specific myeloid cell types may be sources of IL-17A in PsA. Furthermore, not lymphoid cells but IL-17A/IL-17RC positive myeloid cells such as monocytes, neutrophils, eosinophils, mast cells and mast cells may be potential IL-17A producers in PsA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5916

THE IDENTIFICATION OF IL-17A+ - IL-17RA+ AND IL-17RC+ LYMPHOID AND MYELOID CELLS IN BLOOD OF TREATMENT NAÏVE EARLY AND IN SYNOVIAL FLUID OF ESTABLISHED PSORIATIC ARTHRITIS PATIENTS
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Background: Interleukin (IL)-17A is a pro-inflammatory cytokine and is involved in the pathogenesis of psoriatic arthritis (PsA) (1,2). Various cells can produce IL-17A. However, it is not clear which cell types in PsA patients are responsible for the production of IL-17A. In addition, the expression of IL-17RA and IL-17RC on different cell types is not well defined.

Objectives: To identify IL-17A, IL-17RA and IL-17RC positive cells in blood of first diagnosed PsA patients with arthritis and in synovial fluid of established PsA patients with active disease.

Methods: Fresh blood was taken from first diagnosed DMARD and steroid naïve PsA patients (n=10), having arthritis in 1 or more joints (PsA blood). The diagnosis was made by a rheumatologist according to the CASPAR-criteria. In addition, fresh synovial fluid was obtained from established PsA patients (PsA SF) with arthritis in 1 or more joints (n=3) or NSAIDs (n=4). Multicolor flow cytometric analysis was performed on PsA blood and PsA SF.

Conclusions: Hemoglobin levels of RA patients were significantly (p<0.05) lower than the levels of control group (p>0.05). ESR, CRP, NLR and PLR values were significantly higher in patients with active AOSD than in those with active SLE [34,648 (IQR, 10-6), 22 active rheumatoid arthritis (RA) patients (disease activity score 28 with 28-joint counts >10) and 10 healthy individuals]. Together, these data suggest a more broad, but specific IL-17A-IL-17RA/RC signaling network between different cell types important in the IL-17A-driven pathogenesis of PsA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3337

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3689
and CRP scores (p=0.005, p=0.003) were significantly lower respectively. No statistical significance was found in terms of NLR and PLR (p>0.05). Significant positive correlation was found in RA patients with high disease activity between ESR, CRP, NLR and PLR. In AS patients with high disease activity significant positive correlation was found between ESR, CRP, NLR and PLR. No correlation was found between indices, NLR and PLR.

Conclusions: With the advantage of cost effectiveness and easy calculation NLR and PLR in RA patients, and NLR in AS patients might be used as indicators of inflammation together with ESR and CRP or instances when they are not applicable. Although NLR and PLR are useful in the discrimination of healthy and diseased subjects, they are not sufficient to determine disease activity because not only laboratory parameters but clinical findings and self assessment of the patient are also included in activity measurement.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4800

AB0035 ANGIOPOIETINS: THE MISSING LINK IN POEMS SYNDROME?

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Background: The overproduction of VEGF and angiopoietin-1, which plays an essential role in the stabilization and the maturation of blood vessels, and angiopoietin-2 that facilitates angiogenesis in the presence of VEGF.

Methods: Circulating levels of VEGF, Angiopoietin-1 and angiopoietin-2 were determined by ELISA in the serum of 3 patients with POEMS syndrome, before and after therapy. All patients had polyclonar gammopathy, and monoclonal gammopathy (2 IgG1, 1 IgGk) and osteosclerotic lesions. Two patients had typical skin lesions, oedema and one patient had a Castleman disease.

Results: As expected, the serum of patients before treatment exhibited high levels of VEGF (2901±920 pg/mL). Strikingly, angiopoietin-1 levels were highly abundant before treatment (6728±20395 pg/mL) and successful treatment led to a strong reduction in both VEGF and angiopoietin-1. Angiopoietin-1 levels strongly correlated with levels of VEGF (p=0.83). By contrast, angiopoietin-2 levels did not alter significantly before and after treatment.

Conclusions: Thus, angiopoietin-1 seems to be a crucial proangiogenic cytokine overproduced in patients with POEMS syndrome that might explain some of the features of the pathology. The overproduction of VEGF and angiopoietin-1 is likely to promote manifestations encountered in POEMS syndrome such as organomegalgy, osteosclerotic lesions or glomeruloid hemangioma. Restoring the balance between angiopoietin-1, angiopoietin-2 and VEGF could constitute a very promising therapeutic strategy in this disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3697

AB0036 ASSOCIATION BETWEEN SYNOVITIS AND INFLAMMATORY CYTOKINE SERUM LEVELS IN ANKLE KNEE JOINTS: AFFECTED BY PRIMARY KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is characterized by progressive loss of cartilage, deterioration of subchondral bone and mild synovial inflammation. Classified for a long time as a non-inflammatory arthropathy, a growing number of evidences has suggested that OA course could be driven by systemic and localized inflammation. In particular, serum levels of Interleukin (IL)-6 have been associated with higher prevalence of osteophytes in older adults with knee OA. Furthermore, high levels of other inflammatory cytokines have been identified in serum and synovial fluid of OA patients.

Objectives: In the present cross-sectional study, we aimed at analyzing the correlation between articular inflammatory state, reflected by ultrasonographically-detected synovitis, and the serum levels of 27 cytokines, chemokines and growth factors in a cohort of primary knee OA.

Methods: 50 consecutively enrolled 47 patients (M/F 16/31, mean age ±SD 53.8±7.8 years, mean onset interval ±SD 70.0±78.6 months) affected by knee OA according to clinical and radiographic ACR criteria. Patients were excluded if they had received non-steroidal anti-inflammatory drugs or other analgesics within 7 days before enrollment. Pain was assessed with a 100-mm visual analog scale (VAS), and the Lequesne algo-functional index was used to measure the OA severity. BMI was registered. Each patient underwent ultrasonographic (US) assessment of both knees performed by a single operator. According to OMERACT definitions, we assessed the presence of synovial effusion, synovial hypertrophy and power Doppler. These elementary lesions were scored according to a semi-quantitative scale (0 = absent, 1 = mild, 2 = moderate and 3 = severe), the sum of them allows obtaining a total score of the patient’s inflammatory state (0-18).

Results: Blood samples for laboratory assays were obtained and commercially available multiplex bead based immunoassay kits (Human 27-bios, Bio-Rad laboratories, Hercules, CA) were used. Twenty-five serum cytokines (APRIL/TNFSF13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IL-1α, IL-1β, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, IL-17F-Basic, G-CSF, GM-CSF, interferon-γ, IP-10, MCP-1, MIP-1α, MIP-1β, PDGF, RANTES, TNF, VEGF).

Conclusions: The results of the study enactment, OA patients showed a mean±SD US synovitis score of 4.4±2.7, a mean±SD VAS pain rating of 35.3±16.6 mm (range 18–90 mm), a mean±SD Lequesne index of 10.2±4.2 (range 1.5–19), a mean±SD BMI of 26.8±4.2 (range 20–34.7). Positive correlations among US synovitis score and serum levels of IL-6 (r=0.3, p<0.01), IL-8 (r=0.3, p<0.01), IL-12 (r=0.2, p=0.04), VEGF (r=0.3, p=0.01), MCP-1b (r=0.3, p=0.01), VEGF (r=0.3, p=0.04) and BMI (r=0.4, p=0.04).

Conclusions: The results of the present study confirmed that OA may be associated with systemic inflammatory changes, as demonstrated by the positive correlation between US synovitis and several inflammatory cytokines serum levels.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5289

AB0037 SERUM CYTOKINE SIGNATURE IN MUCOCUTANEOUS AND OCULAR BEHÇET’S DISEASE

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Background: Behcet’s disease (BD) is a multi-systemic inflammatory disorder characterized by recurrent oral and genital ulcers, ocular involvement, chronic constitutional bilateral uveitis. However, many other organs including the vascular, gastrointestinal, neurological, and musculoskeletal systems can be affected. Pathogenetically, both innate and adaptive immunity have shown to play a pivotal role, and several proinflammatory cytokines derived from Th1 and Th17 lymphocytes seem to be involved in different pathogenic pathways leading to development of the clinical manifestations.

Objectives: The primary aim of our study was to compare a core set of proinflammatory cytokines between patients with BD and healthy control (HC). The secondary aim was to determine correlations between these putative circulating biomarkers, the status of disease activity, and the specific organ involvement at the time of sample collection.

Methods: Fifty-four serum samples were collected from 46 BD patients (17 males, 29 females, mean age 45.5±11.3 years), and 19 HC (10 males, 9 females, mean age 43±8.3 years). Twenty-five serum cytokines (APRIL/TNFSF13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IL-1α, IL-1β, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, IL-17F-Basic, G-CSF, GM-CSF, interferon-γ, IP-10, MCP-1, MIP-1a, MIP-1β, PDGF, RANTES, TNF, VEGF).

Results: Levels of Chitinase3-like1, gp130/sIL-6Rb, IL-1α, IL-1β, IL-2, IL-6, IL-17 (p<0.05), IL-10 (p<0.01), IFN-γ (p<0.001), TNF-α (p<0.001), sTNF-R1 (p<0.001) resulted higher in BD patients than in HC. No differences were observed between active- and inactive-BD group. In addition, comparing cytokines levels in patients affected by mucocutaneous manifestations with (MO-BD) or without (M-BD) ocular
increased interferon-alpha production by plasmacytoid dendritic cells stimulated with a TLR-7 agonist in systemic lupus erythematosus

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Background: Type I interferon (IFN) appears to contribute to the development of systemic lupus erythematosus (SLE). IFN-\(\alpha\) production is known to be increased in peripheral blood mononuclear cells (PBMCs) from SLE patients. Although plasmacytoid dendritic cells (pDCs) is a major source of IFN-\(\alpha\), recent studies reported that IFN-\(\alpha\) production by pDCs stimulated with a TLR-7 agonist was decreased in SLE compared to healthy controls (HC).

Objectives: We set out to investigate an endosomal TLR-signaling pathway in SLE by using TLR-7 agonist stimulation.

Methods: Blood samples were obtained from 55 HC and 73 SLE patients, diagnosed according to the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus (2012). PBMC from SLE patients and HC were stimulated with a TLR-7 agonist, CpG-A oligodeoxynucleotides (CpG-A ODN)-2216, and a TLR-9 agonist, imiquimod. The proportion of pDCs producing IFN-\(\alpha\) was investigated by intracellular cytokine staining and flow cytometry. PBMC were pretreated with IFN-\(\alpha\) for 24 hours, and then IFN-\(\alpha\) production by pDCs was assessed after stimulated with CpG-A.

Results: As previously reported, the level of IFN-\(\alpha\) production by pDCs stimulated with CpG-A CDN was reduced in SLE compared with HC. However, the proportion of IFN-\(\alpha\) production by pDCs stimulated with imiquimod was significantly increased in SLE patients. The percentage of IFN-\(\alpha\) producing pDCs stimulated with imiquimod was positively correlated with SLE disease activity index (SLEDAI) score, and that of pDCs stimulated with CpG-A ODN was negatively correlated with SLEDAI.

Conclusions: IFN-\(\alpha\) production by pDCs from SLE patients was increased when stimulated with a TLR-7 agonist, and this was accompanied with upregulated TLR7 expression in these cells. In murine lupus-models, TLR7-deletion has been shown to reduce autoimmune disease. The enhanced TLR7-signaling pathway in pDC may play an important role in lupus pathology.

References:

AB0038 REDUCTION OF TH17+ LYMPHO CYTES IN PART OF SAPHO PATIENTS ON TREATMENT WITH SECUKINUMAB

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Background: The SAPHO syndrome has to be considered as a rare subtype of the disease entity of the seronegative spondylarthropathy. The characteristic defining symptoms are synovitis, acne, pustulosis, hyperostosis, and osteitis with ostetiit.

Objectives: To evaluate the count of Th17+ lymphocytes in patients with SAPHO syndrome and psoriatic arthritis before and under treatment with secukinumab.

Methods: Peripheral blood was derived from 4 patients with SAPHO syndrome and 4 patients with psoriatic arthritis, respectively before and under 12 week treatment with secukinumab 200mg (dosage: 4 times weekly, then monthly). All patients received at least one conventional DMARDs and one TNF blocking agent in their medical history. All patients showed active disease with elevated scores of DAS28 and/or HAQ. The patients activity scores of ostetiit (from 0 to 6) and PPP (0–6) were estimated by physician. The blood specimen were separated in EDTA containing tubes to separate lymphocytes, which were analyzed using FACScan-cytometry.

Results: The Th17+ lymphocytes were detectable in 4 patients with psoriatic arthritis and 2 of 4 SAPHO patients before and under 12 week treatment with secukinumab. In 2 of 4 SAPHO patients the fractions of Th17+ lymphocytes were prominent prior to secukinumab application; after treatment duration of 12 weeks one of both developed a depletion of Th17+ cells (figure), the other SAPHO patient a Th17+ cell reduction. Only the two SAPHO patients with diminishing Th17+ lymphocytes have developed treatment response evaluated by reduction of HAQ score (from 1.75 to 1.25), ostetiit score (4.5 to 3.0), and PPP score (5.0 to 4.0). Three of 4 psoriatic arthritis patients showed reduced diseases activity under treatment with secukinumab (DAS28 score from 4.22 to 3.45, HAQ 2.25 to 1.5).

Conclusions: The measurement of Th17+ lymphocytes in the peripheral blood of SAPHO patients could be suggested for further evaluation as possible predictor of treatment response by secukinumab.

References:
[1] Firini D, et al. (Ref.) has previously published data of higher Th17+ lymphocytes in the peripheral blood in SAPHO patients compared with psoriatic arthritis patients or healthy controls. Activation of the Th17 pathway leads to pro-inflammatory effects mediated by interleukin 17 with stimulation of osteobe last, macrophages, and neutrophils with the consequences of secretion pro-inflammatory cytokines such as interleukin 6 and 1, TNF alpha, and MMPs. The interleukin 17 blocking agent secukinumab has been introduced in the armamentarium of antirheumatic drugs against seronegative spondylarthritids including psoriatic arthritis.
AB0040

IMMUNE MODULATORY EFFECTS OF MESENCHYMAL STEM CELL TO MONONUCLEAR CELLS FROM PATIENTS WITH ACTIVE ADULT ONSET STILL’S DISEASE

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Background: Adult onset Still’s disease (AOSD) is an inflammatory disorder of unknown etiology, which is accompanied by increased levels of serum pro-inflammatory cytokine. Mesenchymal stem cells (MSCs) have immunomodulatory capacities and might be a promising therapeutic option in the treatment of refractory autoimmune diseases. Both cell-to-cell contact and the release of soluble factors mediate immune modulatory functions of MSCs.

Objectives: We aimed to determine if MSCs could modulate serum cytokine level in patients with active untreated AOSD, either through paracrine secretion or via direct interaction with the MSCs.

Methods: Human peripheral blood mononuclear cells (PBMCs) from 6 patients with active AOSD were co-cultured for 72 hours with human MSCs (hMSCs at a ratio of 1:10) in each culture. We compared the cytokine levels before and after direct or indirect (transwell cultures) exposure to activated mononuclear cells (LPS, 10ng/ml) or T-cell inducing conditions (anti-CD3 [5 μg/ml], anti-CD28 [5 μg/ml]) recombinant human IL-2 (5 ng/ml). Cytokine levels were detected by multiplex cytokine detection kit by flow cytometry, or ELISA with culture supernatant. In vitro platform for studying the effects of MSCs on individual cytokines, the Wilcoxon signed-rank test was employed for comparison of serum cytokine levels.

Results: Treatment of MSCs with hMSCs resulted in a significant reduction of mean TNF-α level (mean 463.4 pg/ml vs 137.8 pg/ml, p < 0.05) and IL-1β (mean 1887.1 pg/ml vs 1127.9 pg/ml, p < 0.05). When the hMSCs were present during the T-cell differentiation, there was a significant decrease in the mean secreted TNF-α (mean 10953.5 pg/ml vs 454.9 pg/ml, p < 0.05) IFN-γ (mean 14301.0 pg/ml vs 5094.9 pg/ml, p < 0.05) and IL-2 receptor (mean 3550.8 pg/ml vs 2506.4 pg/ml, p < 0.05). On the contrary, level of TGF-β was significantly increased (mean 4088.8 pg/ml vs 5104.8 pg/ml, p < 0.05). But, there was a significant increase in the amount of IL-6 (mean 2215.5 pg/ml vs 25130.6 pg/ml, p < 0.05) and IL-17 (mean 1327.0 pg/ml vs 2453.6 pg/ml, p < 0.05). Two chamber experiments also showed similar pattern of cytokine modulation.

Conclusions: This preliminary experiment demonstrated that MSCs can modulate cytokine profiles of AOSD mononuclear cells by decreasing pro-inflammatory cytokines, and increasing anti-inflammatory cytokine such as TGF-β. However, up-regulation of IL-6 and IL-17 might be a hurdle to overcome in the clinical application of MSCs in AOSD patients.

References:


Acknowledgements: none.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5719

AB0041

LARGE VESSEL VASCULITIS INDUCED BY CANDIDA ALBICAN WATER-SOLUBLE-FRACTION (CAWS) IN THE C57BL/6J MOUSE MODEL IS ASSOCIATED WITH OVEREXPRESSION OF IL-6, TNF-α, AND IL-10 WITH MODEST CHANGE IN SOCS-1

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Background: We have previously demonstrated that mast cell degranulation acutely downregulates lipopolysaccharide induced aerobic expression and serum levels of IL-6 in vivo. This is accompanied by aortic upregulation of suppressor of cytokine signaling-1 (SOCS-1) gene expression. This effect is not seen in histamine H1 receptor-knockout mice suggesting that mast cell-derived histamine is a key mediator involved in IL-6 homeostasis. Mice injected with Candida albican water-soluble-fraction (CAWS) have been shown to develop coronary and aortic vasculitis. Our long-term objective is to determine the pathogenic mechanisms of large vessel vasculitis (LVV).

Objectives: The aim of this pilot study was to replicate and develop a working mouse model to determine the regulatory role of mast cells in LVV.

Methods: Eight to ten weeks-old male C57Bl/6J mice were randomly distributed into two groups [CAWS, N=8; and Control, N=8] and were injected i.p. daily for 5 days with either CAWS in normal saline (2 mg/day/mouse) or normal saline alone (controls). All mice were sacrificed 30 days after the 5th injection. We examined serum levels of IL-6 and TNF-α, as well as aortic tissue expressions of IL-6, TNF-α, IL-10 and SOCS-1 mRNA. Heart and aortic sections were evaluated for inflammation and mast cells after staining with H & E and toluidine blue, respectively.

Results: Treatment of mice with CAWS for 5-consecutive days led to overexpression of IL-6, TNF-α and IL-10 genes in the aortic tissue with modest upregulation of SOCS-1. At the root of the aorta, all animals in the CAWS group had intense inflammatory infiltrates composed of mixed acute and chronic inflammatory cells. There is also evidence of vasculitis in the coronary arteries. In contrast, none of the control mice had any evidence of aortic inflammation or vasculitis. Serum IL-6 concentrations were below detectable levels in both controls and CAWS-treated mice whereas TNF-α levels were elevated in 3 out of 8 mice in the CAWS group. There were no signs or increased presence of intact or degranulating mast cells in the area of inflammation.

Conclusions: These results suggest that CAWS-induced LVV involves acute and chronic inflammatory response and vascular tissue expression of both pro- and anti-inflammatory cytokines and SOCS-1. Detailed kinetic studies are warranted to determine the optimum windows of peak inflammatory response and the expression of these genes to understand the pathobiology of CAWS-induced LVV.

References:


Acknowledgements: Supported by Basic Science Development Award from Department of Medicine at the University of Kansas.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.4884

AB0042

HIGH EXPRESSION OF S100 CALGRANULIN GENES IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TA) is inflammatory disorder that affects aorta and its branches. Toll-like receptors (TLR) 1 to 4 are highly expressed in aorta (1). Activation of TLR4 causes transmural arteritis in human temporal artery-SCID chimera model (2). Ligand responsible for TLR4 activation is not known in TA.

Objectives: Aim of the study is to examine the expression of TLR4 and its endogenous ligands in peripheral blood mononuclear cells (PBMCs) of patient with TA.

Methods: RNA from PBMCs of 24 TA patients and 19 sex and age matched healthy controls were extracted. The mRNA expression of various endogenous TLR4 ligands, TLR4, RAGE, interleukin-6 (IL-6) and IL-8 were quantified in real time PCR using specific primers and SYBR Green qPCR master mix. Serum S100A9A8 and S100A12 level were measured using commercial ELISA kits. S100A8A9 and S100A12 were measured in cell culture supernatant of un-stimulated and lipopolysaccharides (LPS) stimulated PBMCs, cultured for 4 hours. t-test was used to compare between the groups. P < 0.05 was considered as statistically significant.

Results: The mRNA of S100A8, S100A9, S100A12 and TLR4 were highly expressed in TA as compared to healthy controls, while RAGE, HSP70 and IL-6 had lower expression in TA. No difference in serum levels of S100A8A9 and S100A12 was noted between TA and healthy controls. LPS induced high secretion of both S100A8A9 and S100A12 levels in both TA and healthy controls (Figure-1). However, the stimulatory response in healthy controls [2.86 (1.7–3.53) fold] was significantly higher as compared to TA [1.345 (1.1–1.82) fold; p < 0.05] as measured by delta S100A12 (LPS/unstimulated control). Numerically delta S100A9A8 was also higher in healthy controls [2.04 (1.7–5.6) fold] as compared to TA [1.38 (1.09–3.6) fold; p<0.129].

Acknowledgements: Supported by Basic Science Development Award from Department of Medicine at the University of Kansas.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2610

Scientific Abstracts
Conclusions: mRNA expression of S100A8, S100A9, S100A12 and TLR4 in PBMCs of TA patients were higher as compared to healthy controls. Despite this, S100A12 secretion was lower in TA as compared to healthy controls upon LPS challenge.

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Background: Toll-like receptor 4 (TLR4) is a pattern recognition receptor involved in the initiation of inflammatory responses to control pathogen infections, but its role in rheumatic diseases is becoming evident, as well as its potential role as a therapeutic option.

Objectives: The aim of this study was to evaluate the effect, both on articular histophatology and pain behaviour, of a TLR4 antagonist (TLR4-A1) on an experimental model of OA. The effect of the TLR4-A1 on the activating transcription factor-3 (ATF-3) signalling pathway was also assessed.

Methods: OA was induced in adult Wistar rats through an intra-articular injection of 2mg of sodium mono-iodeacetate (MIA) into the left knee. Control animals received a similar injection with saline. TLR4-A1 (10 mg/kg), synthesized by Dr. Quesada from a compound previously described 3. Although the principal TAC action is thought to be the recognition host-derived endogenous molecules called damage-associated molecular patterns (DAMPs). The role of TLR4 in rheumatic diseases is becoming evident, as well as its potential role as a therapeutic option.

Results: TLR4-A1 significantly reduced the nociceptive behavior of OA animals both in the Knee-Bend and Catwalk tests, before and after TLR4-A1 or vehicle administration, at several time-points. Animals were sacrificed 28 days after OA induction. L3-L5 Dorsal Root Ganglia (DRG) were used for immunohistochemistry for TLR4 and ATF-3, signal cords were immunoreacted for TLR4 and knee joints were processed for histopathological evaluation.

Objectives: Methods: A novel TAC structure (SAF2012–40075-C02–02) was intraperitoneally administered, daily, from days 14 to 28 after OA induction. At several time-points, animals were sacrificed 28 days after OA induction. L3-L5 Dorsal Root Ganglia (DRG) were used for immunohistochemistry for TLR4 and ATF-3, signal cords were immunoreacted for TLR4 and knee joints were processed for histopathological evaluation.

Results: Antagonism by TLR4-A1 significantly reduced the nociceptive behavior of OA animals both in the Knee-Bend and Catwalk tests. The effect was immediately observed 1 day after TLR4-A1 administration, but became more evident 4 days later, maintaining thereafter. No improvement in the cartilage histology was observed. The increased ATF-3 expression observed in DRG of OA animals was significantly reduced by TLR4-A1. On the contrary, TLR4 expression slightly increased after antagonist administration both at DRG and superficial dorsal horn levels.

Conclusions: Chronic treatment with TLR4-A1 showed an antinociceptive effect on OA animals, not related to articular histopathological improvement, possibly through an ATF-3 dependent mechanism.

References:

Acknowledgements: This research was supported by Grand-in-Aid for Scientific Research (C) (26462309) and 16K10913 from the Japan Society for the Promotion of Science.


DOI: 10.1136/annrheumdis-2017-eular.2878

AB0045 IL-17 INDUCED GLUCOCORTICOID INSENSITIVITY MIGHT BE DEPENDENT ON THE REDUCED 11β-HSD1 ENZYME ACTIVITY

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Background: It has been demonstrated that IL-17A is able to induce GC insensitivity. Although several studies have reported the role of IL-17 in GC insensitivity the mechanism underlying remains still largely unclear.

Objectives: To understand the effects of interleukin-17 (IL-17) on the enzyme 11β-hydroxysteroid dehydrogenases (11β-HSDs) in the two main classes of monocytes, CD14 and CD16.

Methods: Peripheral Blood Mononuclear Cells (PBMCs) were isolated from healthy donors and were sorted into CD14 and CD16 subpopulations using cell sorting. Effect of IL-17 on 11β-HSD1 enzyme activity was measured in terms of conversion of cortisone to cortisol in sorted and unsorted monocytes using Homogeneous Time-Resolved Fluorescence (HTRF). The direct involvement of 11β-HSD1 in the conversion of cortisone to cortisol was confirmed using carbonoxylene, an inhibitor of 11β-HSD1.

Results: Monocytes showed a concentration-dependent decrease in the 11β-HSD1 enzyme activity when incubated with increasing concentrations of IL-17. CD14 and CD16 cells stimulated similarly with IL-17 showed a significant
difference in the enzyme activity between the untreated and stimulated cells in all treatment groups. However, a dose dependent decrease was observed only in case of CD14 cells. Both unsorted monocytes and monocyte sub-populations showed a significant decrease in the concentration of cortisol measured when co-incubated with carbenoxolone, indicative of the direct involvement of 11β-HSD1 enzyme in the conversion of cortisone to cortisol.

Conclusions: The results of this study showed that IL-17 induced GC insensitivity might be dependent on the reduced 11β-HSD1 enzyme activity in inflammatory conditions. We showed that the pro-inflammatory cytokine IL-17 causes a significant decrease in the 11β-HSD1 enzyme activity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2681

AB0044 METABOLISM AND OSTEOARTHRITIS ARE LINKED BY ADIPOKINES

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Background: Obesity and hyperinsulinemia are of increasing importance in the Western society. Both obesity and insulin resistance lead to changes in expression of adipokines such as adiponectin, visfatin or leptin, which appear to be immunomodulatory factors also in rheumatic diseases.

Objectives: Since osteoarthritis (OA) is often accompanied by hyperinsulinemia and obesity, we combined both mouse models (destabilization of the medial meniscus (DMM) and high-fat diet (HFD)). Here, we evaluated and correlated the systemic and local effects of both models at different stages of OA development with special focus on the local/systemic expression of the adipokines adiponectin, visfatin and leptin over time.

Methods: HFD (mainly consisting of saturated fatty acids) to induce obesity and hyperinsulinemia, and ND (normal diet) as control were fed to C57Bl/6 mice for 3 months followed by surgical OA induction (time point 0). Tissue and sera were collected at different time points after DMM-mediated OA induction (4, 6, 8 weeks).

Adipokytine (leptin, visfatin, adiponectin and IL-6) serum levels were measured by ELISA. Histological stainings of the joints (H&E, satirin O, pappenheim and Masson-Golden’s trichrome) were evaluated and arthritis progress was scored. Immunohistochemical stainings of the joints were performed to evaluate the local distribution of adipokines, which were correlated to systemic adipokytine levels and the respective arthritis score.

Results: Low systemic IL-6 levels confirmed that no acute inflammation due to surgery or infection was present in all animals. OA induction was visible at all timepoints, which was aggravated in HFD compared to ND mice (OA score: 4 weeks ND 0.87 vs. HFD 0.93, 6 weeks ND 1.44 vs. HFD 3.69, 8 weeks ND 1.78 vs. HFD 2.18). Systemic levels of leptin were significantly induced by HFD confirming the induction of insulin resistance, but DMM decreased leptin levels at all timepoints (significantly for 3 out of 6 groups, e.g. 4 weeks: HFD healthy vs. HFD DMM 18.4 ng/ml vs. 3.7 ng/ml). Interestingly, the systemic increase of adiponectin by DMM was time dependent (only 8 weeks after surgery: HFD healthy vs. HFD DMM 3176 ng/ml vs. 6149 ng/ml). But independently of diet. However, HFD in combination with DMM did not show significant effects on systemic levels of adiponectin, visfatin or IL-6.

Conclusion: HFD deteriorates OA in the DMM model. Systemic leptin levels were elevated by HFD/insulin resistance but reduced by DMM, which could not be observed for the mainly proinflammatory adipokytine visfatin. Of note, systemic inflammation as shown by systemic IL-6 levels was low in all animals. The stage of OA development influences adipokine levels, which were only increased systemically 8 weeks after surgery. In summary, systemic levels of adipokines are altered by DMM and HFD as well as the combination of both models and the analyzed adipokines show differing reactions to these factors.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4978

AB0047 TYPE I INTERFERON IS HIGHLY EXPRESSED IN RA SYNOVIAL FLUID AND JOINT CARTILAGE CORRELATED WITH SERUM RHEUMATOID FACTOR; A PRELIMINARY EXPERIMENTAL STUDY

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Background: Systemic inflammation has been postulated to be an independent cardiovascular risk factor, particularly in patients with autoimmune rheumatic disorders (ARD), such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), and is associated with accelerated atherosclerosis. There is some evidence to suggest that antiphospholipid antibodies (aPL) may also play a role in the development of atherosclerosis. However, it is few data about the relationship between these autoantibodies and inflammatory mediators in the development of atherosclerosis.

Objectives: To clarify the involvement of inflammatory mediators and aPL in the atherosclerotic process in patients with ARD.

Methods: The study included 87 female patients with ARD (RA n=47), mean age 45.0 (33.0; 51.0) years old, disease duration 9.0 (3.0; 14.0) years, disease activity (DAS28=5.37, 4.69; 5.86 points); SLE (n=40), mean age 33.5 (27.5; 44.5) years old, disease duration 8.0 (5.0; 14.5) years, disease activity SLEDAI-2K 7.0 (4.0; 6.0) points. Sixty healthy women (mean age 40.5 (36.0; 47.0) years old) formed the control group.

Results: A significant increase in the expression of type I interferons was found in RA patients in comparison with SLE patients and healthy controls (Table 1). Serum levels of IFN alpha and beta of RA cartilage were much higher than those of OA whereas tissue IFN gamma was expressed predominantly in both RA and OA. Expression of IFN alpha was not correlated with that of TNF alpha in RA patients. Statistical analysis revealed that IFN was highly expressed in RA synovial fluid, joint cartilage and blood, not in OA. IFN immunotherapy has been reported to induce RA (4–5), therefore abundant IFN might induce RA and inhibit cure of RA. Our results showed that IFN was related with blood and joint IFN. It can be speculated that IFN might be an index of IFN regulation in RA patient, however, more samples must be investigated to prove this speculation.


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4913
We revealed a correlation between IgG aCL, IgG aIgG, IgG aANV and TNF-α, IgG aCL and IL-6 in SLE patients, and only one between IgG aANV and hs-CRP in RA patients. There wasn’t any correlation between aPL and inflammatory mediators in the control group.

Univariate analysis has demonstrated an association of IgG aANV with IMT (r=0.00, p=0.044) and IgG aANV and TNF-α (r=0.362, p=0.028) in RA patients. Furthermore, we found an association between IL-6 and IgG aPT (r=0.426, p=0.038), TNF-α and IgG aCL (r=0.419, p=0.042) in SLE patients with carotid atherosclerosis. There wasn’t any association between investigated parameters in the control group.

Conclusions: The association between inflammatory mediators and disease activity has been confirmed in ARD patients. Increased autoimmune immune has been verified both in patients with SLE and RA. It has been determined that IgG aANV had more significance for IMT in patients with SLE, TNF-α - in RA patients. Our data also suggest that inflammatory mediators and antiphospholipid antibodies are involved in the atherosclerotic process in patients with ARD.

Disclosure of Interest: None declared


AB0049

NF-κB-INDUCING KINASE REGULATES LTβR-DRIVEN NF-κB SIGNALING AND INFLAMMATORY ACTIVATION OF ENDOTHELIUM

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Background: Sites of chronic inflammation, such as rheumatoid arthritis synovial tissue, are characterized by neovascularization and often contain tertiary lymphoid structures with characteristic features of lymphoid organs such as endothelial venules (HEV), and sometimes even true germinal centers. Ligation of the lymphotixin (LT)-β receptor (LTβR) results in activation of both canonical and NF-κB-dependent pathways. This study aimed to determine whether LTβR can promote inflammation-induced angiogenesis and triggers the development of the cuboidal HEV appearance. However, the relative contribution of the individual pathways to the acquisition of leukocyte traffic-regulating properties by ECs is less well understood.

Objectives: To identify the molecular pathways by which LTβR drives inflammatory activation of ECs to promote interactions with leukocytes.

Methods: Primary human ECs were treated with LTβR or LIGHT to activate LTβR. Induction of downstream signaling pathways was assessed by western blot analysis and NF-κB transcription factor ELISA. The expression of adhesion molecules, inflammatory cytokines and chemokines, such as CXCL1, CXCL5, CXCL8 and GM-CSF in ECs was measured by RT-qPCR and cytokine antibody arrays. EC interactions with leukocytes were determined by an adhesion assay, and EC barrier integrity was assessed by a permeability assay. To repress canonical NF-κB signaling pathway, a small molecule inhibitor of IKKβ was used, and inactivation of non-canonical NF-κB signaling was achieved with siRNAs targeting NFκB.E.

Results: LTβR triggering in ECs resulted in activation of both canonical and non-canonical NF-κB signaling pathways and induced the expression of inflammatory cytokines and chemokines (CXCL1, CXCL5, CXCL8, GM-CSF, CCL5). Consistent with inflammatory activation of ECs, LTβR ligation also induced adhesion of immune cells to activated endothelium and increased permeability across EC monolayers. IKKβ inhibition completely repressed LTβR-induced inflammatory activation of ECs, indicating that this process was mediated through canonical NF-κB signaling. Interestingly, inactivation of IKK with small molecule inhibitors and siRNAs significantly decreased LTβR-induced expression of inflammatory cytokines and adhesion of immune cells to endothelium, whereas silencing of NFκB had no effect. This suggests that the non-canonical pathway is not involved in LTβR-dependent activation of endothelial cells through the canonical NFκB pathway. Further analyses, including silencing of NIK and NFκB overexpression, demonstrated a role for NIK in activation of the canonical NFκB pathway by amplifying IKK complex activity.

Conclusions: These findings suggest that in addition to its pivotal role in the non-canonical pathway, NIK can serve as an amplifier of the canonical NFκB pathway and associated inflammatory responses in ECs mediated by LTβR ligation, which may play a role in development and maintenance of chronic inflammation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5306

AB0050

IMPAIRED ADIPOGENIN AND LEPTIN LEVELS DURING OSTEARTHROSI DIS ONSET AND DEVELOPMENT IN STR/ORT MICE


References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5308

AB0051

INTERLEUKIN-6 BLOCKADE WITH TOCILIZUMAB DECREASES METALLOPROTEINASE-9 ACTIVITY IN SYNOVIAL FIBROBLASTS STIMULATED WITH SYNOVIAL FLUIDS OF PATIENTS WITH RHEUMATOID ARTHRITIS OR SPONDYLOARTHRITIS


Background: Fibroblast-like synoviocytes (FLS) exhibit a transformed aggressive phenotype characterized by increased secretion of pro-inflammatory cytokines and matrix metalloproteinases (MMPs). Early pathological mechanisms that explain the change to an altered phenotype in FLS of chronic inflammatory arthropathies remain largely unknown. The composition of synovial fluids (SF) is very complex and strongly influences the microenvironment of joints including FLS thus representing an inseparable element of the disease. The MMP-9 is a
INCREASED PERIPHERAL CD8+ T CELL RESPONSES IN SLE
MANGIFERIN MODULATES TNF-ALPHA AND MMP-9

Methods: Primary FLS were obtained from SF of the RA patients. Furthermore, the SW928 human synovial cell line was used. The SF of patients with OA (n=11), RA (n=11) or SpA (n=9) patients were pooled. The FLS were stimulated with OA SF or SpA SF pools and supernatants (SN) were collected after 24, 48 and 72 h. The IL-6 levels were assessed in the SN by ELISA. The gelatinase activity of the SN was determined by zymography. The IL-6 function was blocked with the anti-IL-6 receptor antagonist tocilizumab (TCZ) (200μg/ml).

Results: Earlier induction of IL-6 in SW928 cell line was observed by RA and SpA SF stimulation since significant levels were detected at 24 h (p<0.001 and p<0.01 compared with non-stimulated cells, respectively), whilst OA SF induced significant IL-6 secretion at 72 h (p<0.01). Similar results were observed in primary FLS. In contrast to SF of OA patients, SF of patients with RA or SpA induced increased and sustained secretion of active MMP-9. Moreover, the molecular weight band corresponding with NGAL-MMP-9 complex, considered a protease inhibitor, was detected with higher intensity in the SN of FLS stimulated with RA or SpA SF compared with OA SF (p<0.001 compared with FLS stimulated with OA SF). In the presence of TCZ, significant inhibition in the gelatinase activity of all MMP-9 forms was observed at 48h of stimulation with RA or SpA SF (p<0.001 for MMP-9 dimer and NGAL-MMP-9 complex; p<0.01 for MMP-9 monomer, compared with FLS stimulated with RA or SpA SF).

Conclusions: We conclude that SF of patients with inflammatory arthritis reiterate a differential microenvironment for FLS that impacts on early phenotypic changes of these cells. The IL-6 provokes augmented and persistent MMP-9 activity in FLS stimulated with RA or SpA SF. This work identifies TCZ as an inhibitor of all forms of MMP-9.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2940

AB0052 INCREASED PERIPHERAL CD8+ T CELL RESPONSES IN SLE BY LOW-DOSE IL-2 TREATMENT
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Background: CD8+ T cell responses to viral pathogens is crucial for the prompt resolution of acute infections. SLE patients are more likely to have infections due to suppression of immune system by long-term glucocorticoid and immunosuppressive agent intake. Our previous study showed that low-dose IL-2 is effective in SLE.

Objectives: The present study is to evaluate the potential anti-infection effect of low-dose IL-2 in refractory SLE patients.

Methods: Nine refractory SLE patients and 9 health controls (HCs) were recruited. Low-dose IL-2 in refractory SLE patients.

Results: Low-dose IL-2 treatment was effective and safe in refractory SLE patients.

Conclusions: Low-dose IL-2 treatment was effective and safe in refractory SLE patients. We investigated the therapeutic potential of Mangiferin; in a clinical relevant chronic model of SLE induced colitis in mice.

Methods: Female BALB/c mice (8 to 12 wks) were randomized into four groups. Colitis was induced by cyclical administration of 5% DSS to mice i.e. 3 cycles of DSS with 1-week cycle comprised of 5% DSS following by 7 days of autoclaved drinking water (7D DSS + 7D water). Group I (Normal control): free access to autoclaved drinking water. Group II (DSS control): free access to 5% DSS. Group III (DSS + Mangiferin_30mg/kg): free access to 5% DSS + oral Mangiferin at 30mg/kg. Group IV (DSS + Mangiferin_60mg/kg): free access to 5% DSS + oral Mangiferin at 60mg/kg. Mangiferin treatment was initiated following second cycle of DSS (i.e. Day 21); after assuring that colitis relapsed in mice. One fragment of the colon was fixed in 10% neutral buffered formalin for microscopic examination while the remaining tissue was divided into parts and stored at -70°C for assessment of biochemical markers of oxidative stress and inflammatory cytokines such as TNF-α, IL-1β, MMP-9.

Results: Mangiferin treatment ameliorated the clinical parameters (body weight loss, stool consistency, occult blood), reduced mucosal damage (re-established mucosal architecture, abridged neutrophil infiltration), restored epithelial barrier integrity (diminished goblet cell loss), attenuated biochemical markers of oxidative stress (GSH, CAT, SOD, MDA, MPO), crucial inflammatory cytokines TNF-α, IL-1β and attenuates MMP-9 levels implicated in the pathogenesis of arthritis and IBD.

Conclusions: Considering the beneficial effects of Mangiferin in arthritis and IBD, we suggest that it would be valuable to use Mangiferin in IBD patients with arthritis as its extra-intestinal manifestation.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4396

AB0054 CXCL4 POTENTIATES TLR-DRIVEN POLARIZATION OF HUMAN DENDRITIC CELLS TOWARDS CYTOKINE PRODUCTION, ANTIGEN CROSS-PRESENTATION AND INCREASES STIMULATION OF CD8+ T-CELLS
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Background: CXCL4 is a chemokine produced by activated platelets and immune cells. Several studies have reported that CXCL4 plays a critical role on physiological processes since it affects the proliferation and maturation of megakaryocyte and hematopoietic progenitor cells, regulates coagulation and wound healing, displays anti-tumoral and angiostatic activity and induces immune cell modulation. Dysregulation of these processes causes the disturbance of the immune system and homeostasis, and might lead to pathological conditions. Indeed, a strong correlation was previously found between elevated CXCL4 levels in the circulation and the clinical features of patients with systemic sclerosis (SSc) (1). Dendritic cells are essential players in innate defence and bridging towards adaptive immune responses, thereby contributing to both immune activation and maintenance of homeostasis.

Objectives: Considering previous observations on the association of dendritic cells and T-cell dysfunction in SSc, we here investigated the effect of CXCL4 on monocyte-derived DC (moDC) differentiation, on Toll-like receptor (TLR)-mediated responses and on activation of polyclonal and antigen-specific CD8+ T-cells.
Methods: To this end, we compared the phenotype, TLR-mediated responses and CD8+ T-cell activation by moDCs and CXCL4-exposed moDCs.

Results: Already prior to TLR stimulation, CXCL4-exposed moDCs displayed a more mature phenotype. We found that CXCL4 exposure can sensitize moDCs for TLR-ligand responsiveness, as illustrated by a dramatic upregulation of CD83, CD86 and MHC class I, and markedly increased secretion of IL-12 and TNF-α in response to TLR3 and TLR7/8-agonists. Next, we analyzed the effect of CXCL4 in modulating DC-mediated CD8+ T-cell activation. CXCL4-exposed moDCs strongly potentiated proliferation of polyclonal CD8+ T-cells and production of interferon (IFN)-γ and IL-4 in an antigen-independent manner. While the internalization of antigen was comparable to moDCs, antigen processing by CXCL4-exposed moDCs was impaired. Yet, these cells were more potent at stimulating antigen-specific CD8+ T-cell responses.

Conclusions: Together our data supports that increased levels of circulating CXCL4 may contribute to immune dysregulation through the modulation of innate and adaptive responses by dendritic cells.

References:
LEVEL OF VASCULAR ENDOTHELIAL GROWTH FACTOR A AND INTIMA-MEDIA THICKNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS


Background: Early development of atherosclerosis (AS) with higher mortality risk is observed in patients with rheumatoid arthritis (RA). Actually, this problem hasn’t been solved. That’s why researches devoted to finding of relationships between RA and AS is still of current interest. In RA pannus formation accompanied by the development of new blood vessels forms main clinical manifestation. Vascular endothelial growth factor A (VEGF-A) is a heparin-binding glycoprotein, that induces the growth of blood vessels and plays a role in differentiation of endothelial cells. The expression of VEGF-A increases when plaque develops. Objective: To determine particular qualities of VEGF-A production in patients with RA and various atherosclerotic damage of vessels.

Methods: 67 Caucasian patients with RA (age - 52 yr., [38;59], DAS28 5,25 [5,5;6,4]) were included in our study. Patients had American Rheumatism (ACR)-defined RA (1987 classification criteria). 45 European patients with OA (56 yr., [50;63]) were in control group. All patients gave written informed consent before enrollment. VEGF-A was determined by ELISA for quantitative detection of human VEGF-A (Bender MedSystem GmbH, Austria). Range of atherosclerotic damage was assessed by ultrasonography with measurement of carotid intima-media thickness (IMT). IMT measured was compared with normal values according to the age and sex classes: younger 40 yr - 0.7 mm, 40–50 yr - 0.8 mm, elder 50 yr - 0.9 mm for men; younger 45 yr - 0.7 mm, 45–60 yr - 0.8 mm, elder 60 yr - 0.9 mm for women. Results is presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]). Descriptive statistics, non-parametric Mann-Whitney U-test, Kruskal-Wallis test were used for analysis of the results.

Results: No significant differences of IMT were found between groups with RA and OA. Abnormal IMT were observed in about half of patients (Table 1).

Table 1. IMT in patients with RA and OA

<table>
<thead>
<tr>
<th>IMT</th>
<th>IMT-N</th>
<th>Plaque without stenosis</th>
<th>Stenosing plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA, n (%)</td>
<td>35 (52.2)</td>
<td>20 (29.9)</td>
<td>12 (17.9)</td>
</tr>
<tr>
<td>OA, n (%)</td>
<td>18 (40)</td>
<td>12 (26.7)</td>
<td>5 (11.1)</td>
</tr>
</tbody>
</table>

The highest level of VEGF-A was in OA-group with stenosing plaque (p<0.01). No significant differences were found between other OA-subgroup. In patients with RA the highest level of VEGF-A was observed in subgroup with abnormal IMT (p<0.05), but not with plagues. Generally, VEGF-A production in patients with normal IMT was higher in RA-patients, but not significantly.

Table 2. Level of VEGF-A in groups with different values of IMT

<table>
<thead>
<tr>
<th>VEGF-A in OA-patients, pg/ml</th>
<th>IMT &lt; 0.8</th>
<th>IMT 0.8 - 0.9</th>
<th>IMT &gt; 0.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>392.30</td>
<td>396.90</td>
<td>651.05</td>
<td>1148.50</td>
</tr>
</tbody>
</table>

Conclusions: Pro-inflammatory cytokine secretion induced by MSU crystals in synovioocytes triggers chondrocyte activation, intensifying the articular inflammatory state in gouty attacks. Furthermore, the increase in reactive species (particularly NO, which inhibits proteoglycan synthesis) compromises the homeostasis of the extracellular matrix of the cartilage. Finally, overproduction of NGF and H2O2 by the chondrocytes functions a pain modulator during gout attacks.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2401

MODELLING DELAYED BONE HEALING IN A MOUSE-OSTEOTOMY MODEL TO EVALUATE THERAPEUTIC STRATEGIES FOR AFFECTED PATIENTS WITH RA

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Background: Anti-inflammatory treatment of rheumatoid arthritis (RA) using non-steroidal anti-inflammatory drugs (NSAID) or glucocorticoids (GC) as well as the disease itself, are supposed to negatively influence bone metabolism and healing. However, in vivo models allowing to evaluate therapeutic strategies for patients suffering from delayed bone healing are scarce and mainly created by critical size defects that are not representative for comorbidity-induced disorders. In addition, there are no adequate rodent models allowing the analyses of the influence on the bone metabolism by the complete dysregulation of the immune system in RA as well as long-term medications with NSAID or GC. Previously, we have shown that immunologically restricted patients lack an adequate adaptation to hypoxia in the fracture hematoma thus facilitating healing disorders (1). The hypoxic microenvironment during the initial fracture-healing phase is known to be stimulative for activating the immunological reactions, which induce the regeneration. Furthermore, we performed a single-center retrospective study on fracture healing disorders showing a significant high prevalence for RA patients to be affected by delayed bone healing.

Objectives: In order to evaluate therapeutic strategies for affected patients with RA, we developed a model for delayed bone healing in a mouse-osteotomy model.

Methods: Female C57BL aged 12 weeks underwent osteotomy of the femur (fracture gap 0.7 mm) that was fixated with an external fixator (RIS-System). Lysostaphin (based on bovine-Col I; mimicking extracellular matrix) was applied in the fracture gap and analysis was performed 2 and 3 weeks after surgery. The ratio of bone volume (BV) per total volume (TV) in the fracture gap was evaluated using in vitro µCT. In addition, Movat’s pentachrome staining was performed to analyze the cellular and tissue composition within the fracture gap. To investigate the number of cells as well as the vessel formation, we used immunofluorescence to stain for Endomucin, CIBER-BBN, A Coruña, Spain.

Background: Osteoarthritis is the most prevalent inflammatory arthritis in young men, in which clinical manifestations are triggered by the deposits of monosodium urate (MSU) crystals in and around joints. From a clinical perspective, gouty attacks and tophaceous deposits have been associated to nodal osteoarthritis [1,2].

Objectives: To determine the molecular mechanisms associating MSU crystals deposit with chondrocyte activation and changes in articular cartilage.

Methods: Primary cultures of synoviocytes were activated with MSU crystals for 24 h, the resulting supernatant was used as a supplementary conditioning basal medium (CBM) for 24 h chondrocyte growth. The expression level profile of cytokines (IL-6, IL-8) and nerve growth factor (NGF) in the supernatant was measured. Production of reactive oxygen and nitrogen species, such as O2, H2O2, and NO*, was also measured intraincellularly.

Conclusions: Secretion of these soluble mediators in synoviocytes inactivated NGF by the chondrocytes directly stimulated with MSU crystals.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4556

SYNOVIAL SECRETION OF PRO-INFLAMMATORY AND PRO-OXIDANT MOLECULES TRIGGERED BY MONOSODIUM URATE CRYSTALS INDUCES NGF AND H2O2 PAIN MEDIATORS IN THE CHONDROCYTE


Background: Gout is the most prevalent inflammatory arthropathy in young men, in which clinical manifestations are triggered by the deposits of monosodium urate (MSU) crystals in and around joints. From a clinical perspective, gouty attacks and tophaceous deposits have been associated to nodal osteoarthritis [1,2].

Objectives: To determine the molecular mechanisms associating MSU crystals deposit with chondrocyte activation and changes in articular cartilage.

Methods: Primary cultures of synoviocytes were activated with MSU crystals.
ratio was significantly higher in the controls (empty gap = normal healing; n=8 per timepoint) as compared to the Lysostaphin group (n=8 per timepoint) 2 weeks after osteotomy and slightly higher after 3 weeks. Histological investigation showed the clear presence of the scaffold on both timepoints without bridging cartilaginous tissue. The cell number as well as the vessel formation was significantly reduced within the fracture gap.

**Conclusions:** The results obtained so far support the hypothesis that we were able to develop a delayed healing or even non-union osteotomy model in mice by avoiding to create a critical size defect. Therefore, this approach represents a promising alternative animal model to evaluate therapeutic strategies to overcome bone healing complications in RA patients and perhaps other immunologically restricted patients.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1488

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**AB0061**

**35SULPHATE INCORPORATION ASSAY AS A NEW TOOL FOR MEASURING EARLY CARTILAGE DEGRADATION FOLLOWING BLOOD EXPOSURE IN VITRO AND IN VIVO IN F8 KO RATS**

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**Background:** Joint damage upon bleeding causes significant morbidity in patients in cartilage, by incorporation of radioactive $^{35}$Sulphate, is a sensitive method often used. However, histological changes take time to develop. To study the pathophysiology, rodent models with histology as primary outcome are often applied. Therefore, histological changes take time to develop and are subject to interpretation. Determining proteoglycan synthesis rate (PSR) in vitro through incorporation of radioactive $^{35}$Sulphate, is a sensitive method previously applied in human tissue and larger animal models to detect early cartilage changes. Isolating cartilage of small animals can be challenging, so a technique to shave off rat cartilage was developed.

**Objective:** To study cartilage degradation following blood exposure, applying the $^{35}$Sulphate incorporation assay on rat tibial cartilage.

**Methods:** A total of 13 factor VIII knock out (F8KO) rats were bred and housed at Novo Nordisk A/S, Maaloev, Denmark. After euthanasia, the legs were removed and transported to UMC Utrecht, The Netherlands.

In vivo: When 24 hours after euthanasia the cartilage of 6 healthy F8KO rats was obtained by shaving off cartilage pieces of the tibia plateau by use of a scalpel. All cartilage explants were cultured for four days; in addition to culture medium, half of the cartilage samples were cultured with 50% v/v whole blood. After four days PSR was determined by adding 4μCi Na$_2$SO$_4$ to the cultures for four hours. $^{35}$SO$_4$ is incorporated into newly synthesized proteoglycans. After digesting the cartilage pieces and precipitating the proteoglycans with cetylpyridinium chloride, the amount of radioactivity was measured by liquid scintillation analysis and normalized to the specific activity of the pulse medium, labeling time and wet cartilage weight.

In vivo: In 7 F8KO rats a unilateral joint bleed was induced by needle puncture and in the following four days until euthanasia, the animals received analgesia. At UMCU, the tibial cartilage was removed and PSR determined as described above.

All animal experiments were performed in accordance with and approved by the Danish Animal Experiments Council, Ministry of Food, Agriculture and Fisheries, Denmark.

**Results:** On average, a total of 1.6mg (0.8–3.1mg) cartilage per tibia could be obtained. The PSR of healthy cartilage determined after four days of culturing in vitro was on average 49.5 nmol/h.g. In vitro blood exposure resulted in a diminished synthesis: 7.7 nmol/h.g (p<0.0191), corresponding to an 84% decrease comparable to previously published experiments using human tissue [1]. In vivo, an induced joint bleed led to a 44% decrease in PSR (13.5 vs. 7.5 nmol/h.g, p=0.0151).

**Conclusions:** This study demonstrates for the first time that PSR, by use of the $^{35}$Sulphate incorporation assay, can be determined in rat tibial cartilage and is affected by blood exposure in vitro and in vivo. As such, this assay can be a valuable tool to detect cartilage changes using joint degenerative rat models.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6578

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**AB0062**

**EX VIVO BACK-TRANSLATION OF FOSTAMATINIB’S EFFECT ON JOINT ECM TURNOVER SHOWS SIGNIFICANT EFFECT ON BONE BUT NO EFFECT ON THE SYNOVIM**


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**Background:** It is important to establish translational methods that aid in pre-clinical go/no-go decision points to increase the success rate of approved DMARDs. The Spleen tyrosine kinase (Syk) inhibitor Fostamatinib (Fosta) was terminated for development for RA, due to insufficient effect on joint structure in phase III.

**Objectives:** The objective was to use a translational system of ex vivo cultures to back-translate the insufficient effect on joint structure described in clinical studies.

**Methods:** Human mature osteoclasts (HOC) seeded on bone, bovine cartilage explants (BEX) and human synovial explants (SME) were treated with R406 (API of Fosta) at 5μM-0.05μM. Osteoclasts were co-stimulated with 25 ng/ml M-CSF and RANKL, while BEX and SME were co-stimulated with TNFα 2 ng/ml and OSM 10 ng/ml (O=O) or TNFa 10 ng/ml respectively. CTX-1 and CaM were measured in conditioned medium (CM) from HOC. Metabolic activity of HOC was assessed with Alamar Blue. C2M and AGN1x were measured in CM from BEX, while acMMP3, C1M, and C3M were measured in CM from SME. The biomarkers in BEX and SME CM were measured at 4 time points and the total release were quantified by area under the curve (AUC). CTX-1, C2M, AGN1x, acMMP3, C1M, CSM and C3M were measured with ELISA. CaM was measured down to 5μM (P=0.034) and measured down to 0.5μM (P=0.012). In SME R406 only decreased the release of C1M and C3M (Fig 1e) significantly at 5 μM (C1M: P=0.03, C3M: P=0.046), and tended to decrease release of acMMP3 (Fig 1f) at 5μM. The later was however not significant.

**Results:** R406 decreased the release of CTX-1 (Fig 1A) and C2M in a dose-dependent manner, with a significant decrease at 1μM (P<0.01). This might be due to a toxic effect of R406 on HOC (Fig 1B) (P<0.05). R406 decreased the total release of C2M and AGN1x in a dose-dependent manner in BEX. C2M was inhibited a concentrations down to 1.25μM (P<0.034), and AGN1x down to 5μM (P<0.012). In SME R406 only decreased the release of C1M and C3M (Fig 1e) significantly at 5 μM (C1M: P=0.03, C3M: P=0.046), and tended to decrease release of acMMP3 (Fig 1f) at 5μM. The later was however not significant.

**Conclusions:** Serum-based biomarkers of the joint ECM turnover were measured in CM from HOC, cartilage and synovial explant cultures. R406 decreased bone resorption and HOC metabolic activity in a dose–dependent manner, together with the MMP-mediated degradation of type II (C2M) collagen and aggrecanase degradation of aggrecan (AGN1x) in cartilage. However, R406 had limited effect on the inflammation driven MMP-mediated degradation of type I (C1M) and III (C3M) collagen and activation of MMP-3. CTX-1, C2M, and C3M have previously been measured in OSKIRA-1, with a profile identical to the ex vivo measurements here [1].

**References:**
ADISO763 THE PROTECTIVE EFFECT OF PFTα ON ALCOHOL-INDUCED OSTEONECROSIS OF THE FEMORAL HEAD

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Background: Epidemiological studies have shown that alcohol plays a pivotal role in the development of osteonecrosis of the femoral head (ONFH). However, few studies have investigated the pathogenesis or interventions for alcohol-induced ONFH.

Objectives: The aim of this study was to explore the underlying mechanism of alcohol-induced ONFH and the protective effect ofpitthrin-α (PFTα).

Results: Through a series of in vitro assessments, we found that ethanol treatment significantly activated p38, suppressed Wnt/β-catenin signaling and inhibited osteogenic-related proteins, including runt-related transcription factor 2 (RUNX2), osteocalcin (OCN), osteopontin (OPN) and collagen I (COL1). Furthermore, by separating the cytoplasmic and nuclear proteins, we found that ethanol inhibited osteogenesis by impairing the accumulation of β-catenin both in the cytoplasm and nucleus in human bone mesenchymal stem cells (hBMSCs), which resulted from activating glycogen synthase kinase-3β (GSK-3β) in this in vivo study, we established alcohol-induced ONFH in rats and investigated the protective effect of PFTα. Micro-C, hematoyxlin & eosin (H&E) staining, immunohistochemical analyses, immunofluorescence staining, TUNEL staining, and immunohistochemical staining were performed to reveal the PFTα-induced therapeutic effects. H&E findings combined with TUNEL, caspase-3/4-cleaved immunohistochemical staining, and micro-CT images revealed obvious ONFH in the alcohol-administered rats, whereas significantly less osteonecrosis developed in the rats injected with PFTα. As the inhibitor of osteogenesis, RUNX2 and its downstream targets OCN, OPN, and COL1 were immunostained in the femoral heads. These results indicated that these osteogenic-related proteins were significantly decreased in the alcohol-administered rats, whereas these results were reversed in the PFTα-injected rats. Fluorochrome labeling showed a similar result in that alcohol significantly decreased the osteogenic activity in the rat femoral head, which was blocked by the injection of PFTα.

Conclusions: Pitthrin-α, a p38 inhibitor, was able to block the ethanol-triggered activation of p38 in hBMSCs and alcohol-induced ONFH in a rat model. Its antagonistic effect against ethanol’s effect on hBMSCs could be a clinical strategy to prevent the development of alcohol-induced ONFH.

Acknowledgements: The current study was supported by grants from the National Natural Science Foundation of China (no. 81272003 and no. 81301572) and the SMC-Chen Xing Xing Plan for Splendid Young Investigators of Shanghai Jiao Tong University.

Disclosure of Interest: None declared


ADISO764 ADIPOSE STROMAL CELLS EXERT SPECIFIC EFFECTS ON OSTEOARTHRITIC SYNOVIAL MACROPHAGES

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Background: Osteoarthritis (OA) is the most common joint disease and the major cause of pain and disability in the aging population [1]. Adipose stromal cells (ASC) are promising candidate for cell therapy in OA, because they have immunomodulatory, trophic and differentiation capacities [2,3]. Synovial inflammation is accepted as important OA feature for the symptoms and disease progression [4]. Synovial tissue is mainly composed of synovial fibroblasts (SF) macrophages (SM) and a low percentage of other cell types [5].

Objectives: Aim of the study was to analyze the effects of adipose stromal cells in co-culture with SF and SM. Methods: GMP clinical grade ASC were isolated from subcutaneous adipose tissue. Synoviocytes were isolated from synovial tissue of OA patients undergoing total joint replacement. Synoviocyte cultures at passage 1 and 5 were analyzed for: 1. different phenotypical markers by flow cytometric analysis, 2. inflammatory factors by multiplex immunoassay, 3. anabolic and degradative factors by qRT-PCR. Both p.1 (mix of SF and SM) and p.5 (only SF) synoviocyte cultures, as different cell models, were co-cultured with adipose stem cells (ASC) to define their effects. Furthermore macrophages type 1 (M1) were isolated and co-cultured with ASC.

Results: Synoviocytes at passage 1 were positive to typical markers of SM (CD14,CD16,CD68, CD80,CD105,CD106) and SF (CD55,CD73,CD90,CD105,CD106), whereas at passage 5 were only positive to SF markers and showed a higher percentage of CD55 and CD106. P1 synoviocytes cells released a significantly higher amount of all inflammatory (IL6,CXCL8,CCL2,CLL3,CLL5) and anabolic (IL10) factors than those at p.5. Moreover, p.1 synoviocytes cells expressed higher amount of some degradative factors (MMP13, MMP1,S100A9) than p.5 synoviocyte cells. Co-culture experiments showed that the amount of SM in p.1 synoviocytes cells specifically orchestrate the up or down-modulation of some inflammatory (IL6,CXCL8,CCL2,CCL3,CCL5) and degradative factors (ADAMTS5,MMP13,S100A9,S100A8) analyzed. Interestingly, p.5 synoviocytes cells induced all factors analyzed, except COL5. Finally, we demonstrated that ASC effects were strictly dependent by M1, that decreased the release of typical macrophages cytokines (IL1,IL, TNFs and CCL3/MIP1α) and that ASC effects are responsible for the switching by M1 like inflammatory macrophages to M2 like phenotype mainly due to IFNγ only made of the information set out.

Conclusions: These data demonstrate that the GMP-ASC effects on OA synovial inflammation are strictly dependent by macrophages, that the switching activated-M1 inflammatory macrophages to a M2-like phenotype, mainly through PG2E.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6081

ADISO765 2-CARBA-CYCLO PHOSPHATIC ACIDIC ACID SUPPRESSES EXPRESSION OF CARTILAGE DEGRADING ENZYMES SUCH AS MMP-13 IN INFLAMMATORY SYNOVIAL FIBROBLASTS AND ARTICULAR CHONDROCYTES INDUCED BY IL-1 Beta AND/OR TNF ALF.

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Background: Cyclic phosphathic acid (cPA) is one of bioactive lipid, has been implicated as a mediator of various biological effects including inhibitory effects of proliferation, invasion and metastasis of cancer cells. cPA is naturally occurring mediator even in normal human serum, 2-carba-cPA (2ccPA) is structurally modified formula of cPA and has shown improved bioactivity. We have previously confirmed that 2ccPA stimulated HAS-2 production on human osteoarthritic chondrocytes and synovial fibroblasts (SFs) in vitro. Furthermore, intra-articular administration of 2ccPA has shown its suppressing effect of pain, swelling, and articular cartilage destruction in rabbit experimental osteoarthritis (OA). We have established experimental osteoarthritis in rabbits and demonstrated that 2ccPA might had direct inhibitory effect of cartilage degrading enzymes on rheumatoid synovial fibroblasts (SFs) in vitro. Inflammatory arthrits such as rheumatoid arthritis (RA) and early stage of OA involves synovial inflammation and subsequent production of cartilage degrading enzymes also from chondrocytes. 2ccPA may be possible another therapeutic option for degenerative arthrits.

Objectives: The aim of this study was to evaluate the direct effects of 2ccPA on cartilage matrix degrading enzymes using SFs and articular chondrocytes under influence of inflammatory cytokines.

Methods: In vitro studies were performed using SFs and chondrocytes obtained from arthritic patients (RA and OA) at joint replacement surgery. First, 2ccPA 0–25 μM was added to cell cultures and effects of 2ccPA on ADAMTS-4, -5, MMP-3, 9, -13 expression was assessed by real time PCR using specific primers for human transcript. Basic fibroblast growth factor was used as endogenous expression control for PCR. As we confirmed that 2ccPA had dose-dependent inhibitory effects on expression of above enzymes, the second experiment was performed. SFs or chondrocytes were pre-cultured with IL-1β (1 ng/ml) and/or TNF-α (10 ng/ml) for 24 hours, then added 10 μM 2ccPA to study attenuated effect of 2ccPA on synthesis of above cartilage degrading enzymes. Newly synthesized MMP-3, -13 from SFs or chondrocytes in cultured media after 24 hours of 2ccPA addition were measured by sandwich ELISA.

Results: 2ccPA itself repressed cartilage degrading enzymes, ADAMTS-4, -5, MMP-3, -9 and MMP-13 expression in both SFs and chondrocytes. 2ccPA was all repressed by low dose of 2ccPA. Even after cells had been stimulated by cytokines, 10 μM 2ccPA repressed expression of cartilage degrading enzymes in SFs or chondrocytes. Expression of MMP-13 was repressed more in chondrocytes by 2ccPA. ELISA results also confirmed the inhibitory effect of 2ccPA on expression of MMP-3 SFs (n=5) by SD±3 or in RA c3, S100A9 3%–43%. In OA, MMP-13 production was reduced by 31% in OA SFs (n=6) and 34% in OA chondrocytes (n=4). However, not significant reduction of MMP-3 in both SFs or chondrocytes. MMP-9 expression by ELISA was under the detectable limit.
Conclusions: The in vitro results confirmed that 2ccPA had suppressing effect of cartilage degrading enzymes expression on SFs and chondrocytes, supports the hypothesis that 2ccPA might have played direct role to suppress inflammation and also protect articular cartilage in arthritic condition.

Disclosure of Interest: I. Masuda:Grant/research support from: SANSHO, K. Okada: None declared, H. Yamanaka: None declared, S. Momohara: None declared

DOI: 10.1136/annrheumdis-2017-eular.5680

AB0066 HUMAN MULTIPOTENTIAL STROMAL CELLS EXPRESS LOW SURFACE LEVELS OF PRO-INFLAMMATORY CYTOKINE RECEPTORS IN BONE HEALING DEFECTS

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Background: Osteoimmunology is an evolving field where the multipotential stromal cells (MSCs) can be considered as an important player linking immune response with bone generation. A group of pro-inflammatory cytokines including IFN-γ, TNF-α, IL-17, IL-1β and IL-1α has been proven to have a licensing effect on MSCs promoting the immunomodulatory activities of MSCs (1). Importantly, these cytokines can regulate the osteogenic differentiation capability of MSCs and in particular, IL-1β and IL-1α can enhance the MSC osteogenesis as shown in previous in vitro studies (2,3). However, little is known about the role of these cytokine-MSC interactions in the bone-related diseases in humans.

Objectives: The main focus of this study was to assess if the immune-dependent licensing process of MSCs could be involved in defective bone regeneration.

Methods: We used samples of bone marrow aspirates (n=15) from two groups of traumatic bone fracture patients; normal union and non-union. Bone marrow MSCs were analyzed for the surface expression of the receptors of the pro-inflammatory licensing cytokines using flowcytometry-optimized panels. Additionally, a comparison of the cytokine effect on the proliferation of cultured MSCs was compared between normal union and non-union groups using the cell proliferation XTT test.

Results: Interestingly, there were significant lower expression levels of IL-1 receptors 1 and 3 (IL-1R1 and IL-1R3) on non-union MSCs compared to normal-union MSCs (p=0.0478 and p=0.0113 respectively). Furthermore, the surface levels of TNF-α-R1 (CD120a) were significantly lesser on non-union MSCs (p=0.0119). There was a clear trend of reduced expression of IL-17 receptors (CD217) on the surface of non-union MSCs but it was not statistically significant (p=0.0119). The XTT data showed a significant less proliferation index for IL-1-treated non-union MSCs compared to normal-union (p=0.0726). The XTT data showed a significant less proliferation index for IL-1-treated non-union MSCs compared to normal-union MSCs (p=0.0446). Also, a consistent trend of lower proliferation index of non-union MSCs was detected when these cells were treated by IFN-γ, TNF-α or IL-17.

Conclusions: Together, the lower levels of the pro-inflammatory cytokine receptors indicated a possible mechanism for a defective response of non-union MSCs to the inflammatory signals (particularly IL-1). Further understanding of the impact of immune-MSC interactions on human bone healing and regeneration will help to develop new therapies for musculoskeletal diseases involving osteolytic lesions.

References:

Acknowledgements: This project (no. S-16-132E) was supported by the AO Foundation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8309

AB0067 INFLUENCE OF ADIPOKINES ON DIFFERENTIATION OF CULTURED SPONGIOSA-DERIVED MESENCHYMAL STEM CELLS FROM OSTEOPOROTIC AND OSTEARTHRITIS PATIENTS

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Background: Osteoporosis (OP) and osteoarthritis (OA) are two common age-related disorders leading to chronic pain and disability in elderly people. Age-related bone loss and articular cartilage damage are associated with increased bone marrow adiposity due to a possible shift of osteogenic differentiation towards adipogenic differentiation of bone marrow mesenchymal stem cells (MSC). The differentiation of MSC into adipocytes or osteoblasts is an important determinant of bone structural integrity. Adipose tissue is an metabolically active tissue. Therefore adipocyte-derived factors -adipokines- might influence differentiation of bone marrow-derived MSC.

Objectives: The role of adipocyte interactions in the pathogenesis of OP is poorly understood. Therefore, we analyzed the presence of distinct adipokines (visfatin, resistin and leptin) in the bone marrow cavity and their effects on MSC differentiation.

Methods: Spongosia from femoral heads was collected (hip replacement surgery or revision surgery) from patients with a history of osteoarthritis (OA) (n=7, mean age 62±7 years) or non-osteoporotic bone (n=14). In contrast to leptin and resistin, visfatin induced the secretion of proinflammatory cytokines (IL-6, IL-8, MCP-1) during both, osteogenic and adipogenic differentiation. Visfatin significantly increased the matrix mineralization and downregulated collagen type I expression (e.g. fold 4.6) in osteogenic differentiated cells. Visfatin also reduced the expression of MMP2, MMP13, Runx2, Timp1 and Timp2 (e.g. fold 2-4, 3.18-5.85, fold 3.2-4 fold respectively) during osteogenic differentiation, but not leptin and resistin. In contrast to osteogenesis, visfatin significantly induced MMP13 expression (e.g. fold 104.4) during adipogenic differentiation under standard cell culture conditions. However, visfatin-induced MMP13-expression was markedly reduced during differentiation on purified autologous cancellous bone.

Conclusions: Visfatin and leptin levels were increased in OP bone vs. non-osteoporotic bone (n=14). In contrast to leptin and resistin, visfatin induced the secretion of proinflammatory cytokines (IL-6, IL-8, MCP-1) during both, osteogenic and adipogenic differentiation. Visfatin significantly increased the matrix mineralization and downregulated collagen type I expression (e.g. fold 4.6) in osteogenic differentiated cells. Visfatin also reduced the expression of MMP2, MMP13, Runx2, Timp1 and Timp2 (e.g. fold 2-4, 3.18-5.85, fold 3.2-4 fold respectively) during osteogenic differentiation, but not leptin and resistin. In contrast to osteogenesis, visfatin significantly induced MMP13 expression (e.g. fold 104.4) during adipogenic differentiation under standard cell culture conditions. However, visfatin-induced MMP13-expression was markedly reduced during differentiation on purified autologous cancellous bone.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2845

AB0068 HYPOXIA AND RHEUMATOID PHENOTYPE DECREASE THE CAPACITY OF ADIPOCYTES TO SUPPRESS HELPER CELL PROLIFERATION THROUGH IDO1-MEDIATED TRYPTOPHAN CATABILISM

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Background: The pathogenesis of rheumatoid arthritis (RA) is linked to functional changes in synovial fibroblasts (SF) and local infiltration of T lymphocytes. Increased synovial inflammation is also associated with a hypoxic joint microenvironment. Oxygen levels in the joints of RA patients are significantly decreased compared to those of osteoarthritis (OA) patients with values of about 22.5mMhg corresponding to ambient oxygen tensions of 3.2%. So far, little is known about the effects of hypoxia on the interaction between fibroblasts and T lymphocytes and its implications on the pathophysiology of RA.

Objectives: The aim of this study was to compare the influence of SF from RA versus OA patients on T helper (Th) cell responses both under normoxic and hypoxic conditions.

Methods: SF were isolated from synovectomy tissues of OA or RA patients, Th cells were isolated from peripheral blood of RA patients or healthy donors. Cell cultures were performed under normoxic or hypoxic (3% O2) conditions. Th cell proliferation was determined by PKH26 labelling and flow cytometry. Cytokine secretion was quantified by ELISA. Indoleamine 2,3-dioxygenase 1

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1070

AB0069 SCIENTIFIC ABSTRACTS
(IDO1) expression was analysed by Western Blot and expression of enzymes of the kynurenine pathway by real-time PCR. Tryptophan's kynurenine levels in culture supernatants were quantified by HPLC.

Results: SF strongly inhibited the proliferation of co-cultured TH cells. Tryptophan was completely depleted within a few days in co-cultures of SF and TH cells, resulting in erythrocyte-initiation factor (eIF2α) phosphorylation, TCR:chain down-regulation and proliferation arrest. Blocking of IDO1 completely restored TH cell proliferation, indicating that SF suppressed the proliferation of TH cells through IDO1-mediated tryptophan catabolism. Interestingly, RASF showed a significantly lower IDO1 expression, tryptophan metabolism and a weaker TH cell suppressive capacity compared to OASF. Under hypoxic conditions, the secretion of IFNγ, the expression of IDO1, the tryptophan metabolism and the TH cell suppressive capacity of both OASF and RASF were significantly reduced.

Conclusions: SF suppressed TH cell growth through IDO1-mediated tryptophan catabolism, playing an important role in preventing addipogenic differentiation. TH cell responses under normal conditions. The reduced tryptophan metabolism under hypoxia together with the inferior efficiency of RASF to restrict T cell proliferation likely supports the development of synovitis in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5146

AB0069 STRONG AGE-DEPENDENT EFFECTS OF DOPAMINE ON JOINT INVASION IN ARTHRITIS

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Background: Preventing synovial fibroblasts (SF) from migrating into the adjacent cartilage is a desirable therapeutic target in rheumatoid arthritis (RA) in order to avoid joint destruction and disability. In our previous studies we could show that RASF as well as SF from osteoarthritis (OA) patients express all dopamine receptor (DR) subtypes and dopamine stimulation alters pro-inflammatory cytokines (Capellino S et al, AAR 2014).

Objectives: Therefore, we aimed to elucidate a potential dopamine-mediated impact on joint invasion and destruction in arthritis.

Methods: SF from RA and OA patients were obtained from patients undergoing knee joint replacement surgery (mean age: 74.3±11.3yrs at OA and 73.7±10.3yrs at RA patients) to investigate dopamine receptor (DR)-distribution within the RA synovium and in the invasion zone. Immunohistochemistry was performed for all five DR-subtypes. Migration and motility assays were performed under D1-like (D1DR and D5DR) and D2-like (D2DR, D3DR and D4DR) receptor stimulation. Dopamine effects on MMP3 and proMMP1 were evaluated using ELISA. Migration of SF from RA and OA and the invasion zone were studied under hypoxia together with the inferior efficiency of RASF to restrict T cell proliferation. There was no difference between RA and OA patients and between all dopamine receptor (DR) subtypes and dopamine stimulation alters pro-inflammatory cytokines.

Conclusions: SF strongly inhibited the proliferation of co-cultured TH cells. Tryptophan was completely depleted within a few days in co-cultures of SF and TH cells, resulting in erythrocyte-initiation factor (eIF2α) phosphorylation, TCR:chain down-regulation and proliferation arrest. Blocking of IDO1 completely restored TH cell proliferation, indicating that SF suppressed the proliferation of TH cells through IDO1-mediated tryptophan catabolism. Interestingly, RASF showed a significantly lower IDO1 expression, tryptophan metabolism and a weaker TH cell suppressive capacity compared to OASF. Under hypoxic conditions, the secretion of IFNγ, the expression of IDO1, the tryptophan metabolism and the TH cell suppressive capacity of both OASF and RASF were significantly reduced.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4830

AB0070 CHONDROPROTECTIVE EFFECTS LINKED TO REDUCTION OF ADIPOGENESIS AND REGULATION GAP JUNCTION INTERCELLULAR COMMUNICATION: REGENERATIVE POTENTIAL THERAPEUTIC APPROACH FOR OSTEOARTHRITIS

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Background: Human bone marrow mesenchymal stem cells (hMSCs) exhibit an age-dependent reduction in osteogenesis and an increased propensity toward adipocyte differentiation. This switch has been associated with different bone disorders characterized by reduced bone formation and increased bone marrow fat accumulation. Connexin43 (Cx43) is an integral membrane protein that forms gap junction channels (GJs) and is implicated in multiple cellular functions including cellular differentiation and control of bone remodelling and cartilage structure and function.

Objectives: In this study we investigated the effect of oleuropein and other molecules isolated from the Olea europaea in cellular differentiation to test if these molecules act as adiogenic suppressors in order to promote bone ad cartilage regeneration through a Cx43-dependent mechanism.

Methods: hMSCs were obtained from bone marrow donors. Human chondrocytes were isolated from cartilage of healthy donors and patients with osteoarthritis (OA). Differentiation assays were carried out in the presence of different concentrations of oleuropein and olive extract (OE). Cellular differentiation was evaluated using histological stains. Scrape loading assays, western-blot, real-time qPCR and Western-blot analysis of hMSCs supplemented with oleuropein/OE showed increased levels of Cx43. On the other hand, OA chondrocytes showed higher levels of Cx43 in comparison with normal chondrocytes; oleuropein and OE treatments significantly decreased Cx43 levels and dye transference through GJ channels. The treatment of OA chondrocytes micromass culture with oleuropein and OE increased the expression of proteoglycans and Col2 in the extracellular matrix. These changes in the micromasses were accompanied by a decrease in Cx43 levels improving protein subcellular localization.

Conclusions: Together, our results suggest that the molecules used in this assays, via Cx43 and GJ intercellular communication increase the propensity towards osteogenesis and chondrogenesis, reducing adipocyte differentiation. Our assays indicate that these molecules may represent a potential therapeutic approach for cartilage and bone age-related disorders such as OA in order to avoid joint destruction. We thus conclude that hMSCs treated with olive-derived molecules could be used for cartilage regeneration through a Cx43-dependent mechanism.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5266

AB0071 ANALYSIS OF SYNOVIAL EXPRESSION OF PARVOVIRUS B19 ASSESSED IMMUNOHISTOCHEMICALY AND CORRELATED TO SYNOVITIS SCORE

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Background: Apart from systemic symptoms of viral infection parvovirus B19 (B19) could lead to acute and chronic arthropathy. It has been found in synovial tissue of rheumatoid arthritis (RA) patients, sometimes, being associated with some forms of undifferentiated arthritis. Possibly, it could promote inflammation in various forms of arthritis.

Objectives: To determine the expression of B19 antigens in different compartments of synovial membrane; correlate these findings to the estimated synovitis score.

Methods: 7 RA and 54 osteoarthritis (OA) patients were enrolled in this study. nPCR was used to detect the presence of B19 genomic sequence in 61 samples of synovial tissue. PCR B19 positive tissue samples were immunohistochemically treated with the anti-B19 antibodies detecting B19 capsid proteins’ VP1/VP2 expression estimated thereafter semiquantiitatively. The intimal and subintimal layers of synovium as well as vasculature were estimated. Synovial inflammation was evaluated using synovitis score.

Results: 3 RA and 3 OA patients were PCR B19 tissue positive. B19 antigens’ expression was observed in synovial lining, immune infiltrates and vascular endothelium. Correlation between B19 expression observed in synovial cells and inflammatory infiltrates’ lymphocytes and macrophages was r=0.555 (p<0.0001) and r=0.793 (p<0.0001), respectively. Likewise, correlation between vascular endothelial B19 expression and synovial lymphocytic infiltration was demonstrated r=0.616 (p<0.0001). Determined synovitis score varied from low up to intermediate revealing median value 2. Simultaneously, there was no correlation found between the synovitis score and B19 antigens’ expression.

Conclusions: B19 capsid proteins’ VP1/VP2 expression is detectable in different structural constituents of synovial membrane. Under conditions studied, the tissue expression of B19 antigens does not correlate with the inflammatory indices scored.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6411
RATIONAL DESIGNED GOLD NANOPIRATE SUPPRESSES RANKL-INDUCED OSTEOSTALOGENESIS IN RAW264.7 CELLS VIA NF-KAPPA B PATHWAY AND MAPK PATHWAYS

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Background: Bone erosion in joint is the most deleterious effect induced by rheumatoid arthritis (RA) and is the major cause of disability. New therapies are urgently required to prevent RA-associated bone destruction. The excessive bone resorption in RA was proved to be mediated by osteoclasts which are derived from the monocyte/macrophage lineage and induced by RANKL. Therefore, RANKL could be a potential target for the preservation of bone mass in RA.

Objectives: Chrysotherapy showed potential effects in reducing of joint destruction but with serious side-effects in RA therapy. A rational designed gold nanoparticle named GN was prepared to provide a choice for suppressing bone loss in RA therapy with more safety.

Methods: Mouse macrophage cell line RAW264.7 was activated by RANKL to evaluate the potential osteoclastogenesis suppressing effects of GN. The differentiation, fusion and function of osteoclast were assessed by tartrate-resistant acid (TRAP) staining, actin ring formation assay and osteologic discs detection respectively. Relative expressions of osteoclast-specific genes were evaluated by RT-PCR and the activity of NF-κB pathway as well as MAPK pathways were analyzed by immunoblotting.

Results: Osteoclast differentiation, fusion and bone resorption were activated by RANKL in RAW264.7 cell, while GN significantly attenuates this process in a dose-dependent manner. The expressions of osteoclast-specific genes including TRAP and OSCAR were increased by RANKL stimulation but were effectively suppressed by GN. The activation of NF-κB pathway and MAPK pathways induced by RANKL was also suppressed by GN treatment.

Conclusions: Our findings revealed that treatment with GN could prevent RANKL-induced osteoclastogenesis and reduce increased expression of osteoclast-specific genes which may through the suppression of NF-κB and MAPK activation in macrophage. GN may provide a basis for the design of chrysotherapy drugs that effect in progression of RA-associated articular erosions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2087

ACCUMULATION OF ADVANCED GLYCAATION END PRODUCTS (AGEs) IN OSTEARTHRITIC CARTILAGE IS RELATED TO AN IMPAIRMENT OF THE ADAPTIVE MECHANISM OF GLYXALASE-1

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Background: Advanced glycation end-products (AGEs) that result from a non-enzymatic reaction between a sugar and a protein, are generated during tissular ageing. Accumulation of AGEs could also be part of the osteoarthritis (OA) process by modifying the biomechanical properties of cartilage and by inducing chondrocyte activation. Glyxalase-1 (Glo-1) is the main enzyme involved in the removal of AGEs precursors, especially the AGE carboxymethyllysine (CML).

Objectives: We aimed to quantify CML in human osteoarthritic cartilage, to investigate Glo-1 expression in chondrocytes and to study chondrocytic Glo-1 regulation in an inflammatory context.

Methods: 1) Ex vivo: Osteoarthritic cartilages from patients undergoing knee replacement were collected, dissected and incubated for 24h with or without IL-1β (5 ng/mL). Osteoarthritic CML in these cartilage explants was measured using liquid chromatography and mass spectrometry. Glo-1 protein expression (Western Blot and immunohistochemistry) and Glo-1 enzymatic activity by measuring the kinetic release of particles or ions from arthroplasty may exert local effects in the peri-prosthetic tissue. Cobalt and chromium ions are released through corrosion from metal-on-metal arthroplasty and modulate the gene expression level of several cytokines, chemokines and other mediators in bone cells.

Objectives: It was the aim of the study to analyse the effect of Co2+ and Cr3+ ions on the expression of TGF-β isoforms in bone forming cells and their impact on mineralization.

Methods: The study investigated the effect of Co2+ and Cr3+ ions on the expression of TGF-β1-3 in the human osteosarcoma cell lines (MG63 and SaOs2) and primary human osteoblasts. Cells (3x105) were seeded in 2 ml DMEM (10%FCS) into 12 well plates and stimulated with CoCl2 and CrCl3 in concentrations between 50–250 μM for 24 hours. Total RNA was extracted and changes of expression levels of TGF-β1-3 were analysed by real-time PCR using sequence-specific primers and probes. For mineralization cells were cultivated for up to 4 weeks in DMEM (10% FCS) supplemented with 0.2mM ascorbic acid, 10nm dexamethasone and 10mM gliceroxide and Co2+ and Cr2+. Calcium deposits were detected by 1% Alizarin Red S (pH 4.1) staining.

Results: The osteoarthritic cells as well as primary human osteoblasts isolated from bone explants expressed all three TGF-β isoforms, with TGF-β1 as most abundantly expressed isoform. A dose dependent reduction of all TGF-β isoforms by Co2+ ions was observed, the strongest effect was found for TGF-β2. In MG63 cells and primary osteoblasts the mRNA levels of TGF-β2 decreased to 15±4% and 17±15% compared to the unstimulated control. The effect was lesser in SaOs2 cells with a reduction to 61±7% compared to control. In contrast to bivalent Co ions, the trivalent Cr ions had no significant effect on the expression of all TGF-β isoforms.

Conclusions: The results of our study show that bivalent cobalt ions and trivalent chromium ions have different effects on bone forming cells. While Co2+ affects the expression of the different TGF-β isoforms in osteoblast-like cells and primary osteoblasts, no inhibitory effect on mineralization in the tested concentrations was seen. Cr3+ however, did not influence the expression of TGF-β but strongly inhibited the mineralization in vitro.

Our data imply that the inhibitory effect of metal ions such as Co and Cr ions on the transcription of the bone regulating cytokines TGF-β1-3 and on bone forming activity may influence bone homeostasis.

Acknowledgments: Funded by Stiftung Endoprothetik (S01/16).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6218

TARGETING IMMUNE AND NON-IMMUNO SYNOVITIS BY 1,3,5-TRIZINE-THIAZOLE VIA DUAL INHIBITION OF NF-KB AND EGFR-TK IN POSSIBLE BENEFIT IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which is easily recognised by unrelenting inflammation, joint erosion, joint immobility and severe debilitation. The cause of the disease suggests that, T cells, B cells, macrophages, and dendritic cells gain access to the inflamed synovium causing progression of disease via generation of cytokines and autoantibodies.

Methods: The study investigated the effect of Co2+ and Cr3+ ions on the expression of TGF-β isoforms in bone forming cells and their impact on mineralization.

Results: The osteoarthritic cells as well as primary human osteoblasts isolated from bone explants expressed all three TGF-β isoforms, with TGF-β1 as most abundantly expressed isoform. A dose dependent reduction of all TGF-β isoforms by Co2+ ions was observed, the strongest effect was found for TGF-β2. In MG63 cells and primary osteoblasts the mRNA levels of TGF-β2 decreased to 15±4% and 17±15% compared to the unstimulated control. The effect was lesser in SaOs2 cells with a reduction to 61±7% compared to control. In contrast to bivalent Co ions, the trivalent Cr ions had no significant effect on the expression of all TGF-β isoforms.

Conclusions: The results of our study show that bivalent cobalt ions and trivalent chromium ions have different effects on bone forming cells. While Co2+ affects the expression of the different TGF-β isoforms in osteoblast-like cells and primary osteoblasts, no inhibitory effect on mineralization in the tested concentrations was seen. Cr3+ however, did not influence the expression of TGF-β but strongly inhibited the mineralization in vitro.

Our data imply that the inhibitory effect of metal ions such as Co and Cr ions on the transcription of the bone regulating cytokines TGF-β1-3 and on bone forming activity may influence bone homeostasis.

Acknowledgments: Funded by Stiftung Endoprothetik (S01/16).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6218
Rheumatoid arthritis - etiology, pathogenesis and animal models

AB0076 PERIODONTAL MICROBIA IN EGYPTIAN RA PATIENTS AND THEIR RELATION TO SERUM AND GINGIVAL ANTIBODIES AND OTHER DISEASE PARAMETERS

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Background: A possible infectious trigger for RA is suspected at the gingival site. Emerging data implicates the microbiome in RA pathogenesis. Mucosal sites representative of the initial site of autoimmune generation. If validated, these findings could lead to the discovery of potential biomarkers and therapeutic approaches in the pre-clinical and clinical phases of RA.

Objectives: To determine the causes causing periodontitis in Egyptian RA patients and their relation to serum and gingival ACPA level and other disease parameters.

Methods: This study was carried out on 100 Egyptian RA patients fulfilling the 2010 ACR/EULAR classification criteria for RA and of less than 5 years disease duration, recruited from Rheumatology Unit, outpatient clinic and Dental clinic at Alexandria Main University Hospital. RA disease activity was assessed by applying DAS28 and functional state of the patients was assessed by applying HAQ score. Dental examination, serum RF, and ACPA in serum and GCF were done for all patients. X-ray of both hands to detect erosions and severity of the disease.

Results: Of the 100 patient, 66 patient had periodontitis, for them, GCF culture was performed and Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia were found in 60.8%, 15.2%, and 30.3% of RA patients with periodontitis respectively. Gingival ACPA was detected in the 3 studied organisms, being of significant higher level with P. gingivalis than P. intermedia (p=0.047).

Conclusions: P. gingivalis is the most prevalent periodontal microbiota in Egyptian RA patients with periodontitis, that associated with significant higher level of gingival ACPA. None of the detected organisms correlated with the degree of RA activity or other disease parameters, apart from significantly higher CRP level with A. actinomycetemcomitans.

References:
TRANSDERMAL DELIVERY OF METHOTREXATE IN RHEUMATOID ARTHRITIS: ARE WE DEEP ENOUGH?


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Background: Methotrexate (MTX), at low doses, is the first choice in the management of rheumatoid arthritis (RA). Despite its effectiveness, the probability of its discontinuation remains high due to adverse effects such as gastrointestinal intolerance, bone marrow toxicity as well as hepatotoxicity with conventional oral and parenteral therapy. Transdermal delivery epitomizes an attractive alternative for drugs with systemic toxicities. The physicochemical characteristics of MTX such as high polarity and ionisation at physiologic pH make the development of its topical route of delivery challenging. A new class of liposomes termed deformable or flexible liposomes have been reported to possess the virtue of stratum corneum and increase the depth of skin penetration.3

Methods: MTX entrapped in deformable liposomes were prepared and characterised for particle size (PS) and entrapment efficiency (EE). They were incorporated into a hydroxyethyl cellulose gel base and evaluated for ex vivo skin permeation. Optimized liposomal gel was applied on the back of rats (3x4 cm area) and evaluated for its acute dermal toxicity and pharmacokinetics. Biodistribution was studied by topical application of 125I labelled MTX incorporated liposomal gel in rats. Furthermore the efficacy of optimized gel was determined in collagen induced arthritis (CIA) in rats.

Results: The optimized deformable liposomes exhibited a small PS of 110±20 nm and EE 35–50% while the liposomal gel showed a transdermal flux of 17.37±1.5 μg/cm²/hr in ex vivo skin permeation study. Topical application of liposomal gel demonstrated no clinical abnormalities or pathological changes at the site of application in rats. Pharmacokinetic data indicated sustained systemic delivery of MTX from its liposomal gel up to 48 hours. The gel resulted in lower accumulation of MTX in liver, kidneys and gut in contrast to intravenous administration of plain125I labelled MTX solution. In the CIA model, topical MTX gel administration demonstrated significant reduction in hind paw swelling and arthritic score, also validated by histological and radiographic examination of ankle joints and lowering of serum levels of cytokines like TNF-α and IL-6 in comparison to disease control group.

Conclusions: The liposomal gel delivered dermal safety, sustained systemic delivery of MTX at its lower distribution to the organs of toxicity which may enable alleviating systemic side effects. Moreover, topical gel of MTX holds appreciable therapeutic efficacy in the CIA model.

References:

AB0079 TRANSDERMAL DELIVERY OF METHOTREXATE IN RHEUMATOID ARTHRITIS: ARE WE DEEP ENOUGH?

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8113

AB0080 MODULATION OF IMMUNOGLOBULIN G2B BINDING IN COMBINATION OF METHOTREXATE AND ACONITE IN A COLLAGEN-INDUCED ARTHRITIS SETTING

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Background: Our previous study showed synergistic responses in TNF-alpha (TNF-α) and interleukin-6 with the combination of methotrexate (MTX) and aconite. Modulation of those cytokines has not been applied to rheumatoid arthritis (RA)-mimicked in vivo models.

Objectives: To translate in vitro effects of MTX, aconite, and MTX/aconite combination towards anti-arthritic responses in vivo, we investigated arthritis index (AI), histopathologic changes, and levels of TNF-α, immunoglobulin G (IgG) 2a and 2b in a collagen-induced arthritis (CIA) setting.

Methods: CIA was induced in male DBA/Claitlnd mouse group by intradermal injection of bovine collagen type II and Complete Freund’s Adjuvant. In Day21, a bovine collagen type II and Incomplete Freund’s Adjuvant were given for booster infection. The mice of arthritis onset were treated daily throughout Day49 with per oral administration of pre-investigated ratios of three to one; MTX (3 mg/kg), aconite (Aconibal®, 1 mg/kg), and MTX/aconite (3 and 1 mg/kg) combination. The AIs were evaluated every week. Histological changes, levels of TNF-α as well as IgG2a and IgG2b in blood using ELISA kit were evaluated at finals. Repeat measure and one-way ANOVA were analysed using SPSS (ver. 18.00.0, Windows; SPSS Inc., Chicago, IL, USA) to evaluate inter-period and inter-group differences with Tukey’s post-hoc tests.

Results: The CIA phenotypes adequately presented through three groups’ AI reductions (CIA vs. MTX, aconite, or MTX/aconite; p<0.001, for three). There were differences of AI scores in aconite group from MTX one in week 4, 5, and 6 (MTX vs. aconite; p=0.038, p=0.001, p=0.042, respectively). Synergistic responses of AI were not shown any of three groups. The recoveries of synovial tissues were observed in MTX and MTX/aconite groups. The levels of TNF-α were not changed (aconite vs. MTX/aconite; p=0.200 and MTX vs. MTX/aconite; p=0.700). MTX group showed IgG2a reduction (CIA vs. MTX; p<0.001). Interestingly, MTX/aconite combination and aconite group slightly downregulated IgG2b levels as 89.845.6% and 90.5±7.4%, respectively (CIA vs. MTX/aconite; p=0.001 and CIA vs. aconite; p=0.010).

Conclusions: Synergistic in vitro effects of MTX and aconite combination brought...
the partial in vivo phenotypic responses: Acomite showed more Al changes than MTX did in 4, 5, and 6 weeks. However, we found the presence of partial FcγRIIB affinity of binding modulation that MTX/Acomite could enhance preventing monocye/macrophage activation via immune complex in RA pathogenesis, as was other benefits of the combination except direct synergies.

References:


Acknowledgements: This study was supported by KIOM (Grant # K17252). The commercial product was donated by the virtue of HanPoong Pharmaceutical Company.

Disclosure of Interest: None declared

AB0081

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Background: Protein citrullination is catalysed by peptidylarginine deiminase (PAD) and plays an important pathogenic role in anti-citrullinated protein antibody (ACPA)-positive rheumatoid arthritis (RA), and possibly in other inflammatory diseases. PAD activity is dependent on calcium and reducing conditions.

Objectives: To determine the ability of H2O2 and reactive oxygen species (ROS) induced by the nitricamide adenine dinucleotide phosphate (NADPH) oxidase to regulate PAD activity.

Methods: Activity of recombinant human (rh) PAD2, rhPAD4 and PAD4 released from phorbol 12-myristate 13-acetate (PMA)-stimulated leucocytes was measured using an in-house PAD activity assay detecting citrullination of fibrinogen. PAD2 released from cells was measured using a luminex-based assay. The NADPH oxidase inhibitor diphenyleneiodonium (DPI) was used to inhibit ROS production in cells.

Results: At concentrations above 40 μM, H2O2 inhibited the catalytic activity of reduced rhPAD2 and rhPAD4. The inhibitory effect increased with increasing H2O2 concentration, reaching complete abrogation at 600 μM. PMA-stimulated leucocytes showed markedly higher PAD activity following inhibition of ROS formation with DPI. At a concentration of 10,000 μM, exogenously added H2O2 inhibited the catalytic activity of PAD released from PMA-stimulated leucocytes.

Conclusions: The ROS H2O2 directly inhibits enzymatic activity of PAD, and generation of ROS by NADPH oxidase down-regulates the activity of PAD released from stimulated leucocytes. This mechanism may play an important role in preventing hypercitrullination of proteins and thereby generation of self-antigens in RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3162

AB0082

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Background: Alkaline phosphatase (AP) functions as a gate-keeper of the innate immune system [1] by detoxifying inflammation triggering moieties (ITMs). As an eptophosphatase, AP thus acts extracellurally by dephosphorylating ITMs that originate and are released from endogenous sources, e.g. by converting ADP and ATP nucleotides into adenosine to establish a key signalling anti-inflammatory effect. Consequently, AP activity prevents the production of pro-inflammatory cytokines by activated leucocytes and their downstream effects. Due to its broad mechanism of action, AP may potentially serve as an attractive therapeutic moiety in chronic inflammation disorders, including rheumatoid arthritis (RA).

Objectives: To examine the anti-arthritic effects of prophylactic and therapeutic AP interventions in arthritic rats.

Methods: Wistar rats were immunized twice with methylated bovine serum albumin (mBSA), followed by local arthritis induction (intra-articular i.a.) mBSA injection with 3 repeated injections) in the right knee (arthritic knee) with the contralateral left knee serving as internal control [2]. Interventions were performed using 200 μg human recombinant placental AP, administered subcutaneously, either before i.a. mBSA injections (2x, every 3 days, 2 rats/group; prophylactic setting) or after arthritis induction (4x, every 3 days, 4 rats/group; therapeutic setting). AP treatment, ex vivo tissue sections, knees were dissected, cryo-processed, embedded in paraffin and paraffin-embedded. Knee sections were examined for synovial macrophage infiltration by immunohistochemistry with ED1 (CD68) and ED2 (CD163) macrophage specific antibodies. Results were compared with untreated arthritic rats and arthritic rats receiving MTX therapy (1 mg/kg, intraperitoneally, 4x, every 3 days, 4 rats/group).

Results: Prophylactic and therapeutic schedules of AP treatment were well tolerated and reduced knee swelling comparable with MTX treatment. Following AP prophylactic intervention, synovial macrophage infiltration in the arthritic setting was reduced 4-fold (ED1) and 6-fold (ED2) when compared with affected knees of untreated arthritic rats, approaching macrophage counts in contralateral (non-arthritic) knees of AP treated rats. Therapeutic AP interventions resulted in 3.5-fold lower synovial infiltration of both ED1 and ED2 macrophages in arthritic knees, comparable with effects of MTX treatment.

Conclusions: AP, both as prophylactic and as therapeutic intervention, demonstrated favourable anti-arthritic efficacy in a rat model of arthritis. These studies warrant further preclinical and clinical evaluation as a putative novel therapeutic entity for arthritis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4630

AB0083

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Background: The role of adipose tissue in RA pathogenesis has been acknowledged since the high frequency of dyslipidemia and insulin resistance in these patients. Leptin, a pleiotropic adipokine, has been associated with inflammation markers and articular damage in RA and the anti-citrullinated protein antibodies. Notwithstanding, these findings have not been consistent across different populations. These points towards that single nucleotide polymorphism (SNP) in leptin and its receptor might influence the participation of this adipokine in RA pathogenesis.

Objectives: To determine the association of the SNPs LEP -2548 G>A and LEPR +668 A>G with adiposity, metabolic and inflammation markers in RA patients.

Methods: We enrolled 116 patients with RA (ACR 1987) matched with 133 control subjects by age, gender, body mass index (BMI) and overweight/obesity. There was no difference in genotypes distribution of LEP -2548 G>A and LEPR +668 A>G were determined by PCR-RFLP using Hhal and MspI restriction enzymes. Results: There was no difference in genotypes distribution of LEP -2548 G>A and LEPR 668 A>G between RA and control. LEPR 668 A=G was associated with higher anti-CCP titers and disease activity score compared to LEPR 668A/A homozygotes, 4.2±1.7 vs. 3.46±1.2 P=0.012. LEPR -2548A allele was associated with younger age of RA diagnosis vs. G/G homozygotes, 35.8±11.5 vs. 41.8±13.9 years old (P =0.045). OR for diagnosis before 40 years old was 2.7 (95%CI 1.04 – 7.45).

Conclusions: LEP -2548 G:A is related with a younger age at diagnosis of RA and LEPR 668 A=G was associated with increased anti-CCP titers and disease activity. This suggests that there is an additive effect between chronic inflammation of RA and obesity were leptin may favor humoral immune response against citrullinated proteins and influence the severity of RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6729
AB0084 BREADTH OF BASELINE AUTOANTIBODY PROFILE AND TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Seropositive and seronegative rheumatoid arthritis (RA) are distinct disease entities with regard to pathophysiological mechanisms and disease outcomes. However, over the past years it has become clear that the autoantibody profile of seropositive RA is very diverse, involving multiple post-translational modifications and isotypes, and it seems unlikely that a single autoantibody will be informative for identifying groups at risk of poor treatment response. Instead of individual autoantibodies, we hypothesized that the breadth of seropositive patients’ profile may be the best reflection of the underlying immunopathology, and would be able to identify homogenous treatment response and inform treatment decisions.

Objectives: To investigate whether baseline autoantibody profile is associated with treatment response and the ability to taper off medication in RA patients.

Methods: All RA patients fulfilling the 2010 ACR/EULAR Criteria included in the IMPROVED study1 that were seropositive for routine clinical testing for anti-cyclic citrullinated peptide-2 (anti-CCP2 IgG), rheumatoid factor (RF IgM), or our in-house assay for anti-carbamylated protein antibodies (anti-CaP IgG) were selected (n=381). In baseline sera of these patients, we measured IgG, IgM, and IgA isotypes for each family (except IgG for RF) and reactivity against 4 citrullinated peptides (cit-vimentin 59–74, cit-fibronogen 36–52 and α–27–43, and cit-elosine 5–20). We investigated associations between autoantibody profile and 1) change in disease activity score (DAS)-44 over time and 2) sustained drug-free remission, defined as the ability to taper off medication and remain in remission for ≥1 year after achieving DAS44<1.6.

Results: The initial treatment response (mean ∆DAS 0–4 months) in seropositive patients with a broad autoantibody profile (7–8 isotypes present) was better than in those with fewer isotypes present (∆DAS 0–4 months of 7–8 isotypes vs 1–2, 3–4, and 5–6 isotypes, respectively: -2.2 vs -1.5 [p<0.001], -1.7 [p<0.04], and -1.8 [p<0.04]). In contrast, the presence of multiple autoantibodies was unfavorable regarding the long-term outcome of sustained drug-free remission.

Within seropositive disease, patients with more isotypes and more reactivities to citrullinated peptides significantly less often achieved sustained drug-free remission (SDFR) (Figure).

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3193

AB0085 INTERACTION OF HLA-SHARED EPITOPE (SE) AND SMOKING ON THE DEVELOPMENT OF ANTI-CCP POSITIVE RHEUMATOID ARTHRITIS IN GREEK POPULATION

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Background: Rheumatoid Arthritis (RA) is a complex, multifactorial autoimmune disease, whose etiopathogenesis involves genetic and environmental factors.

Objectives: The aim of the study was the assessment of the association of HLA-DRB1*SE in the presence/absence of anti-CCP autoimmunity in Greek patients with RA (smokers and non-smokers).

Methods: Eighty-three (83) RA patients (41 smokers, 42 have never smoked) were typed for HLA-DRB1* alleles by molecular techniques (PCR-SSOP and -SSP). In 62 out of 83 (74.7%) anti-ccp abs were detected by ELISA.

Results: In RA pts and in comparison to the controls, increased frequency of HLA-DRB1*01:01 (28.9% vs 6.8%, OR=4.4), 10.01 (16.9% vs 2.4%, OR=8.4), 04.04 (7.2% vs 2%, OR=1.8), 04.03 (7.2% vs 1%, OR=7.6) and 04.05 (15.7% vs 3.7%, OR=4.8), as well as decreased frequency of 04.02 (1.2% vs 2%, OR=0.6) and 04.03 (4.8% vs 6.8%, OR=0.7) were found. Among the RA patients, 77.1% possess 1SE vs 18.9% of controls (OR=14.4), whereas 10.8% possess 2SE vs 1% of controls (OR=11.8). In CCP (+) RA patients and in comparison to CCP (-) patients, we assessed the association of HLA-DRB1*01:01 (27.4% vs 14.3%, OR=2.3) and 10.01 (21% vs 4.8%, OR=5.3) was observed. Furthermore, 88.7% of CCP (+) carry 1SE vs 42.9% of CCP (-) patients (OR=10.5). CCP (+) smokers patients in comparison to CCP (+) non-smokers are presented with an increased frequency of DRB1*01:01 (41.9% vs 12.9%, OR=4.9). Among the CCP (+) smokers, 96.8% possess 1SE vs 80.6% of CCP (+) non-smokers (OR=7.2), whereas 12.9% possess 2SE vs 12.9% of CCP (+) non-smokers (OR=1).

Conclusions: a) An increased frequency of HLA-DRB1*01:01, 10.01, 04.05 alleles, as well as the protective role of 04.02, 04.03 alleles in Greek patients with RA were confirmed b) The presence of any SE, particularly *01:01 allele, strongly influences the production of anti-CCP abs and c) Interaction between smoking and any SE, particularly *01:01 allele, is associated with anti-CCP positive RA in Greek patients.

References:
[2] Voulgari PV, Tarassi K, Voulgari IP, Voulgari CA, Voulgari V, Voulgari PA. HLA-DRB1 alleles, as well as the protective role of *04:02, *04:03 alleles in Greek patients with RA were confirmed. c) Interaction between smoking and any SE, particularly *01:01 allele, is associated with anti-CCP positive RA in Greek patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5213

AB0086 PREVENTIVE EFFECTS OF ANGIOTENSIN 1-7 ON NEOANGIOGENESIS AND LEUKOCYTE TRAFFICKING INCREASE IN THE EARLY PHASES OF AN EXPERIMENTAL MODEL OF ANTIGEN INDUCED ARTHRITIS

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Background: Renin Angiotensin System (RAS) might be supposed to be involved in the early and late phases of development of synovitis, since data exist showing that Angiotensin (AT)-II contributes to the development of vascular damage under early inflammatory conditions (1, 2). Little is known about AT 1–7 functions, which is supposed to play counteracting actions vs AT II, under these conditions (2, 3).

Objectives: to evaluate if, in the early phases of an experimental model of arthritis, namely the antigen-induced arthritis (AIA), treatment with AT 1–7 could interfere with the synovial development of capillary vascular growth, and prevent leukocyte trafficking activation, in vivo, either at synovial and at mesenteric post-capillary venules.

Methods: in compliance with European (86/609/EEC) and the Italian (D.L.116/92) ethics committees, 2 groups each of 8 male (240–270 gr) Wistar rats were randomly chosen and treated respectively with sterile saline, or with AT 1–7 (576 μg/kg/day), during the time of immunization with methylated serum bovine albumin (mBSA). Arthritis was induced by intracutaneous administration of mBSA (0.1mg in 100ml sterile saline) into the right knee of each animal, after previous immunization to mBSA emulsified in complete Freund’s adjuvant. The left knee, injected with the same volume of sterile saline, served as a control. Then, aortic arch, artheritic joint, the count of capillary branches, and the number of fluorescently-labelled leukocytes, showing transient or stable adhesion to the endothelial microvascular layer (EL), were assessed by using an in vivo videomicroscopy technique.

Results: synovial branchung vessels with diameter >20μm were not modified after AIA induction, while microvessels having diameter less than 20 μm were significantly increased. After 2 and 5 days, AT 1–7 reduced the number of neo expressed <20μm diameter vessels (Day2: 3.7±3.4 vs 7.7±5.05, p=ns; Day5: 12.7±6.9 vs 21.0±7.3, p<0.05; both significantly greater than control joints). Transient and stable adhesion to EL showed to be partially reduced 2 days after AIA induction and significantly reduced after 5 days (Day5, transient=12.5±6.2 vs 26.0±9.0, p<0.05; stable=27.0±8.3 vs 41.7±10.6, p<0.05; both significantly greater than control joints). Comparable results were found when analysing the number of leukocytes adhering to mesenteric EL.

Conclusions: we suggest that AT 1–7 could play an immune modulating role in the early phase of synovitis with possible prevention of further inflammatory and secondary structural tissue alterations. These data further support the hypothesis that mechanisms leading to synovial AT-II activation have a detrimental role in the development of arthritis.
SONIC HEDGEHOG PROMOTES FIBROBLAST-LIKE SYNCOYOCITES PROLIFERATION VIA MODULATING THE MAPK/ERK SIGNALING PATHWAY IN RHEUMATOID ARTHRITIS

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Background: The Sonic hedgehog (Shh) signaling pathway has been reported to be activated in synovium of RA patients and RA-FLS in vitro [1]. Further, Shh signaling plays an important role in RA-FLS proliferation [2]. As for the extracellular signal-regulated kinase (ERK), is a member of mitogen-activated protein kinase (MAPK) [3], which has been reported to be involved in proliferation of RA-FLS [4]. However, the role of MAPK/ERK signaling pathway in the proliferation of RA-FLS modulating by Shh is unclear.

Objectives: To study the effect of MAPK/ERK signaling pathway on cell proliferation modulated by Sonic hedgehog (Shh) signaling in fibroblast-like synoviocytes isolated from patients with active rheumatoid arthritis (RA-FLS).

Methods: The RA-FLS were primarily cultured by the explant culture, and then were treated with Shh agonist Purmorphamine, inhibitor Cyclopamine or MAPK/ERK signaling pathway inhibitor U0126, respectively. Western blots was used to examine the phosphorylation level of ERK 1/2 (p-ERK1/2), which was the critical protein of MAPK/ERK signaling. The cell proliferation activity was detected using cell proliferation and cytotoxicity kit-8 (CCK8), and the cell proliferation rate was detected using a flow cytometry.

Results: Compared with the control group, Purmorphamine transiently increased p-ERK1/2 protein at the concentration of 1 μM, and the peak activations of p-ERK1/2 took place at 15min (P < 0.01). Cyclopamine and U0126 decreased the expression of p-ERK1/2 protein (P < 0.01). After the RA-FLS treated with Purmorphamine (1 μM) for 48 hours, the cell proliferation activity was 114±54% and the percentage of S phase cells was 8.39±0.60%, significantly higher than those of the control group 100±5% (P < 0.01) and 3.29±0.69% (P < 0.01). After treated with Cyclopamine (10 μM) for 48 hours, the cell proliferation activity of RA-FLS was 89±1% (P < 0.05) and the percentage of S phase cells was 1.53±0.22% (P < 0.05). When co-treated with purmorphamine (1 μM) and U0126 (10 μM), the cells proliferative activity was 89% (P < 0.05) and the percentage of S phase cells was 1.70±0.25% (P < 0.05).

Conclusions: Shh might promote proliferation of RA-FLS via modulating MAPK/ERK signaling, subsequently contributing to hyperlasia of synovium and ultimately leading to RA disease.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4027

AB0089 ELECTROKINETIC CHARACTERISTICS OF SYNCOYOCITES (SC) AND THE LEVEL OF ANTIOXIDANT PROTECTION IN RHEUMATOID ARTHRITIS (RA)

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Background: Known role of SC in the pathogenesis of RA. It is impossible, however, at this level of knowledge to ascertain all the mechanisms for their involvement in the pathological process. Reduced tissue antioxidant protection can affect cellular metabolism, and as might be expected, through the mechanism of autophagy inducing mitochondrial and lysosomal degradation, facilitating cell membrane depolarization.

Objectives: The aim of this work was to study the electrophoretic mobility (EM) of SC of RA patients and its relationship with the activity of antioxidant enzymes: Cu-Zn superoxide dismutase (Cu-Zn SOD), Se-glutathione peroxidase (Se-GPO) and catalase (CAT).

Methods: SC has been obtained from the knee of 7 patients with RA and 5 donors. SC isolated by standard methods. EM of SC determined by the automatic microscope. Se level in SC determined by atomic absorption spectrometry. The activity of the antioxidant enzymes was determined by classical methods of enzymology.

Results: A significant depolarization of the RA SC, resulting in a reduction of their EM as compared to the normal level of the average in 4 times. Activity of antioxidant enzymes is dramatically reduced by a significant decrease of Se concentrations in SF (150 μg/l normally up to 80 μg/l in RA), which is particularly reflected in the activity of Se GPO (note that SC can be up to 100 Se-containing proteins).

Table 1

<table>
<thead>
<tr>
<th>EM of SC (nV/sec)</th>
<th>Cu-Zn SOD (Units/mg of protein)</th>
<th>Se-GPO (Units/mg of protein)</th>
<th>CAT (μmol/min/mg of protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal SF</td>
<td>1.62±10^9</td>
<td>23.4±0.8</td>
<td>1.3±0.3</td>
</tr>
<tr>
<td>RA SF</td>
<td>3.73±10^9</td>
<td>11.7±0.4</td>
<td>0.2±0.0</td>
</tr>
</tbody>
</table>

Conclusions: We can assume that aggravated by RA catabolic processes that caused the dysfunction of the lysosomal and mitochondrial structures (autophagy), consistently shoot antioxidant protection of SC and cause depolarization and the decrease in electrophoretic mobility of these cells.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4111
AB0000
N-ACETYL-L-CYSTEINE (NAC) CONTROLS OSTEOCLASTOGENESIS THROUGH REGULATING TH17 DIFFERENTIATION AND RANKL PRODUCTION IN RHEUMATOID ARTHRITIS
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Background: NAC is a thiol antioxidant produced by the body and serves as a precursor of glutathione synthesis. In rheumatoid arthritis (RA), oxidative stress is an important mechanism causing destructive proliferative synovitis. NAC is a thiolic antioxidant produced by the body and serves as a precursor of glutathione synthesis. In rheumatoid arthritis (RA), oxidative stress is an important mechanism causing destructive proliferative synovitis.

Objectives: This study aimed to determine the regulatory role of N-Acetyl-L-cysteine (NAC), an antioxidant, in IL-17-induced osteoclast differentiation in RA.

Methods: After RA synovial fibroblasts were stimulated by IL-17, the expression and production of RANKL were determined by real-time PCR and ELISA. Human peripheral blood monocytes were cultured with M-CSF, IL-17, RANKL, and/or various concentrations of NAC, followed by counting of the cells for trarrrate-resistant acid phosphatase activity to determine osteoclast formation. Osteoclastogenesis was also determined after cocultures of IL-17-stimulated RA synovial fibroblasts, Th17 cells and various concentrations of NAC with monocytes. After human peripheral CD4⁺ T cells were cultured with NAC under Th17 condition, IL-17, IFN-γ, IL-4, Foxp3, RANKL and IL-2 expression and production was determined by flow cytometry or ELISA.

Results: When RA synovial fibroblasts were stimulated by IL-17, IL-17 stimulated the production of RANKL, and NAC reduced the IL-17-induced RANKL production in a dose-dependent manner. NAC decreased IL-17-activated phosphorylation of mTOR, JNK and IkB. When human peripheral blood CD14⁺ monocytes were cultured with M-CSF and IL-17 or RANKL, osteoclasts were differentiated, and NAC reduced the osteoclastogenesis. After human peripheral CD4⁺ T cells were co-cultured with IL-17-pretreated RA synovial fibroblasts or Th17 cells, NAC reduced their osteoclastogenesis. Under Th17 polarization condition, NAC decreased Th17 cell differentiation and IL-17 and RANKL production.

Conclusions: NAC inhibits the IL-17-induced RANKL production in RA synovial fibroblasts and reduces osteoclast differentiation. NAC also reduced Th17 polarization. NAC could be a supplementary therapeutic option for inflammatory and bony destructive processes in RA.

Acknowledgements: This research was supported by a grant of the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology, Republic of Korea (NRF-2014R1A2A2A01007223) and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HI13C1704).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1506

AB0001
SURFACE PHENOTYPE OF CIRCULATING PLATELETS IS ALTERED IN PATIENTS WITH RHEUMATOID ARTHRITIS
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Background: Rheumatoid arthritis (RA) is a connective tissue disease and characterized with multiple synovitis. However, pathogenesis of RA and systemic characteristic of RA is still under the investigation (1). Platelets distribute systemically through blood circulation and classically contribute to hemostasis physiologically (2). On the other hand, platelets can contribute to disease process by producing humoral factors such as cytokines or growth factors (3). Also, platelets have surface molecules not only associated with hemostasis but with other functional properties. Thus, these molecules can trigger the activation of other cells by cell-to-cell contact (4).

Objectives: To examine the association between characteristics of phenotype of circulating platelets based on the expression of surface molecules and clinical characteristics of RA and to seek the possibility as novel biomarkers.

Methods: Eighty patients with RA were involved and 9 with scleroderma and 13 healthy controls were used as controls in this study. Surface expression of CD62P (P-selectin), membrane-bound TGF (transforming growth factor)-beta, CD147 (emmprin), CD142 (tissue factor) component, CD31 (platelet endothelial cell adhesion antigen) on CD62P+CD45+CD142+ platelets was examined using flow cytometry. Comparison between two groups was by non-parametric Mann-Whitney U-test. Clinical parameters at blood drawing were retrospectively obtained from clinical records, and correlation between proportion of platelet subsets and clinical parameters were examined.

Results: Proportion of CD62P+ activated platelets were higher in both RA and SSc compared to HC (P < 0.0005, P < 0.0002, respectively). Interestingly, CD147+ platelets were significantly higher in RA (P < 0.0004), whereas not only proportion of CD147+ platelets but that of TGF-beta+ platelets were higher in SSc compared to healthy controls (P < 0.0001, respectively). In patients with RA, proportion of CD147+ activated platelets was correlated with inflammatory markers such as CRP and ESR and markers for disease activity such as SDAI (P < 0.05, respectively) and these proportion were decreased after treatment (P < 0.03).

Conclusions: In patients with RA, proportion of CD62P⁺ and CD147⁺ platelets were increased compared to healthy controls. Furthermore, phenotype of platelets of RA was altered compared to SSc. Interestingly, proportion of CD62P⁺ platelet is associated with the inflammatory markers and disease activity of RA. These results suggest that platelets reflect disease process of RA and could be utilized as novel biomarkers.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4596

AB0002
EFFECT OF METHOTREXATE, LEFLUNOMIDE AND HYDROXYCHLOROQUINE ON THE INSULIN RESISTANCE AND OBESITY ASSOCIATED WITH RHEUMATOID ARTHRITIS: OBESE MOUSE MODELS OF RHEUMATOID ARTHRITIS

Background: Numerous studies have demonstrated the closely association between rheumatoid arthritis (RA) and metabolic complications such as obesity and insulin resistance. Thus, there is an urgent need for the use of therapies targeting both the activity of the disease and such metabolic disorders. Nowadays, the conventional treatment of RA consists of disease-modifying antirheumatic drugs (DMARDs) in monotherapy or combined. Yet, its negative/beneficial effect on the metabolic complications associated with cardiovascular disease prominent in RA patients is still unravelled.

Objectives: To analyze and compare the effects of methotrexate, leflunomide and hydroxychloroquine on the obesity and insulin resistance in an obese collagen-induced arthritis (CIA) mouse model.

Methods: CIA was developed in obese and lean mice. 55 C57Bl/6 mice (4–5 weeks) were used. Forty-one mice were fed with high fat diet (60%) until reaching 30g (obese) (OB). Groups of study: 5 non-diseased lean mice, 9 CIA lean mice, 5 non-diseased OB mice, 9 OB-CIA mice treated with leflunomide (10 mg/kg daily), 9 OB-CIA mice treated with methotrexate (3mg/kg three times/week) and 9 OB-CIA mice treated with hydroxychloroquine (60 mg/kg daily) for 15 days. Mice were weighted and the number of total inflamed digits was recorded daily. After treatment, before 72 hours of termination, glucose tolerance test (GTT) was performed. Buffy coat, plasma and metabolic tissues (gonadal and inguinal adipose tissue, skeletal muscle and liver) were collected.

Results: CIA obese mice developed the arthritis earlier and more severe (increased number of inflamed digits) compared with CIA lean mice. Regarding the progression of the disease, the three drugs significantly reduced the number of affected joints from the second day of treatment. However, after 15 days of treatment, the therapies more effectively reducing the generation of inflamed digits were hydroxychloroquine and methotrexate. The development of RA in both obese and lean mice did not have effect on the body weight. Among the therapies used, only the hydroxychloroquine significantly reduced the body weight after 11 days of treatment. Glucose tolerance test revealed that the area under the curve was markedly smaller in OB-CIA mice after treatment with hydroxychloroquine compared to other treatments and OB-CIA mice untreated, suggesting an improvement of insulin sensitivity. Analysis on the metabolic tissues of these mice is currently ongoing in order to completely elucidate the effect of these therapies in the metabolic state.

Conclusions: 1) Obesity accelerates the development and aggravates the outcome of the arthritis in CIA mice. 2) Among the three DMARDS administered, hydroxychloroquine promoted a beneficial effect on the metabolism of CIA obese mice, reducing body weight and improving the insulin sensitivity. These results suggest that hydroxychloroquine could be used as a valuable therapeutic strategy in RA patients to reduce the disease activity and ameliorate the metabolic complications associated.

Acknowledgements: Funded by PI2013–0191, ISCIII-FIS (CP15/00158), RD16/0012/0015 and Roche Pharma S.A

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4684
BLYS AND APRIL OVEREXPRESSION IN EARLY RHEUMATOID ARTHRITIS: ASSOCIATION WITH B CELLS AND MYELOID SUBSETS

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Background: studies on B cell-mediated autoimmune diseases highlight the relevance of the B Lymphocyte Stimulator (BLyS) and A Proliferation-Inducing Ligand (APRIL), but emerging evidence points to an interaction with cell lineages other than B subsets. Although disturbances in the B cell compartment underlie the early stages of rheumatoid arthritis (RA), this phenomenon is poorly understood.

Objectives: to investigate the cellular populations responsible of BLyS expression and their association with the soluble forms of BLyS, APRIL and its receptor TACI (Transmembrane Activator and CALM Interactor) in early RA and to evaluate the changes in these parameters upon TNFα-blockade.

Methods: membrane BLyS (mBLyS) expression was assessed on B cells, monocytes (MØ), myeloid (mDC) and plasmacytoid (pDC) dendritic cells and neutrophils (NØ) by flow cytometry in fresh blood samples from 37 RA patients ([DAS28 score (mean±SD): 4.84±1.44, disease duration (mean range): 1.26 (0–11) years, 23 (62.1%) RF+, 19 (51.3%) ACPA+, 19 untreated] and 31 healthy controls (HC). A subgroup of 13 biologic-naïve RA patients was prospectively followed for three months upon TNFα-blockade. Serum levels of soluble BLyS (sBLyS), APRIL (sAPRIL) and TACI (sTACI) were quantified by immunoassays.

Results: mBLyS expression was increased on B cells (p=0.002), MØ (p<0.001), pDC (p<0.001) and NØ (p=0.014) in RA patients. Higher sBLyS (p=0.018) and sAPRIL (p=0.001) serum levels were found in RA, whereas those of sTACI were not different compared to HC (p=0.460). Serum sAPRIL levels paralleled those of sTACI (r=0.325, p=0.040), and mBLyS expression on B cells (r=0.463, p=0.009), MØ (r=0.521, p=0.003), mDC (r=0.438, p=0.014) and NØ (r=0.509, p=0.009) in HC but not in RA patients. Serum levels of sTACI were negatively associated with DAS28 score (r=-0.272, p=0.006) in RA. However, sAPRIL was associated with mBLyS expression on MØ in patients with longer disease duration (>3 months) (r=0.779, p<0.001), but not with mBLyS expression on B cells (r=0.245, p=0.361). In the whole RA group, TNFα serum levels were found to be correlated with sAPRIL (r=0.499, p<0.001) and sBLyS (r=0.362, p=0.013). Similarly, IFNα and sAPRIL were positively associated (r=0.423, p<0.001). TNFα-blockade was associated with decreasing mBLyS expression on B cells, MØ, mDC and NØ (all p<0.050), and a slight increase in sTACI (p=0.044). Higher levels of mBLyS on MØ and mDC at baseline were associated with a poor clinical response upon TNFα-blockade (n=8; p=0.006 and p=0.010 compared to HC, respectively).

Conclusions: a role for B cell-activating factors in the pathogenesis of early RA is supported. B cells and myeloid populations (MØ, mDC and NØ) can account for the BLyS overexpression in RA, although important differences arise in their involvement. TNFα and IFNα are related to sBLyS and sAPRIL levels. An increased production of the soluble forms of BLyS and APRIL in addition to a less efficient feedback from their decay receptors may delineate its detrimental effect.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2687

BY INTRAVENOUS INFUSION MARKED BY GREEN FLUORESCENT PROTEIN TO REVEAL BONE MARROW MESENCHYMAL STEM CELLS' DISTRIBUTION AND DIFFERENTIATION OF COLLAGEN INDUCED ARTHRITIS RATS

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Background: Rheumatoid arthritis (RA) is a autoimmune disease, which is characterized by the osteoclasta or the high deformity rate of cartilage and bone. According to some materials, Mesenchymal stem cells (MSCs) were defined as the cell full of proliferation, differentiation capacity, and potential immune regulation. MSCs transplantation could be a appropriate-design pattern to the joint damaging from rheumatoid arthritis (RA). However, the repairing mechanism against osteoclasta of cartilage and bone is still unclear.

Objectives: This study used collagen induced arthritis (CIA) rats as animal model to explore MSCs’ tissue repairing mechanism.

Methods: We observed the ability of BMSCs differentiating into cartilage cells by toluidine blue staining in vitro; Then, BMSCs were labeled by the green fluorescent protein (GFP), infused into CIA through rats’ tail vein infusion. In different point time, the rat’s joints were made paraffin section, we observed the differentiation of GFP positive cells and the distribution of GFP-positive cells differentiated chondrocytes by immunohistochemically method.

Results: First, we found BMSCs in vitro can differentiate into cartilage cells under a certain-culture condition. Then, BMSCs were labeled by the green fluorescent protein (GFP), infused into CIA through rats’ tail vein infusion. In different point time, the rat’s joints were made paraffin section, which the GFP positive cells were observed in synovium and bone marrow tissues after transplantation on the 3th day, and in cartilage tissues on the 11th day, then increased in cartilage tissues on the 30th day, 42th day by laser scanning confocal microscope. Anti-type II collagen, GFP double positive cells were found in articular cartilages (especially damaged part) by Anti-II collagen immunofluorescence technology.
Conclusions: BMSCs were restricted to the joint injury or inflammatory site, differentiated into chondrocytes, and then participated in the cartilage repair.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3090

**AB0096 EFFICACY AND SAFETY OF ORAL ADMINISTRATION OF PURE CELASTROL IN AIA RATS**

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**Background:** Celastrol, a pentacyclic-triterpene isolated from Tripteris willordii roots, has shown great therapeutic potential for the treatment of several inflammatory diseases, including rheumatoid arthritis (RA). We have previously demonstrated that celastrol has significant anti-inflammatory and bone protective effects in the adjuvant-induced rat model of arthritis (AIA), when administered via intraperitoneal route. For further preclinical evaluation of celastrol as a candidate compound for RA treatment, an effective and safe oral administration is crucial.

**Objectives:** In this work we aimed to study the dose range for both therapeutic and toxic effects for oral administration of pure celastrol using the AIA rat model.

**Methods:** Celastrol (1, 2.5, 5, 7.5, 12.5 and 25 μg/g/day, N=5/group) was administrated orally in female AIA rats after 8 days of disease induction (therapeutic model) for a period of 14-days. A group of healthy (N=8) and non-treated (N=20) and 10 animals under tofacitinib treatment. Rats were monitored during 22 days after disease induction for the inflammatory score, ankle perimeter and body weight. Healthy non-arthritic rats were used as controls.

**Results:** Oral administration of pure celastrol at 2.5, 5 and 7.5 μg/g/day reduced the inflammatory score and ankle swelling, preserved articular joint structure with a reduction in synovial inflammatory infiltrates and proliferation, halted articular bone destruction, and diminished the number of synovial CD68+ macrophages (a biomarker of response to anti-arthritic treatment). This compound also reduced the number of osteoclasts and osteoblasts present in joints. Bone resorption and turnover was also reduced at both 5 and 7.5 μg/g/day, with a significant decrease in bone turnover markers in the levels of TRACP-5b, P1NP and CTX-1. Of note, no significant variation in body weight, evidence of nephro-, hepato- or cardiotoxic effects, nor alterations in bone metabolism, and/or with kinetics of its bone effects that might need longer exposure.

**Conclusions:** Our results clearly show that 2.5 μg/g/day is the lowest and 5 μg/g/day is the highest effective and safe oral doses of celastrol in the setting of AIA rat model. These findings suggest that while celastrol is potentially very effective to treat RA, it has a narrow therapeutic window.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2886

**AB0097 METHOTREXATE AND LOW DOSE PREDNISOLONE DOWNREGULATE OSTEOCLAST FUNCTION IN MONOCYTES FROM EARLY RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Rheumatoid arthritis (RA) is a systemic, immune mediated inflammatory disease that is associated with bone erosions and joint destruction. Methotrexate (MTX) slows bone damage but the mechanism by which it acts is still unknown.

**Objectives:** In this study we aimed to assess the effect of MTX and low dose prednisolone (MTX+P) on circulating osteoclast (OC) precursors and OC differentiation in RA patients.

**Results:** RA patients before and at least 6 months after MTX therapy were analyzed and compared with healthy donors. A blood sample was collected to assess receptor activator of NF-κB (RANK) ligand (RANKL) surface expression on circulating leukocytes and frequency and phenotype of monocyte subpopulations. Serum quantification of bone turnover markers and cytokines and in vitro OC differentiating assays were performed.

**Research question:** The number or RANKL+ neutrophils increased in RA patients when compared to healthy donors (p=0.006) and after treatment with MTX+P their count was reduced to healthy control numbers (p=0.0155). Classical activation markers of monocytes such as HLA-DR, CD86, CCR2 and CD11b, and also RANKL were increased in RA patients at baseline, comparing to control healthy donors. After MTX+P exposure, expression decreased to healthy control levels. Serum RANKL levels were increased at baseline comparing to healthy donors (p=0.0164) and normalized after therapy.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6935

**AB0098 EFFECTS OF TOFACITINIB IN EARLY ARTHRITIS BONE LOSS**

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**Background:** Rheumatoid arthritis (RA) causes immune mediated local and systemic bone damage.

**Objectives:** The main goal of this work was to analyze, how treatment intervention with tofacitinib prevents the early disturbances on bone structure and mechanics in adjuvant induced arthritis rat model. This is the first study to assess the impact of tofacitinib on the systemic bone effects of inflammation.

**Methods:** Fifty Wistar adjuvant-induced arthritis (AIA) rats were randomly housed in experimental groups, as follows: non-arthritis healthy group (N=20), arthritis non-treated (N=20) and 10 animals under tofacitinib treatment. Rats were monitored during 22 days after disease induction for the inflammatory score, ankle perimeter and body weight. Healthy non-arthritis rats were used as controls for comparison. After 22 days of disease progression rats were sacrificed and bone samples were collected for histology, micro-CT, 3-point bending and nonindentation analysis. Blood samples were also collected for bone turnover markers and systemic cytokine quantification.

**Results:** At tissue level, measured by nonindentation, tofacitinib increased bone cortical and trabecular hardness. However, micro-CT and 3-point bending tests revealed that tofacitinib did not revert the effects of arthritis on cortical and trabecular bone structure and on mechanical properties.

**Conclusions:** Possible reasons for these observations might be related with the mechanism of action of tofacitinib, which leads to direct interactions with bone metabolism, and/or with kinetics of its bone effects that might need longer exposure.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3491
AB0009 TAXOL ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY INHIBITING THE FORMATION OF MICROVESSELS

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Background: Angiogenesis is one of the critical features in rheumatoid arthritis (RA). Uncontrolled neovascularization could help the infiltration of inflammatory cells and lead to synovial hyperplasia and bone destruction further. Precious studies have demonstrated that the medicine taxol (PTX) has anti-angiogenesis effects.

Objectives: To evaluate the inhibitory effects of PTX on angiogenesis in a collagen-induced arthritis (CIA) mouse model.

Methods: A total of 50 mice were used to induce a CIA mouse model with collagen II (CII) and complete Freund’s adjuvant (CFA). Twenty-four with obvious arthritis syndrome were randomly divided into four groups: CIA model group, PTX 1.5 mg/kg group, PTX 1.0 mg/kg group, PTX 0.5 mg/kg group. In addition, 6 normal mice was regarded as the control group. PTX was administered by intraperitoneal injection in the PTX treatment groups 8 times every other day. Arthritis index scores, tissue pathology scores after HE staining and synovium macrophage density analysis after immunohistochemical (IHC) staining were performed. Immunohistochemistry and ELISA were used to detect the expression of vascular endothelial growth factor (VEGF) and hypoxia-inducible factor-α (HIF-1α). Additionally, the correlation between MVD and pathological scores, level of VEGF and HIF-1α in the synovium were also evaluated.

Results: After PTX treatment, the three intervention group arthritis index scores (1.33±0.52, 2.00±0.63, 3.33±1.03) declined when compared with the CIA group (5.67±1.03, p<0.001, p=0.016). The total histological scores in the three PTX treatment groups (2.50±0.6, 3.89±0.86, 3.98±0.66) were lower than those in the CIA group (7.67±0.79, p<0.001, p=0.007). Similarly, PTX significantly alleviated the scores for synovitis, pannus formation and bone destruction. Compared with the CIA group (110.32±6.06/mm²), the MVD of the three intervention groups decreased in dose-dependent manner (53.67±9.77/mm², 34.73±2.36/mm², 57.65±7.22/mm²; p<0.001, p=0.001, p=0.016). In addition, the expression of VEGF and HIF-1α in synovial tissues and serum level also decreased significantly after PTX treatment. Further analysis showed that MVD and pathological scores and levels of VEGF and HIF-1α in the synovium were positively correlated (r=0.921, r=0.944, r=0.889, r=0.969, r=0.933; r=0.001, respectively).

Conclusions: PTX may alleviate CIA by suppressing angiogenesis, providing new insights into the treatment of RA. VEGF and HIF-1α may be the target for PTX suppression of microvessel formation.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2515

AB0100 MTX COMBINED WITH CTX INHIBITED IL-6 INDUCED JAK2-STAT3 ACTIVATION AND THE INDUCTION OF P-GP IN PERIPHERAL BLOOD LYMPHOCYTES OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by irreversible joint destruction and disability. At present, the biggest challenge in the field of RA treatment is the emergence of multidrug resistance (MDR) in the application of disease-modifying anti-rheumatic drugs (DMARDs). The Multidrug resistance Related Protein and Multi Drug Resistance protein 1, also called P-glycoprotein can decreases the intracellular concentration of different drugs. Moreover, cytokines play an increasingly important role in the expression regulation mechanisms of P-gp, especially inflammatory cytokines IL-6. Previous research showed that interleukin-6 up-regulates P-gp in peripheral blood lymphocytes via the JAK2-STAT3 pathway in RA patients. Through more than ten-years’ clinical research, we observed that the therapeutic cycle alliance of MTX and CTX overcome MDR in RA patients? This study will give the answer.

Objectives: To Clarify whether the therapeutic alliance of MTX and 4-hydroperoxyxycyclophosphamide (4-HC) suppress expression and mRNA of P-gp in peripheral blood lymphocytes of RA through JAK2-STAT3 pathway.

Methods: RA patients without any DMARDs and biologic therapy (n=15) were enrolled. P-gp expression level was detected by Flow Cytometry. P-gp mRNA of peripheral blood lymphocytes and the intracellular signaling pathway mediating the effects of MTX and 4-HC on IL-6-stimulated JAK2-STAT3 activation was assessed by RT-PCR.

Results: Compared with blank control group, IL-6 induced P-gp, JAK2 and STAT3 expression levels increased significantly (P<0.05). Compared with IL-6 group, P-gp, JAK2 and STAT3 expression levels of 4-HC group and low MTX+4-HC group both decreased (P<0.05). the expression levels of P-gp, JAK2 and STAT3 in low MTX group, middle MTX group and high MTX group were lower than IL-6 group, but there was no statistically significant differences (P>0.05).

Conclusions: Our data indicated that MTX combined with CTX significantly inhibited IL-6 induced JAK2-STAT3 activation, as well as the induction of P-gp. inhibition of IL-6-mediated multidrug resistance signaling pathways by the alliance of MTX and CTX may represents a new reversing drug-resistance therapeutic strategy for RA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5019

AB0101 NEW MUTATED PEPTIDYLARGININE DEIMINASE FROM PORPHYROMONAS GINGIVALIS A TARGET IN EARLY RA CITRULLINATES MAJOR RA-AUTOANTIGENS

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Objectives: Previous reports showed that peptidylarginine deiminase (PPAD) form Porphyromonas gingivalis (Pg) is not able to citrullinate proteins internaly. New mutated PPAD (mPPAD) from Pg. involved in periodontal disease (PD) clonout of Pg. strain was characterized and analyzed for its reactivity in sera from patients with systemic autoimmune diseases

Methods: We cloned a new enzymatically active recombinant mutated PPAD from Pg. mPPAD mutations and citrullination sites were analyzed by DNA sequencing and/or protein mass spectrometry. Autoantibod indiction of enzymatic activity and human autoantigen protein citrullination was investigated by 2D-Elektrophoresis, Mass spectromobol analysis and ELISA. Furthermore we tested anti-mPPAD/ict-mPPAD with human sera (n=83) from early RA before and after onset of RA (n=30), established RA (n=32), SLE (n=16) and healthy blood donors (n=15) in ELISA assays. To study a potential impact on the RA mouse model (CAIA), mPPAD-containing vesicles from Pg. were injected by intraperitoneal injection (IP).

Results: Recombinant mPPAD lacks 43 amino acids at the N-terminus and exhibits so far two new amino acid mutations (amino acid position 73 (F-L) and 447 (E-V)). We were able to demonstrate, mPPAD is enzymatically active over a huge pH-range (3–10) and autoantibodies at amino acid position 63 the arginine to citrulline. Moreover mPPAD citrullinates major autoantigons in RA (Fibrinogen, Vimentin and hNRNP-A/B1) which are detectable by RA patient sera and specific anti-citrulline monoclonal antibodies. mPPAD citrullinates HeLa-protein extracts and these specific citrullinated proteins are recognized by RA patient sera. Anti-citrullinated mPPAD antibodies were detected in 41% (n=32) of patients with RA but not in SLE (n=16) and control sera (n=15). In a RA follow-up study (n=30), we detected nearly similar antibody-sensitivities for citrullinated mPPAD before and after onset of RA (13/20%), Only a minority (7%) of RA patients show higher mPPAD antibody levels after RA diagnosis. In the Collagen antibody-induced arthritis (CAIA) RA mouse model mPPAD containing Pg vesicles when injected IP showed a TL2-dependent protective anti-inflammatory effect like Pg. LPS and Lipomannan.

Conclusions: Pg. infection and RA disease diagnosis occurs on different time points and Pg. infection induces a TL2-dependent protective anti-inflammatory effect. We show the first time that mPPAD can citrullinate major human autoantigens internally and their immunologically and diagnostic relevance.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3651
AB1002

IMPAIRMENT OF GRANZYME B-PRODUCING REGULATORY B CELLS EXACERBATED RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a common and complex autoimmune disease characterized by chronic inflammation and cartilage/bone damage involving numerous cells, such as T cells, B cells, chondrocytes, fibroblasts [1]. B cells had long been well-demonstrated to participate in the development of RA [2]. B cells producing specific antibody and inducing T cell activation, impaired immunosuppressive function of B cells further emphasized their roles in RA recently [2].

Objectives: To investigate whether B cells could produce granzyme B and the potential role in the pathogenesis of Rheumatoid arthritis (RA).

Methods: To reveal the expression of granzyme B in B cells, flow cytometry, PCR and Eilispot were performed. The role of IL-21 and anti-BCR stimulation on granzyme B expression was assessed by in vitro stimulation assay. CD4+ T cell-B cell co-culture in the presence of granzyme B neutralizing antibody was performed to demonstrate the function of these cells. Then the levels of granzyme B in B cells between RA patients, OA patients as well as HCs were compared. Next, the correlation analysis between granzyme B-producing B cells and clinical features in RA patients was performed. Finally, the frequencies of granzyme B-producing B cells in RA patients before and after therapy were also evaluated using flow cytometry.

Results: B cells could spontaneously produce granzyme B, which could be perpetuated by IL-21 and anti-BCR stimulation. The frequencies of Th1 and Th17 cells were significantly elevated under the condition of granzyme B blockade when granzyme B was neutralized in CD4+ T cell-B cell co-culture. In RA patients, but not OA patients and HCs, the frequencies of granzyme-B producing Bregs decreased significantly, which was functionally impaired and negatively correlated with disease activity score 28. Moreover, after effective clinical therapy, the frequencies could recover to normal levels.

Conclusions: B cells exert the regulatory functions via granzyme B production. Under RA circumstance, these granzyme B-producing Bregs were impaired and contributed to the disease progression.

References:

AB1003

ANTI-INFLAMMATORY AND IMMUNOMODULATORY EFFECTS BY HUMAN UMBILICAL CORD MENSECHYMAL STEM CELL DERIVED MICROVESICLES IN RATS WITH COLLAGEN INDUCED COLLAGEN EROSION

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Background: Immunologic deranging and persistent inflammation is closely associated with the arising and developing of rheumatoid arthritis (RA). Increasing investigators demonstrated microvesicles (MVs) derived from mesenchymal stem cell (MSC-MVs) might simulate immune regulation and tissue repair of the parental cells. However, the immunotherapeutic potential of MVs in RA remains unknown.

Objectives: We investigated the therapeutic effects of MSC-MVs in RA model collagen induced arthritis (CIA) rats.

Methods: We tested the therapeutic effects of MSC-MVs on CIA rats, levels of T helper 17 (Th17), regulatory T cell, and cytokines related, as well as specific transcriptional regulation factor Foxp3 and ROR-γ T analysis was performed.

Results: Here, we show that MSC-MVs administration effectively improve arthritis symptoms, inhibit synovial hyperplasia, thus delaying the progression to inflammation, bone destruction, as effective as their original cells, exerting arthralprotective effects. MSC-MVs treating inhibited the proliferation of T cell, accelerated the apoptosis. MSC-MVs treating reducing proinflammatory cell Th17, cytokines IL-17, while a decline in the level of an-inflammatory cell Treg, cytokines TGF-β.

In the spleen and ankle joint of CIA rats, MSC-MVs treating increasing the expression level of Foxp3 and coinciding with the ROR-γ T suppressed, which, the enhanced therapeutic effects correlated with the increase of dosage in a certain range.

Conclusions: MSC-MVs showed anti-inflammatory and immunomodulatory activities on CIA rats, suggesting a new and feasible strategy for protection against RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2269

AB1004

ALTERATIONS OF SPLICOSOME COMPONENTS IN LEUKOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS INFLUENCE THEIR AUTOIMMUNE AND INFLAMMATORY PROFILE, AND THE DEVELOPMENT OF CARDIOVASCULAR DISEASE

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Background: A significant percentage of genetic and inflammatory diseases derive from splicing alterations. Therefore, the understanding of what modifications in splicosome determine an alternative splicing and its association with the development of such pathologies is of critical importance.

Objectives: To study the alterations present in the splicosome machinery of patients with rheumatoid arthritis (RA), its influence on the development and activity of the disease and their atherothrombotic profile.

Methods: An array of selected components of the major- (n=12) and minor-splicosome (n=4) and associated splicing factors (n=28) was developed, and their expression levels were measured in splicosome fluidic methodology, in purified leukocytes from 14 RA patients and 14 healthy donors (HD). In parallel, an extensive clinical and serological evaluation was performed. Carotid intima media thickness (CIMT) was used as atherosclerosis marker. Endothelial activity was monitored by laser-doppler flowmetry, and pro-inflammatory and oxidative stress markers were quantified. Association of these splicing components with clinical and analytical features were investigated.

Results: A significant alteration in various components of splicosome and splicing factors was found in all the leukocytes subtypes from RA patients vs HD. Interestingly, we found a specific altered profile of splicing factors and splicosome components when compared monocytes (CA150, PRPS, SRM160, U2AF1, RNU4atc, PTB81, RAVER1, RBM17, SFR54, SFR510), lymphocytes (RNU12, RNU4, RNU6, PRPB, MAGOCH, NOVA1, SRSF3) and neutrophils (SNR111, RNU6, SC5B, RBM3).

Altered levels of various splicosome elements in monocytes were associated with the presence of atheromatous plaques, while in neutrophils were found related to radiological involvement. In lymphocytes, the alteration of these components were linked to the positivity for Rheumatoid Factor and anti-CCP antibodies, indicating that modifications in the splicosome machinery could contribute to the increase in the production and assembly of autoantibodies, inducing autoantibody production.

Correlation studies showed a significant relationship between altered levels of various splicosome components in different leukocyte subtypes and high disease activity (DAS, HAQ), increased expression of proinflammatory mediators (CRF, TF, TNF, IL-8, TLR4) and oxidative stress markers (peroxides, GPX, SOD) as well as with parameters associated with insulin resistance.

Conclusions: These results reveal that there is a significant alteration of splicosome components in RA patients that could be associated with the development and activity of this autoimmune condition, and influence mechanisms that drive the development of cardiovascular disease. Studies in progress will help to clarify the physiological implications of these findings, which could constitute novel diagnostic biomarkers, as well as new therapeutic tools for the treatment of RA.

Acknowledgements: Funded by CTS7940, and ISCIII (PI15/01333, CP15/00158, and RIER RD16/0012/0015).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3462

AB1005

DOXYCYCLINE AND DEXAMETHASONE-INDUCED REPROGRAMMING OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN A MODEL OF ARTHRITIS WITH THE SYSTEMIC MANIFESTATIONS IN WISTAR RATS

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Background: The systemic juvenile idiopathic arthritis (sJIA) is a problem with high social significance all over the world. Targeted cell reprogramming becomes one of the most important lines for modern medicine and can be regarded as

 Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4907
EFFECT OF SERUM CYTOKINES ON COLLAGEN INDUCED ARTHRITIS RATS AFTER INTRA-ARTICULAR INJECTION OF OZONE

Objectives: To observe the effects of intra-articular ozone injection on the contents of tumor necrosis factor-α (TNF-α), Interleukin-6 (IL-6), IL-17A and vascular endothelial growth factor (VEGF) in the serum of rats with collagen-induced arthritis (CIA) and to explore the therapeutic mechanism of ozone treatment.

Methods: Thirty-two Wistar rats were randomized into 4 groups, including ozone group (O 3 group), Ca blank group (Ca blank group), Doxy group (Doxy group) and DEXA-group (DEXA-group). The rats were divided into 3 equal groups and an additional subcutaneous injection was performed as follows: Doxy-group − doxycycline (50 mg/kg, Saratov, Russia), DEXA-group − dexamethasone (4 mg/kg, KRKA, Slovenia), control group − 0.9% sodium chloride solution (Belarus).

Conclusions: Intra-articular injection of 40 μg/ml ozone can attenuate synovitis in rats with CIA, the mechanism of which may involve the inhibition of TNF-α, IL-6 and VEGF in the serum.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3447

AB0107 THE MODULATION OF MACROPHAGE POLARIZATION BY SIRT1 MAYBE NEW TARGET THERAPY IN RHEUMATOID ARTHRITIS


Background: The polarization of macrophages was the expressed to M1/M2 phenotype by various stimuli or environment signals. The M1 macrophage was the pro-inflammatory phenotype and was key effector cells in the immune response of rheumatoid arthritis (RA). So, M1 macrophage influenced the inflammation of RA synovial membrane and joint destruction in RA, whereas M2 macrophage was anti-inflammatory phenotype and could down-regulate the production of proinflammatory cytokines in RA. The SIRT1 attenuated the RA inflammation via down-regulation of NF-κB signaling. However, the effect of SIRT1 on macrophages polarization remained unclear.

Objectives: We aimed to check out that activated SIRT1 modulated macrophages polarization into M1 phenotype and controlled the inflammation of RA.

Methods: Monocytes from synovial fluid of RA patients, bone marrow-derived monocytes (BMDCs) from mice were studied. monocytes were cultured with M-CSF for 7days to differentiate into M0 macrophages (monocyte-derived mature macrophages M0 phenotype); M0 macrophages were incubated with LPS and IFN-γ to obtain M1 macrophages. M1 macrophages were incubated with M-CSF for 7days to differentiate into M2 macrophages (M2 phenotype). The polarization of macrophages was expressed by M1/M2 ratio.

Conclusions: SIRT1 modifies macrophages polarization and inhibits the inflammation of RA synovial membrane and joint destruction in RA. SIRT1 may be a new target to treat RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3996

AB0106 EFFECT OF SERUM CYTOKINES ON COLLAGEN INDUCED ARTHRITIS RATS AFTER INTRA-ARTICULAR INJECTION OF OZONE

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Background: Ozone is a new treatment method, study confirmed that the ozone intra-articular injection can reduce the level of TNF-α in rat synovial TNF-α, a synovial tissue, the regulation of rat apoptosis inhibiting gene Bcl-2 decreased expression, thereby promoting apoptosis of synovial cells. However, there are few reports on the effects of ozone on the inflammatory cytokines such as serum TNF-α in the pathogenesis of RA.

Objectives: To investigate the effects of intra-articular ozone injection on the contents of tumor necrosis factor-α (TNF-α), Interleukin-6 (IL-6), IL-17A and vascular endothelial growth factor (VEGF) in the serum of rats with collagen-induced arthritis (CIA) and to explore the therapeutic mechanism of ozone treatment.

Methods: Thirty-two Wistar rats were randomized into 4 groups, including ozone group (O 3 group), Ca blank group (Ca blank group), Doxy group (Doxy group) and DEXA-group (DEXA-group). The rats were divided into 3 equal groups and an additional subcutaneous injection was performed as follows: Doxy-group − doxycycline (50 mg/kg, Saratov, Russia), DEXA-group − dexamethasone (4 mg/kg, KRKA, Slovenia), control group − 0.9% sodium chloride solution (Belarus).

Conclusions: Intra-articular injection of 40 μg/ml ozone can attenuate synovitis in rats with CIA, the mechanism of which may involve the inhibition of TNF-α, IL-6 and VEGF in the serum.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3447
DECREASED EXPRESSION OF PTPN22 GENE IN PATIENTS WITH RHEUMATOID ARTHRITIS CARRYING THE RISK ALLELE OF PTPN22 RS2488457 POLYMORPHISM

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J. González-Vela1, T. Pina1, G. Ocejo-Vinyals3, J. Irure-Ventura3, R. Blanco1,
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Background: Mutations in the protein tyrosine phosphatase non-receptor 22 (PTPN22) gene are associated with numerous connective tissue and autoimmune diseases [1]. In particular, PTPN22 has been recognized as the main non-HLA genetic risk factor involved in rheumatoid arthritis (RA) susceptibility [2]. Moreover, it has been suggested that PTPN22 modulation may influence on inflammatory processes associated with RA [3,4].

Objectives: To determine if PTPN22 (rs2476601, rs33996649 and rs2488457) polymorphisms, associated with RA, may influence on PTPN22 expression in RA patients compared to healthy controls. Moreover, the association between PTPN22 expression in patients with RA and their clinical characteristics was studied.

Methods: PTPN22 messenger RNA (mRNA) expression was quantified by quantitative real-time PCR in peripheral blood samples from 42 RA patients and 24 healthy controls. PTPN22 rs2476601 (G→A), PTPN22 rs33996649 (C→T), and PTPN22 rs2488457 (C→G) single-nucleotide polymorphisms (SNP) were genotyped by TaqMan SNP genotyping assays. Differences in PTPN22 expression between patients and controls were analyzed by Student’s t test, according to their genotype. Correlation coefficients were also assessed between PTPN22 expression in RA patients and their clinical characteristics.

Results: A significant down-regulation of PTPN22 expression in RA patients carrying PTPN22 rs2488457 risk allele (G) compared to controls was observed (relative mean values of PTPN22 mRNA levels ± standard deviation: 2.93±0.76 vs 4.33±0.63, p=0.0004). Furthermore, an inverse relationship between PTPN22 expression and disease duration (r=0.38, p=0.03) was found. These results were adjusted by sex, age at time of study and cardiovascular risk factors.

Conclusions: Our study shows for the first time that the risk allele of PTPN22 rs2488457 polymorphism influences on the down-regulation of PTPN22 in patients with RA. This result suggests a transcriptional suppression of PTPN22 gene in RA, which in turn may play an important role in disease diagnosis and progression.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2646

AB0108

AB0109 AUTOPHAGY INHIBITOR REGULATES APOPTOSIS AND PROLIFERATION OF SYNOVIAL FIBROBLASTS THROUGH THE INHIBITION OF PI3K/AKT PATHWAY IN COLLAGEN-INDUCED ARTHRITIS RAT MODEL

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Background: Mounting studies have illustrated an important role of autophagy in various diseases, but few studies have reported its contribution to rheumatoid arthritis (RA) and the underlying mechanism is largely unknown.

Objectives: This study aimed to investigate whether autophagy inhibitors could regulate apoptosis and proliferation through PI3K/AKT pathway in RA.

Methods: RA animal model was established by collagen induction. General observations and degree of joint swelling were observed. Inflammatory response, cell survival related factor and apoptosis were also detected in synovial fibroblasts. In addition, cultured rheumatoid arthritis fibroblast-like synoviocytes (RA-FLS) were subjected to TNF-α treatment in vitro, and TNF-α induced cell apoptosis, synovial cell proliferation and apoptosis were detected. Moreover, cell cycle and cytokine secretion protein, along with the above parameters, were analyzed.

Results: Results from the animal model showed that autophagy inhibitors could attenuate inflammatory reaction and synovial hyperplasia, while promoted synovial fibroblasts apoptosis. Meanwhile, inhibition of autophagy promoted cell apoptosis and reversed cell proliferation in vitro, also blocked cell in the G2/M arrest, and reduced the S phase cells. Furthermore, inhibition of PI3K/AKT pathway reversed TNF-α mediated autophagy and cytokine secretion.

Conclusions: Autophagy inhibitors could mitigate inflammation response, inhibiting RA-FLS cell proliferation while promoting cell apoptosis by PI3K/AKT pathway.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5839

AB0109

EVALUATION OF THE EFFECT OF CHUANTENTONGBI DECOCTION ON DBA / 1 MICE CIA MODEL

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Background: DBA/1 mouse (H2q type) CIA model as a mature model of rheumatoid arthritis is widely used in pharmacology and pharmacodynamics research[1]. Chinese medicine treatment of rheumatoid arthritis has accumulated rich experience. The study of Tripterygium glycosides treatment of rheumatoid arthritis had good effect[2]. ChuanTengTongBi decoction is also the effective prescription commonly used for the treatment of rheumatoid arthritis.

Objectives: To investigate the pathological damage degree of DBA/1 mouse CIA model and the effects of different doses of ChuanTengTongBi decoction on the CIA model mice.

Methods: The mice were divided into normal group, model group, leflunomide group (3.11mg/kg/d), low-dose of ChuanTengTongBi group (0.44g/ml/d), medium-dose group (0.88g/ml/d) and high-dose group (1.76g/ml/d).

Results: The arthritis index (AI) was evaluated every week to determine whether the model was successful. We defined AI score ≤ 4 as successful model (AI score

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2044
standard:0. No swelling;1. Slight redness and swelling;2. Moderate redness and swelling of ankle; 3. Severe redness and swelling of the entire paw; 4. Maximally inflamed limb with involvement of multiple joints (p<0.05%). Day 28–42, hind foot redness and swelling of the mouse continued to develop and extended to the forefoot. Compared with the normal group, incidence of CIA model group reached 100%. Day 49, compared with the model group by joint scores, medium-dose group, high-dose group and leflunomide group have significant differences on CIA model (p<0.01). Compared with the Leflunomide group, low-dose group, medium-dose group and high-dose group have no obvious difference (p>0.05). Compared with the low-dose group, medium-dose group and high-dose group have no difference (p>0.05).

Table 1. Joint scores (mean ± SD)

<table>
<thead>
<tr>
<th>groups</th>
<th>28d</th>
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<th>42d</th>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>b</td>
<td>8.05±1.62</td>
<td>12.40±2.10</td>
<td>14.68±1.77</td>
<td>12.33±1.68</td>
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<tr>
<td>c</td>
<td>8.66±0.14</td>
<td>11.99±0.23</td>
<td>12.10±0.23*</td>
<td>11.30±0.22**</td>
</tr>
<tr>
<td>d</td>
<td>7.90±0.34</td>
<td>11.40±0.18</td>
<td>12.80±0.22**</td>
<td>12.00±0.13</td>
</tr>
<tr>
<td>e</td>
<td>7.45±0.23</td>
<td>10.90±0.13*</td>
<td>10.40±0.44*</td>
<td>10.60±0.36*</td>
</tr>
<tr>
<td>f</td>
<td>8.80±0.24</td>
<td>10.60±0.30*</td>
<td>11.30±0.22**</td>
<td>8.80±0.55**</td>
</tr>
</tbody>
</table>

a. Blank group. b. Model group. c. Leflunomide group. d. Low-dose group. e. Medium-dose group. f. High-dose group. Compared with the model group, *p<0.05, **p<0.01.

Conclusions: CIA model has a high morbidity, long duration, macroscopic pathological manifestation and irreversible ankle joint deformation, which is consistent with the progress of human RA disease and pathological damage. Medium-dose of ChuanTengTongBi decoction, high-dose and leflunomide group had inhibitory effect on the progress of arthritis, and the effect of high-dose was better than that of leflunomide group.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3396

AB0111  CADIUM NANOPARTICLES CITRULLINATE INTRACELLULAR CYTOKERATINS: CADMIUM POTENTIALLY LINKS RHEUMATOID ARTHRITIS TO SMOKING AND NUMEROUS WORKING CLASS OCCUPATIONS

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Background: Smoking has emerged as a consistent risk factor for ACPA positive RA, although the specific constituents of cigarette smoke that induce citrullination are unknown. It has been hypothesised that cadmium triggers RA as its inhalation risks various well established risk factors for RA such as smoking (the most important environmental source of cadmium) and numerous working class occupations [1].

Objectives: To determine whether the cadmium-derived materials induce intracellular citrullination.

Methods: Human A549 lung epithelial cells were exposed to cadmium in ionic and particulate form represented by cadmium chloride and cadmium oxide, respectively, and their combinations with ultrafine carbon black (uCB) nanoparticles produced following high temperature combustion, imitating cigarette burning. Protein citrullination in cell lysates was analysed by SDS-PAGE electrophoresis with western blotting and verified by immunofluorescence staining and confocal microscopy. Target citrullinated proteins were identified by proteomic analysis.

Results: Cytotoxicity studies demonstrated that cadmium compounds were toxic to the cells. Based on the results of cytotoxicity measurements, all the materials utilised in the experiments were subsequently applied to the cells in sub-toxic concentrations. Cadmium oxide, uCB and its combination with cadmium chloride and cadmium oxide after high temperature combustion induced citrullination of multiple proteins in cultured human lung epithelial cells of A549 cell line, as demonstrated by SDS-SDS-PAGE electrophoresis and western blotting. This phenomenon develops via a peptidylargininedeiminase-dependent mechanism, as demonstrated in our previous studies [2]. The majority of citrullinated proteins were represented by the bands corresponding to the molecular weights between 55 and 72 kDa, and several less abundant bands at the level of ~25 kDa and over 130 kDa. Acidic cytokeratin of type I (9, 10) and basic/neutral cytokeratins type II (1, 2, 5, 6, 6A, 6B and 77) were identified as major intracellular citrullination targets. Immunofluorescent staining demonstrated that the citrullinated proteins were localised both in the cytoplasm and nuclei of cells exposed to cadmium particles, similar to the distribution patterns observed in cells exposed to uCB.

Conclusions: Cadmium nanoparticle exposure facilitates post-translational citrullination of proteins.

Spondyloarthritis - etiology, pathogenesis and animal models

AB0112  INTERFERON-REGULATED GENES (IRG) SIGNATURES DIFFERENTIATE GROUPS OF AS PATIENTS AND ARE ASSOCIATED WITH ANTI-TNF RESPONSE: PILOT DATA

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Background: Ankylosing Spondylitis (AS) is a chronic inflammatory arthritis characterised by sacroiliac/lumbar spinal inflammation and extra-articular manifestations. Currently, TNF inhibitors (TNFi) are licensed for treatment-refractory AS; however, many patients do not respond to treatment and there is no way to predict Response/Non-Response (R/NR). The expression of several Interferon (IFN) signaling related genes (IRG) are associated with inflammatory diseases, including AS. Furthermore, an IRG expression signature has been used to predict treatment response in phase-Ia trials in systemic lupus erythematosus (1), demonstrating the feasibility of the use of IRG signatures as biomarkers in routine clinical practice.

Objectives: To explore whether IRG signatures differentiate groups of AS patients, and can be associated with response to TNFi in AS.

Methods: Twenty-six week-0 peripheral blood mononuclear cell (PBMC) samples...
from AS patients participating in a previously reported in-house clinical trial [infliximab (IFX), n=15 vs. placebo (P), n=11] (2) were selected from our tissue bank. R/NR was defined as a ≥1.1 point reduction in AS Disease Activity Score (ASDAS) at week-30, or a reduction in the number of sacroiliac/vertebral MRI lesions. Expression of 96 IRG was quantified from PBMCs using custom TaqMan assays and analysed using unsupervised hierarchical clustering, Chi-Squared, and Mann-Whitney U tests.

Results: A total of 11 patients were clinical responders [IFX=7; P=4/11]. At week-0, patients clustered into 2 groups (C1/C2) based on expression of 14 IRG. Clinical/demographic characteristics were not significantly different between C1/C2 and groups were not biased for treatment (C1, IFX=8; P=4, C2, IFX=7; P=7, p≤0.735). Improvement in ASDAS was weakly associated with C2 (C2, R=8/14, C1, R=7/12, p=0.098). Looking at IFX treated patients only (n=15), 2 cluster groups were observed (T1/T2) driven by 12 IRG. T2 was associated with a reduction in MRI lesions (T2 R=6/7, T1 R=3/8, p≤0.057). Finally, paired week-0 and week-22 samples from 10 IFX-treated patients were analysed and clustered in 2 groups (H1/H2). Changes in IRG signature following treatment were observed towards segregating pre- and post- IFX treatment samples (H1, 6/8 week-0; H2, 8/12 week-22 p≤0.7).

Conclusions: This pilot study suggests a possible association between IRG and response to IFX treatment in AS. These results now require assessment in a larger cohort in order to determine statistical and possible clinical significance, and to refine the signature further to construct potential predictive algorithms.

References:


Acknowledgements: The authors would like to thank the George Drecler Foundation and BTCure EU/IMI for funding this project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4471

AB0114 THE RELATIONSHIP OF POLYMORPHISMS OF ANTXR2 GENE EFFECTS OF ANTI-IL17A BLOCKADE WITH SECUKINUMAB ON SYSTEMIC AND LOCAL IMMUNE RESPONSES: A MECHANISM-OF-ACTION STUDY IN PERIPHERAL SPONDYLOARTHRITIS

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Background: IL-17A blockade is an effective therapy for ankylosing spondylitis (AS) and psoriatic arthritis (PsA), the two prototypical forms of spondyloarthritis (SpA). How IL-17A blockade affects the systemic and local immune responses in SpA patients with peripheral disease (pSpA) is unknown.

Methods: 20 active pSpA patients were included in a 12wk open-label trial followed by 2yrs non-investigational extension. All patients received secukinumab 300mg/wk from baseline to wk4 and then every 4wks. Clinical response was measured 4wkly. TruCulture tubes with SEB and zymosan were drawn at baseline, day3, and wk12. Synovial biopsies were obtained by needle arthroscopy at baseline and wk12, analyzed by immunohistochemistry (IHC) and qPCR.

Results: The 20 pSpA patients consisted of 13 PsA, 3 undifferentiated SpA, 2 AS, 1 reactive arthritis, and 1 inflammatory bowel disease associated pSpA. There were no SEAs in the 12wk core study. However, two SEAs occurred in the extension of the study: tosilsitis (suspected to be related to study drug) and myocardial infarction (non related), both fully recovered. Secukinumab induced a rapid and highly significant improvement in SJC (Baseline: 2.5 [IQR1–4] vs wk12: 0.5 [IQR0–1]–p=0.001), TJC (6 [2–8] to 0.5 [0–3]–p=0.001), VASglobal (46 [28–65] to 13 [6–24]–p=0.001). 18/20 patients reached EULAR DAS response at wk12 (10 good and 8 moderate responders). This was paralleled by significant improvements in other activity outcomes such as BASDAI (53 [25–63] to 20 [9–30]–p=0.001) and PASI (5,7 [4,5–7,1] vs 0,6 [0,1–1,8]–p=0.001). Systemic inflammatory response revealed a decrease in CRP (3.85 [1.55–16.6] to 2 [1,15–3.63]–p=0.001) and ESR (16 [6–35] to 6 [2.8–16.3]–p=0.001), which was associated with decreased production of MMP-3, a validated biomarker of inflammation in pSpA, by peripheral blood cells in the TruCulture system (see figure). With exception of a decrease in IL-17A, the TruCulture system did not reveal any impact of secukinumab on the capacity of peripheral blood cells to produce a broad panel of cytokines and chemokines upon stimulation. In contrast with this preserved systemic immune response, IHC confirmed the positive impact of secukinumab on peripheral disease (pSpA).

Conclusions: Secukinumab has a profound beneficial clinical and biological impact on pSpA. Further systemic immune analysis will delineate which inflammatory pathways are blocked by secukinumab in the diseased target tissue.

References:


Disclosure of Interest: L. Van Mens: None declared, M. van de Sande Speakers
M. Castelino 1,2, M. Tutino2, J. Moat3, U.Z. Ijaz4, R. Parslew5, A. Al-Sharqi 5, R.B. Warren6, C. Quince7, P. Ho1, M. Upton 8, S. Eyre 2, A. Barton 1,2.
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Background: Psoriatic arthritis (PsA) is a complex inflammatory condition with both genetic and environmental risk factors contributing to disease. A potential environmental risk factor, known to modify the immune system, is the intestinal microbiota. In PsA there is evidence of intestinal inflammation [1,2] and recently dysbiosis of the gut microbiota has been reported in treatment naïve PsA patients [3]. However, there is no information on the temporal stability of the microbiota over time in established PsA on treatment compared to matched PsC controls.

Objectives: To explore the temporal stability of gut microbiota composition and reveal associations with PsA compared to PsC while on stable on treatment with methotrexate.

Methods: Patients with PsA and PsC were recruited to the study if they had been on a stable dose of methotrexate for 6 months. Bacterial DNA was extracted and the V3-V4 hypervariable region of the 16S rRNA was amplified and sequenced on MiSeq. The resultant data was analysed using a bespoke bioinformatics pipeline and taxa were assigned using the Ribosomal Database Project classifier according to the SILVA119 database. The Wilcoxon rank sum test was used to assess alpha diversity indices, while permanova testing using Bray Curtis distance and DESeq2 values corrected for false-discovery rate (FDR) were used to compare beta diversity indices after removing low abundance (<0.5%) Operational Taxonomic Units (OTU). The ALDEx2 analysis package was used to assess effect size.

Results: Stool samples were available from 9 PsA (n=13) and 6 PsC (n=12) individuals. Second stool samples were also obtained from the PsA (n=5) and PsC (n=4) groups. No significant difference in the alpha diversity indices was observed between PsA and PsC. The beta diversity index showed no significant difference between the two conditions using permovana test. However, using the DESeq2-FDR analysis, 8 OTUs were identified which had significantly (p<0.01) different abundances in PsA compared to PsC. The taxa (Lachnospiraceae & Ruminococcaceae) predominately belonged to the Firmicutes phylum, family Lachnospiraceae and Actinobacteria phylum, family Bifidobacteriaceae. The significant OTUs with DESeq2 had an effect size <1 using ALDEx2 but the BH p-value was not significant (p<0.01), which may be due to the small sample size. There were no significant differences in the diversity measures over time.

Conclusions: These results suggest that a gut enterotype with predominant Firmicutes/Actinobacteria composition is associated with stable/well controlled disease and is stable over time. This requires replication in a larger cohort.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3404

Identifying the AS Patient at Risk: Is Aortic Root Dilatation Associated with HLA-B27?

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Background: Cardiac involvement is more common in Ankylosing Spondylitis (AS) patients with HLA-B27 genotype, especially aortic valvular regurgitation (AVR). AVR in AS is caused by aortic root dilatation and fibrotic thickening of the aortic cusps, both linked to inflammation. Inflammation of the aortic root might lead to a weakening in aortic wall strength and dilatation with AVR. Severe AVR can result in heart failure and is an indication for valve replacement or repair. The prevalence of AVR in AS is estimated at 14–18%, which is significantly higher compared to the general population. Therefore, some advocate regular echocardiographic screening of AS patients [1]. However, the cost-benefit of echocardiographic screening in AS is currently unknown and the precise effect of AS specific cardiac pathology on clinically overt cardiovascular morbidity and mortality remains to be elucidated. Hence, we should aim to identify a specific ‘at risk’ AS population that might benefit from routine echocardiographic monitoring.

Objectives: Primary: To assess the association between the aortic root diameter in HLA-B27 positive versus HLA-B27 negative patients.
Secondary: To assess the association between the aortic root diameter with disease duration and inflammation biomarkers.

Methods: We performed a cross-sectional study in AS patients between 50–75 years who were recruited from a large rheumatology outpatient clinic. Patients underwent echocardiography, with 2D, spectral and colour flow Doppler. The aortic root was measured at sinuses of Valsalva during diastole. The aortic root was measured at sinuses of Valsalva during diastole. The aortic root diameter/BSA and disease duration and inflammation biomarkers were assessed.

Results: 132 Consecutive AS patients were included with a mean age of 60.5 years, of whom 110 (83%) were HLA-B27 positive. The median aortic root diameter was corrected for body surface area (BSA). Correlation between aortic root diameter/BSA and disease duration and inflammation biomarkers were assessed.
AB0117 CADHERIN-11 MRNA EXPRESSION IS INCREASED IN THE PERIPHERAL BLOOD OF PATIENTS WITH ACTIVE SPONDYLARTHROPATHY: A PILOT STUDY


Background: Cadherin-11 is a key regulator of synovial architecture and has a central role in the formation of the rheumatoid pannus. Immunohistochemical studies have shown upregulation of cadherin-11 in the synovium of patients with severe psoriatic arthropathies (SpA), comparable to that in rheumatoid arthritis (RA), as well as in the intestinal tissue of patients with inflammatory bowel disease (IBD). Moreover, cadherin-11 mRNA transcripts have been identified in the peripheral blood of patients with RA and independently associated, among various disease characteristics, with the presence of active inflammation in multiple joints [1].

Objectives: To test the hypothesis that cadherin-11 mRNA transcripts are increased in the peripheral blood of patients with active SpA and search for possible associations with clinical features.

Methods: Fifteen patients with active SpA (SpA-FLS), aged between 21 and 71 years, 11 men, and 30 age- and gender-matched healthy controls were examined. Peripheral whole blood samples (3 ml) were subjected to cDNA synthesis and cadherin-11 mRNA expression was quantified by real-time PCR. Available cDNA from 33 IBD patients without axial or peripheral active arthritis served as disease controls and were studied in parallel.

Results: Cadherin-11 mRNA was detected in the peripheral blood of 9/15 (60%) patients with SpA versus 5/30 (17%) healthy controls and 10/33 (30%) patients with IBD (SpA vs healthy controls: p = 0.006, SpA vs IBD: p = 0.06). Notably, cadherin-11 mRNA was not assayed in patients with basal diseases like neoplasia or psoriasis present in 10 patients, but was detected with increased frequency among SpA patients with clinically active peripheral arthritis at the time of sampling (7 out of 10.70%) than the remaining patients (2 out of 5, 40%). Moreover, cadherin-11 positivity associated significantly with increased erythrocyte sedimentation rate in SpA but not in IBD.

Conclusions: Cadherin-11 mRNA is upregulated in the peripheral blood of patients with SpA and may correlate with “spreading” of inflammation in peripheral joints. Since an anti-cadherin-11 mAb is in early clinical development for RA, further studies in patients with inflammatory arthritis are warranted.

References:

Disclosure of Interest: N. Vlaichogiannis: None declared, P. Christopoulos: None declared, G. Bamias: None declared, K. Fragiadaki: None declared, M. Tektonidou: None declared, P. Sfikakis: Grant/research support from: Educational grant from Janssen.

DOI: 10.1136/annrheumdis-2017-eular.3650

AB0110 THE LYMPHATIC SYSTEM: A GATEKEEPER FOR MIGRATION OF T-CELLS TOWARDS SYNOVIAL JOINTS AND ENTESSES IN PSORIASIS

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Background: The factors underlying the transition of psoriasis (PsO) to psoriatic arthritis (PsA) are poorly understood. The lymphatic system may control the homing of disease-associated T-cells to skin and extra-cutaneous sites like synovial joints and entheses.

Objectives: To study the capacity of lymphatic endothelial cells (LEC) to regulate T-cell homing capabilities in PsA.

Methods: Human dermal LEC (1.0x10⁴), and fibroblast-like synoviocytes of a patient with PsA (PsA-FLS; 1.0x10⁵) were pre-incubated for 3 days with PsA synovial fluid (PsA-SF; 0/100% v/v) and co-cultured with 2.5x10⁴ allogeneic CD4+CD45RO+CD25- T-cells that were sorted from peripheral blood mononuclear cells of 3 donors (with or without stimulation with αCD3/αCD28). After 72 h, T-cell viability was analyzed by the Cytotoxicity. The CCR4+ (Th2) and Th17 (CCR4-/CXCR3-) T-cells were identified. We also looked at lymphocyte-associated antigen (CLA) expression (CLA-). CD11b-IL-22, and TNF protein levels were determined by ELISA. Statistical analysis included unpaired t-test (two-sided) for two-group comparison or one-way ANOVA with the Tukey-Kramer post hoc test for multi-group comparisons.

Results: Stimulation of CD4+CD45RO+ T-cells in co-culture with PsA-FLS skewed towards the CCR6+ subset Th17/Th22, which were predominantly Th17 cells. Th17 differentiation upon stimulation was suppressed in co-culture with LEC, even when LEC were pre-incubated with PsA-SF. T-cell stimulation in co-culture with PsA-FLS, as compared to PsA-SF, promoted the generation of the Th17 secreting receptor CD11b that was co-cultured with PsA-FLS. The proportional reduction in CLA expression on T-cells in the co-cultures with LEC pre-incubated with PsA-SF 20% was comparable to PsA-SF, however LEC conserved CLA expression on CD4+CD45RO T-cells at a higher level than PsA-FLS. The expression of Th22 phenotypic markers was affected by the LEC, with a trend towards lower IL-17A and higher IL-22 levels were observed in the co-cultures with LEC that were pretreated with PsA-SF 20%, as compared to the co-culture with PsA-FLS. No differences were seen for TNF protein levels.

Conclusions: LECs are directly involved in T-cell differentiation and homing capabilities, as well as suppression of Th17 differentiation upon stimulation, as compared to PsA-FLS. LEC, promoted Th22 generation, and conserved CLA expression in CCR6+ T-cells, even when LEC were preincubated with PsA-SF. Studies are underway to confirm that LECs from relevant biological tissues (e.g. synovium and lymph nodes) are critical for tissue-restricted T-cell migration to skin and synovial membranes in PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3560
protein 1 (CHD1L1, also known as YKL-40) were validated with ELISA. Further, pirfenidone decreased the secretion of both DKK1 (p=0.006) and OPG (p=0.02) by SpA FLs stimulated with TGFβ1, TNFα, and INFγ, while the concentration of RANKL was below the detection limit of the ELISA assay in all cultures. Finally, pirfenidone inhibited the deposition of hydroxyapatite by osteoblasts in a dose-dependent manner (p=0.0001). This inhibition was partly reversible when removing pirfenidone after the first week of the mineralization assay.

Conclusions: Taken together, pirfenidone inhibited SpA myofibroblast formation and activity and osteoblast mineralization. This encourages further research in anti-fibrotics as treatment of new bone formation in SpA.

Disclosure of Interest: None declared

AB0120 ACCELERATED OSTEOGENIC DIFFERENTIATION OF HUMAN BONE-DERIVED CELLS IN ANKYLOSING SPONDYLITIS
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Background: Ankylosing spondylitis (AS) is characterized by excessive bone formation with syndesmophytes, leading to bony ankylosis. The contribution of osteoblasts to the pathogenesis of ankylosis is poorly understood.

Objectives: The aim of this study was to determine molecular differences between disease controls (Ct) and AS bone-derived cells (BdCs) during osteogenic differentiation.

Methods: We confirmed osteoblastic differentiation of Ct and AS BdCs under osteogenic medium by observing morphological changes and measuring osteoblastic differentiation markers. Osteoblast differentiation was detected by alkaline phosphatase (ALP) staining and activity, and alizarin red S and hydroxyapatite staining. Osteoblast-specific markers were analyzed by qRT-PCR, immunoblotting, and immunostaining.

Results: Results showed that AS BdCs showed significantly increased osteoblast activity and differentiation capacity by regulating osteoblast-specific transcription factors and proteins compared to Ct BdCs. Active inflammation caused by adding AS serum accelerated bony ankylosis. Our study could provide useful basic data for understanding the molecular mechanism of ankylosis in AS.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4885

SLE, Sjögren’s and APS - etiology, pathogenesis and animal models

AB0121 DYSREGULATED CIRCULATING miRNA LEVELS ARE CHARACTERISTIC OF BOTH NON SJÖGREN’S SICCA AND PRIMARY SJÖGREN’S SYNDROME PATIENTS
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Background: MicroRNAs are small non-coding RNAs that play important regulatory roles in a variety of biological processes. They can regulate the post-transcriptional expression of target genes and play an important role in gene regulation. Specific microRNAs are stably present in serum and changes in their abundance are potentially disease-specific. Considering their important role in regulation of the immune system, we investigated circulating levels of miRNAs in patients with primary Sjögren’s syndrome (pSS) and those with non-Sjögren’s sicca (nSS) in relation to disease activity.

Objectives: To assess the expression of a large number of miRNAs in the serum of pSS and nSS patients as compared to healthy controls and to investigate their correlation with disease activity.

Methods: Two independent cohorts (discovery and validation) were established, consisting of a total of 37 pSS patients classified according to the 2002 criteria, 20 nSS patients that were not clinically considered to be pSS and did not meet the classification criteria, and 18 healthy controls (HC). Serum miRNAs were isolated and microRNA profiling was performed using the OpenArray platform in the discovery cohort. A selection of 10 miRNAs found to be differentially expressed between the groups was measured in the independent validation cohort using single TaqMan microRNA Assays.

Results: miRNA profiling revealed 10 miRNAs to be differentially expressed between the groups: 2 in pSS vs HC, 7 in nSS vs HC and 1 in both pSS and nSS vs HC. One miRNA was excluded from further analysis after technical validation by single TaqMan microRNA Assay. The other 9 miRNAs were measured in the validation cohort. Surprisingly, 2 miRNAs were validated to be increased in the nSS group as compared to HC (snRNA-U6 and miR-661). Using the discovery cohort of both cohorts of miRNAs, levels of miR-U6 and miR-661 was associated with serum Ig and C4 in the nSS group, but also in the pSS group. This prompted us to investigate miRNA expression in subgroups of pSS patients. snRNA-U6 and miR-661 levels are significantly increased compared to HC in pSS patients negative for autoantibodies. In autoantibody positive pSS patients, levels of miRNA-U6 and miR-661 are comparable to those found in HC and both miRNAs are significantly increased in autoantibody negative patients as compared to autoantibody positive pSS patients. In addition, their expression is strongly associated with leucocyte numbers in the autoantibody positive patients, but not in the negative patients.

Conclusions: Increased circulating levels of snRNA-U6 and miR-661 in patients with nSS and autoantibody negative pSS patients are associated with normal B cell activity and normal numbers of circulating leukocytes. Reduced miRNA levels in autoantibody positive pSS patients are associated with B cell hyperactivity and decreased leucocyte counts, which is possibly the result of immune cell migration to the inflammatory sites. Considering the important role of miRNAs in the control of immune cell activation, this work points to a significant role of miRNAs in pSS and nSS patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4961
AB0123

**T-CELL SURFACE GLYCOSYLATION PATTERN ALTERATIONS IN SLE – A PUTATIVE LINK TO GALECTIN-1-MEDIATED IMMUNOREGULATORY DEFICIENCY**

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**Background:** We have previously found that activated T-cells from systemic lupus erythematosus (SLE) patients express lower amount of intracellular galectin-1 (icGal-1) than those of healthy controls and are resistant to the apoptotic effect of extracellular galectin-1 (ecGal-1), an endogenous immunoregulatory lectin. We also demonstrated that the de novo synthesized icGal-1 level affects apoptosis of T-cells induced by ecGal-1, since low icGal-1 expression resulted in reduced sensitivity to ecGal-1 (Deák M et al). We have therefore proposed the defective ecGal-1 production to be an explanation to the insufficient regulatory effects of ecGal-1 in SLE. However, altered binding of ecGal-1 to T-cells due to changes in surface glycosylation may also regulate the apoptotic activity of ecGal-1.

**Objectives:** We have herein hypothesized that the cell-surface glycosylation pattern, and consequently, lectin-binding ability in SLE T-cells is altered, and that an abnormal expression of glycosylation enzymes may account for these changes.

**Methods:** In order to analyse the glycosylation pattern of cell surface glyco-proteins, lectin binding assays were performed using 5 different plant lectins and human recombinant Gal-1 on resting and activated T-cells from patients with active SLE (n=8) with multi-colour flow-cytometry, and were compared with 15 healthy controls. mRNA levels of 13 glycosylation enzymes involved in the development of N-glycan structures on T-cells were measured with qPCR, and were correlated with the specific lectin binding data.

**Results:** As compared with the resting state, the increase in Gal-1 binding during activation was significantly lower in SLE T-cells than in controls, and the level of Gal-1 binding maximum was significantly reduced in SLE activated T-cells than in controls. Binding maximum of plant lectins that recognise high complexity N-glycans was increased less in SLE T-cells than in controls during activation. In addition, mRNA level of sialyltransferase ST3GAL6 was increased and neuraminidase Neu1 was decreased in active SLE patients as compared to controls. The ST6GAL1/NEU1 ratio in SLE patients positively correlated with the SLEDAI activity index.

**Conclusions:** SLE T-cells show decreased complexity of N-glycan structures. Increased ST3GAL6 and decreased Neu1 expression result in an increased density of terminal sialic acids, and this may explain the impaired Gal-1 binding. In addition, to the previously described deficiency in icGal-1 expression upon activation, our present results suggest that an abnormal glycan complexity and a shift toward terminal sialylation provide a further mechanism of pathological T-cell activation and regulation of T-cell viability in SLE.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5657

AB0124

**SEROLOGICAL MEASURES OF B CELL FUNCTION IN PATIENTS WITH SLE; HOW ROBUST ARE THEY OVER TIME?**

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**Background:** In SLE the precise mechanisms whereby parent autoreactive B cells are generated and permitted to escape tolerance checkpoints, proliferate, persist and evade normal regulatory mechanisms remain poorly understood. Hypotheses include defective negative central selection, defective peripheral selection with enhanced germinal center activity as well as positive selection of B cells via autoantigen presentation or T-independent mechanisms. Biomarkers to identify possible breaches in tolerance checkpoints would allow more effective intervention. We have therefore measured relative levels of soluble sCD23 (released during B cell differentiation from naïve to memory B cell status) and the B cell activation factor, BAFF (survival factor and class-switch/differentiation promoter) in SLE sera to determine if relative levels of sCD23 and BAFF were of use as biomarkers to group patients based on B cell kinetics rather than clinical features. BAFF is often raised in SLE patients and can stimulate the aberrant differentiation of transitional B cells and of plasmablasts in vitro. Combining the 2 biomarkers could therefore indicate whether there was an increased expansion of naïve B cells, and whether BAFF was a possible driver/consequence of autoimmune disease in different patients.

**Objectives:** To determine whether relative levels of sCD23 and BAFF reflect disease activity or remain stable over time.

**Methods:** Stored SLE serum from patients who were Rituximab-naïve, had >5 samples available in the biobank over at least 6 months (n=38). Samples were analysed for levels of sCD23 and BAFF via ELISA. Wilcoxon matched-pairs signed rank test were used to compare serial values. Clinical details including BILAG scores were also collected for the available time points. If positive dsDNA at any time during the time period this was deemed positive. The latest BILAG was utilised and reviewed, a patient was deemed not to have system involvement if the final value was an “E” for that system.

**Results:** Sera from 38 SLE patients (32 female, 6 male) with mean age of first sample 42 (range: 25–72). Minimum interval between 1st and last sample was 101 weeks (range: 35–192 weeks). Patients were then sorted into clinical groups according to levels of these serum markers. Normal ranges defined as: sCD23 (1235–5023pg/ml), BAFF (584–1186pg/ml). Group I (n=9): – High (H) sCD23, Normal (N) BAFF; Group II (n=11) – H sCD23, H BAFF; Group III (n=17) – N sCD23, N BAFF; Group IV (n=2) – N sCD23, H BAFF. Figure 1 shows the p values generated from the Wilcoxon matched-pairs signed rank test for each time period demonstrating no significant change over time. Analysis of clinical data showed no differences in terms of organ involvement or anti-dsDNA Ab status.

**Conclusions:** Within a cohort of SLE patients, soluble CD23 and BAFF is stable over time despite variation in disease activity. Grouping patients based on sCD23 and BAFF profile may be useful in identifying distinct B cell maturation pathways reflecting underlying autoimmune pathways which vary between patients.

**Disclosure of Interest:** A. Hennessy: None declared, R. Marques: None declared, M. Leandro Consultant for: Roche UK, Roche Basel and Genentech, D. Isenberg: None declared, G. Cambridge: None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6790

AB0125

**BRAIN IMMUNOPATHOLOGY OF LUPUS-PRONE FC′RIIB−/−/YYA MICE - IMPLICATION TO THE INNATE IMMUNE RELATED MECHANISM OF NEUROPSYCHIATRIC SLE**

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**Background:** Neuropsychiatric SLE (NPSLE) is a common manifestation of SLE and problems such as cognitive impairment or depression are elusive. The importance of innate immune related inflammation in the pathomechanism of neurodegenerative or psychiatric diseases has been recognized recently, and the importance of innate immunity in the pathogenesis of NPSLE has also been suggested. Therefore, we investigated innate immune mechanism of NPSLE by using lupus prone mice.

**Objective:** This study is conducted to understand the brain immune pathology of lupus-prone Fc′RIIB−/−/YYA mice in which innate immune stimulation is potentiated by the finding of Toll-like receptor 7 activation in brains of lupus-prone mice.

**Methods:** Immune cell subsets and histopathology of brains were analyzed by flow cytometry and immunohistochemistry in Fc′RIIB−/−/YYA mice compared with congenic mice at around 16 week-old when glomerulonephritis had developed. For flow cytometric analysis, microglia, myeloid lineage cells and lymphocytes were defined by staining with CD11b and CD45. Subsets of those cells and their activation status were analyzed. For histopathological analysis, microglia, brain macrophages, astrocytes and lymphocytes were immunostained and expression of MHC class I and class II were also analyzed.

**Results:** Flow cytometric analysis revealed increase in the number of microglial cells (CD11b+ CD45+R) and myeloid lineage cells (CD11b+ CD45+R) in the brains of Fc′RIIB−/−/YYA mice compared with congenic Fc′RIIB−/−/YYA mice. Mean fluorescence intensity of MHC class I was increased in microglia and myeloid lineage cells in Fc′RIIB−/−/YYA mice. An increased percentage of CD3 positive cells and CD19 positive cells were observed and their expression of CD69, an activation marker, were increased in Fc′RIIB−/−/YYA mice. In histopathology, number of macrophages and microglia identified by Iba1 (ionized calcium binding adapter molecule 1) positive cells were increased in Fc′RIIB−/−/YYA mice. In areas where MHC class I and II were highly expressed on macrophages, the sensitivity to Fc′RIIB−/−/YYA mice showed no differences in terms of organ involvement or anti-dsDNA Ab status.
reaction of astrocytes and patchy increase of lymphocytes were also observed. Furthermore, MHC class I and class II were also highly expressed in the vascular endothelium in FcγRIIB⁻ Yaa mice.

**Conclusions:** Activation of myeloid lineage cells and reactive changes of glial cells and endothelial cells were observed in the central nervous system of lupus-prone FcγRIIB⁻ Yaa mice. These results imply the role of innate immune mechanisms in the pathology of NPSLE.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2849

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**AB0126 AUTOPHAGY AND SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE OF ATG14⁺, FOXP3⁺, AND CD56⁺ EXPRESSION ON T REGULATORY CELLS AND NK CELLS**

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**Background:** Autophagy is a highly conserved protein degradation pathway, essential for removing protein aggregates and misfolded proteins in healthy cells. Autophagy and autophagy-molecules expression have been implicated in autoimmune diseases. Systemic Lupus Erythematosus (SLE) is a prototype of autoimmune illness whose main characteristic is the loss of immune tolerance. Recent evidences suggest that autophagy, and autophagy-related proteins participate in SLE immune regulation. However, little is known about the SLE clinical significance of autophagy-related proteins, T regulatory, and NK cells.

**Objectives:** To evaluate the expression of ATG14⁺ (autophagy-related key regulator protein), FOXP3⁺, CD25⁺ T regulators, CD56⁺NK cells in active and inactive SLE patients.

**Methods:** The expression of ATG14⁺, FOXP3⁺, CD25⁺, and CD56⁺ were measured by flow cytometry, and expressed in percentages in T and NK cells.

**Results:** A total of 40 SLE patients and 20 healthy controls were included. The expression of ATG14⁺, FOXP3⁺, CD25⁺, and CD56⁺ were measured by flow cytometry, and expressed in percentages in T and NK cells.

**Conclusions:** We found that in active patients autophagy is higher than in inactive patients. Inactive patients FOXP3 expression in NK cells is normal. These results can be due to the effect of the different treatments given according to clinical manifestations. Autophagy-related key regulator protein may be a new target of SLE treatment.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6883

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**AB0127 ANTI-DS-DNA ANTIBODIES REGULATE ATEROTHROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH THE INDUCTION OF NETOSIS, INFLAMMATION AND ENDOThelial ACTIVATION**

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**Background:** The role of anti-dsDNA in the pathogenesis of the systemic lupus erythematosus (SLE) has been clearly established. However, the influence of these autoantibodies in the atherothrombotic status of SLE patients has not yet been evaluated.

**Objectives:** 1. To analyze in vivo the involvement of anti-dsDNA antibodies in the development of CVD in SLE patients. 2. To evaluate in vitro the mechanisms underlying the effects of anti-dsDNA antibodies in these processes.

**Methods:** The study was conducted in 50 SLE patients and 38 healthy donors. Endothelial function was assessed by measuring the post-occlusive hyperaemia using Laser-Doppler. Various markers of oxidative stress, inflammatory cytokines, prothrombotic mediators and NETosis, were quantified in purified leukocytes and plasma from SLE patients and controls. Activation of intracellular pathways was analyzed in monocytes using intracellular immunocytochemistry. Purified neutrophils, monocytes and lymphocytes from healthy donors and endothelial cells (ECs) were treated separately and in a trans-well co-culture system with anti-dsDNA antibodies isolated from the serum of SLE patients. Then, markers of inflammation, thrombosis, oxidative stress and NETosis were evaluated by flow cytometry (cytometry), RT-PCR (mRNA) and electron microscopy.

**Results:** SLE patients showed impaired micro-vascular endothelial function (reduction of hyperaemia post occlusion area) and altered expression levels of pro-inflammatory proteins (IL6, IL8, MCP-1 and P-CR), prothrombotic molecules (TF), oxidoreductases and prooxidant enzymes, and netosis-related molecules (NE, MPO and cell free-DNA). Monocytes from anti-dsDNA-positive SLE patients showed activation of various pathways related to inflammation, thrombosis and apoptosis (Erk, STAT3, p38, JNK, GSK, Bad and Caspase-3). Association studies demonstrated that molecules related to inflammation and thrombosis, endothelial dysfunction, oxidative stress and netosis were linked to the occurrence of thrombotic events, as well as to the presence of anti-dsDNA antibodies. In vitro treatment of purified leukocytes with anti-dsDNA antibodies promoted an increase in the production of NETosis, level of peroxides and percentage of cells with altered mitochondrial membrane potential, as well as enlarged expression of a number of proinflammatory and prothrombotic molecules. In vitro treatment of HUVEC with anti-dsDNA antibodies promoted an increase in endothelial activation molecules (ICAM-1, VCAM-1 and E-selectin).

**Conclusions:** 1. Positivity for anti-dsDNA antibodies is linked to an increased pro-atherothrombotic status in SLE patients. 2. Anti-dsDNA antibodies, in vitro, promote NETosis on neutrophils, apoptosis on monocytes, modulate the expression of molecules related to inflammation and thrombosis, and induce endothelial activation. Together, that data suggest the involvement of these autoantibodies in atherothrombotic development in SLE.

**Acknowledgements:** CTS-794 and ISCIII (FIS15/1333.RIER16/0012/015)

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4735

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**AB0128 ALTERATIONS IN THE SPlicing MACHINERY COMPONENTS IN LEUKOCYTES FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS INFLUENCES ITS DEVELOPMENT AND ATEROTHROMBOTIC PROFILE AND DRIVES THE THERAPEUTIC RESPONSE**

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**Background:** Recent studies emphasize the relevance of alternative splicing in the development of genetic and autoimmune diseases and suggest therapeutic possibilities based on the modulation of this process.

**Objectives:** To identify alterations in the leukocyte splicing machinery of patients with systemic lupus erythematosus (SLE) and to evaluate its influence on the development and activity of the disease, its atherothrombotic profile, and the response to specific therapies.

**Methods:** An array of selected components of the major-(n=12) and minor-splicing machinery (n=4) and associated splicing factors (n=28) was developed, and their expression levels were evaluated using a Fluidigm methodology, in purified leukocytes from 36 SLE patients and 29 healthy donors (HD). In parallel, an extensive clinical/serological evaluation was performed. Carotid intima media thickness (CIMT) was used as atherosclerosis marker. Endothelial activity was

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6883

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monitored by laser-doppler, and pro-inflammatory and oxidative stress markers were quantified by flow cytometry and RT-PCR. In a parallel cohort of SLE patients (n=12), the effects of in vivo treatment with ubiquinol on spliceosome components was evaluated.

**Results:** As a general feature, a significant reduction in splicing factors and spliceosome components was found in all leukocytes of SLE patients. Interestingly, we found a specific altered profile of splicing factors and spliceosome components when compared monocytes (UZAF1, FBPI11, SRFS9), lymphocytes (RBBM22, PRP8, S1RFSF5) and neutrophils (RN4U, CA150). The reduced levels of some components of spliceosome in both monocytes and neutrophils was linked to the occurrence of thrombotic events, foetal loss and arterial hypertension. In lymphocytes, those reduced levels were strongly related to the positivity for anti-dsDNA antibodies in SLE patients, thus suggesting that reduced spliceosome machinery would contribute to increase in altered autoantigen assembly, inducing immune complexes autoantigen production. Correction studies have demonstrated an inverse relationship among reduced levels of spliceosome components/splicing factors and high activity of the disease (measured as SLEDAI), endothelial dysfunction, and increased expression levels of peroxides and peroxynitrites, as well as of altered mitochondrial membrane potential in monocytes and neutrophils. In vitro treatment of leukocytes from HDs with anti-dsDNA promoted a reduction in spliceosome components associated with the expression of proinflammatory and oxidative mediators. Finally, in vivo treatment with ubiquinol reversed reduced expression in SLE of spliceosome components related to their prothrombotic phenotype.

**Conclusions:** These results reveal the existence of SLE-associated spliceosome alterations -promoted by anti-dsDNA antibodies- which could be related to the development and activity of this autoimmune condition and have influence on the induction of mechanisms that drive atherothrombosis as well as the therapeutic response.

**Acknowledgements:** Funded by CTS7940 and ISCIII (PI15/01333 and RIER RD16/0012/0015).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5036

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**AB0129**

**HMGB1+ MICROPARTICLES IN SYSTEMIC LUPUS ERTHROMYOSITIS PATIENTS WITH LUPUS NEPHRITIS**

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**Background:** High mobility group box protein 1 (HMGB1) is a nucleic acid-binding protein that can function as an alarm when is released from activated and dying cells. In association with nucleosomes, HMGB1 may contribute to the pathogenesis of systemic lupus erythematosus (SLE). Some previous reports have associated HMGB1 with the pathogenesis of cutaneous lupus and lupus nephritis (LN). HMGB1 may also be contained in microparticles (MPs). These vesicles have a wide spectrum of biological activities in intercellular communication, and they compete with apoptotic cells to bind mononuclear phagocytes.

**Objectives:** To evaluate the association of MP-HMGB1+ circulating with LN and to correlate them with LN activity.

**Methods:** Blood samples from 60 SLE patients were used to isolated MPs from platelet-poor plasma by centrifugation and their count, cell source and phenotype were characterized by flow cytometry. Renal pathology was reported using the standardized International Society of Nephrology/Renal Pathological Society classification. Inactive lupus nephritis (LN) was defined by the presence of one or more of the following criteria: 24 hrs proteinuria 500 mg/dl or inactive urine sediments (<5 red cells/HPF) and no red leucocytes (<5 white cells/HPF) and stable serum creatinine.

**Results:** Mean age of SLE patients was 31.9±10.8 years, and mean disease duration was 7.8±6.2 years. 73% patients had LN and LN were female. Patients with LN had significantly higher frequency of MP-HMGB1+, no significant differences were found among patients with active versus inactive LN or among patients with complete versus non-renal manifestations. A moderate positive correlation with disease activity (SLEDAI, r=0.367, p=0.020), anti-C1q antibodies titers (r=0.42, p=0.032), and no correlation was found with activity or chronicity indexes on renal biopsies. A ROC curve for MP-HMGB1+ and renal involvement showed a good discriminative ability (AUC 0.705). A cutoff of 15.7% of MP-HMGB1+ showed the best discrimination threshold with a sensitivity of 63.3% and specificity of 83.3%.

**Conclusions:** In our cohort of patients with SLE, MP-HMGB1+ was significantly higher in patients with LN and in patients with active disease. Given the multiple implication of HMGB1 in SLE, including the active kidney recruitment of mononuclear phagocytes, we consider that MP-HMGB1+ could be a potential biomarker for LN in SLE patients.

**References:**

**Acknowledgements:** C. Burbano is recipient of a doctoral scholarship from COLCIENCIAS (call 617–2013). The authors thank to the grants “Sostenibilidad y Sistema Universitario de Investigaciones, CODI (2013–05–42869836) from Universidad de Antioquia, and to COLCIENCIAS (11156574057)".

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4397
Antiphospholipid Syndrome Patients show an Altered Profile of Endothelial Progenitor Cells and Endothelial Microparticles

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Background: Antiphospholipid Syndrome (APS) is an autoimmune disease characterized by recurrent thromboembolic events and pregnancy morbidity associated to the presence of specific serum antibodies directed against membrane phospholipids and proteic co-factors. APS represents the earlier and reversible stage of subclinical atherosclerosis that characterizes these patients. An altered profile of endothelial progenitor cells (EPCs) and endothelial microparticles (EMPs) could promote endothelial damage compared to who did not. Kaplan-Meier survival curve showed no difference compared to healthy subjects.

Objectives: Our aim was to evaluate circulating EPCs and EMPs in primary APS patients (PAPS).

Methods: We studied primary APS patients with previous thromboembolic events and sex and age-matched healthy controls (HC). Circulating EPCs was identified by flow cytometry analysis as CD34+/KDR+ positive cells isolated from peripheral blood mononuclear cells (PBMCs); EMPs was obtained by centrifugation of whole blood and quantified by flow cytometry (CD31+/CD41a+). Data were expressed as mean±standard deviation or median (interquartile range) when appropriate; correlations between EPC and EMP levels with anti-cardiolipin and anticardiolipin like protein I, both IgM and IgG, were scored blindly by a renal pathologist. To identify factors related to the development of LN, Cox proportional hazard regression model and Kaplan-Meier curves were used.

Results: The concentrations of pIGBP1 in SLE patient were higher than those in healthy individual (9.6±8.4 ng/mL vs 4.5±2.4 ng/mL) and positively correlated with SLEDAI score. However, the concentrations were not different between LN and non-nephritis SLE and were not associated with activity index score in renal pathology. During follow-up more than 5 years, nephritis was developed in 20 patients (20.5%) among 39 SLE patients who did not have renal involvement at baseline. Interestingly, levels of pIGBP1 (p=0.002), CRP (p=0.009), or anti-dsDNA antibody (p=0.03) were significantly elevated in 8 patients who developed LN compared to who did not. Kaplan-Meier survival curve showed that initial pIGBP1 (>10.71 ng/mL) as well as anti-dsDNA (>0.7IU/mL) were associated with high probability of LN development in the future.

Conclusions: Based on our results, high concentration of pIGBP1 could be a valuable marker to represent high SLE activity and a predictor for developing nephritis in SLE patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4292
**AB0135** BLOOD LYMPHOCYTE SUBSETS ACCORDING TO THE CLINICAL PROFILE IN SJÖGREN'S SYNDROME


**Background:** It has been recently described the occurrence of disturbances in lymphocyte subsets in Sjögren’s syndrome (SS) which may reflect B cell hyper activation and a T cell adjaent role.

**Objectives:** We aim to characterize circulating lymphocyte subsets in SS patients, according to disease activity and antibody profile.

**Methods:** We have included in this study 53 SS patients (2002 AECG criteria) of which 22 with >10 years since diagnosis and 31 with <2 years since diagnosis, and 22 healthy controls. Lymphocyte subsets, including follicular (Thf) and regulatory T (Treg) cells, maturation subsets, plasmablasts (PB) and regulatory B (Breg) cells, were characterized by flow cytometry. Statistical analysis was performed with GraphPad. Significance was considered for p<0.05.

**Results:** Compared to controls, SS patients had lower absolute counts of B (p=0.0337) and T cells (p=0.0012), lower CD4 (p=0.0002) and higher CD8 percentages (p=0.0006), resulting in an increased CD4/CD8 ratio (p=0.0006). Additionally, there was decrease in absolute counts of Tregs (p=0.0008) and Th17 cells (p=0.0005) in SS patients. Moreover, there was a decreased absolute counts (Th1) and Tfh17 cells, identified by CXCR5 expression, though higher levels of IL21+CD4 T cells (p=0.0299) and Th1 cells (p=0.0092). SS patients also presented higher % of naïve B cells (p=0.0412), lower % and absolute counts of memory (% =0.0161; abs p=0.0002) and unswitched memory (% =0.0106; abs p=0.0005) B cells and lower absolute counts (p=0.0001) of switched memory B cells. SS patients had higher naive/memory B cell ratios, compared to healthy subjects (p=0.0219). Accordingly, using the Bm1–5 classification, we have found decreased Bm1 (% =0.0087; Abs p=0.0007), eBm5 (Abs p=0.0005) and Bm5 (Abs p=0.0015) in SS patients. Similar Bm2+Bm3/eBm5+Bm5 ratios were observed in patients and controls. CD24+CD27+ Bregs were also decreased (p=0.0102) in SS patients.

**Conclusions:** SS patients had also an increase in IL21+CD4 T cells, particularly in patients with extra-glandular manifestations (EGM) (n=12), who also presented less Tfh17 cells compared to SSA-. Moreover, there was a decreased absolute count (Bm1) and Bm17 cells, identified by CXCR5 expression, though higher levels of IL21+CD4 T cells (p=0.0299) and Th1 cells (p=0.0092). SS patients also presented higher % of naïve B cells (p=0.0412), lower % and absolute counts of memory (% =0.0161; abs p=0.0002) and unswitched memory (% =0.0106; abs p=0.0005) B cells and lower absolute counts (p=0.0001) of switched memory B cells. SS patients had higher naive/memory B cell ratios, compared to healthy subjects (p=0.0219). Accordingly, using the Bm1–5 classification, we have found decreased Bm1 (% =0.0087; Abs p=0.0007), eBm5 (Abs p=0.0005) and Bm5 (Abs p=0.0015) in SS patients. Similar Bm2+Bm3/eBm5+Bm5 ratios were observed in patients and controls. CD24+CD27+ Bregs were also decreased (p=0.0102) in SS patients.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3030

**AB0136** MICROPARTICLES FROM SLE PATIENTS ARE A SOURCE OF INTERFERON-ALPHA

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**Background:** Systemic lupus erythematosus (SLE) is the prototype of systemic autoimmune disorders. In the late 1970s, increased serum levels of interferon (IFN) were shown for the first time to be significantly associated with SLE and to correlate with disease activity. IFNα is a pleiotropic cytokine that can affect multiple cell types involved in lupus. Plasmacytoid dendritic cells have a special role in the production of IFN and are the main sources of serum interferon. IFNα has the potential to dramatically influence the development, progression, and pathogenesis of SLE as it can influence the function and activation state of most major immune cell subsets and function as a bridge between innate and adaptive immunity. Lupus-prone mouse models, indicates that the type I interferon system may play a pivotal role in the pathogenesis of several lupus and associated clinical features, such as nephritis, neuropsychiatric and cutaneous lupus. Circulating microparticles (MPs) are ubiquitous in the blood of healthy individuals. These MPs play an active role in coagulation and intercellular communication and assist in activation or suppression of the immune system, depending on their parent cell origin. Changes in the concentration and/or composition of circulating microparticles have been described in various autoimmune diseases, including rheumatoid arthritis (RA) systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). For SLE, the reported microparticle-related changes remain somewhat inconclusive.

**Objectives:** To better understand the role of MPs in SLE patients, we analyzed the presence of interferon alpha on MPs surface.

**Methods:** MPs were isolated from citrate-treated plasma; blood cells were removed by two steps of Ficoll gradients (2500g for 15min at 20 C two time). The resulting platelet-poor-plasma (PPP), was analyzed by flow cytometry with specific antibody against IFN alpha.

**Results:** 20 consecutive SLE patients (10 with active lupus nephritis) and 10 sex- and age-matched healthy control subjects were included in the study. We found that MPs from SLE patients carry on their surface IFN alpha. Moreover, the percentage IFNα+MPs was higher in SLE patients and in lupus nephritis patients than in healthy controls. There was no significant difference between patients with and without renal involvement.

**Conclusions:** The results of the present study show for the first time the presence of IFN alpha on MPs surface. We may assume that INF+MPs derive from dendritic cells. In lupus nephritis patients the increased recruitment of dendritic cells was at tubular interstitial level, with subsequent IFN alpha production. Interestingly, MPs (containing RNA and DNA) could stimulate type I IFN production in plasmacytoid dendritic cells and MPs releasing.

**Disclosure of Interest:** None declared


**AB0137** ALTERATIONS IN MICRONA EXPRESSION PROFILES IN PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** MicroRNAs (miRNAs) are single-stranded, endogen non-

- PS) and antibodies against surface markers endothelial cells (CD31+CD41-).

**Mann-Whitney and Spearman correlation tests were used.** A p value ≤0.05 was considered statistically significant.

**Results:** Sixty SLE patients (55F/5M, age 41,7±9.6 Y disease duration 149±12 months) and 29 healthy controls were studied. Twenty-eight patients had renal involvement and the total number of plasmatic MPs was lower in SLE patients than HC (p=0.001). In contrast there was no significant difference in levels of EMPs between the two groups. When the patients were divided according to renal involvement, the patients with active lupus nephritis (A-LN) showed lower plasmatic level of EMPs in comparison to inactive LN (I-LN) (p=0.01), while the patients with LN had higher levels of EMPs than HC (p=0.002). There was no significant difference of total urinary level of MPs between SLE patients and HC. Urinary levels of EMPs were higher in SLE and in lupus nephritis patients than HC.

**Conclusions:** The results of the present study show increased urinary and plasmatic levels of EMPs in patients with lupus nephritis in remission. Circulating EMPs have been considered as a potential biomarker of endothelial activation and damage in several autoimmune disorders, and higher EMP levels have been detected in patients with vasculitis and associated with disease activation. According to our results, plasmatic EMPs levels are higher in inactive LN patients than in healthy donors. These results may suggest a potential role of EMP as a biomarker of lupus nephritis.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5003

**AB0135** PLASMATIC AND URINARY ENDOTHELIAL MICROPARTICLES ARE INCREASED IN PATIENTS WITH LUPUS NEPHRITIS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease presenting with a wide array of clinical manifestations and incompletely understood pathogenesis. It is characterized by alterations in the innate and adaptive immune system ultimately leading to the loss of immunologic tolerance and occurrence of autoantibodies against nuclear material. Lupus nephritis is one of the most severe features of SLE determining an increase in morbidity and mortality rates. Renal biopsy still represent a fundamental diagnostic and prognostic tool for LN. Therefore, non-invasive surrogate biomarkers of active LN are urgently needed. Circulating, heterogeneous submicroparticles (MPs) are released from cells and platelets constitutively and upon cellular activation or apoptosis. Such MPs may reflect the state of their parental cells and tissues and could serve as markers of pathology. Particularly in SLE, MPs are potential biomarkers and triggers of autoimmunity. Recent studies have demonstrated increased levels of plasmatic EMPs in patients with SLE active disease and their reduction after treatment.

**Objectives:** The aim of this study was to investigate plasmatic and urinary levels of microparticles in a cohort of SLE patients with and without renal involvement compared to healthy controls.

**Methods:** Consecutive SLE patients and sex- and age-matched HC were included in the study. MPs were isolated from plasma and urine and characterized by flow cytometry using AnXV (a probe that binds to the exposed phosphatidilserine
cording small RNAs, ranging from 18 to 25 nucleotides in length. miRNAs are essential in regulating gene expression, cell development, differentiation and function. Dysregulation in miRNA expression may contribute to the development of autoimmunity. However, a given miRNA may have hundreds of different mRNA targets and a target might be regulated by multiple miRNAs, thus the conclusion of dysregulated miRNA expression profiles could give a better insight into the development of immunological disturbances in autoimmune diseases.

**Objectives:** The aim of our study was to examine the changes in miRNA expression profiles in patients with primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE).

**Methods:** Eight pSS patients, 8 SLE patients and 7 healthy control subjects were enrolled in the investigation. miRNAs were isolated from peripheral blood mononuclear cells, and expression patterns were determined with Illumina next-generation sequencing technology. Since the immune system, pSS and SLE encompasses pronounced B cell hyperactivity along with specific autoantibody production, we paid a special attention on the association between miRNA expression levels and altered peripheral B cell distribution.

**Results:** In SLE patients 135, while in pSS patients 26 miRNAs showed altered expression. Interestingly, the 25 miRNAs including miR-146a, miR-16 and miR-21, which were over-expressed in pSS patients, were found to be elevated in SLE group, as well. On the contrary, we observed the down-regulation of miR-150-5p, which is a novel and unique finding in pSS. Levels of several miRNAs observed in SLE, were modulated in the pSS group as well, such as miR-148a-3p, miR-152, miR-155, miR-223, miR-224, miR-326 and miR-342. Expression levels of miR-223-5p, miR-150-5p, miR-155-5p and miR-342-3p, which miRNAs are potentially linked to B cell functions, showed associations with the B cell proportions within peripheral blood mononuclear cells.

**Conclusions:** The observed differences in miRNA expression profiles and the better understanding of immune regulatory mechanisms of miRNAs may help to elucidate the pathogenesis of pSS and SLE.

**Acknowledgements:** This work was supported by the ÚNKP-16–4-III New National Excellence Program of the Ministry of Human Capacities.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3205

**AB0138**

**INTERFERON-GAMMA CHALLENGE OF PBMC FROM PATIENTS WITH LUPUS NEPHRITIS IN REMISSION DECREASES SUPPRESSOR OF CYTOKINE SIGNALING 1 (SOCS1) AND REGULATORY T CELLS (TREGS) AND PROMOTES IMMUNE ACTIVATION**

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**Background:** Interferon-gamma (IFN-γ) plays an important role in the development of lupus nephritis (LN). Regulation of IFN-γ signaling that occurs in disease remission and in active LN is herein addressed.

**Objectives:** To study the impact of IFN-γ on PBMC obtained from patients with LN in remission as compared to active LN.

**Methods:** Sixteen patients fulfilling the ACR classification criteria for systemic lupus erythematosus were recruited. All patients had a history of LN of whom 10 were in remission (as defined by EULAR criteria) and 6 had active LN (as defined by SLEDAI-2K or BILAG). Healthy subjects (n=10) were included as a control group. Sera and PBMC were obtained from each individual. Flow cytometry, western blots and real time RT-PCR were used in processing and detection of cell subtypes, protein and mRNA levels. Recombinant human IFN-γ (rhIFN-γ) and anti-IFN-γ neutralizing antibody were used in vitro. Mann-Whitney and student t-tests were used for statistical analysis.

**Results:** In active LN there was a significant 2-fold increase in CD4+CD69+ activated T cells as compared to healthy subjects and patients in remission. Reactivity to interferon-gamma receptor was determined by the phosphorylation of its predominant transcription factor, signal transducer and activator of transcription 1 (STAT1) in the cells that were incubated with rhIFN-γ. Its predominant transcription factor, signal transducer and activator of transcription 1 (STAT1) in the cells that were incubated with rhIFN-γ all groups had elevated its predominant transcription factor, signal transducer and activator of transcription 1 (STAT1) in the cells that were incubated with rhIFN-γ during 24h and 48h, respectively, and healthy subjects responded likewise. In active LN there was a significant 2-fold increase in CD4+CD69+ activated T cells as compared to healthy subjects and patients in remission.

**Conclusions:** In LN remission a challenge with IFN-γ could lead to immune activation and a risk of flare-up, as it results in a decrease in both SOCS1 and Tregs and a robust STAT1 phosphorylation. In active LN, STAT1 phosphorylation is less diminishing, as both SOCS1 and Tregs are saturated, which could affect their suppressive effectiveness.

**Disclosure of Interest:** None declared

**AB0139**

**ROLE OF MUCOSAL-ASSOCIATED INVARIANT T (MAIT) CELLS IN A LUPUS MODEL**

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**Background:** Mucosal associated invariant T (MAIT) cells are innate T cells that are regulated by MHC-related molecule-1 (MR1) and express a semi-invariant TCRγ chain. Vα7.2-Jα33 in humans and Vα19-Jα33 in mice. Previously, we have demonstrated that MAIT cells played a protective role against experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis. We found that MAIT cells are activated in patients with systemic lupus erythematosus (SLE) and that the activation state of MAIT cells correlated with SLE disease activity index (SLEDAI) score, suggesting their association in lupus pathology.

**Objectives:** We set out to clarify functions of MAIT cells in a lupus model by using FcγRIIB+ Yaa mice.

**Results:** Yaa mice were crossed to MR1 deficient mice lacking MAIT cells, and disease progression was compared between MR1+ FcγRIIB+ Yaa and MR1– FcγRIIB+ Yaa mice at 1–4 months of age. Serum anti-dsDNA antibody levels were measured and urinary microalbumin were evaluated. At the time of sacrifice, at 4 months of age, the severity of nephritis and dermatitis were assessed by histologically and IgG deposition in skin and glomeruli was measured.

**Conclusions:** Survival rate was significantly reduced in MR1– FcγRIIB+ Yaa mice compared with MR1+ FcγRIIB+ Yaa mice. Anti-dsDNA antibody levels were remarkably higher in MR1– FcγRIIB+ Yaa mice compared with MR1+ FcγRIIB+ Yaa mice at 4 months of age. Even though Glomeruli were significantly enlarged both in MR1+ and MR1– FcγRIIB+ Yaa mice due to a marked cellular proliferation in glomeruli, the glomerulonephritis score tended to be lower in MR1+ FcγRIIB+ Yaa mice compared with MR1– FcγRIIB+ Yaa mice. A larger amount of IgG deposition was observed in mesangial area and along glomerular capillary walls in MR1+ than MR1– FcγRIIB+ Yaa mice. However, MR1+ FcγRIIB+ Yaa mice showed exacerbated inflammation in the skin lesions. There was a high degree of inflammatory cells infiltration into the skin and a significant worsening of dermatitis score in MR1+ FcγRIIB+ Yaa mice compared with MR1– FcγRIIB+ Yaa mice.

**Conclusions:** These data suggests that MAIT cells exhibit dual roles in lupus pathogenesis. MAIT cells enhance autoantibody production and the disease severity of nephritis, but have a suppressive effect on dermatitis. Further studies are under going to uncover the mechanisms by which MAIT cells are involved in each target tissues.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3086

**AB0140**

**LUPUS-PRONE SLAM HAPLOTYPE EXERTS MONOCYTOSIS AND DEVELOPS SPECIFIC PHENOTYPE OF AUTOIMMUNE DISEASE INTRODUCED BY YAA MUTATION**

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**Background:** We previously obtained a 129-derive FcγRIIB-deficient C57BL/6 (B6) congenic strain of mice, which spontaneously developed severe rheumatoid arthritis (RA)1. The introduction of the Yaa (Y-linked autoimmune acceleration) mutation, which is a consequence of a translocation from the telomeric end of the X chromosome containing the Ya gene onto the Y chromosome, to the FcγRIIB-deficient B6 mice (B6.FcγRIIB–/–Yaa) developed lupus-like nephritis but not RA2.

**Objectives:** By extensively backcrossing 129-derived FcγRIIB-deficient mice to B6 mice, we established wildtype FcγRIIB and 129-derive autoimmune-prone SLAM haplopyte (SLAM) strains.2 We examined the phenotypes of SLAM mice, and also Yaa mice by introducing Yaa mutation to these mice.

**Methods:** We analyzed peripheral blood monocyte subset and also serum autoantibodies as well as immunohistopathological findings of kidneys and lungs.

**Results:** SLAM mice showed age-associated monocytosis with marked expan-
sion of Gr-1 negative monocytes, also perivascular inflammatory cell infiltration in lungs. But they did not show any pathogenic autoantibodies. When introducing Ya mouse, Slam129. Ya mice showed significant increase the serum levels of anti-RNP antibodies and anti-Sm antibodies. Although they showed significant increase of serum levels of IgM class anti-dsDNA antibodies, they did not show the elevation of IgG class anti-dsDNA antibodies. Also they developed nephritis but the pathological score was significantly lower than B6.FcRRIIB-/-, Ya mice.

Conclusions: Autoimmune-prone SLAM haplotype plays a role for Gr-1 negative monocytosis and Slam129. Ya mice developed specific lupus phenotype with elevation of anti-RNP and anti-Sm autoantibodies.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4175

**AB0141**

LOW DOSE IL-2 CIRCUMVENTED CD3 SIGNAL TRANSMITTING IN T CELLS IN THE TREATMENT OF SLE

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Background: mTOR signaling is proved to be one of the most important pathway in the pathogenesis in SLE. However, in patients with SLE, whether mTOR pathway can be inhibited by low-dose IL-2 remains controversial.

Objectives: To clarify the effects of low-dose IL-2 therapy on mTOR signaling in the treatment of SLE.

Methods: Eight patients with active SLE were treated with 1 million IU IL-2. Phophrylation of S6 ribosomal protein (S6RP), AKT and pSTAT5 were measured before and after the first 2 week of low-dose rhlIL-2 administration. C57BL/6 mice (male, 8–12 weeks old) were intraperitoneally immunized with SRB and followed by administration of different doses (low:10,000 IU and high:300,000 IU) of rhlIL-2 or PBS from day 3 to day 9. The ratio of Th1, Th2, Th17, Treg and Treg as well as the level of S6RP, AKT and pSTAT5 were assayed by flow cytometry.

Results: Low-dose IL-2 was efficient and well tolerated in active SLE, and was associated with expansion of Treg cells (P<0.001) and reductions of Th17 and Th17 cells (P<0.001). No significant change of pS6RP and pAKT was observed. On the other hand, there was a significant induction of the activation of STAT5. In mouse studies, low-dose IL-2 inhibited the differentiation of Th17 cells and T1h cells. Comparing with high dose IL-2 group, there was no significantly increased mTOR activity after low-dose IL-2 administration.

Conclusions: Low-dose IL-2 might circumvent mTOR pathway and play a regulatory role in the treatment of lupus.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3482

**AB0142**

IGM ANTIBODIES AGAINST PHOSPHORYLCHOLINE PROMOTE POLARIZATION OF T REGULATORY CELLS FROM PATIENTS WITH ATHEROSCLEROTIC PLAQUES, SYSTEMIC LUPUS ERYTHEMATOUS AND HEALTHY DONORS: A NOVEL IMMUNOLOGICAL CONCEPT


Background: Igm antibodies against Phosphorycholine (anti-PC) are negatively associated with atherosclerosis, cardiovascular disease (CVD) and systemic lupus erythematous (SLE) where the risk of CVD and atherosclerosis is very high. Here we study effects of Igm anti-PC on Th17 and T regulatory cells (Tregs).

Objectives: Immunomodulation in atherosclerosis and SLE could have a huge impact on disease prevention and treatment.

Methods: Mononuclear leukocytes were isolated from peripheral blood (PBMC) obtained from healthy blood donors, from six SLE patients with age- and sex-matched controls and from symptom-giving human atherosclerotic plaques. The patient and SLE group on Th17 (CD4+CD14+CD25+CD127−) and Treg (CD4+CD25+CD127+CD102−) cells were determined by flow cytometry in CD4+ T cells after 6 days culture with Th17 or Treg-polarizing cytokines, with PMA and Ionomycin stimulation. IgM anti-PC were extracted from total IgM, with flow-through IgM as controls. Dendritic cells (DC) were differentiated from PBMC. Antibody peptide/protein characterization was done by ELISA.

Results: IgM anti-PC increased significantly the proportion of Tregs from healthy donors, SLE patients and from atherosclerotic plaque cells while control antibodies did not. T cells from SLE patients had a significantly lower proportion of Tregs and higher proportion of Th17 cells as compared to matched controls. IgM anti-PC but not control antibodies significantly reduced production of IL-17 and TNF-alpha in cell culture from SLE patients and from atherosclerotic plaque cells. IgM anti-PC interacted with CDA40 and kept DCs in an immature stage potentially being tolerogenic. We identify differences on the IgM peptide expression level in anti-PC compared to control antibodies.

Conclusions: IgM anti-PC increase Tregs and having low levels could contribute to both SLE and atherosclerosis (and CVD) and could thus represent a novel underlying mechanism in these conditions. This finding could also have therapeutic implications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5076

**AB0143**

IMMUNOMODULATION FOLLOWED BY QUANTITATIVE TRANSSCRIPTOMIC PROFILING TO CHARACTERIZE THE FUNCTIONAL ROLE OF THE SJÖGREN’S-ASSOCIATED NCRNA AC092580.4


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Background: Despite concerted efforts to characterize dysregulated transcriptional responses observed in Sjögren’s syndrome and related autoimmune disorders, both in whole blood and target tissues), the functional roles of non-coding RNAs (ncRNAs), many of which have been identified as critical players in transcriptional regulation of disease, remain poorly defined.

Objectives: In the present study, we describe ongoing efforts to functionally characterize the upregulated ncRNA identified by RNA-seq and in silico approaches, AC092580.4 (FC=2.54), which we hypothesize plays a role in T and NK cell responses.

Methods: To study the immunomodulation of the ncRNA AC092580.4, we carried out a time-course experiment (0–36 hrs) using either PMA/I (500x dil) or universal Type I Interferon. Relative gene expression changes were determined using the 129 strain-derived Sle16 locus in rheumatoid arthritis and related autoimmune disease, both in whole blood and target tissues), the functional roles of non-coding RNAs (ncRNAs), many of which have been identified as critical players in transcriptional regulation of disease, remain poorly defined.

Objectives: In the present study, we describe ongoing efforts to functionally characterize the upregulated ncRNA identified by RNA-seq and in silico approaches, AC092580.4 (FC=2.54), which we hypothesize plays a role in T and NK cell responses.

Results: Of the transcripts showing DE in our SS RNA-seq study, we identified 98 as having significantly correlated expression with AC092580.4 in the SS with expression matrix (r=0.70 or < −0.65). To understand the possible effects of immunomodulation on relevant cells, we stimulated HS-2 cells with PMA/I at various time points and assessed AC092580.4 expression by. We observed downregulation of AC092580.4 and the co-expressed transcript GLMAM (tough: 12–16hrs; FC=0.09) followed by slow recovery at 36hrs (FC=0.59). To characterize these transcriptional changes further, we performed RNA-seq using healthy PBMCs exposed to various T cell stimulants. We observed marked upregulation of both AC092580.4 and GLMAM 24/36hrs by all stimulants (FC=4.85–5.98). Other transcripts showed variable responses. Cav2 was upregulated by PMA/I, but downregulated by CD3/CD28 and PHA. Stimulation by PHA leads to upregulation of CD3D (FC=1.56) and SNRPD1 (FC=3.28) with little change in RPL3FA (FC=1.09). Stimulation by CD3/CD28 similarly leads to upregulation of SNRPD1 (FC=2.85) and SNRPD1 (FC=10.04), but clear downregulation of RPL3FA (FC=0.64). We assessed AC092580.4 expression in HS-2 cells exposed to I IFN and observed initial upregulation (6hrs, FC=1.46) followed by gradual downregulation (36hrs, FC=0.18).

Conclusions: In the present study, we have initiated stimulation studies with 1Rheumatology; 2Pediatrics; 3Gynecology and Obstetrics, Faculty of Medicine of the University of Porto, Porto, Portugal

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8672

**AB0144**

PREGNANCY OUTCOMES IN IMMUNE-MEDIATED RHEUMATIC DISEASES: A RETROSPECTIVE LONGITUDINAL STUDY IN A TERTIARY HOSPITAL

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Background: Autoimmune rheumatic diseases such as systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS) and Sjögren’s syndrome (SS) are part of a clinical spectrum eligible to affect women in child-bearing ages, increasing pregnancy morbidity and affecting neonatal outcomes. Pregnancy complications include the teratogenic risk from immunosuppressive drugs, pregnancy-related disease flares, recurrent pregnancy loss, premature

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4175
delivery, intrauterine growth restriction (IUGR) and preeclampsia. Conceiving in periods of low disease activity helps to reduce these complications.

Objectives: This project aims to describe the occurrence of pregnancy complications among women with immune-mediated rheumatic diseases and to study the associated clinical factors.

Methods: A retrospective, longitudinal study was performed including consecutive pregnant women with immune-mediated rheumatic diseases seen in a multidisciplinary group for autoimmune diseases during pregnancy, in a tertiary hospital, between January 2010 and December 2015. Clinical and demographic data, as well as pregnancy outcomes, were collected through consultation of clinical files. They were compared with pregnancy manifestations (premature delivery, flares during pregnancy, recurrent pregnancy loss and foetal growth restriction) were studied using Mann-Whitney, quiz-square and fisher tests (SPSS 24.0).

Significance level was set as <0.05.

Results: We included 384 gestations from a total of 140 women with a mean age of 32.5±4.4 years; 4 gestations were twin pregnancies. Within these 151 gestations, 54 (35.8%) women had SLE, 17 (11.3%) had Sjögren’s syndrome, 17 (11.3%) had rheumatoid arthritis, 41 had APS (27.2%), 11 (7.3%) had Behçet’s disease, 4 (2.6%) had systemic sclerosis, 8 (5.3%) had mixed connective tissue disease and 16 (10.6%) had other immune-mediated diseases. 35 (23.2%) had anti-SSA/La antibodies, 18 (11.9%) had anti-SSB antibodies, 6 (4.0%) had anti-URNP antibodies and 43 (28.5%) had anti-nuclear antibodies. Seven (4.6%) of the women developed gestational diabetes and 4 (2.6%) developed gestational hypertension. Furthermore, 54 (35.8%) women had pre-existing miscarriages. Pregnancy outcomes were frequently affected with increased GFR (58.8% vs 46.1%; p=0.04), and was associated with gestational diabetes (21.4% vs 2.9%; p=0.018). It also occurred more frequently in multiple pregnancies (75% vs 16.4%; p<0.001), mothers taking glucocorticoids (28.6% vs 9.2%; p=0.003) and active rheumatic disease (23% vs 6.8%; p=0.03). No statistically significant differences were observed in the occurrence of different pregnancy complications among different diseases or in presence of different antibodies.

Conclusions: Our study proved a link between immune-mediated rheumatic diseases and specific pregnancy outcomes such as prematurity and IUGR. Outcomes were worse when taking glucocorticoids, when gestational diabetes were developed and when conception occurred in a period of active disease.


AB0145 TLR4 SIGNALING PATHWAY MEDIATES THE SENESCENCE OF BONE MARROW-MESENCHYMAL STEM CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Previous studies of our research group revealed the senescence of bone marrow-mesenchymal stem cells from systemic lupus erythematosus patients, which participated in the development of SLE. "Inflammatory microenvironment" played a very important role in cellular senescence. In the preliminary experiments, we discovered the level of HMGB1 in serum and Peripheral blood mononuclear cells from SLE patients was higher than those of The healthy control group.

Objectives: The aim of this study was to investigate whether HMGB1 can lead to senescence BM-MSCs from SLE patients and its possible mechanism.

Methods: We included 151 gestations from a total of 140 women with a mean age of 32.5±4.4 years; 4 gestations were twin pregnancies. Within these 151 gestations, 54 (35.8%) women had SLE, 17 (11.3%) had Sjögren’s syndrome, 17 (11.3%) had rheumatoid arthritis, 41 had APS (27.2%), 11 (7.3%) had Behçet’s disease, 4 (2.6%) had systemic sclerosis, 8 (5.3%) had mixed connective tissue disease and 16 (10.6%) had other immune-mediated diseases. 35 (23.2%) had anti-SSA/La antibodies, 18 (11.9%) had anti-SSB antibodies, 6 (4.0%) had anti-URNP antibodies and 43 (28.5%) had anti-nuclear antibodies. Seven (4.6%) of the women developed gestational diabetes and 4 (2.6%) developed gestational hypertension. Furthermore, 54 (35.8%) women had pre-existing miscarriages. Pregnancy outcomes were frequently affected with increased GFR (58.8% vs 46.1%; p=0.04), and was associated with gestational diabetes (21.4% vs 2.9%; p=0.018). It also occurred more frequently in multiple pregnancies (75% vs 16.4%; p<0.001), mothers taking glucocorticoids (28.6% vs 9.2%; p=0.003) and active rheumatic disease (23% vs 6.8%; p=0.03). No statistically significant differences were observed in the occurrence of different pregnancy complications among different diseases or in presence of different antibodies.

Conclusions: Our study proved a link between immune-mediated rheumatic diseases and specific pregnancy outcomes such as prematurity and IUGR. Outcomes were worse when taking glucocorticoids, when gestational diabetes were developed and when conception occurred in a period of active disease.


AB0146 INVOLVEMENT OF PERIPHERAL CD8 T CELL SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Although the mainstream of pathogenesis of systemic lupus erythematosus (SLE) is thought to be interactions between antigen-presenting cells, CD4 T cells, helper T cells, B cells and cytokines, previous reports suggested CD8 T cells also involve in the pathogenesis of SLE1,2. However the associations between subsets of CD8 T cells and clinical manifestations remains unclear.

Objectives: We conducted standard immunophenotyping analysis with peripheral blood from SLE patients and focused on CD8 T cell subsets to elucidate the association with clinical phenotype and serological markers.

Methods: Peripheral blood was obtained from inactive SLE patients and healthy subjects as controls and also from active SLE before and 3 months after treatment. CD8 T cell subsets were measured by flow cytometry with fresh whole blood samples.

Results: Thirty-four active SLE patients and 38 inactive patients and 22 healthy controls (HCs) whose age and sex were matched with those in SLE patients were enrolled. Mean SLE disease activity index (SLEDAI) was 14.2 and 1.8 in active and inactive patients respectively. Anti-dsDNA antibody (120%, p=0.016, rho =-0.283), and was also higher in patients with nephritis than patients without nephritis (p=0.074), though it did not correlate with SLEDAI. The expression levels of HLA-DR+ cells was significantly higher in SLE patients than HCs and positively correlated with SLEDAI (p=0.016, rho =-0.283), and was also higher in patients with nephritis than patients without nephritis (p=0.074), though it did not correlate with SLEDAI. The expression levels of HLA-DR+ cells was significantly higher in SLE patients than HCs and positively correlated with SLEDAI (p=0.016, rho =-0.283), and was also higher in patients with nephritis than patients without nephritis (p=0.074), though it did not correlate with SLEDAI.

Conclusions: Pathological state of SLE positively correlated with the proportion of naive CD8 T cells negatively correlated with SLEDAI only with those who were treated with cyclophosphamide.


AB0147 THE EFFECTIVE TREATMENT WITH HYDROXYCHLOROQUINE ON SOLUBLE TISSUE FACTOR LEVELS IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES AND ANTIPHOSPHOLIPID SYNDROME WITH AND WITHOUT UNDERLYING SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Antiphospholipid syndrome (APS) is characterized by venous, arterial, or microvascular thrombosis, and/or arterial or venous thrombosis, and/or fetal losses, in the presence of antiphospholipid antibodies (aPL). The mainstay of treatment is based on anticoagulation therapy; however, increasing interest is currently received by the antimalarial hydroxychloroquine (HCQ). The use of HCQ has been associated with a reduced risk of thrombosis but HCQ’s anti-inflammatory mechanism of action is unclear particularly in patients with aPL and APS.

Objectives: The aim of our study was to assess soluble tissue factor (TF) levels in HCQ naïve-patients with persistent aPL or APS at baseline and 12 weeks after commencing HCQ. We hypothesise that HCQ lowers levels of soluble TF.
Methods: Twenty-two individuals with APS with or without other associated autoimmune disease (20 females, two males, median age 55 (range 18–70) years) had blood samples taken before and 12 weeks after starting HCQ 200mg. Plasma was stored at -80°C and thawed to measure TF using Lumibind TF kit (Invittech Ltd, Cambridgeshire, UK). The assay was performed according to the manufacturer's instructions. Patient characteristics are outlined in Table 1. Statistical analysis was performed using SPSS Version 22. For continuous normally distributed data a two-tailed student's paired t-test was performed. A value of p=0.05 was considered as significant. There are no previous data in this area, so we were unable to do a power calculation to work out study size. Our study is therefore a pilot study.

Results: Soluble TF levels were above our normal range (40–300 pg/ml) prior to the commencement of HCQ and were significantly reduced (pre level mean (SD) 401.8 (152.8) pg/ml versus post 300.9 (108) pg/ml (p=0.010).

Conclusions: There was a significant reduction in soluble TF levels in this patient cohort of patients with aPL and APS after commencing HCQ. Our previous work has shown that HCQ has not affected complement turnover, VEGF levels, thromboelastometry findings or CRP levels. Our findings of a reduction of soluble TF levels in aPL positive patients after the commencement of HCQ maybe a key mechanism by which HCQ reduces thrombotic risk. Further studies of a larger patient cohort are required to conform our observation.

References:


Disclosure of Interest: K. Schreiber Shareholder of: Novo Nordisk, Grant/research support from: educational support from Daiichi Sankyo, K. Breen: None declared, K. Parmar: None declared, B. Hunt: None declared

DOI: 10.1136/annrheumdis-2017-eular.4746

AB0148

INDUCTION OF HO-1 EXPRESSION IN MONOCYTES MIGHT PREVENT KIDNEY DAMAGE IN LUPUS NEPHRITIS (LN)

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Background: Systemic lupus erythematosus (SLE), is an autoimmune disease characterized by autoantibody synthesis and inflammation. During disease course, up to 70% of SLE patients will develop LN. Emerging evidence has demonstrated that infiltrating monocytes and macrophages are associated with LN pathogenesis. We have previously demonstrated that HO-1, a haem-degrading enzyme with anti-inflammatory properties is decreased in peripheral monocytes of SLE patients. Therefore, we decided to explore the contribution of HO-1 expression to LN pathogenesis.

Objectives: To explore the role of HO-1 in modulating innate immunity through a cytoprotective effect in monocytes of LN nephritis patients. Accordingly, we examined the expression of HO-1 in circulating monocytes, and the effect of HO-1 induction in reactive oxygen species (ROS) production and the phagocytic activity of monocytes from peripheral blood of LN patients and healthy controls (HC).

Methods: SLE patients with proliferative LN confirmed by renal biopsy (Class III, IV or V ISN/RPS) were recruited at Hospital Clínico de PUC. All individuals signed an informed consent form. Monocytes were purified from peripheral blood mononuclear cells (PBMCs) of LN patients and HC using pan-monocytes MACS kit. Subpopulations of monocytes and HO-1 expression were measured by FACS. ROS was determined using CellRox Kit. The phagocytic ability of monocytes was assessed by FACS and the total phagocytosis was calculated as the percentage of cells with engulfed beads.

Results: We found that monocytes from LN patients show significant differences when compared to HC in all the parameters analyzed. The percentage of CD16+ inflammatory monocytes was higher in LN patients (6.72±0.98%) compared to HC (4.07±0.48%) (p<0.05). HO-1 protein expression is decreased in circulating LN monocytes (4789±911 vs 1572±481, p=0.005). Baseline levels of ROS are elevated in LN monocytes with similar values that the ones found in monocytes from HC treated with a ROS inducer (HC+TBP: 843±199; LN: 8355±1714). Furthermore, phagocytic activity is increased in LN monocytes (77.97±3.31%) compared to HC (39.63±2.75%). Moreover, our preliminary data indicate that HO-1 induction, using cobalt protoporphyrin (CoPP), leads to downregulation of ROS production in LN (~60%) and HC (~40%) leaving both in similar levels of ROS production. In addition, phagocytic activity is also decreased in LN and HC monocytes in the presence of CoPP (~30%).

Conclusions: Decreased HO-1 expression in circulating monocytes of LN patients leads to higher ROS production and phagocytic activity. ROS level and phagocytosis are reduced when we induce HO-1 expression with CoPP. We propose that HO-1 induction might exert a cytoprotective role in LN by regulating innate immunity. FONDECYT N°1150173.

Acknowledgments: We would like to extend our appreciation to all the volunteers that participated in this study. None declared

DOI: 10.1136/annrheumdis-2017-eular.6428

AB0149

PROLACTIN AND AUTOPHAGY IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE OF CORRELATION BETWEEN PRL-R+ (RECEPTOR), CD19+, ATG14+, AND CD25+ EXPRESSION ON B AND T REGULATORY CELLS

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Background: Systemic Lupus Erythematosus (SLE) is a prototype of autoimmune diseases with excessive anti-nuclear autoantibodies production. B cells activation with immune complex formation is the main characteristic of SLE with abnormalities in immune cells, dysregulation of apoptosis, and defects in the clearance of apoptotic materials. Autophagy, a highly conserved protein degradation pathway, is essential for removing protein aggregates and misfolded proteins in cells and its defects contributes to SLE pathogenesis. On the other hand, multiple evidences in humans and experimental models suggest that prolactin (PRL) is associated with active SLE and participates in the immune dysregulation, and one of the mechanisms of PRL action is the inhibition of apoptosis.

Objectives: Analyze the relationship between PRL receptors (PRL-R) on B and T regulatory cells and markers of autophagy in SLE patients and the association, if any, with clinical characteristics of SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4746
Methods: The expression of PRL-R on B cells CD19+ and autophagy-related key regulator protein ATG14+ on T regulatory cells CD25+, were measured by flow cytometry, and expressed in percentages of SLE patients (1997, ACR criteria), and healthy controls. Active SLE was considered by SLEDAI (≥4). The organs affected and treatments were evaluated.

Results: A total of 40 SLE patients and 20 healthy controls were included. Mean age of patients and controls was 30.67±4.16. Mean duration of disease was 6±4.6 years. Twenty patients were active (SLEDAI 8.45±1.9) and of these, lupus glomerulonephritis was observed in 13 patients (65%). The expression of PRL-R on B cells of active SLE was higher than in inactive SLE (50.5% vs 26.5%). In active SLE especially in patients with glomerulonephritis, the mean amount of PRL-R on B cells/ml was 6.645/ml (range 3167–6957). In contrast, patients with inactive SLE, had a low amount of PRL-R, 52.5/ml (range 15–895). In the relation of autophagy, the mean expression of ATG14+ in 20 active SLE patients was 11.19% in comparison with inactive SLE patients, 7.13%, (p=0.04), and in healthy donors, 7.45% (p=0.028).

Conclusions: Our study suggest: In active SLE patients the expression of PRL-R and autophagy-related key regulator protein ATG14+ are very high in B cells and T regulators respectively, in comparison with inactive SLE and healthy donors. These novel findings suggest the interaction between PRL-R and autophagy in order to promote clinical/immune activation with overproduction of autophagosomes. PRL-R and ATG14+ may be a new target of SLE therapy.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8887

AB0150 INCREASED ERYPTOSIS LEVELS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME PATIENTS

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Background: Erythrocytes (RBCs) hold a crucial role in hemostasis and their integrity is influenced by different stimuli including circulating inflammatory mediators. Even though RBCs do not have nuclei and mitochondria, they have developed a process allowing them to undergo a rapid self-destruction named eryptosis. The exact mechanism of eryptocytes cell death is not fully clarified yet but it seems to involve Ca2+ and ceramide formation, leading to cell shrinkage and externalization of phosphatidylserine (PS) (1). Interaction between platelets and eryptocytes could participate in an increasing risk of thrombotic episodes typical of several diseases including antiphospholipid syndrome (APS). In fact, not only signals triggering eryptosis are involved in thrombosis activation, but also recent studies have demonstrated how PS-exposing eryptocytes are able to adhere to the vascular wall causing an impairment of circulation (2,3).

Objectives: Enhanced eryptosis is known to contribute to several pathological conditions (1) but the involvement of this process in APS has not been investigated yet. For this reason the aim of the study was to evaluate eryptosis levels in APS healthy subjects positive for antiphospholipid antibodies without clinical manifestations (aPL carriers), autoimmune haemolytic anemia (AIHA) and healthy donors (HD).

Methods: 27 patients with primary APS (M/F 5/22, mean age 51.1±7.6 years), 14 aPL carriers (M/F 3/11, mean age 48.9±8.4 years) were recruited after written informed consent. Moreover 10 AIHA patients and 12 HD were also enrolled as positive and negative control group respectively. RBCs were isolated from whole blood after centrifugation and eryptosis levels were analysed by flow cytometry, and expressed in percentages of SLE patients (1997, ACR criteria), and healthy controls. Moreover, 10 AIHA patients and 12 HD were also enrolled as positive and negative control group respectively. RBCs were isolated from whole blood after centrifugation and eryptosis levels were analysed by flow cytometry, and expressed in percentages of SLE patients (1997, ACR criteria), and healthy controls.

Results: APS patients showed higher levels of eryptosis compared to HD (p<0.01). Interestingly, the percentage of annexin V-positive RBCs was lower in aPL carriers respect to APS patients (p=0.001). Moreover, an inverse correlation between RBCs volume and eryptosis was found in APS patients (r=-0.4, p=0.03).

Conclusions: Our study provides for the first time evidence of eryptosis enhancement in APS patients suggesting a possible contribution of RBCs apoptosis in the pathogenesis of the disease.

References:
expression revealed suppression in the relative fold change of IL-6 by 23%, IL-8 by 30%, TNF-α by 11%, and IFN-γ by 21% with Tai Chi.

Conclusions: These data suggest that moderate exercise and stress management can have potent immunoregulatory effects on the chronic, systemic inflammation associated with SLE and identify Tai Chi exercise as a viable and effective therapy to complement current pharmacological interventions.

References:

Acknowledgements: Funding: Center for Integrative Health and Wellness and Wexner Medical Center.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5455

AB0152
DISEASE ACTIVITY AND DAMAGE SCORES CORRELATED DIFFERENTLY WITH THE PATIENT REPORTED OUTCOMES IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME COMPARED TO LUPUS ASSOCIATED WITH SECONDARY SJÖGREN’S SYNDROME


Background: Previous studies showed a poor correlation between EULAR Disease Activity Index (ESSDAI) and assessing comparatively patients with primary (pSS) (1). There are no previous studies correlating these scores with the SS Syndrome Disease Activity Index (ESSDAI) in patients with Sjögren’s syndrome (SLE/SS) patient groups.

Objectives: To that end, WT and RAGE−/− animals were injected intra-peritoneally with a single dose of pristane. Disease manifestations were determined after 7 months and included the determination of proteinuria and renal pathology by evaluating the glomerular cellularity and matrix on H&E stained paraffin-embedded kidney sections. Immunofluorescence for glomerular depositions of IgG and IgC. In addition to that we checked for auto-antibody production at several time points during disease development and immune cell distribution, differentiation and phenotype in infected kidneys and spleen.

Results: Apart from a slight decrease in CD71+/Fas+ germinal center B cells and B220−CD21+CD23− follicular B cells in RAGE−/− animals, we did not detect differences in auto-antibody secretion or disease manifestations between RAGE−/− and WT mice.

Conclusions: Our data contrast with recently published data showing that a deletion of RAGE exacerbates lupus nephritis and lymphoproliferation in a different SLE model (B6-MRL Fas lpr/j). Therefore, we are currently looking into the effects of RAGE deletion in additional models of auto-antibody-mediated immune disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6419

AB0153
DELETION OF RECEPTOR FOR ADVANCED GLYCACTION END PRODUCTS (RAGE) DOES NEITHER AFFECT AUTO-ANTIBODY PRODUCTION NOR DEVELOPMENT OF RENAL DISEASE IN PRISTANE-INDUCED LUPUS

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Background: Systemic lupus erythematosus (SLE) is characterized by autoantibodies to diverse autoantigens, especially to nuclear components such as double-stranded DNA (dsDNA) or nucleosomes. Still, it remains unclear why poorly immunogenic molecules such as dsDNA and nucleosomes become targets of humoral autoimmunity in SLE. Increased signaling via pattern-recognition receptors (PRRs) through pathogen-associated molecular patterns (PAMPs) or endogenous damage-associated molecular patterns (DAMPs) released from damaged or stressed tissues, may contribute to the break of tolerance against such nuclear antigens. One important PRR in this context may be RAGE. Among many others, RAGE recognizes High mobility group box 1 (HMGB1). HMGB1 is a DNA-binding nuclear protein that has been found at elevated levels in patients with SLE and other autoimmune diseases; likewise perpetuation of RAGE signaling sustains inflammation and leads to the establishment of chronic inflammatory disorders.

Objectives: We therefore examined, using the Pristane-induced SLE model, if increased RAGE signaling may be involved in the break of tolerance against autoantigens in chronic inflammation.

Methods: To that end, WT and RAGE−/− animals were injected intra-peritoneally with a single dose of pristane. Disease manifestations were determined after 7 months and included the determination of proteinuria and renal pathology by evaluating the glomerular cellularity and matrix on H&E stained paraffin-embedded kidney sections. Immunofluorescence for glomerular depositions of IgG and IgC. In addition to that we checked for auto-antibody production at several time points during disease development and immune cell distribution, differentiation and phenotype in infected kidneys and spleen.

Results: Apart from a slight decrease in CD71+/Fas+ germinal center B cells and B220−CD21+CD23− follicular B cells in RAGE−/− animals, we did not detect differences in auto-antibody secretion or disease manifestations between RAGE−/− and WT mice.

Conclusions: Our data contrast with recently published data showing that a deletion of RAGE exacerbates lupus nephritis and lymphoproliferation in a different SLE model (B6-MRL Fas lpr/j). Therefore, we are currently looking into the effects of RAGE deletion in additional models of auto-antibody-mediated immune disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5455

Table

<table>
<thead>
<tr>
<th>Demographic</th>
<th>pSS (n=55)</th>
<th>SLE/SS (n=15)</th>
<th>Significance</th>
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<td>Sex (female/male %)</td>
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<td>15 (100/0)</td>
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<td>Ethnicity</td>
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<td>Age (mean range)</td>
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<td>56 (25–78)</td>
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<td>Disease duration mean (range)</td>
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<td>23 (3–40)</td>
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<td>Anti-Ro%</td>
<td>76 (43)</td>
<td>73 (11)</td>
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<td>Anti-La+% (n)</td>
<td>49 (27)</td>
<td>27 (4)</td>
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<td>ESSDAI median [IQR]</td>
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<td>2 [1–4]</td>
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<td>SSDDI median [IQR]</td>
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<td>Global BILAG median [IQR]</td>
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<td>Treatment</td>
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<td>Methotrexate (%)</td>
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<td>33</td>
<td>P&lt;0.0092</td>
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Unpaired T test performed; **p<0.01, n = total number, % percentage, IQR = interquartile range, ethnicity: C = Caucasian, A = Asian, MN = African Caribbean, O = Chinese, anti-La = anti-Sjögren’s-syndrome-related antigen A, anti-Ro = anti-Sjögren’s-syndrome-related antigen B.

We found significant correlations of SSDDI score with disease duration and maximum ESSDAI score in patients with pSS (r=0.27, p=0.05 and r=0.67, p=0.001, respectively). In SLE/SS patients, ESSPRI scores correlated with both BILAG and maximum ESSDAI score (r=0.55, p=0.03 and r=0.7, p=0.02, respectively). The SSDDI score correlated with the disease duration only in pSS patients (r=0.27, p=0.05).

Conclusions: Our study showed that there was no similar correlation between various disease scores in patients with pSS compared to SLE/SS patients. If the patient reported outcomes correlated with the disease activity (ESSDAI and BILAG) in SLE/SS patients, this correlation was not seen in pSS patients, in which the significant correlations were found only between damage scores, highest disease activity score and disease duration.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2470

AB0154
CIRCULATING CGP DNA PROMOTER FRAGMENTS IN SLE ACTIVATE INTRARENAL TLR9 SIGNALING AND ACCELERATE RENAL INFLAMMATION AND FIBROGENESIS

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Background: In systemic lupus erythematosus (SLE), lupus nephritis (LN) is associated with chronic inflammation and perpetuated fibroblast activation, both determined by epigenetic mechanisms involving aberrant CpG DNA promoter methylation. During SLE progression, global methylation patterns are commonly lost. These CpG DNA promoter methylation patterns are not limited to the kidney, circulating CpG-rich DNA is also detectable in the blood allowing for biomonitoring (‘liquid biopsy’). However, little is known about its specific contribution to determining disease progression. In the kidney, CpG-rich DNA activates TLR9 signaling mechanisms involved in inflammation and fibrogenesis. Based on these observations, we hypothesized that CpG-rich DNA promoter fragments potentially accelerate renal inflammation and fibrogenesis in SLE-associated LN.

Objectives: To analyze the role of circulating CpG-rich DNA on endothelial TLR9 signalling and the effect of experimental modification of oligonucleotides on kidney inflammation in the Pristane-induced murine model of SLE.

Methods: We isolated circulating CpG-rich DNA from blood samples in a cohort of SLE patients. Then, we tested how these DNA promoter fragments influenced the LN phenotype in a TMPD (‘pristane’)-induced mouse model. Further, we investigated how this renal response could be influenced by the administration of either human or synthetic methylated/unmethylated CpG-rich DNA oligonucleotides. Additionally, the effects of the administration of circulating CpG-rich DNA fragments on TLR9-signalling was analyzed in endothelial cell cultures.

Results: We show that circulating CpG-rich DNA promoter fragments are detectable in SLE patients’ blood. Furthermore, SLE-associated LN is associated with accumulation of unmethylated CpG-rich DNA promoter fragments, implicating a mechanistic connection. These observations were further corroborated in a rodent model of TMPD-induced SLE where administration of CpG-rich DNA (iso-lated from LN patients or synthetic unmethylated CpG-rich DNA oligonucleotides) worsened the renal phenotype in terms of inflammation and fibrogenesis. Causal contribution of TLR9 was further confirmed in Thr29−/− knockout mice with protection from renal inflammation and kidney fibrosis after administration of unmethylated CpG-rich DNA promoter oligonucleotides. TLR9-mediated intrarenal...
inflammation can be therapeutically targeted by administration of synthetic methylated CpG-rich DNA oligonucleotides, ultimately associated with suppression of TLR9-mediated signaling responses and renal injury in experimental SLE/LN.

**Conclusions:** Collectively, our results implicate accumulation of unmethylated CpG-rich promoter DNA fragments in SLE-associated LN. Furthermore, these unmethylated CpG-rich promoter DNA fragments causally contribute to TLR9-mediated inflammation and renal fibrogenesis. Administration of methylated CpG-rich oligonucleotides antagonizes intrarenal TLR9-mediated inflammatory signaling responses and fibrogenesis. Therefore, biomonitoring of CpG-rich promoter DNA fragments and modulation of intrarenal TLR9 signaling is a promising therapeutic target in SLE-associated LN.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4493

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**AB0155 LEARNING SLE PATHOLOGICAL MECHANISMS FROM MULTI-OMICS PROFILES**

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**Background:** Precision medicine aims at providing intervention based on clinical and molecular stratification of patients, and is an important approach for targeting heterogeneous diseases. Multiple types of omics data may give rise to different biological hypotheses of disease etiology. Therefore, the integrated analysis of multi-omics data provides a rich dataset to explore associations between molecular and clinical readouts.

**Methods:** We have recently developed a method allowing us to graphically visualize the relationships between molecular and clinical readouts. To overcome this problem we present a method based on L1 regularization of parameters of interest. However, variable selection approaches are often employed in this context.

**Results:** The proposed method allows us to graphically visualize the relationships between molecular and clinical readouts. To overcome this problem we present a method based on L1 regularization of parameters of interest. However, variable selection approaches are often employed in this context.

**Conclusions:** Systemic lupus erythematosus is a complex autoimmune disease characterized by a variety of clinical manifestations. While multi-omics profiling in multi-omics profiles provides a rich dataset to explore associations between molecular and clinical readouts, the specific relationship between molecular and clinical phenotypes is often underexplored for datasets that contain fewer samples than the number of variables. To overcome this problem we present a method based on L1 regularization and variable selection to generate networks of predictive markers across multiple data types.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5009

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**AB0156 THYMIC STROMAL LYMPHOPOIETIN (TSLP) IN PRIMARY SJÖGREN’S SYNDROME AND RELATED LYPHOMA: THE POSSIBLE CONTRIBUTION OF A NOVEL GROWTH FACTOR**

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**Background:** Primary Sjögren’s syndrome (pSS) is an autoimmune lymphoproliferative systemic disease with a higher risk of non-Hodgkin B cell lymphoma (NLH) evolution. In SS, salivary gland (SG) epithelium plays a crucial role in initiating and perpetuating the autoimmune response. Thymic stromal lymphopoietin (TSLP) is an epithelial and lymphoproliferative cytokine involved in the maintenance of immune tolerance at interfaces between body and environment and in the regulation of lymphocytes homeostasis.

**Objectives:** To study TSLP in serum and SG biopsies of pSS patients stratified by the lymphoproliferative histopathologic status, from fully benign lesions (fbSS) to more malignant ones (nSS) and to NLH, in order to evaluate a possible role of TSLP in SS pathogenesis and in lymphoma evolution.

**Methods:** Serum TSLP levels were determined by ELISA in pSS patients (n=30; 12 fbSS, 10 MESA, 8 NLH) and in controls (healthy blood donors - HD n=20; non-autoimmune sicca without SS - nSS n=10). TSLP was also studied by immunohistochemistry in SG biopsies of the same patients and nSS controls. Correlations with clinical and histopathologic parameters were performed. Of note, sequential samples were also included from three patients evolving from fbSS to NLH.

**Results:** TSLP serum levels were significantly higher in pSS compared to nSS (p<0.01) and HD (p<0.01). A progressive significant increase from fbSS to MESA (p<0.004) and finally to NLH (NLH vs fbSS p=0.0001; NLH vs MESA p=0.003), where the increase was dramatic. This was observed also in metastatic samples from the three pSS patients evolving to NLH. A positive significant correlation between TSLP serum levels and disease activity assessed by ESSDAI was found (r=0.7).

**Conclusion:** Of note, in the affected tissue, TSLP showed an opposite pattern of expression than in the serum. Concerning the salivary epithelium, a declining expression of TSLP was shown from fbSS (expression was similar to nSS) to MESA and finally to NLH. Strikingly, however, the three pSS patients evolving to lymphoma were the only ones showing a low TSLP epithelial expression also at baseline. Concerning the glandular lymphoid infiltrate, the TSLP expression again decreased with progression to NLH. Again, the three pSS patients evolving to lymphoma were the only ones showing a low TSLP inflammatory expression also at baseline.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6450

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**AB0157 TREX1 MUTATION IN THE MEMBERS OF A FAMILY WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTI-PHOSPHOLIPID SYNDROME**

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**Background:** We report a familial SLE and Antiphospholipid Syndrome (aPL) who are positive for TREX1 mutation and complicated with AA amyloidosis.

**Objectives:** Here we report a family with SLE and Anti-phospholipid Syndrome (aPL) who are positive for TREX1 mutation and complicated with AA amyloidosis.

**Methods:** DNA samples were extracted from peripheral blood samples of two affected (mother and daughter) and two unaffected individuals of the same family. Exome sequencing was performed for the four family members and data was processed according to GATK Best Practices recommendations. Exome variants were used to search for a rare candidate variant causing the disease. Identified variant was screened in four family members using Sanger sequencing.

**Results:** The index case (mother) was a 63 year-old woman who had developed polyarthritis and recurrent cerebrovascular accident (CVA) at the age of 44. She was positive for ANA, anti-ds-DNA and IgG anti-cardiolipin antibodies. On anticoagulant therapy she still experiences frequent CVAs. The daughter who is 43 years old had experienced depression, non-erosive arthritis and alopecia at the age of 13. She was positive for ANA, dsDNA and ACA and was treated with hydroxychloroquine, prednisolone, and rituximab. She had attacks of deep vein thrombosis despite anticoagulant therapy. A renal biopsy was performed because of an increase in her creatinine level, with no proteinuria and normal urinary sediment, which revealed AA amyloidosis. She was heterozygous for the p.T300C variant in MEFV gene. Further genetic testing was performed for the mother and the daughter as well as two other non-affected members of the family. Candidate variant search in exome data resulted a novel c. 27T>A (p.M17?) variant in TREX1 gene. Candidate variant search in exome data resulted a novel c. 27T>A (p.M17?) variant in TREX1 gene. Candidate variant search in exome data resulted a novel c. 27T>A (p.M17?) variant in TREX1 gene. Candidate variant search in exome data resulted a novel c. 27T>A (p.M17?) variant in TREX1 gene. Candidate variant search in exome data resulted a novel c. 27T>A (p.M17?) variant in TREX1 gene. Candidate variant search in exome data resulted a novel c. 27T>A (p.M17?) variant in TREX1 gene.

**Conclusions:** Since the variant disrupts translation initiation codon (ATG/AAG) it is predicted to cause loss of complete protein production.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6231
TAUROURSODEOXYCHOLIC ACID DECREASES THE EXPRESSION OF ERAD COMPONENTS AND THE ACCUMULATION OF SALVARY MUCINS INDUCED BY PRO-INFLAMMATORY CYTOKINES

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Background: The salivary glands of Sjögren's syndrome patients show en-doplasmatic reticulum (ER) stress characterized by intracellular accumulation of secretory products such as MUC1, dilated cisternae of proteins in the ER, by decreasing ERAD activity and ER stress induced by the presence of TUDCA suggests that this chemical chaperone promotes folding of proteins.

Objective: The aim of this study was to evaluate if TUDCA decreases EDEM1, SEL1L and MUC1 expression induced by pro-inflammatory cytokines in salivary gland epithelial cells.

Methods: HSG-cells were incubated with 10 nM of IFN-γ or TNF-α for 24h. After 24h, increased expression for both molecules was determined by Western Blot and RT-qPCR, respectively. EDEM1 and SEL1L localization was determined by immunofluorescence.

Results: HSG cells stimulated with IFN-γ or TNF-α showed a significant increase of EDEM1 and SEL1L protein and mRNA levels. Importantly, TUDCA co-incubation caused a significant decreased expression of both molecules.

Conclusions: Decreased expression of MUC1, SEL1L and EDEM1 in the co-incubation caused a significant decreased expression of both molecules. TUDCA might alleviate the ER stress of salivary glands from Sjögren's syndrome of proteins in the ER, by decreasing ERAD activity and ER stress induced by the presence of TUDCA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5822

INTERFERON-Γ-INDUCIBLE KYNURENINES INFLAMMATION PATHWAY: THE MISSING LINK BETWEEN DISEASE ACTIVITY AND SYMPTOMS IN SJÖGREN’S SYNDROME

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1Medicine, Federal University of Espirito Santo, Vitória, Brazil; 2Clinical Science Department, University of Bergen, Bergen, Norway; 3Statistic Department, Federal University of Espirito Santo; 4Locomotor System Department, Federal University of Minas Gerais, Vitória, Brazil; 5Broegelmann Research Laboratory, University of Bergen, Bergen, Norway; 6Bevital Laboratory A/S, University of Bergen, Vitória, Brazil

Background: Tryptophan (TRP) can be converted to kynurenine (KYN) by indoleamine 2,3-dioxygenase (IDO) driven by interferon-γ. Recent studies have suggested that the KYN pathway reflects an important interface between the immune and nervous system modulation.

Objective: The aim was to study KYN pathway and their correlation to clinical and immunological parameters in primary Sjögren’s syndrome (pSS).

Methods: We included 97 pSS (AECG) and 63 healthy controls matched to age, sex, ethnicity, and body mass index (BMI). KYN metabolites and TRYP were analysed by liquid chromatography/tandem mass spectrometry.

Results: Patients aged 50±11 years showed anti-SSA-Ro of 63%, anti-SSB-La 31%, anti-nuclear antibody 81%, rheumatoid factor 24%, and systemic manifestations 67%. Most (88%) showed low disease activity measured by Eular Sjögren's Syndrome Disease Activity Index (ESSDAI). 22% moderate to high, 10% high ESSDAI. The kynurenine:tryptophan ratio (KTR) was (0.031±0.014 vs. 0.024±0.007, p<0.001), KYN (1.890±0.580 vs. 1.652±0.426, p=0.000), quinolinic acid (QA) (477.82±251.55 vs. 382.05±128.06, p=0.018), hydroxyindoleacetic acid (3HK) (53.45±52.05 vs. 39.15±9.67, p=0.056), anilinic acid (AA) (19.86±6.26 vs. 16.94±4.17, p=0.001) were higher while xanthurenic acid (XA) (11.52±8.87 vs. 10.33±6.58, p=0.019), and TRYP (64.90±13.43 vs. 71.02±8.88, p=0.012) were lower in pSS compared to controls. Higher KTR was associated with disease duration (r=0.211, p=0.042), CRP (r=0.254, p=0.029), lower hemoglobin (r=−0.219, p=0.034), creatinine (r=−0.586, p=0.000), hypergammaglobulinemia (r=0.254, p=0.014), hyper IgG (r=0.354, p=0.004), lower C3 (r=0.233, p=0.014), and C4 (r=−0.294, p=0.004). Higher KTR was observed in those with Biological ESSDAI domain involvement (0.033±0.016 vs. 0.029±0.013, p=0.003), glandular manifestation (0.037±0.014 vs. 0.029±0.013, p=0.007), in the other hand lower KTR in those with presence of musculoskeletal pain (0.029±0.011 vs. 0.032±0.015, p=0.003). ESSDAI showed a tendency to correlate with KTR (r=0.177, p=0.091) and ESSPRI inversely correlated with AA (r=−0.233, p=0.071). Either patient with pain showed lower AA (20.66±6.67 vs. 17.22±5.07, p=0.021).

Conclusions: TRYP is decreased and KYN metabolites pathway is increased in pSS. IDO activity expressed like KTR was positively correlated with disease activity and glandular manifestations but negatively with pain. A better understanding of the KYN pathway can clear the dissociation of symptoms and disease activity in pSS.

Disclosure of Interest: None declared

References:

Disclosure of Interest: None declared
ANTIPHOSPHOLIPID ANTIBODIES DIFFERENTIALLY REGULATE THE EXPRESSION & ACTIVITY OF THE PROTEINASES WITH EFFECTS UPON MONOCYTE AUTOPHAGY

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Background: Antiphospholipid antibodies (aPLs) are known to activate monocytes in the pathogenesis of antiphospholipid syndrome (APS), although the precise mechanisms by which this activation occurs are not fully understood. We have recently identified several novel protein targets using a comprehensive proteomic analysis of human monocytes treated with IgG from patients with APS. Amongst these novel targets lysosomal proteases, including cathepsin B and cathepsin D were identified. These proteases are important in protein degradation, clearance of autolysosomes, apoptosis and autophagy. Dysregulation of these homeostatic cellular functions may be important in the importance of autoantigens and pathogenesis of the APS. Therefore, we have now studied the effects of APS IgG upon the expression/activity of different cathepsins and their effects upon autophagy.

Objectives: Determine the effect of pathogenic aPl antibodies on monocyte autophagy and its association with the regulation of lysosomal activity.

Methods: Healthy monocytes were treated with 200 µg/ml IgG purified from (n=9) patients with APS or (n=9) healthy control (HC) IgG for 6 h. The expression of cathepsin B and cathepsin D were measured by western blotting. Activity assays for lysosomal proteases cathepsin D, cathepsin B and cathepsin L were performed using fluorescence based assays (Tryp200™). Intracellular proteolytic activity of monocytes was determined using DQ-BSA (Molecular probes) and flow cytometry analysis. Autophagy was induced by treating monocytes with 50 µg/ml GM-CSF for 14 h.

Results: Consistent with our previous label free quantification mass spectrometry proteomic analysis, western blot analysis confirmed that levels of cathepsin B and cathepsin D were decreased in monocytes treated with APS IgG compared to HC IgG. Similarly, enzymatic assays revealed that cathepsin B and cathepsin D activities were significantly reduced in monocytes treated with IgG from patients with APS compared to HC (p=0.0188, 0.0323). In contrast, levels of enzymatic activity of cathepsin L were increased in monocytes treated with APS IgG compared to HC IgG (p=0.0106). To determine the effect of APS IgG on autophagy, we exposed healthy monocytes to IgG and induced autophagy by treating them with GM-CSF for 14 h. Subsequently we tested the intracellular proteolytic activity with DQ-BSA. Stimulation of monocytes with APS IgG reduced the lysosomal activity of GM-CSF-treated monocytes whereas HC IgG had no effect, indicating that APS IgG disrupts lysosomal degradation during monocyte autophagy.

Conclusions: We found that IgG from patients with APS regulate the expression and activity of lysosomal proteases cathepsin B/D and cathepsin L in opposite directions. Activity of cathepsin B and D was down-regulated by exposure to IgG from patients with APS whereas cathepsin L was up-regulated. Furthermore, we found APS IgG disrupts lysosomal degradation during monocyte autophagy. Animal experiments are now underway to increase our understanding of how modulation of cathepsin activity and autophagy may be important in the pathogenesis of APS and provide new therapeutic targets.

Disclosure of Interest: None declared


SERUM LEVEL OF PRO-INFLAMMATORY CYTOKINES IS NEGATIVELY ASSOCIATED WITH FATIGUE IN PRIMARY SJÖGREN’S SYNDROME

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Background: We have previously described a model of fatigue in patients with primary Sjögren’s syndrome (PSS) based on the levels of serum cytokines, pain and depression scores. Importantly, removal of cytokines from this model substantially reduced the accuracy suggesting that cytokines may have a key role in the biological basis of fatigue [1]. However, interpreting the model is complicated by the complexity of the immune system and the likely multiple interactions between numerous cytokines and other variables [2]. Structural equation modelling (SEM) is a statistical technique that allows for analysis of one or multiple independent variables with one or multiple dependent variables. SEM consists of two components – the structural model, which represents the relationships between the theoretical variables, and the measurement model, which are the relationships between the latent variables and their measures [3]. Objectives: To use SEM to test our hypothesis that the balance between pro-inflammatory and anti-inflammatory cytokines play an important role in determining severity of fatigue in patients with PSS.

Methods: We used Canonical Correlation Analysis (CCA) to investigate the variation in cytokine expression across our spectrum of fatigue patients to explore interactions and dependencies between cytokines. We then built a conceptual model based on the literature representing the likely relationships between fatigue and various proinflammatory and anti-inflammatory cytokines and other soluble molecules in the serum. This conceptual model was then challenged using serum data and fatigue scores of 161 PSS patients from the UK primary Sjögren’s syndrome registry. Model fit was assessed using the Confirmatory Factor Index, the Root Mean Square Error of Association and the Standardised Root Mean Square Residual. We also analysed changes in fatigue scores over a period between 1–4 years.

Results: CCA revealed the first axis ofordination (CCA1) broadly correlates with fatigue, consists of many pro-inflammatory cytokines including TNFα, IL6, IL12 and IFNy, IL17, which were negatively correlated with fatigue while IL-6 and MCP1, which were positively associated with increased fatigue severity. The second axis (CCA2) reflects a trend in cytokines which appear to relate to patients’ age. Fatigue scores were largely stable over time and therefore data were not included in the SEM analysis. The main pro-inflammatory SEM model showed fatigue was negatively associated with pro-inflammatory cytokine activity (p=0.019); IL-10 drove IP-10 (p<0.001); and IL-10 was driven by IL-6 (p=0.006) (Fig 1).

Conclusions: Chronic fatigue in PSS is negatively associated with many pro-inflammatory cytokines. We hypothesize that it reflects adaptive biological processes, which occurs after chronic exposure to inflammation in conditions such as PSS.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5811

MESENCHYMAL STEM CELLS INDUCE CD1C+ TOLERGENIC DENDRITIC CELLS IN HUMAN SYSTEMIC LUPUS ERYTHEMATOSUS VIA UP-REGULATING FLT-3 LIGAND

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Background: CD1c+ tolerogenic dendritic cells (DCs) play important roles in the induction of peripheral tolerance and control of adaptive immune response. Umbilical cord (UC)-derived mesenchymal stem cells (MSCs) exhibit immunoregulation effects in systemic lupus erythematosus (SLE). However, the underlying immunosuppression mechanism of MSCs via tolerogenic DCs in SLE remains unclear.

Objectives: The aim of this study was to examine tolerogenic DCs levels in SLE patients, and to further investigate the mechanism of MSCs in the regulation of tolerogenic DCs.

Methods: Tolerogenic DCs were isolated as Lin (CD3/19/56/14)+CD11c+CD1c+ from peripheral blood mononuclear cells (PBMCs). Levels of tolerogenic DCs were determined by flow cytometry, and serum concentration of Flt-3 ligand (FLT3L) were determined by ELISA from 17 healthy controls and 25 SLE patients. Eight SLE patients were given UC MSCs infusions. We compared the levels of tolerogenic DCs and serum FLT3L before and 24 hours after UC
Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

**AB0164 AMYLOIDOSIS IN PROGRESSIVE SYSTEMIC SCLEROSIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 12 PATIENTS**

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**Background:** Systemic sclerosis (SSc), like all chronic autoimmune disorders, may be complicated by AA amyloidosis (AAa). An associated B-cell lymphoma or cause amyloid nodal involvement and amyloidosis in SSc patients, but not dose-dependently. The supernatant regulated peripheral CD1c+ DCs, but not dose-dependently. The supernatant level significantly increased after co-cultured with MSCs. However, the addition of FLT3L siRNA significantly abrogated the up-regulation of CD1c+ DCs by MSCs.

**Conclusions:** UC MSCs induce CD1c+ tolerogenic DCs through up-regulating FLT3L in lupus patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3334

**References:**


**AB0165 CXCL4 MAY PLAY A KEY ROLE IN SYSTEMIC SCLEROSIS BY DRIVING CD4 T CELLS TO PRODUCE IL-17**

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**Background:** CXCL4 regulates multiple facets of immune response and its level is higher in various Th17-associated autoimmune diseases, including systemic sclerosis (SSc)-1. Recently, CXCL4 was shown to induce type I interferon production as well as endothelial activation in SSc patients1. Th17 skewing has been demonstrated in SSc1,2, however, whether CXCL4 plays a role in the induction of IL-17 production is currently unclear.

**Objectives:** To investigate the effect of CXCL4 on human CD4 T cell phenotype in particular IL-17 production in the absence or presence of antigen presenting cells.

**Methods:** Blood was obtained from healthy donors and CD4 T cells, monocytes, dendritic cells, were isolated using magnetic-based sorting (n=20). In addition, CD4 T cells from SSc patients were isolated (n=10). CD4 T cells were activated using anti-CD3/CD28, or in co-cultures with antigen presenting cells, stimulated using superantigen Staphylococcal enterotoxin B. Exogenous recombinant human CXCL4 was added during (co)-culture in different concentrations. Cytokine production and proliferation were analyzed using Luminex immunoassays, intracellular cytokine staining, and flow cytometry.

**Results:** CXCL4 directly induced CD4 T cells secreting both IL-17 and IFN-γ, as well as IL-22, when costimulated with anti-CD3/CD28 (p<0.05). In many SSc patients, similar IL-17 increase upon CXCL4 treatment was observed, although this did not reach statistical significance. This might be due to the fact that CD4 T cells from SSc patients had already significantly higher levels of IL-17 as compared to healthy donors (2182±222.2 vs 1053±263.6 pg/ml, mean±SEM, p<0.05). Furthermore, in co-culture system of CD4 T cells with monocytes or myeloid dendritic cells, CXCL4 treatment induced IL-17 production upon triggering by superantigen (p<0.05). Moreover, when monocyte-derived dendritic cells were differentiated in the presence of CXCL4, they orchestrated significantly increased levels of IL-17, IFN-γ, and proliferation by CD4 T cells (all p<0.05).

**Conclusions:** Altogether, we demonstrate that CXCL4 may potentially activate immune responses in Th17-mediated rheumatic diseases such as systemic sclerosis.

**References:**


**Acknowledgements:** This study was supported by the Dutch Arthritis Association (Reumafonds) to A.J.A. and T.R.D.J.R., the Netherlands Organization for Scientific Research (NWO) to A.J.A. (Mosaic grant 017.008.014) and T.R.D.J.R. (Pre-Seed grant), the Portuguese Fundação para a Ciência e a Tecnologia S.S.C.S. (SRH/FB/89643/2012) and the European Research Council to T.R.D.J.R. (ERC Starting grant).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6100

**AB0166 INTERLEUKIN-6-POLARISED MACROPHAGES PROMOTE DERMAL MYOFIBROBLAST DIFFERENTIATION**


**Background:** Macrophages and fibroblasts are key effector cell types present in scleroderma tissue. While the effect of scleroderma fibroblast conditioned medium on macrophages has been previously studied2, less is known about the effect of scleroderma macrophages on fibroblasts. Interleukin-6 (IL-6) is an important mediator of fibrosis and is overexpressed in scleroderma sera and cells of skin fibroblasts, macrophages and endothelial cells3. Given the increase in IL-6 levels in scleroderma and presence of the IL-6 receptor on the cell surface of macrophages, we are now investigating the phenotype of macrophages exposed to IL-6. Here we present our work into the paracrine function of IL-6-treated macrophages in stimulating fibroblasts using a media transfer approach.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1226
AB0167 CALCULUM INFUX KINETICS AND THE CHARACTERISTICS OF POTASSIUM CHANNELS IN PERIPHERAL T LYMPHOCYTES IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic connective tissue disorder characterized by microvascular injury, fibrosis and autoimmunity that affects the skin and internal organs. The short-term activation of peripheral blood T lymphocytes plays a crucial role in initiating and maintaining the chronic inflammation. The transient increase of the cytoplasmic free calcium level plays a key role in the process of lymphocyte activation. Kv1.3 and IKCa1 potassium channels are important regulators of the maintenance of calcium influx during lymphocyte activation. The influx of calcium is maintained by the function of potassium channels that conserve the electrochemical potential gradient via the efflux of potassium from the cytoplasm. Recent reports raised the notion that the inhibition of lymphocyte potassium channels, especially that of the Kv1.3 channel would be an straightforward solution for specific immunosuppression in autoimmune diseases. Furthermore, our previous studies described an alteration of the short-term activation of peripheral lymphocytes in rheumatoid arthritis and primary Sjögren’s syndrome (pSS), and the overexpression of Kv1.3 channels in pSS.

Objectives: Therefore, in this study we aimed to characterize the effects of lymphocyte potassium channel inhibition on short-term peripheral blood T lymphocyte activation in major lymphocyte subsets in SSc.

Methods: We enrolled 12 healthy individuals and 16 SSc patients. We evaluated calcium influx kinetics following activation in CD4, Th1, Th2 and CD8 cells applying a novel kinetic flow cytometry approach. We assessed the sensitivity of the above subsets to specific inhibition of the Kv1.3 and IKCa1 potassium channels. We also assessed the Kv1.3 expression on lymphocytes.

Results: We observed increased parameters of calcium influx in CD8+ lymphocytes as compared with Th1 cells in SSc. However, the activation of CD8+ cells was lower in SSc compared to healthy controls. Moreover, activation of Th1 lymphocytes was slower in SSc than in healthy controls. The inhibition of IKCa1 potassium channel decreased the activation of CD8+ lymphocytes in healthy controls and the activation of Th1 cells in SSc. The inhibition of Kv1.3 channel modified the dynamics of activation of Th1 and Th2 lymphocytes in SSc.

Conclusions: The altered function of CD8+ cells and the specific inhibition of potassium channels seem to be a consequence of altered calcium influx kinetics in SSc, distinguishing it both from healthy controls and other autoimmune diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4868

AB0168 PROTECTIVE EFFECTS OF EPIGALLOCATECHIN 3 GALLATE ON FIBROSIS IN SCLERODERMA MODEL

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Background: Scleroderma (SSc) is a disease that shows involvement in internal organs or on the skin characterized by fibrosis (1). Dermis thickening and uncontrolled extracellular matrix (ECM) increase are seen in this disease whose pathogenesis is not fully understood. TGF-β/Smad 2/3 pathway is pivotal role in SSc pathogenesis via induction of profibrotic molecules including collagen and by decrease of matrix metalloproteinases (MMPs) synthesis (2,3). The occurrence of the myofibroblast phenotype at fibrosis is thought to be responsible for the contracted regions of the affected tissues (4).

Objectives: The aim of this study is to investigate the potential effects of epigallocatechin-3-gallate (EGCG) against fibrosis.

Methods: 32 Balbc female mice were randomly selected into four groups. For 21 days: (1) Control group (n: 8) was given 100 μL subcutan (sc) saline (SF) once a day, 100 μL intraperitoneal (ip) SF twice a week, (2) BLM group (n: 8) was given 100 μL (100 μg) sc BLM once a day, 100 μL ip SF twice a week, (3) BLM + EGCG group (n:8) was given 100 μL (100 μg) sc BLM once a day, 100 μL (100 μg) ip EGCG twice a week, (4) EGCG group (n: 8) was given 100 μL sc SF once a day, 100 mL (100 μg) ip EGCG twice a week. Hematoxylin&eosin and Masson trichrome staining of dermal areas were performed. Myofibroblast activity was measured using alpha smooth muscle actin antibody (α-SMA) by immunohistochemistry. Expression levels of MMP-1, MMP-8, MMP-13 and p-SMAD protein were examined by western blot. Expression levels of TGF-β1 mRNA were examined by qPCR. All of the statistical analyses were performed using SPSS software and the quantitative data were expressed as the mean±SEM. The quantitative variables were compared using the a ANOVA-Sidak. Statistical significance was defined as p<0.05.
EVALUATION OF FREQUENCY AND TYPE OF PHYSICAL DIMINISHED PERIPHERAL T-CELL ACTIVATION ALONG WITH ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN PATIENTS

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References:

DOI: 10.1136/annrheumdis-2017-eular.2076

Disclosure of Interest: Medicine Faculty of Research Laboratory (R-LAB).

Acknowledgements:

This research was supported by a grant supplied from “Dokuz Eylul University Research Fund” and carried out at Dokuz Eylul University Medicine Faculty of Research Laboratory (R-LAB).

Disclosure of Interest: None declared


AB0169 EVALUATION OF FREQUENCY AND TYPE OF PHYSICAL THERAPY IN MORE THAN 3400 PATIENTS WITH SYSTEMIC SCLEROSIS


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Background: Systemic sclerosis (SSc) is a chronic fibrosing autoimmune disease which leads to severe musculoskeletal dysfunction, disability and contractures. Little is known on the type and extent of physical therapy (PT) prescribed to SSc patients in daily practice.

Objectives: To determine the type and frequency of PT received by SSc patients.

Methods: The data of 3430 clinically well defined SSc patients registered in the database of the German Network for Systemic Sclerosis were analyzed using SPSS.

Results: 48.5% (1662/3430) of the patients were treated with PT. The most frequently used form of PT was lymphatic drainage (23.6%/876), followed by physical exercise therapy (18.1%/671) and paraffin wax bath (10.5%/389). About 30% of the patients (46.9%) received two or three different forms of PT simultaneously. The prescription of PT did not correlate with the SSc subtype, as 49.5% (503/1016) of dcSSc patients, 50.3% (850/1689) of lcSSc patients and 45.7% (143/313) of SSc-Overlap patients received PT. PT was significantly more often prescribed to patients with pulmonary fibrosis in 51.1% (617/1208), synovitis in 61.6% (299/485) and CK elevation in 61.1% (174/285) (p=0.001–0.029). PT did not correlate with patients with pulmonary fibrosis in 51.1% (617/1208), synovitis in 61.6% (299/485) and CK elevation in 61.1% (174/285) (p=0.001–0.029). PT did not correlate with patients with pulmonary fibrosis in 51.1% (617/1208), synovitis in 61.6% (299/485) and CK elevation in 61.1% (174/285) (p=0.001–0.029).

Conclusions: Although SSc is characterized by considerable disability and restriction of motion, less than 50% of patients received PT. The significant decrease in PT prescription during recent years may reflect lack of knowledge how to prescribe PT and more restrictive insurance regulations.

Disclosure of Interest: None declared

AB0171 ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN INTRIGUING ASSOCIATION WITH SKIN INVOLVEMENT

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Background: Systemic sclerosis (SSc), one of the most complex connective tissue disease, is characterized by three pathogenic events namely, vascular damage, autoimmunity and fibroblast activation, leading to a widespread fibrosis of skin and internal organs (1,2). Previous studies showed that 1) carbanhylation mainly affects structural proteins undergoing to a low turn-over rate, namely dermal skin and tendons-associated proteins; and that 2) carbanhylated proteins accumulate in skin in an age-dependent manner, contributing to tissue alteration (3).

Objectives: As dermis is a disease target and anti-carbanhylated protein antibodies (anti-CarP Ab) have been reported in patients with SSc (4), we sought to evaluate any relationship between anti-CarP Ab and clinical parameters reflecting skin involvement in SSc.

Methods: Serum samples and clinical data from 123 patients with SSc were collected. The samples were collected by indirect ELISA, using carbamylated bovine serum albumin as the antigen. Serum Anti-CarP Ab levels were also measured in 41 healthy aged-matched individuals. Clinical data were retrieved as previously reported (5).

Results: The mean serum levels of anti-CarP Ab did not statistically differ
between healthy and SSc group. In SSc, Spearman analysis showed that anti-CarP was inversely correlated with the modified Rodnan skin score (R) (R=-0.325, p<0.001), independently of patients’ age. Receiver operating characteristics (ROC) analysis identified the anti-CarP cut-off that best discriminated dichotomized clinical variables related to skin involvement. This cut-off was employed to study CarP expression in patients with anti-CarP positive and anti-CarP negative patients. Three SSc skin-related clinical parameters were significantly different between groups: RSS (p=0.001), SI skin (p=0.002), and sclerodema (p=0.001). A worse skin involvement was associated with low anti-CarP levels.

Conclusions: The study shows that anti-CarP Ab serum level inversely associates to the severity of skin involvement in SSc patients. One possible mechanism to explain the inverse association is that the disease-dependent accumulation of carboxamidated proteins in the skin may neutralize circulating anti-CarP Ab, thus contributing to their serum levels decrease. However, further investigation is needed to clarify this issue and to assess whether the levels anti-CarP Ab can be useful in the clinical setting of SSc.

References:

Disclosure of Interest: None declared

PSGL-1 AND ADAM8 ON DENDRITIC CELLS ARE ASSOCIATED WITH SYSTEMIC SCLEROSIS AND COULD ACT AS BIOMARKERS FOR INTERSTITIAL LUNG DISEASE

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Background: Systemic Sclerosis (SSc) is a chronic autoimmune disorder with cutaneous, vascular and immune cells abnormalities that lead to extensive cutaneous and visceral fibrosis with high morbidity and mortality. P-Selectin interacts with PSGL-1 and proteolytically processes it, what could be a regulatory mechanism to control the expression of this inflammatory markers in the immune system.

Objectives: To investigate whether PSGL-1 and ADAM8 expression on leukocytes could be implicated in the pathogenesis of SSc.

Methods: PBLS from 47 SSc patients and 35 healthy donors were analyzed by flow cytometry. The percentage of cells expressing PSGL-1, HLA-DR and ADAM8, as well as the membrane (without cell permeabilization) and total (after cell permeabilization) expression were assessed for each leukocyte subset. For ADAM8, as well as the membrane (without cell permeabilization) and total (after cell permeabilization) expression were assessed for each leukocyte subset. For PSGL-1 and ADAM8 expression in CD16+ monocytes. Remarkably, highest PSGL-1 expression on CD16+ monocytes. Remarkably, highest PSGL-1 expression on conventional DC (CDc) and high levels of ADAM8 on plasmacytoid DC (pDC) associate with interstitial lung disease (ILD), one of the most severe SSc clinical manifestations, suggesting that PSGL-1 and ADAM8 could be prognostic markers of ILD.

Conclusions: This study highlights that PSGL-1 and ADAM8 expression on conventional DC, monocytes and lymphocytes could be implicated in SSc pathogenesis and particularly on DC might act as biomarkers for ILD.

References:

Disclosure of Interest: None declared

AB0173 MYCOBACTERIAL INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE AND ASSOCIATED FACTORS. DATA FROM THE REGISTRY OF PATIENTS WITH SLE OF THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSER)

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Objectives: To study the prevalence of mycobacterial infection (MI), the associated factors and their clinical significance in patients included in a large SLE cohort.

Methods: Retrospective descriptive study of RELESSER patients with a history of MI and analysis of the factors associated with this infection.

Results: In RELESSER, 3,658 patients with ≥ 1 ACR SLE criteria were included. Three SSc skin-related clinical parameters were significantly different between groups: RSS (p=0.001), SI skin (p=0.002), and sclerodema (p=0.001). A worse skin involvement was associated with low anti-CarP levels.

Conclusions: The study highlights that PSGL-1 and ADAM8 expression on CD16+ monocytes and plasmacytoid DC might act as biomarkers for ILD.

Disclosure of Interest: None declared

AB0174 LYMPHOCYTE SUBSETS T, B AND NK CELLS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a rare multisystem disease with underlying immune mechanisms, whose pathogenesis remains unclear. Few previous reports have evaluated lymphocyte subpopulations in SSc and your results are conflicting.

Objectives: The present study aimed to analyze the lymphocyte subsets in SSc patients in comparison to healthy individuals.

Methods: Peripheral blood (PB) samples to analyze lymphocyte subsets were obtained from 47 SSc patients who were divided into two groups: ACR SLE criteria were included. Three SSc skin-related clinical parameters were significantly different between groups: RSS (p=0.001), SI skin (p=0.002), and sclerodema (p=0.001). A worse skin involvement was associated with low anti-CarP levels.

Conclusions: The study highlights that PSGL-1 and ADAM8 expression on CD16+ monocytes and plasmacytoid DC might act as biomarkers for ILD.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2974

AB0174 LYMPHOCYTE SUBSETS T, B AND NK CELLS IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a rare multisystem disease with underlying immune mechanisms, whose pathogenesis remains unclear. Few previous reports have evaluated lymphocyte subpopulations in SSc and your results are conflicting.

Objectives: The present study aimed to analyze the lymphocyte subsets in SSc patients in comparison to healthy individuals.

Methods: Peripheral blood (PB) samples to analyze lymphocyte subsets were obtained from 47 SSc patients who were divided into two groups: ACR SLE criteria were included. Three SSc skin-related clinical parameters were significantly different between groups: RSS (p=0.001), SI skin (p=0.002), and sclerodema (p=0.001). A worse skin involvement was associated with low anti-CarP levels.

Conclusions: The study highlights that PSGL-1 and ADAM8 expression on CD16+ monocytes and plasmacytoid DC might act as biomarkers for ILD.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2974
29.6%, p<0.026) (Table 1). No statistically significant differences were found in the percentages or the absolute numbers of T, B or NK cells.

**Conclusions:** Our data support previous reports indicating that depletion of lymphocyte in the PB of SSc patients. However, we found no significant difference in relation to lymphocyte subtypes, which differs from the literature data.

**References:**

**Results:** Sitaxentan and/or ambrisentan significantly blocked the migration of neutrophils and tumor cell lines. In more detail, neutrophil migration in response to N-formylmethionyl-leucyl-phenylalanine (FMLP) or Protease-activated receptor 2 (Par-2) agonist. Because it has been shown before [2], IgGs from HD and SSc patients were used as additional stimulus for the effects of ETAR antagonists on migration of neutrophils and tumour cells remain to be determined.

**Conclusions:** This is the first attempt to validate circulating biomarkers defining disease phases in SSc patients. These results support that patients diagnosed as early SSc have the highest likelihood of disease progression. Moreover, the presence of autoreactive IgGs in SSc sera can be used to identify patients at risk for particular disease outcomes, such as cardiac involvement or pulmonary fibrosis.

**Acknowledgements:** FONDECYT 3150623 & 1151383; FONDAP 15150012.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3889
setting, our results confirm that defSSc might represent an intermediate entity between pre-clinical stages and the most severe subsets of disease, thereby opening new perspectives on SSC pathophysiology and disease intervention.

References:

Acknowledgements: Supported by a grant from Gruppo Italiano per la Lotta alla Sclerodermia (GILS). MC and TR are partly supported by the VIDI laureate and Dutch Arthritis Foundation (NWO, Netherlands Institute for Science) and ERC starting grant (Figure). The LTI MultiPlex Core Facility is acknowledged for technical performance of the multiplex immune assays.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5295

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**AB0178 PHENOTYPING OF NATURAL KILLER (NK) RECEPTORS ON NK AND NKT-LIKE CELLS DISCLOSES DEFECTIVE IMMUNE-REGULATORY CAPABILITY IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by dysregulation of the immune system, vasculopathy and fibrosis of the skin and internal organs. Natural Killer (CD56+CD3- NK) and NKT-like (CD56+CD3+) cells display receptors (NKR) whose expression pattern determines their cytotoxic and immune-regulatory activity. The role of NK and NKT-like cells in the dysregulation of the immune system in SSc has not been fully elucidated yet.

Objectives: To improve our knowledge on the contribution of NK, NKT -like and iNKT cells as immune check-points in fibrotic SSc.

Methods: NKR were assessed by flow cytometry using two 13-color panels on whole blood of 84 SSc patients and 20 healthy controls (HC). In particular, 15 patients with early SSc (EsAaSSc) without signs or symptoms of evolutive disease (2001 LeRoy and Medsger criteria). 24 patients with definite SSc without skin or lung fibrosis (defSSc); 26 patients with limited (iSSc) and 19 patients with diffuse cutaneous SSc (dcSSc) 2013 EULAR/ACR classification for SSC were included. NK degranulation in response to K562 target cells was assessed in iSSc and dcSSc patients versus HC.

Results: The number of circulating lymphocytes, NK-like and iNKT cells - but neither CD3+ T nor NK cells - was reduced in dcSSc versus HC. NKp46+ NK cells were decreased in both iSSc and dcSSc versus HC and EsAaSSc. Consistently with these observations, dcSSc exhibited lower degranulation capability (CD56+KIR+) and activating NKR-expressing NK-like cells were diminished in both iSSc and dcSSc versus HC.

Conclusions: dcSSc patients showed a defective NK cytotoxicity potential, possibly due to the decreased NKp46+ fraction. The regulatory, cytotoxic KIR+ NK-like fraction was also reduced with a parallel decrease of activating receptors expression in both iSSc and dcSSc. Overall these results point towards an impairment of NK and NKT-like cells as immune check-points in fibrotic SSc.

References:

Acknowledgements: Supported by a grant from Gruppo Italiano per la Lotta alla Sclerodermia (GILS). MC and TR are partly supported by the VIDI laureate and Dutch Arthritis Foundation (NWO, Netherlands Institute for Science) and ERC starting grant (Figure). The LTI MultiPlex Core Facility is acknowledged for technical performance of the multiplex immune assays.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5689

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**AB0179 DEGRADATION OF TYPE VII COLLAGEN (COL7) IS ASSOCIATED WITH SYSTEMIC SCLEROSIS – DEVELOPMENT OF A NOVEL NEO-EPITOPE SPECIFIC ASSAY**

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Background: Idiopathic pulmonary fibrosis (IPF) is characterized by an increased rate of extracellular matrix (ECM) turnover resulting in fibrosis. The pathologic remodeling process increases levels of protein synthesis and degradation mediated by proteases such as matrix metalloproteinases (MMPs). Acute exacerbations of IPF (AE-IPF) represent periods of increased disease activity. Pulmonary involvement, especially pulmonary fibrosis, is common in patients suffering from systemic sclerosis (SSc) and ankylosing spondylitis (AS).

Objectives: The objective was to investigate if ECM remodeling was altered during AE-IPF by serological neo-epitope biomarkers.

Methods: Serum samples were collected from patients with IPF at clinically stable disease (S-IPF, n=29) and at AE-IPF (n=68). Of these, 11 and 28 patients, respectively, had idiopathic pulmonary fibrosis (IPF). 28 IPF patients had paired samples. Biomarkers released from MMP-mediated degradation of collagen type I (C1M), III (C3M), IV (C4M), and VI (C6M), elastin (ELM7), versican (VCAN), biglycan (BGM), and C-reactive protein (CRP) were assessed in serum by competitive ELISAs utilizing neo-epitope specific monoclonal antibodies. Data were analysed using Mann-Whitney test, Wilcoxon test, Spearman’s rank correlation, and Kaplan-Meier curves as appropriate.

Results: Mean age of patients was 71 (range 54–88) at AE-IPF and 69 (range 55–83) at S-IPF. Mean forced vital capacity in percentage of predicted value (%FVC) was 55.6% (SD 19.5) at AE-IPF and 79.0% (SD 26.5) at S-IPF. Serum fibilics that connects the basement membrane to the underlying interstitial matrix and has mainly been investigated for its role in blistering skin diseases. It has been investigated for its role in dystrophic epidermolysis bullosa, a severe skin disease. Furthermore, increased levels of type VII collagen in skin has been reported for patients with systemic sclerosis (SSc).

Objectives: The objectives here were to develop and characterize a bio-functional marker assessing col7 degradation in patients with SSc.

Methods: We identified a specific fragment of col7 in serum from COPD patients, which was not found in controls, using mass spectrometry. A monoclonal antibody was raised against the first ten amino acids of the neo-epitope (KLH-CGG-GPPGPPGRLV) and employed in a competitive ELISA (C7M). The C7M assay was validated technically and was subsequently evaluated in 2 cohorts including SSc patients. The first cohort (SSc#1; n=35) consisted of early (≤2 years of SSc symptoms; n=16) and late (>10 years of disease with stable skin for at least 6 months, n=19) diffuse SSc patients, while the second cohort (SSc#2; n=119) consisted of limited (n=78) and diffuse (n=41) SSc patients. Serum C7M levels were likewise measured in healthy subjects and compared to the levels of SSc patients using the Kruskal-Wallis test with Dunn’s multiple comparisons test comparing healthy individuals with the two SSc cohorts.

Results: A technically robust competitive ELISA (C7M), which was highly specific for a col7 fragment was developed. The assay showed acceptable inter- (13%) and intra-assay (9%) variation, linearity (102% dilution recovery), analyte stability (102% recovery after 4 freeze/thaw cycles), and interference. The C7M marker was evaluated by comparing serum levels in healthy donors with patients with SSc (Figure). Serum C7M levels were not associated with age, gender, BMI, or disease duration. The mean geometric serum C7M level in healthy donors was 4.6 ng/mL (95% CI 3.7–5.6 ng/mL). The geometric mean serum C7M levels were significantly elevated in both cohorts of patients with SSc (SSc#1: 13.6 ng/mL [95% CI 11.1–16.5], p<0.0001; SSc#2: 9.2 ng/mL [95% CI 8.3–10.2], p<0.0001). Furthermore, a significant difference were observed between the two cohorts (P<0.05).

Conclusions: The C7M ELISA enabled quantification of type VII collagen degradation in serum. Elevated serum C7M levels indicated that the remodeling of type VII collagen was significantly increased in patients with SSc, suggesting a pathological role.

Acknowledgements: We thank Biogen Idec’s SSc department for their contribution.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5059
levels of C4M, C6M, and CRP at AE-IIP were positively correlated with %FVC (r=0.37, p=0.008; r=0.36, p=0.011; r=0.33, p=0.020, respectively). Serum levels of C4 (p=0.002) and C6 (p=0.024) were increased while LEM7 (p=0.024) and VCANM (p=0.0001) were decreased at AE-IIP as compared with S-IIP when analyzing all patients. IPP patients had lower levels of VCANM at AE-IIP (p=0.001). IPP patients had significantly elevated serum levels of C4M (p=0.004) and decreased levels of LEM7 and VCANM (p=0.036 and p=0.0001, respectively) at AE-IIP. C1M and C6M levels at AE-IIP were borderline related to mortality outcome for IPP patients (both p=0.059) with levels above median associated with a higher risk of mortality. Analyses of all or paired patients showed no associations with mortality.

Conclusions: Serological levels of neo-epitope biomarkers of ECM degradation were associated with AE-IIP and weakly with mortality outcome. These results indicate that the rate of ECM remodeling in the lungs of patients with IIP is significantly altered during periods of high disease activity such as an acute exacerbation. The difference in degradation profile for the proteins studied is intriguing and indicate activation of different processes contributing to AE-IIP. Neo-epitope biomarkers of the ECM might be useful in identifying patients diagnosed with rheumatic disease as SSC and AS with pulmonary involvement.

Acknowledgements: The Danish Research Foundation

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5699

AB0181 DIFFUSING CAPACITY AND CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS – DATA FROM THE GERMAN NETWORK FOR SYSTEMIC SCLEROSIS

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Background: Lung involvement, i.e. interstitial lung disease (ILD) and pulmonary hypertension (PH), is commonly in patients with systemic sclerosis (SSc), significantly limiting quality of life and survival. Data on clinical correlations between lung function and clinical subsets of SSc are sparse.

Objectives: To investigate the relationship of DLCO and clinical characteristics in patients SSc patients within the registry of the German Network for Systemic Sclerosis.

Methods: Clinical data of the patient registry, currently including DLA data of 1917 patients were evaluated. In total, these patients were clinically evaluated 5997 times (i.e., at the first visit and during follow-up visits). At the initial visit and during follow-up visits DLCO were correlated with clinical characteristics.

Results: At initial presentation, 64% of the patients had DLCO levels <75% predicted. Impaired DLCO levels were observed in 74% of dcSSc patients, in 64% of SSc-Overlap patients and 57% of lcsSc patients (p=0.0001). Furthermore, male patients (62%), patients with PH (80%), ILD (80%), dyspnea (78%), and those with presence of anti-topoisomerase I antibodies (71%) exhibited significantly more often DLCO levels <75% (p=0.01). Patients suffering from dcSSc had the lowest DLCO levels (mean value, 62%), followed by patients with SSc-Overlap syndrome (mean value, 67%) and lcsSc patients (mean value, 71%). In addition, significant differences between subsets. Long-term follow-up evaluation (mean follow up, 6.0 years) revealed that in comparison to lcsSc patients dcSSc patients (OR 2.1; p=0.0001; 95%-CI 1.7–2.5) and SSc-Overlap patients (OR 1.55; p<0.0001; 95% CI 1.2–2.0) had a significantly increased risk to a decrease in DLCO levels <75%.

Conclusions: Impairment of pulmonary function as determined by diffusing capacity DLCO is more common and more pronounced in patients with dcSSc and SSc-Overlap Syndrome compared to lcsSc. DLCO may be useful for diagnosing and monitoring pulmonary involvement in SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5878
subjects (CNTs). PBMCs, isolated from 9 among the SSc patients, were cultured on fibronectin-coated plates [5]. The non-adherent cells were removed and after 8 days (t0) of culture (standardized time), the adherent spindle shaped cells were lifted through incubation in 0.05% EDTA (ice-cold). Fibrocyte identification (at both t0, t8), was performed by FACS, using anti-CD45, anti-COL I, anti-CXCR4 and anti-CD163, indicating pro-fibrotic and endothelial markers.

**Results**: FACS analysis revealed that, at basal time (t0), among the CD45+ cells, the percentage of fibrocytes, identified as triple positive (CD45+, COL I+, CXCR4+) was 1.0±2.1% in SSc patients and 0.4±0.3% in healthy subjects (CNTs). In addition, the HLA-DR expression on fibrocytes in both SSc patients and CNTs showed low values (22.1±11.1 and 7.1±14.1, respectively). After 8 days (t8) of culture, fibrocytes presented adherent and spindle shaped morphology. Interestingly, the FACS analysis at t8 of culture, demonstrated that the percentage of SSc fibrocytes CD45+, COL I+, CXCR4+ increased up to 50.8±27.3%, compared to basal time (t0), as well as strongly increasing the HLA-DR expression (10.0±22.7%).

**Conclusions**: Fibrocytes isolated from CPCS of SSc patients were confirmed to express CD45, COL I and CXCR4 molecules, but in very low percentage at the beginning. Already after 8 days of culture in proper conditions, the percentage of differentiated fibrocytes (CD45+, COL I+ and CXCR4+) increased up to 50.8±27.3%, compared to basal time (t0), as well as strongly increasing the HLA-DR expression (10.0±22.7%). Additional markers of progressive fibrocyte differentiation are now under test to further characterize the fibrocyte phenotype(s) of SSc patients vs healthy controls.

Long-term administration of fenspiride has no negative impact on bone mineral density and selected markers on bone turnover in young growing rats.

Methods: The experiment was carried out on 118 young (8-week-old) male Wistar rats receiving standard diet containing 1.2% of calcium and 0.7% of phosphate. Rats were randomly assigned to two groups (9 in each group): group F—rats receiving fenspiride (15 mg/kg) in saline solution (4ml/kg), and group C (control group)—rats receiving saline solution (4ml/kg). Saline solution and fenspiride were given intragastrically once daily for 90 days (from day 3 to day 93). Blood samples and 93 blood cultures for serum isolation were collected. Markers of bone turnover were assessed with commercial ELISA kits according to producers' instruction. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA) with Hologic DXA equipment (Hologic Discovery W 9600) using a small animal software. The experiment was performed with the approval of the Local Ethics Committee for Experiments on Animals in Wroclaw.

Results: On Day 1 there was no difference in age and body weight between groups. On Day 1, no difference in total body bone mineral density (BMD) (0.160±0.0065 g/cm² vs. 0.1608±0.0056 g/cm²), lower limbs BMD (0.230±0.0267 g/cm² vs. 0.233±0.0315 g/cm²), serum levels of bone turnover markers (osteocalcin: 1000.921±109.0705 pg/ml vs. 952.577±178.5306 pg/ml; BCTX: 280.089±54.4298 pg/ml vs. 292.8979±116.0042 pg/ml; osteoprotegerin: 3.5±0.6338 pg/ml vs. 3.7963±0.6894 pg/ml; RANKL: 0.167±0.4099 pg/ml vs. 0.201±0.2717 pg/ml) was detected. On Day 93 there was no difference in body weight, total body BMD and lower limbs (0.212±0.0104 g/cm² vs. 0.205±0.0242 g/cm²; 0.264±0.0159 g/cm² vs. 0.252±0.0271 g/cm², respectively) between groups. On Day 93 no difference between groups in serum bone turnover markers was detected (OC: 422.756±32.3316 pg/ml vs. 429.2071±83.0520 pg/ml; BCTX: 307.748±77.6753 pg/ml vs. 285.3486±79.1334 pg/ml; OPG: 5.466±7.815 pg/ml vs. 5.3520±1.6458 pg/ml; RANKL: 0.647±0.8457 pg/ml vs. 0.5639±0.8608 pg/ml).

Conclusions: Long-term administration of fenspiride has no negative impact on bone mineral density and bone turnover in young growing rats.

Acknowledgements: Research was supported with Wroclaw Medical University Grant for Young Researchers Pbnm 138.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3055

Basic science in paediatric rheumatology

AB0187 LONG-TERM ADMINISTRATION OF FENSPIRIDE HAS NO NEGATIVE IMPACT ON BONE MINERAL DENSITY AND BONE TURNOVER IN YOUNG GROWING RATS

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Background: In young organisms intensive bone turnover is observed and it allows the skeleton to achieve proper size, shape and weight of bones. It is extremely important to assess the influence on various drugs on growing bones. Fenspiride is registered for therapy of acute and chronic respiratory tract infections in children and adolescence. It decreases the synthesis of proinflammatory cytokines, blocks H1 receptors and has bronchodilatatory properties.

Objectives: The aim of the study was to assess the influence of long-term administration of fenspiride on bone mineral density and selected markers on bone turnover in young growing rats.

Methods: The experiment was carried out on 118 young (8-week-old) male Wistar rats receiving standard diet containing 1.2% of calcium and 0.7% of phosphate. Rats were randomly assigned to two groups (9 in each group): group F—rats receiving fenspiride (15 mg/kg) in saline solution (4ml/kg), and group C (control group)—rats receiving saline solution (4ml/kg). Saline solution and fenspiride were given intragastrically once daily for 90 days (from day 3 to day 93). Blood samples and 93 blood cultures for serum isolation were collected. Markers of bone turnover were assessed with commercial ELISA kits according to producers' instruction. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA) with Hologic DXA equipment (Hologic Discovery W 9600) using a small animal software. The experiment was performed with the approval of the Local Ethics Committee for Experiments on Animals in Wroclaw.

Results: On Day 1 there was no difference in age and body weight between groups. On Day 1, no difference in total body bone mineral density (BMD) (0.160±0.0065 g/cm² vs. 0.1608±0.0056 g/cm²), lower limbs BMD (0.230±0.0267 g/cm² vs. 0.233±0.0315 g/cm²), serum levels of bone turnover markers (osteocalcin: 1000.921±109.0705 pg/ml vs. 952.577±178.5306 pg/ml; BCTX: 280.089±54.4298 pg/ml vs. 292.8979±116.0042 pg/ml; osteoprotegerin: 3.5±0.6338 pg/ml vs. 3.7963±0.6894 pg/ml; RANKL: 0.167±0.4099 pg/ml vs. 0.201±0.2717 pg/ml) was detected. On Day 93 there was no difference in body weight, total body BMD and lower limbs (0.212±0.0104 g/cm² vs. 0.205±0.0242 g/cm²; 0.264±0.0159 g/cm² vs. 0.252±0.0271 g/cm², respectively) between groups. On Day 93 no difference between groups in serum bone turnover markers was detected (OC: 422.756±32.3316 pg/ml vs. 429.2071±83.0520 pg/ml; BCTX: 307.748±77.6753 pg/ml vs. 285.3486±79.1334 pg/ml; OPG: 5.466±7.815 pg/ml vs. 5.3520±1.6458 pg/ml; RANKL: 0.647±0.8457 pg/ml vs. 0.5639±0.8608 pg/ml).

Conclusions: Long-term administration of fenspiride has no negative impact on bone mineral density and bone turnover in young growing rats.

Acknowledgements: Research was supported with Wroclaw Medical University Grant for Young Researchers Pbnm 138.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3055
Rheumatoid arthritis - prognosis, predictors and outcome

**AB0189**

**RAID COMPOSITE INDEX IN THE EVALUATION OF RA PATIENTS RECEIVING BIOLOGICAL TREATMENT: HUR-BIO REAL-LIFE RESULTS**

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**Background:** Rheumatoid Arthritis Impact of Disease (RAID) is a composite index. There are seven domains of this index (pain, function, fatigue, sleep disturbance, physical wellbeing, psychological/emotional well-being and coping). This index is validated and recommended to be used in clinical trials to measure the effect of RA.

**Objectives:** The aim of this study is to examine the relationship between RAID composite index and other indexes.

**Methods:** This study was carried out from the HUR-BIO reserved database since August, 2016. In addition to the demographic characteristics of the patients, DAS-28, HAQ-DI, pain, fatigue, Patient Global Assessment (PGA), Tender joint counts (TJC), Swollen joint counts (SJC), CRP and ESR are recorded. Since August, 2016. In addition to the demographic characteristics of the patients, DAS-28, HAQ-DI, pain, fatigue, Patient Global Assessment (PGA), Tender joint counts (TJC), Swollen joint counts (SJC), CRP and ESR are recorded. Since August, 2016.

**Results:** HUR-BIO database contains 1235 RA patients as of August 2016. A RAID form was filled for 149 of these patients before initiating biological agent.

**Conclusions:** RAID has moderate correlation with pain, fatigue and PGA. RAID also has moderate correlation with pain, fatigue and PGA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4469

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**AB0190**

**ASSESSMENT OF PLASMA MICRO-RNA 155 IN RHEUMATOID ARTHRITIS**

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**Background:** Several observations have indicated that Epigenetics now play a role in the pathogenesis of many diseases including Rheumatological and Inflammatory diseases (Rheumatoid Arthritis). Unlike the genetic code, the epigenome is altered by endogenous (e.g. hormonal) and environmental (e.g. diet, exercise) factors and changes with age. There are three main and interrelated mechanisms: DNA methylation, post-translational modification of histone proteins and non-coding RNA which includes Micro RNA (miR).

**Objectives:** 1. To determine the level of miR-155 in plasma of RA patients. 2. To determine the potential value of miR-155 as molecular biomarker for diagnosis, prognosis of disease outcome, and prediction of therapeutic response in RA patients, and to test the relation miR-155 and serum levels of Matrix Metalloproteinase 3 (MMP). 3. To determine the potential value of miR-155 as molecular biomarker for diagnosis, prognosis of disease outcome, and prediction of therapeutic response in RA patients, and to test the relation miR-155 and serum levels of Matrix Metalloproteinase 3 (MMP).

**Methods:** The study group consisted of 50 female RA patients in active disease and 25 controls of matched age and sex. Disease duration of 1 to 10 years and age range from 20 to 45 years old. They underwent detailed history taking including questionnaire for disability and health assessment scoring, clinical examination, radiological assessment by modified Sharp score. Routine laboratory investigations in addition to assessment of Plasma miR-155 expression levels and serum MMP-3 levels were done for all patients. Ten of the cases were resampled for miR-155 and MMP-3 after receiving treatment and entering disease remission (By DAS 28 score).

**Results:** Plasma miR-155 expression levels and serum MMP-3 titers were significantly higher in RA patients than in controls (mean 4.071 and 1, p < 0.001, mean 323.7 and 84.5, p<0.001 respectively). MMP-3 titers in serum were significantly higher in erosive than in non-erosive arthritis (mean 366.9 and 163.4, p<0.001). There was a significant positive difference between serum MMP-3 levels in disease activity and remission (mean 630 and 390, p<0.001). Mean values of the clinical parameters of our study group: STLV score (37.4±15.90), HAQ score (56.8±16.69), ACR disability class (2.224±0.672), DAS 28 score (4.86±1.222), ESR (58.16±29.44), Sharp score (32.63±23.91). There was a significant positive moderate correlation between Plasma miR-155 and serum MMP-3 (r=0.596, p<0.001). Correlation between Plasma miR-155 expression levels and HAQ (p=0.612, r=0.03744), with ESR (p=0.13, r=0.219) with DAS 28 score (p=0.187, r=0.192), with Sharp score (p=0.675, r=0.0179). There was a significant positive moderate correlation between Plasma miR-155 and serum MMP-3 (r=0.596, p<0.001). Correlation between Plasma miR-155 expression levels and HAQ (p=0.612, r=0.03744), with ESR (p=0.13, r=0.219) with DAS 28 score (p=0.187, r=0.192), with Sharp score (p=0.675, r=0.0179).

**Conclusions:** miR-155 is indeed related to the presence of Rheumatoid arthritis, although not directly related to disease activity like MMP-3, miR-155 significantly but moderately correlates with MMP-3 in blood, but whether it plays a role in the pathogenesis of the disease with or without directly influencing MMP-3 in the joint will require more work on both markers inside the synovial fluid, tissue and the synovial fibroblasts. MMP-3 was re-established in our study as a marker of disease activity and predictor of erosive arthritis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4469

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**AB0191**

**CLINICAL SIGNIFICANCE OF MULTIPLE AUTOANTIBODY SPECIFICITIES IN RHEUMATOID ARTHRITIS: THE ROLE OF ANTI-CITRULLINATED ALPHA ENOLASE AND ANTI-INTERFERON INDUCIBLE PROTEIN 16**

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**Background:** Anti-cyclic citrullinated peptide antibody (anti-CCP) auto-antibodies (auto- Abs) represent the current gold standard for the diagnosis of rheumatoid arthritis (RA). However, growing evidence suggests that a variety of other citrullinated or not citrullinated self-proteins may act as autoantigens and lead to the production of auto-Abs. The identification of the diagnostic and/or prognostic value of such novel auto-Abs is under intense investigation. We recently demonstrated that RA patients display a higher prevalence of auto-Abs against the interferon-inducible protein 16 (anti-IF16) but these auto-Abs do not have a good diagnostic value (1). Recently, it was shown that auto-Abs against citrullinated alpha-enolase (anti-CEP1) are associated with erosive RA (2).

**Objectives:** The purpose of this study was to investigate the possible prognostic value of anti-CEP1-1 and anti-IF16 as well as the clinical implication of their association with anti-CCP in a cohort of RA patients.

**Methods:** Two hundred and fifty two RA patients were enrolled and serum samples were collected. Auto-Ab were assessed as follows: anti-CCP EIA second generation ELISA kit (Euroimmun); anti-CEP-1 IgG ELISA kit (Euroimmun). In a subgroup of 113 patients also anti-IFI16 auto-Abs were assessed with an in-house ELISA kit (1). Clinical and serumological records of patients were collected and statistical analysis was performed with SPSS 21.0 software.

**Results:** One hundred and twenty two patients (44%) displayed anti-CEP1-1 auto-Abs and of these 97 patients (87%) also displayed anti-IF16. Logistic regression analysis revealed an association between both anti-Abs and RA-associated pulmonary disease (odds ratio 10.21, 95% CI: 1.98–69.7; p=0.04). We also confirmed that anti-CEP1-1 are associated with erosive RA but of interest to a greater extent compared to anti-CCP (anti-CEP1-1: OR=4.12; p=0.04; anti-CCP: OR=2.1; p=0.03). The analysis that included anti-IF16 auto-Abs revealed that a small proportion of patients display all the three auto-Abs (9%) but
the triple positivity was significantly associated with male gender (OR=3.5; p<0.02), the presence of rheumatoid nodules (OR=5.3; p=0.015) and pulmonary involvement (OR=2.6; p<0.007). Anti-IF16 auto-Abs were associated to male gender independently of the presence of the other two auto-Abs.

Conclusions: Our study demonstrated that anti-CEP-1 auto-Abs may participate to the development of RA-associated pulmonary manifestation together with anti-CCP and that the assessment of multiple auto-Abs in daily practice may help clinician to stratify RA patients at identify those at higher risk to develop extra-articular manifestations.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3564

AB0192

SERUM MEASURES OF TYPE I COLLAGEN DEGRADATION ARE SURROGATE MARKERS OF JOINT DESTRUCTION AND PROGRESSION; FIRST STEPS TOWARDS A PROGNOSTIC SCORE

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Background: Monitoring of patients with rheumatoid arthritis (RA) requires assessment of biomarkers reflecting disease activity and its progression. There is a need for non-invasive markers for frequent monitoring of disease severity and progression as well as response to therapy.

Objectives: Serological markers together with clinical parameters was tested in a multi-marker model to assess its ability to objectively predict progression of RA.

Methods: Current post-hoc analysis included RA patients from the biomarker substudy of the phase III clinical study LITHE investigating the safety and efficacy of tocilizumab 1–4. Patients had moderate/severe, active RA. In addition, only patients of the placebo arm and with total sharp score (SHP) recorded at baseline (BL), week 24 (W24) and W52 were included. Progressors were defined as the delta from BL to W24 and W24 to W52. Biochemical markers reflecting tissue turnover (table) were assessed at BL and W16. Associations with structural progression (deltaSHP) were investigated by spearman’s r, least squared multivariate and logistic regression. Covariates were CRP, sex, BMI, age, disease duration, DAS-ESR, no. prior DMARDs/antiTNF use and SBL/SHP. The data were divided into a training and confirmation set; 1) association between markers/W16 and deltaSHP/W24 (n=31 prog./42 non-prog.), 2) association reflecting tissue turnover (table) were assessed at BL and W16. Associations with structural progression (deltaSHP) were investigated by spearman’s r, least squared multivariate and logistic regression. Covariates were CRP, sex, BMI, age, disease duration, DAS-ESR, no. prior DMARDs/antiTNF use and SBL/SHP. The data were divided into a training and confirmation set; 1) association between markers/W16 and deltaSHP/W24 (n=31 prog./42 non-prog.), 2) association

Results: The training set. Eight markers were correlated (R=0.2–0.7) with deltaSHP/W52. Of these C1M, PINP, ICTP and MMP3 were predictive for of progression (deltaSHP/W52=0) with ORs of 3.2 [1.3–8.0], 4.0 [1.4–12], 8.5 [2.4–31], and 2.5 [1.3–5.1]; all p<0.01, respectively. A logistic model for prediction of disease progression incorporating C1M, ICTP, disease duration and BMI demonstrated an AUC of 0.77 [0.66–0.86], p<0.01. The model correctly identified 72% of the progressors. The confirmation set: The results were confirmed in the second dataset with an AUC of 0.75 [0.64–0.81], p<0.01. The model correctly identified 65% of the progressors.

Table 1. Barriers to medication adherence

<table>
<thead>
<tr>
<th>Biochemical marker</th>
<th>Description</th>
<th>Biomarker of</th>
<th>Spearman correlation between deltaSHP/W24 and biomarker of and lower biochemical marker BL or W16</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1M</td>
<td>MMP-mediated type I collagen degradation</td>
<td>Connective tissue destruction</td>
<td>0.677</td>
</tr>
<tr>
<td>C1M</td>
<td>MMP-mediated type II collagen degradation</td>
<td>Cartilage degradation</td>
<td>0.688</td>
</tr>
<tr>
<td>CAM</td>
<td>MMP-mediated type II collagen degradation</td>
<td>Connective tissue destruction</td>
<td>0.277</td>
</tr>
<tr>
<td>CAM</td>
<td>MMP-mediated type III collagen degradation</td>
<td>Basement membrane destruction</td>
<td>0.537</td>
</tr>
<tr>
<td>CEP</td>
<td>MMP-mediated type IV collagen degradation</td>
<td>Connective tissue destruction</td>
<td>0.617</td>
</tr>
<tr>
<td>CRP</td>
<td>C-Reactive protein</td>
<td>Acute reactant</td>
<td>0.954</td>
</tr>
<tr>
<td>CRISP</td>
<td>Collagenase 3</td>
<td>Acute reactant</td>
<td>0.248</td>
</tr>
<tr>
<td>CA5/OCX</td>
<td>Ratio between sulfated hialuronate/ hialuronate</td>
<td>Bone turnover bone: turnover (proportion/bone)</td>
<td>0.602</td>
</tr>
<tr>
<td>Gender</td>
<td>-</td>
<td>-</td>
<td>0.059</td>
</tr>
<tr>
<td>HAA</td>
<td>Health assessment questionnaire</td>
<td>-</td>
<td>0.052</td>
</tr>
<tr>
<td>K2P</td>
<td>MMP-mediated type I collagen degradation</td>
<td>Connective tissue destruction</td>
<td>0.564</td>
</tr>
<tr>
<td>KSFP</td>
<td>Male metatarsus bone</td>
<td>Joint inflammation</td>
<td>0.26</td>
</tr>
<tr>
<td>FMX</td>
<td>Free fatty acids</td>
<td>-</td>
<td>0.073</td>
</tr>
<tr>
<td>JI</td>
<td>Inflammatory score</td>
<td>-</td>
<td>0.130</td>
</tr>
<tr>
<td>PRISM</td>
<td>Proprietary type of I collagen</td>
<td>Cartilage formation</td>
<td>0.077</td>
</tr>
<tr>
<td>FNPP</td>
<td>Proprietary type of I collagen</td>
<td>Cartilage formation and BMD</td>
<td>0.237</td>
</tr>
<tr>
<td>VCAH</td>
<td>MMP-mediated Visceral degradation</td>
<td>Epithelial turnover</td>
<td>0.054</td>
</tr>
<tr>
<td>VCLN</td>
<td>MMP-mediated degradation of chondrocytes</td>
<td>Macroscopic activity</td>
<td>0.282</td>
</tr>
</tbody>
</table>

Table 2. Medication adherence and disease activity

<table>
<thead>
<tr>
<th>DAS 28</th>
<th>Low adherence (Morsky = 2)</th>
<th>Moderate adherence (Morsky = 6–7)</th>
<th>High adherence (Morsky = 8)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission (&gt;2.6)</td>
<td>2 (5.6%)</td>
<td>5 (13.9%)</td>
<td>28 (80.6%)</td>
<td>36</td>
</tr>
<tr>
<td>Low activity (2.6–3.2)</td>
<td>7 (38.8%)</td>
<td>3 (15.8%)</td>
<td>17 (94.9%)</td>
<td>37</td>
</tr>
<tr>
<td>Moderate disease activity (&lt;3.2–5.1)</td>
<td>17 (68.0%)</td>
<td>5 (20%)</td>
<td>3 (12%)</td>
<td>25</td>
</tr>
<tr>
<td>High disease activity (&gt;5.1)</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>13</td>
<td>41</td>
<td>82</td>
</tr>
</tbody>
</table>

DAS: Disease activity score.

Conclusions: Our RA patients who were closely followed had 50% high medication adherence. This rate is quite high compared to other studies using MMAS-8. It should be kept in mind that tight control and adequate communication increase medication adherence but different parameters may also be effective. Assessing cognitive disorders and emotional problems of the patient will be beneficial for improving adherence and controlling disease activity.

References:
AB0194  JOURNEY OF A PATIENT WITH RHEUMATOID ARTHRITIS: DELAY IN DIAGNOSIS AND TREATMENT


Background: It has been shown that there is a window of opportunity for treatment in Rheumatoid Arthritis (RA). Several Argentinian studies showed an average of 8 months to arrive to a rheumatology visit and 12 months to receive DMARDs. There aren’t recent studies.

Objectives: To establish delay time from onset of rheumatoid arthritis (RA) symptoms to the first rheumatology visit, to diagnosis of the disease and to the beginning of treatment with DMARDs; and to assess impact of such delay on structural damage, in a cohort of RA patients.

Methods: A retrospective study was performed including all patients with RA (fulfilling ACR/EULAR 2010 criteria) seen at a Prepaid Medical Health Plan between 2002–2015. Diagnosis delay and its impact on functional capacity measured by HAQ and structural damage by Sharp van der Hejde score (SvDH) were estimated. Descriptive and clinical data, and rates of clinical remission, onset of symptoms and HAQ-A were extracted from electronic medical records. Svdh score was performed by an experienced rheumatologist.

Results: 246 patients (mean age at diagnosis 67.25±14 years, 199 (81%) female) were included. Clinical presentation was poliarthritis in 49% of the cases, oligoarticular in 47% and monarticular in 3%. 79% had high titers of anti-citrulline-cyclic peptide antibodies, 12% low titers, and 9% were negative. Rheumatoid factor was positive in 82.5%. Mean time of follow up was 7 years (SD: 3.8). At the end of the follow-up,median HAQ-A (n=145) was 0.125 (IQR: 0–0.87). Hands and feet of 171 patients, Median Sv Dh score was 15 (IQR: 6–33), 242 patients (98.4%) received DMARDs as initial treatment: methotrexate monotherapy (76%) was the most frequent one. 41 patients (17%) received biological agents at some point of their disease. Table 1 shows different delay times in accessing rheumatology consultation, diagnosis and beginning of treatment.

Conclusions: Delay in diagnosis greater than 12 months was associated with more radiological damage. At the end of follow up, 21 patients (12.8%) had noradiological damage (SvDH score =0). In the ROC curve (AUC 0.57,95% CI: 0.45 - 0.69), 5.6 months of diagnosis delay was the best cut off value to discriminate the presence of erosions (SvDH erosions score>0), with a sensitivity and specificity of 54.17% and 61.90%, respectively. Delay in diagnosis greater than 12 months (n=70) was associated with significantly radiological damage: Svdh mean 30.91 (IC 95% 21.99–39.79) vs 21.32 (IC 95% 16.93–25.72); p=0.0325.

Table 1. different delay times

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from first symptoms to first rheumatology visit (months)</td>
<td>9.21 (20.50)</td>
<td>3 (1–7)</td>
</tr>
<tr>
<td>Time from first symptoms to diagnosis (months)</td>
<td>14.2 (24)</td>
<td>4.8-24 (13-24)</td>
</tr>
<tr>
<td>Time from first symptoms to DMARDs indication (months)</td>
<td>16.9 (25.4)</td>
<td>7 (3–17)</td>
</tr>
<tr>
<td>Time from first symptoms to biological indicators (years)</td>
<td>6.2 (4.8)</td>
<td>5.7 (2.4–7.2)</td>
</tr>
</tbody>
</table>

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2387

AB0195  IS THERE AN ASSOCIATION BETWEEN PERIODONTITIS AND LEVELS OF ANTI-CITRULLINATED PEPTIDES ANTIBODIES IN RHEUMATOID ARTHRITIS?

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Background: There is evidence for chronic periodontitis (PD) in RA autoimmune response by periodontopathogenic bacteria such as P gingivalis, through citrullination of L-arginine.

Objectives: 1. To determine whether there is an association between PD and its severity with ACPA titres and number of periodontal pockets ≥5mm (NPP),2. To assess relationship between PD and ACPA titres.3. To identify association between certain periodontal parameters and ACPA titres and their possible cutoff points.

Methods: Observational, cross-sectional study RA patients ≥18 with ≥4 teeth, no tooth cleaning, antibiotic intake 6 months before.Socio-demographic and anthropometric variables, annual dental prophylaxis and comorbidities.Serum ACPA detection: Ab IgA against CCP2 (ELISA) Eurodiagnostica.positive≥25; ACPA titres stratification: Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), bleeding on probing (Bop), probing pocket depth, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tenneti): T0 level (absence), T1 (mild), T2 (severe). Statistical analysis: t-student, Kruskal Wallis, Chi- squared tests by Stata program 13.1.

Results: 187 RA patients included (table 1). ACPA determined in 168 patients: 67.86% (+) with similar titles distribution: low 18%, moderate 26%, high 23%. PD:182 patients (97.3%); T1 52.4%, T2 44.9%. Although prevalence of severe PD (ACPAs+) was higher compared to PD/ACPAs (69.2% vs 30.7%), there was no association between PD and ACPA positivity/titres. Regarding the association with periodontal parameters, there was tendency of association between ACPAs+ and number of periodontal pockets ≥5mm (NPP), OR 1.02 (95% CI 0.9–1.04) assessed. There was a gradient effect, where NPP increased as ACPA titre increased, which was significant for high ACPA titres (p=0.05, OR 1.03 95% CI 1.0–1.05). When ACPAs+ was related to %PI and BoP, a strong association was observed for PI, OR 10.32 (p<0.026), and only a tendency for BoP (p<0.062). With cutoff points of 8% PI and 65% BoP, a risk for ACPAs+ was detected with an OR 2.19 and OR 2.45, respectively.

Table 1

<table>
<thead>
<tr>
<th>RA (N)</th>
<th>RA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>147</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>54.4 (10.8)</td>
</tr>
<tr>
<td>Follow up time, median (SD), years</td>
<td>8.88 (7.32)</td>
</tr>
<tr>
<td>Early RA</td>
<td>35</td>
</tr>
<tr>
<td>Rheumatoid factor, seropositive</td>
<td>138</td>
</tr>
<tr>
<td>Disease Activity Ranges</td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>39</td>
</tr>
<tr>
<td>Low</td>
<td>45</td>
</tr>
<tr>
<td>Moderate</td>
<td>85</td>
</tr>
<tr>
<td>High</td>
<td>18</td>
</tr>
<tr>
<td>Medication RA</td>
<td></td>
</tr>
<tr>
<td>Without Treatment</td>
<td>10</td>
</tr>
<tr>
<td>DMARDs</td>
<td>99</td>
</tr>
<tr>
<td>≥2 DMARDs</td>
<td>22</td>
</tr>
<tr>
<td>Biologic Drugs</td>
<td>56</td>
</tr>
</tbody>
</table>

Conclusion: 1.Despite higher prevalence of severe PD in ACPA(+), patients were not associated between the presence of PD and ACPA positivity nor with serum titres. 2. On analysis of ACPA titres in relation to the severity of the periodontal parameters, there was a “gradient” risk, where NPP increased as ACPA titres increased, which was significant for high ACPA titres.3. Risk cutoff points for ACPA+ were 8% for PI and 65% for BoP.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4420

AB0196  VASCULAR ENDOTHELIAL GROWTH FACTOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The level of vascular endothelial growth factor (VEGF) may reflect the intensity of angiogenesis, which is an important step in the initiation and development of chronic rheumatic arthritis (RA).

Objectives: To study features of VEGF level changes in the blood of RA patients, depending on the duration of the disease, the degree of activity, the level of antibodies to cyclic citrullinated peptide (anti-CCP)

Methods: 194 patients were examined with a diagnosis of RA (verified according to criteria ACR/EULAR 2010), without concomitant pathology. Among the examined patients with RA women predominated 168 (86.6%), and there were 26 men (13.4%). The age of patients was 22 to 65 years (mean age 47±10.22 years), mean duration of the disease was 3.82±3.43 years. Assessment of RA activity was done by DAS28 index in the form of VEGF measurement for the presence of anti-CCP (≥20 U/ml) (78%) and 42% (22%) - negative. Serum CRP concentrations (Vector-Russia), anti-CCP (Orengect, Germany), VEGF BCM Diagnostic, Canada) were determined by ELISA. Statistical processing of the data was performed using non-parametric methods, univariate (ANOVA) variance analysis on a personal computer using a licensed software packages (“Microsoft-Excel” and “Statistica-Stat-Soft”, USA).

Results: Analysis of VEGF level changes in the blood depending on the duration of RA revealed that the measure was high in patients with small diseases duration (194 patients) and the intensity of angiogenesis, which is an important step in the initiation and development of chronic rheumatic arthritis (RA).

Conclusions: The level of vascular endothelial growth factor (VEGF) may reflect the intensity of angiogenesis, which is an important step in the initiation and development of chronic rheumatic arthritis (RA).

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2967


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2387
showed a significant increase in VEGF level (343.35 (190.62; 561.28) pg/ml) in the group of high positive ACCP (>60 U/ml) compared with the group of low positive ACCP (≤60 U/ml) – 470.23 (324.3, 676.65) pg/ml (p=0.005). Using ANOVA variance analysis, it was found that the level of anti-CCP in the blood of studied RA patients influences the VEGF level in high degree in blood (K=7;8; p=0.005).

Objectives: The objective of this study is to assess VEGF levels in the blood of RA patients, to examine the correlation between VEGF levels in the blood and clinical parameters of RA activity, and to determine the role of VEGF in the development of early joint destruction.

Disclosure of Interest: None declared.


**AB0198**

**DIFFERENTIAL CHARACTERISTICS OF PATIENTS DISCONTINUING SEVERAL BIOLOGICAL THERAPIES IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS**

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Background: The treatment of Rheumatoid Arthritis (RA) has been transformed in the last decade with the introduction of biologic therapy. Nevertheless, a significant proportion of patients are primary or secondary nonresponders and will receive several biologics during the course of the disease. Evidence is lacking on the characterization of patients failing several agents and those who have adequate clinical response to their first biologic treatment.

Objectives: To compare demographic, clinical and analytical characteristics in a cohort of RA pts who have failed treatment with at least two biological agents (“switchers”) and another cohort of RA patients showing a sustained clinical good response to their first therapy (“maintainers”). As a secondary objective, reasons for therapy discontinuation were also evaluated.

Methods: A total of 186 patients under biological therapy of the RA-PAZ cohort were included in this observational study. In this cohort, 63 pts were switchers and 123, maintainers. Baseline demographic data and clinical disease activity (DAS 28 –ESR), clinical improvement (delta-DAS 28) and serological data (CRP and ESR) were evaluated at baseline and after six months after starting the first biological treatment. Serum anti-drug antibodies (ADA) were measured by bridging ELISA at the last visit available during the follow-up period under the first treatment. Reasons for discontinuation of the first therapy and the number of biologic treatments received during the course of the disease were also evaluated.

Results: Demographic and clinical characteristics of both groups are shown in Table 1. Mean Age (49.96±10.82 vs 53.77±12.91, p=0.046) and disease duration (6.79±6.19 vs 9.97±8.56, p=0.001) prior to biologic therapy initiation were lower in the switchers. Furthermore, a higher proportion of switchers had extrarticular manifestations in comparison to the maintainers (18/63 (28.6%) vs 16/123 (12.8%), p=0.016). Clinical activity at baseline (DAS28: 5.74±1.26 vs 5.01±1.14, p=0.01) and after 6 months of starting the first biological therapy (DAS28: 4.45±1.6 vs 3.22±1.1, p=0.001) were statistically significantly higher in the switchers. At the last visit under the first biologic, there were also more ADA-positive pts in the switchers (6/25 (24%) vs 1/73 (1.4%), p=0.01). Moreover, duration under biologic treatment was higher in this group. In terms of the reason for discontinuation of the first biologic, 22.2% of pts showed primary lack of efficacy, 38.1%, secondary loss of efficacy; 33.3%, adverse effects; 4.8% interrupted because of other reasons and 1.6% because of death.

Table 1: Demographic and clinical characteristics of switchers and maintainers. Mean (SD) or Median (IQR).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Switchers (n=63)</th>
<th>Maintainers (n=123)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.96±10.82</td>
<td>53.77±12.91</td>
<td>0.046</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>43/20 (69%)</td>
<td>79/44 (64%)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td>6 (9.5%)</td>
<td>14 (11.4%)</td>
<td></td>
</tr>
<tr>
<td>ESR (mm)</td>
<td>32.1±12.4</td>
<td>24.6±12.1</td>
<td>0.04</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>0.8±0.5</td>
<td>0.8±0.5</td>
<td></td>
</tr>
<tr>
<td>DAS28</td>
<td>5.0±4.0</td>
<td>3.2±1.1</td>
<td>0.001</td>
</tr>
<tr>
<td>EROD</td>
<td>5.0±4.0</td>
<td>3.2±1.1</td>
<td>0.001</td>
</tr>
<tr>
<td>TFPI</td>
<td>5.0±4.0</td>
<td>3.2±1.1</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-6</td>
<td>5.0±4.0</td>
<td>3.2±1.1</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: We find a high frequent of lung involvement in early RA, in most of cases subclinical. Performing Respiratory function tests may help in early detection of lung involvement. These results should be ratified in larger series.
remission. There was no association between reasons for discontinuation of the first therapy because of primary or secondary failure and adverse effects (3.4±0.9 vs 3.7±5.1, 11 vs 3.86±1.3, p=0.6) with the number of treatments received.

Conclusions: In our biologic therapy RA-PAZ cohort, we found a subgroup of younger pts, with a more systemic phenotype of the disease and a higher disease activity who required a prompter biological therapy initiation. This subgroup of pts is more susceptible to biological treatment failures. The development of ADA after the first biological agent was also associated with the need to use more biologics.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5494

AB0199 METHOTREXATE RESPONSE IN EARLY RHEUMATOID ARTHRITIS ASSESSED USING A SOMAMER PROTEOMIC ASSAY

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Background: Optimizing treatment in early rheumatoid arthritis (ERA) improves clinical outcomes. Developing approaches that would allow for accurate outcome predictions would be useful. We examined the possibility of employing SOMAscan to identify biomarkers that predict treatment response.

Objectives: To define methotrexate (MTX) 6 month treatment associated response protein changes using SOMAscan.

Methods: Sera from 14 Disease Modifying Antirheumatic Drug (DMARD) naive ERA patients at baseline (PRE) and after six months of MTX (POST) were analyzed using SOMAscan, an aptamer based assay that offers simultaneous relative quantitation of 1310 proteins. RA activity was measured by DAS28ESR3var abbrev DAS3. Data were measured at baseline. SOMAmeter intensity data was log2 transformed and differences (D=POST-PRE) clustered using undirected hierarchical self-organization. Kolmogorov-Smirnov differential analysis determined SOMAmers contributing to these populations at p<0.05. Potential processes associated with these SOMAmers regulation groups were identified using an in-house biological enrichment tool.

The potential for SOMAmers to predict treatment response was also explored: for this we defined a fractional clinical response metric dDAS3= (DAS3_POST- DAS3_PRE)/DAS3_PRE. We then selected a population of proteins (n=3 to avoid over-fitting) with PRE expression levels best correlating to dDAS3. These three PRE expression values formed a weighted average, with weighting coefficients optimized by a simple Monte-Carlo method. We included this weighted average with clinical variables in logistic regression models, where 6 month DAS3 was the dependent variable.

Results: Clustering gave two populations of 6 and 8 patients (POP0, POP1) with mean delta DAS3 values of -1.71 and -0.46 respectively. In POP0 compared to POP1, 113 proteins were upregulated and 121 proteins were downregulated. The upregulated proteins were involved in VEGF signalling and platelet activation. The downregulated proteins were involved in regulation of immune response, cellular response to TNF and cytokine–cytokine receptor interactions. The fractional change dDAS3 correlated well with the treatment response panel (R²=0.8645; p=6.8e-5), with the caution that expression values of the 3 best-correlating proteins exhibited low coefficients of variation (0.1). However, these proteins did reflect RA response. The weighted sum was also independently associated with treatment response in regression models including baseline DAS3 (or components) and RF/ACPA.

Conclusions: This pilot study suggests that high content proteomic approaches such as SOMAscan may be useful for developing prediction tools of patient responses to treatment. Extension of this work to a larger patient population is ongoing.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1435

AB0201 INFUENCE OF SIGA ON CLINICAL ACTIVITY MARKERS IN SPA PATIENTS WITH NON-RADIOGRAPHIC AND PERIPHERAL COMPROMISE


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Background: There are previous evidence about inflammatory signs related with the intestinal mucosa in spondyloarthritis patients with seronegative arthritis and them relation with articular inflammatory activity. It is uncertain the role of these serological markers on the inflammatory/clinical activity in patients with SPA.

Objectives: To establish the relationship among activity variables and indices, and soluble markers associated to mucosal associated lymphoid tissue in a group of SPA patients.

Methods: Patients were selected by rheumatologists with the ESSG criteria. Levels of SigA, IgA, IgA Chlamydia trachomatis, Shigel spp., Verrucomicrobium spp., Campylobacter spp and Salmonella spp, CRP, ESR, HLA-B27, BASDAI, ASAS-CRP and ASDAS-ESR were determined. A principal components analysis (PCA), Poisson Regression and multiple correspondence analysis were performed to find relationships between clinical and laboratory variables and SigA. This study was approved by Ethics Committee.

Results: 46 patients were included (78.2% males with a mean age 34.8±12.3 years). It was reported at least one gastrointestinal sing in 69.2% of patients: abdominal bloating (45%), abdominal pain (43%); all patients showed at least one musculoskeletal symptom, 69.5% enhethesis, 63% inflammatory back pain and 58.6% arthritis, as well as 43.4% previous infection and 47.8% present HLA-B27. The PCA showed three principal factors which cover a contribution of 82.2% to explain the SigA variation. The ASDAS-CRP, ASDAS-ESR, BASDAI variables which provide the 47.12% the regression model shows an inverse association among SigA and BASDAI (prevalence ratio (PR):0.43 95% CI:0.25–0.70 p=0.001), ASDAS-CRP (PR=0.72, 95% CI:0.24–0.95 p=0.021) and ASDAS-ESR (PR=0.69, 95% CI:0.39–0.95 p=0.007); however, a risk was demonstrated among BASDAI and Yersinia IgA (PR:1.68 95% CI:1.03–2.74 p=0.036) and between CRP and ASDAS-ESR with HLA-B27 (PR=1.62 95% CI:1.16–2.19 p=0.002). There was a relationship between the absence of clinical activity (ASDAS-CRP, ASDAS-ESR, and BASDAI), previous infection, Yersinia IgA with SIgA Q1 (27.8–43.0 ug/mL); Chlamydia trachomatis, Shigel spp.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1747

AB0200 MUSCULOSKELETAL ULTRASOUND ADDED TO ROUTINE EVALUATIONS OF RHEUMATOID ARTHRITIS PATIENTS HAS A DIFFERENT IMPACT ON THE TREATMENT PROPOSAL DEPENDING ON PHYSICIAN EXPERIENCE

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Background: Disease activity (DA) is the most important factor in the treatment decision/monitoring during rheumatoid arthritis (RA) patient’s follow-up. In routine clinical practice, it is recommended to regularly evaluate DA level from patients with RA. Musculoskeletal ultrasound has been suggested to add value to establish the level of DA; evaluations that assess a reduced number of joints, as the German ultrasound score of 7 joints (GUS-7) are easy to incorporate in clinical practice (1).

Objectives: To explore the real impact of GUS-7 in the treatment recommendation to RA outpatients, currently attending an Early Arthritis Clinic (EAC). The primary objective was to determine the proportion of patients in whom treatment recommendation differed after GUS-7 examination. We additionally tested the variations of GUS-7 impact according to the physician’s experience (senior rheumatologist [SR] vs. trainee in rheumatology [TR]).

Methods: A sample size of 84 evaluations was calculated to achieve the primary objective. Eighty-seven consecutive and randomly selected RA outpatients were invited to participate; 2 patients denied because of administrative reasons and the 85 pts left underwent 170 assessments (85 each by the SR and the TR). At first, both physicians (blinded to each other evaluations) performed a clinical evaluation that included DAS28 scoring and recommended a RA-treatment. Then, patients underwent GUS-7 by a blinded (to clinical evaluations) rheumatologist that additionally determined the sonographic disease activity. In the final step, the TR and the SR integrated the US findings to their previous evaluation and reviewed their prescription; GUS-7 findings, pre- and post-GUS-7 treatments were recorded on standardized forms. Patients received final recommendation only after the SR. All the patients signed informed consent and were instructed about the process. Descriptive statistics was used.

Results: Patients were primarily middle-aged [(mean±SD) 45.1±12.4 years] female (91.4%), with (mean±SD) disease duration of 7.5±3.9 years. Most of the patients (69.2% according to TR and 71.6% to SR) were in DAS28-ESR-remission, although the four levels of DA were represented. Agreement between both physicians was good (Kappa: 0.82; p<0.001). Most frequent GUS-7 findings were grey scale synovitis in at least one joint in 98.8% of the patients, among whom 22.6% had Power Doppler activity (PD); one third of the patients had tenosynovitis although few (12%) had PD; erosions were detected in 38.6% of the population.

In 34 of 170 clinical scenarios (20%), GUS-7 findings modified treatment; treatment changes (after GUS-7 findings were incorporated to clinical findings) consisted of an increase in 24 (70.6%) scenarios, a decrease in 8 (23.5%) and joint injection with corticosteroids in 2 (5.9%). Interestingly, 24 of the 34 clinical scenarios with GUS-7 treatment impact were performed by the TR vs. 10 performed by the SR: 70.5% vs. 29.5%, p=0.01. Treatment changes (increase, decrease and joint injection) were similar among both specialists.

Conclusions: In routine clinical practice of RA patients, GUS-7 assessments impacted treatment decisions in 20% of the patients; the impact was stronger among TR than among SR.

of BASDAI and ASDAS-CRP, absence of previous infection had a strong relation with low levels of S IgA.

Conclusions: S IgA serum level were the only one serologic maker, which had an inverse correlation with all clinical activity variables of disease, previous infection and some specific antibodies associated with intestinal mucosal infection, suggesting a protective role of this molecular shape of IgA that is characteristic of mucosal immune responses.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6159

AB0202

LOW DOSE ACETYLSALICYLIC ACID AS PRIMARY PROPHYLAXIS OF CARdiovascular EVENTS in RHEUMATOID ARTHRITIS: A LONGITUDINAL, RETROSPECTIVE STUDY

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Background: Cardiovascular events (CV) i.e. acute myocardial infarction and stroke are recognized as a leading cause of mortality in patients with Rheumatoid Arthritis (RA) [1]. Acetylsalicylic acid (ASA) is known to be associated with a significant decrease in the incidence of CV events in patients at high risk for atherothrombotic disease like patients with diabetes [2] and has been recently reported to play a primary prophylactic role of CV events in Systemic Lupus Erythematosus by our team [4].

Objectives: To investigate the so far unexplored role of ASA in reducing CV morbidity in RA.

Methods: We analysed patients admitted to our Outpatient clinic from January to December 2015. Out of 199, 155 patients, who had been followed from January 2000 and had not experienced any CV event at the first visit, were enrolled. The incidence of CV morbidity was recorded at December 2016.

Results: The 115 patients had been followed-up for a median of 8 years (range 1–15 years). Out of them, 111 patients had been treated with ASA, that we currently administer to patients undergoing steroid treatment. During the 15-years of follow up, 5 CV events (2 cerebrovascular, 3 acute myocardial infarction) had occurred (incidence rate 3.33/1000 person/year). Interestingly, only 1 CV event had occurred in ASA treated patients (incidence rate 1.12/1000 person/year) with respect to 4 in the non-ASA group (44 patients) (Incidence rate 10.48/1000 person/year) (p=0.0146).

Conclusion: This study has several limitations including the low number of patients and CV events. Nevertheless, it might suggest a primary prophylactic role of ASA in RA, that awaits to be investigated in large controlled prospective studies.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2653

AB0204

DISEASE FACTORS ASSOCIATED TO ABNORMAL INTIMA-MEDIA THICKNESS IN MEXICAN MESTIZO RHEUMATOID ARTHRITIS PATIENTS

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Background: Atherosclerotic cardiovascular disease (ASCVD) is the main mortality cause in patients with rheumatoid arthritis (RA) [1]. It has been proven that the carotid intima-media thickness (CIMT) measured with carotid duplex ultrasonography is an important ASCVD predictor with a measurement >0.9 mm (2–4).

Objectives: To characterize the disease factors related with abnormal carotid duplex US findings in Mexican mestizo RA patients with RA.

Methods: In a cross-sectional setting, we enrolled consecutive RA patients. Patients with overlap syndromes, personal history of ASCVD, dyslipidemia and previous use of any statin were excluded. A board-certified radiologist performed a bilateral carotid duplex US to all patients. Abnormal CIMT was defined as >0.9 mm (hypertrophy ≤0.9 – 1.2 mm and carotid plaque ≥1.2 mm). A clinical history and blood tests were performed at the time of the patient’s visit. Disease activity was measured with Disease Activity Score using 28 joints-C-reactive protein (DAS28-CRP).

Results: We enrolled 57 patients. Demographic characteristics are shown in table 1. A total of 30 (52.2%) patients had an abnormal CIMT. US findings are shown in table 2. A significant correlation between abnormal CIMT and RA disease duration (p=0.04), as well as between the former and anti-cytokine circulatory peptide antibodies (ACPA) positivity (p=0.033) was found.

Table 1. Demographic and disease characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender, n (%)</td>
<td>54(94.7)</td>
</tr>
<tr>
<td>Age (years), mean ± SD</td>
<td>56±8.9</td>
</tr>
<tr>
<td>Disease duration (years), mean ± SD</td>
<td>12±4.83</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>28±21.4.9</td>
</tr>
<tr>
<td>Smoking status, n (%)</td>
<td>5 (8.77)</td>
</tr>
<tr>
<td>DAS28-CRP, mean ± SD</td>
<td>3±3.3x1.19</td>
</tr>
<tr>
<td>Disease Activity, n (%)</td>
<td>17 (29.8)</td>
</tr>
<tr>
<td>Remission</td>
<td>11 (19.3)</td>
</tr>
<tr>
<td>Low</td>
<td>25 (43.8)</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (7.1)</td>
</tr>
<tr>
<td>Severe</td>
<td>44 (77.19)</td>
</tr>
<tr>
<td>Positive Anti-CCP, n (%)</td>
<td>51 (89.47)</td>
</tr>
</tbody>
</table>

BMM: Body Mass Index.

Table 2. – Carotid Doppler ultrasound findings.

<table>
<thead>
<tr>
<th>Ultrasound findings, n (%)</th>
<th>Disease duration</th>
<th>Disease Activity</th>
<th>Positive Anti-CCP</th>
<th>Positive RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal CIMT</td>
<td>52±14.8</td>
<td>0.022</td>
<td>0.57</td>
<td>0.636</td>
</tr>
<tr>
<td>Plaque</td>
<td>13.13±9.9</td>
<td>0.33</td>
<td>0.75</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td>21.16±8.4</td>
<td>0.52</td>
<td>0.59</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Conclusions: There is a strong relationship between CIMT and the chronic inflammatory process of RA, as well as ACPA positivity. These results might be influenced by the high mean disease duration of our patients. Prospective studies that evaluate CIMT among disease duration intervals are necessary to support these findings.
CAROTID INTIMA-MEDIA THICKNESS LINKED TO THE PRESENCE OF CARDIOVASCULAR RISK FACTORS IN MEXICAN MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS


Objectives: The aim of this study is to relate abnormal carotid intima-media thickness (CIMT) to the presence of cardiovascular risk factors.

Methods: Observational cross-section design. We included patients who fulfilled the 1987 ACR and/or 2010 ACR/EULAR classification criteria for RA, 40 to 75 years old, with no personal history of atherosclerotic CV disease. A board-certified radiologist performed carotid duplex ultrasonograms. Patients were distributed in two groups according to the absence (Group 1) or presence (Group 2) of traditional risk factors for cardiovascular disease (smoking status, dyslipidemia, high blood pressure, and diabetes).

Results: A total of 82 patients were included. Demographic characteristics for each group are shown in Table 1. Ultrasound findings are shown in Table 2. CIMT alterations were more common in Group 2 (66.7%) than in Group 1 (38.7%), with a p-value of 0.013. Presence of carotid plaque was more common in Group 2 (27.5%) than in Group 1 (16.1%), shown clinical relevance, although this effect has not been universally demonstrated [2].

Objectives: The aim of the present study was to investigate if serum IL-17 and CCL20 reflect activity of the disease and whether they could be of prognostic value for predicting therapeutic response to biologic therapy in RA.

Methods: Thirty RA patients qualified to receive biologic treatment were prospectively assessed before and 12 weeks of therapy with either TNF-α blocker (adalimumab, certolizumab, golimumab, and infliximab) or IL-6 blocker (tocilizumab).

Results: The patient baseline characteristics were summarized in Table 1. Serum levels of IL-17 and CCL20 did not change significantly over the course of therapy and they did not correlate with the disease activity, response to therapy, the type of biologic intervention and other medication used.

Conclusions: Serum IL-17 and CCL20 levels showed no correlation with DAS28, and standard inflammatory markers.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2178
**AB0207** CHANGE IN ANTI-CITRULLINATED PROTEIN AUTOANTIBODY LEVELS IN CLINICAL PRACTICE ARE ASSOCIATED WITH RESOURCE USE AND DISEASE ACTIVITY MEASURES


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Background: High anti-citrullinated protein antibody (ACPA) concentration, beyond ACPA positivity, is indicative of more aggressive radiographic progression in patients (pts) with RA. However, there is limited information on changes in ACPA levels in clinical practice settings, and the association of changes in ACPA with measures of resource use and/or disease activity.

Objectives: To evaluate the association between change in ACPA levels with hospitalizations/durable medical equipment (DME) use and change in disease activity.

Methods: Pts enrolled in a tertiary care centre RA registry, established in 2003, were analysed. The registry mostly comprises pts with established RA who were evaluated semi-annually for multiple clinical patient-reported outcomes as well as resource utilization parameters, and annually for disease activity measures such as DAS28 (CRP), SDAI and CDAI. The current analysis is based on pts enrolled in the registry with ACPA values at the time of baseline (BL) and follow-up visits.

BL and follow-up ACPA levels were based on well-documented and validated ELISAs from Euro-Diagnostica (distributed by IBL-America, Minneapolis, MN, USA). Annual mean ACPA change from BL over the first year of enrolment in the registry was calculated. Changes (follow-up – BL)/BL x 100) in ACPA levels were categorized as decrease (–>10%), no change (–10% to +10%) or increase (>+10%). Use of DME (canes, wheelchairs, walkers and commodes) and as well as hospitalizations during 12-month follow-up and annual change in disease activity (DAS28 [CRP], SDAI, CDAI, swollen painful joint counts and pain) were assessed. Multivariate logistic regression analyses for binary outcome variables (DME and hospitalizations) and linear regression for change in disease activity measures were conducted, controlling for BL covariates.

Results: A total of 840 (65%) pts in the registry had BL and follow-up ACPA values and were included in the analysis. Overall, 34.6% (n=291) of pts had a decrease, 31.7% (n=266) had no change and 33.7% (n=283) had an increase in ACPA levels. There were no significant differences in BL characteristics between the three groups except for disease duration. Pts with RA with an increase in ACPA levels had significantly longer disease duration at BL. In univariate analyses, DME use was 23.4%, 30.1% and 28.6%, and hospitalization rate was 13.4%, 16.5% and 20.1% in pts with a decrease, no change or an increase in ACPA levels, respectively. Unadjusted mean (SD) change from BL in DAS28 (CRP), SDAI and CDAI in pts with reductions in ACPA levels was −0.7 (1.4), −6.1 (15.7) and −5.9 (15.1), and 0.5 (1.4), −5.0 (15.7) and −4.7 (14.6) in pts with an increase in ACPA levels. After controlling for BL covariates, the odds ratio (OR) for DME (vs no change) across all cohorts. Unadjusted 12M hospitalization rate in ACPA+ vs ACPA− pts was 10.8 vs 16.4%, 13.7 vs 14.3% and 8.5 vs 10.8% in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively. After controlling for baseline covariates, the hazard ratio for hospitalizations in the ACPA+ (vs ACPA−) group was 0.57 (95% CI: 0.34, 0.98; p=0.04), 0.95 (95% CI: 0.84, 1.09; p=0.47) and 0.88 (95% CI: 0.66, 1.17; p=0.38) in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively (Figure).

Disclosures: ACPA+ pts with RA treated with abatacept have a lower rate of hospitalization than ACPA− pts. This pattern was not observed with cDMARDs or non-abatacept bDMARDs. Further efforts including matching and subgroup analysis should be explored for direct comparisons between the cohorts.

References:

**AB0208** HOSPITALIZATION RATES IN PATIENTS WITH RA BY POOR PROGNOSTIC FACTORS: IMPACT OF ABATACEPT AND OTHER DISEASE-MODIFYING ANTI-RHEUMATIC THERAPIES

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Background: Studies have reported that poor prognostic factors (PPF) in RA, such as high anti-citrullinated protein antibodies (ACPA), are associated with erosions, rapid radiographic progression and/or extra-articular manifestations.1,2 Evidence from clinical trials and clinical practice indicate differences in treatment effects of biologic (b)DMARDs by ACPA status and/or level.3,4 PPF also play an important role in clinical management of patients (pts) with RA, including inpatient admissions.

Objectives: To compare hospitalization rates of ACPA-positive (+) with ACPA-negative (−) pts managed with abatacept (ABA), non-ABA bDMARDs or conventional (c)DMARDs.

Methods: This is a retrospective cohort analysis of Clinformatics Data Mart, a database of administrative health claims including results for outpatient laboratory tests, processed by national laboratory vendors under contract with the managed care organization, for a total of ∼53 million unique lives over 13 years. This analysis was restricted to adult pts (aged ≥18 years) who had at least two ICD-9-CM diagnosis codes for RA between Jan 2007 and Dec 2014 (identification period) and 12 months (M) of membershipdrug benefit. Pts with ankylosing spondylitis, Crohn’s disease, lupus, psoriasis or ulcerative colitis at or before the index date were excluded. ACPA+ was based on >19 or >5 U/mL, depending on the test utilized. Follow-up for pts initiating ABA was from first day of treatment to first hospitalization, end of enrolment or end of 12M follow-up. The primary outcome was all-cause hospitalization at 12M. Descriptive statistics such as Wilcoxon rank-sum test for continuous variables or Pearson’s chi-square test for categorical variables were used. Cox proportional hazard model was used to examine all-cause hospitalization adjusted for age, sex, region and past hospitalization. Additional covariates included co-morbidities that were different between ACPA+/− pts. Similar analyses were performed for pts treated with cDMARDs and non-ABA bDMARDs.

Results: A total of 496 ABA, 7438 cDMARD and 2118 non-ABA bDMARD pts were included, with an overall past hospitalization rate of 35.5, 25.4 and 23.2%, respectively, Overall, 59.5, 51.7 and 51.7% of pts were ACPA+ in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively. ACPA+ pts were older and less likely to have obstructive sleep apnoea, depression and myalgia/myositis across all cohorts. Unadjusted 12M hospitalization rate in ACPA+ vs ACPA− pts was 10.8 vs 16.4%, 13.7 vs 14.3% and 8.5 vs 10.8% in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively. ACPA+ pts were older and less likely to have rheumatoid nodules, depression and myalgia/myositis across all cohorts. Unadjusted 12M hospitalization rate in ACPA+ vs ACPA− pts was 10.8 vs 16.4%, 13.7 vs 14.3% and 8.5 vs 10.8% in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively. After controlling for baseline covariates, the hazard ratio for hospitalizations in the ACPA+ (vs ACPA−) group was 0.57 (95% CI: 0.34, 0.98; p=0.04), 0.95 (95% CI: 0.84, 1.09; p=0.47) and 0.88 (95% CI: 0.66, 1.17; p=0.38) in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively (Figure).

Conclusions: ACPA+ pts with RA treated with abatacept have a lower rate of hospitalization than ACPA− pts. This pattern was not observed with cDMARDs or non-abatacept bDMARDs. Further efforts including matching and subgroup analysis should be explored for direct comparisons between the cohorts.

References:
**AB0209**

**THE CHANGES OF SIGNAL PEPTIDE-CUB-EGF DOMAIN-CONTAINING PROTEIN (SCUBE) AND OTHER ANGIogenesis PROTEINS DURING DISEASE ACTIVITY AND RELATIONSHIP WITH THE JOINT ULTRASOUND FINDINGS IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Rheumatoid arthritis (RA) is a multifactorial, systemic, progressive, inflammatory disease which is characterized with bone and cartilage destruction. Synovial angiogenesis is important at the etiopathogenesis. SCUBE (Signal peptide-CUB-EGF domain-containing protein) is rather a new surface cell protein. Its secretion increases with inflammation and hypoxic conditions. Its relations with inflammation and angiogenesis are shown in preclinical studies.

**Objectives:** To study serum levels of newly identified plasmaSCUBE 1 and 3 and other angiogenesis markers and analysis of changes after treatment in RA patients. Moreover, to determine whether a correlation with this change in SCUBE proteins after treatment, clinical parameters and with joint ultrasound findings.

**Methods:** This study covers patients diagnosed with RA associated with 2010 American Collage of Rheumatology (ACR) diagnosis criteria matched with healthy controllers who are equivalent of RA patients in terms of age and gender. Detailed background information and examination of the patients were recorded and disease activity scores (DAS28) were figured out and US7 scores were calculated. The levels of SCUBE 1–3, Vascular Endothelial Growth Factor (VEGF), Matrix metaloproteinaz-9 (MM-9), Interlökin-6 (IL-6), CD40L were evaluated with the method of Enzyme-Linked ImmunoSorbent Assay (ELISA). Clinical and laboratory measurements were re-evaluated at the third month after treatment.

**Results:** This study covers 56 individuals; 28 of whom were diagnosed with RA and 28 of them were healthy controllers. Significant differences were observed between RA patients and healthy controller groups in terms of MMP-9 levels and 28 of them were healthy controllers. Significant differences were observed in SCUBE proteins after treatment, clinical parameters and with joint ultrasound findings.

**Conclusions:** This study covers patients diagnosed with 2010 American Collage of Rheumatology (ACR) diagnosis criteria matched with healthy controllers who are equivalent of RA patients in terms of age and gender. Detailed background information and examination of the patients were recorded and disease activity scores (DAS28) were figured out and US7 scores were calculated. The levels of SCUBE 1–3, Vascular Endothelial Growth Factor (VEGF), Matrix metaloproteinaz-9 (MM-9), Interlökin-6 (IL-6), CD40L were evaluated with the method of Enzyme-Linked ImmunoSorbent Assay (ELISA). Clinical and laboratory measurements were re-evaluated at the third month after treatment.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5949

**AB0210**

**THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE FOR ASSESSING RESPONSE TO TREATMENT WITH ADALIMUMAB**

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**Background:** The multi-biomarker disease activity (MBDA) score measures 12 serum biomarkers to assess disease activity in patients with rheumatoid arthritis (RA) on a scale of 1–100. The MBDA score was validated in several different cohorts but has not been evaluated in a cohort consisting only of patients initiating TNF inhibitor therapy in clinical practice. We utilized patients enrolled in the Corrona-CERTAIN study to evaluate MBDA scores for patients initiating adalimumab (ADA) in several clinical practices in the US.

**Objectives:** Evaluate the ability of the MBDA score to assess response to treatment with ADA.

**Methods:** We studied 106 biologic-naïve RA patients who had been treated with ADA for at least 12 months, had initiated ADA in CERTAIN while in moderate or high disease activity by CDAI, and for whom sera were available at baseline (BL) and Months 3 and 6. Changes (Δ) in MBDA score and DAS28-CRP were evaluated from BL to Months 3 and 6 by the one-sample paired t-test. MBDA scores were evaluated for patients grouped by EULAR response categories, using the Cochran-Armitage test for trend. Receiver Operating Characteristic (ROC) analysis with bootstrap sampling (20,000 iterations) was used to evaluate MBDA score to discriminate ΔDAS28-CRP improvement ≥1.2 units at Month 3, and to determine the optimal MBDA threshold by maximizing the sum of sensitivity and specificity (Youden’s index criterion).

**Results:** At BL, median values were age 54.5 years, disease duration 2 years. BMI 28.2, DAS28-CRP 4.7, CDAI 24, SDI 25.4; 74.5%/65.4% were RF+/ACPA+. Median MBDA score was 49 with 17 (16%) patients in low (<42), 3 (22%) patients in moderate (30–44), and 66 (62%) patients in high (>44). MBDA categories. The relative magnitude and the direction of median change from BL to Months 3 and 6 were similar for MBDA score (Δ−8, −9) and DAS28-CRP (Δ−4, −8), with statistically significant changes from BL for each (line graphs in Figure). Similar results were observed for SDAI and CDAI. Pearson’s correlations with ΔMBDA score at Months 3 and 6 were 0.56, 0.59, respectively, for ΔDAS28-CRP, 0.48, 0.47 for ΔSDA1, 0.42 for ΔCDAI (all p<0.0001). Median reductions in MBDA score were significantly greater for patients with concurrent DAS28-CRP improvement >1.2 units (n=67) vs. ≤1.2 units (n=39) at Month 3 (15 vs. 2) and Month 6 (13 vs. 1.5) (both p<0.0001); and for patients with EULAR Good vs. Moderate vs. Non-responses (p=0.0002 at Month 3, p<0.0001 at Month 6) (bar graphs in Figure). Area under the ROC curve (AUCROC) for the ability of ΔMBDA score from BL to Month 3 to discriminate DAS28-CRP improvement >1.2 units at Month 3 was 0.82 (95% CI, 0.74–0.90). The optimal threshold for this discrimination was a reduction in MBDA score ≥9 units, with sensitivity/specificity=0.63/0.82 and PPV/NPV=0.86/0.56.

**Conclusions:** This study expands the previous validation of the MBDA score by demonstrating its ability to assess response to treatment with adalimumab in a US clinical practice cohort. The AUCROC value of 0.82 for discriminating improvements in DAS28-CRP >1.2 units indicates a significant association between change in MBDA score and clinical improvement.


**DOI:** 10.1136/annrheumdis-2017-eular.5602

**AB0211**

**THE EFFECT OF SMOKING, ALCOHOL AND CAFFEINE ON EARLY RHEUMATOID ARTHRITIS OUTCOMES**

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**Background:** The aim of early RA treatment is remission. Intensive treatment with MTX achieves remission in 30–50% patients (pts). Modifiable risk factors, as smoking, alcohol, coffee and tea, may affect response to MTX.

**Objectives:** To study the influence of tobacco, alcohol, caffeine on the MTX response in early RA pts.

**Methods:** A case-control study (2010–2015): cases were pts who achieved DSAS28−2.6 (remission) and controls were pts who did not. We collected information from pts 18-years with early RA, treated with MTX, evaluated quantified RA, specialized in early RA. All the pts underwent a structured interview about their smoking history and others habits. A descriptive and comparative study, was performed (SPSS21).

**Results:** 182 pts (age 50,96±13,11y, 67.6% female, 81.3% RF+ and 65.7% ACPA+) was treated with MTX and followed 105,03±7,15 months since 1995. More than 95% pts received MTX in (rapid escalation) in the first 24 months of the onset of symptoms. DSAS28−2.6 was achieved for 67 (36.8%) pts, who required an lower average dose of MTX (15.07mg/w) than those who did not (18,40mg/w) (p=0.000). Age, DAS28 and physical function at baseline, treatment delay, smoking and adverse events by MTX were related to remission.The univariate and multivariate analysis of the baseline pts characteristics and the relationship of their smoking history with age, RF, ACPA and outcome of MTX monotherapy are shown in table 1and 2, respectively. The median survival of MTX monotherapy was 87,39 months (100.27 non-smokers and 47.70 months for current smokers (Log Rank 10.32, p=0.001) (see graphic).

**Conclusions:** The treatment of early RA with MTX alone achieved high rates of remission, especially in non-smokers. Smoking cessation could significantly improve the response to MTX and therefore should be an integral part of the treatment of early RA patients.
**RA-onset and OR as ACAs levels and MTXm duration. MTXm persistence at 5 years was 59% pts and their median survival was 93 months (77.14 to 108.8). We only found significant differences in favor of non-smokers and RF < 100.**

### References:


### Table 1. Clinical and sociodemographic characteristics of RA patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Responders</th>
<th>Nonresponders</th>
<th>Statistic Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset (y) (mean, SD)</td>
<td>53.48 (13.0)</td>
<td>46.65 (11.5)</td>
<td>χ₂ (p &lt; 0.0006)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>80 (65.0)</td>
<td>72 (72.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Current Smokers n (%)</td>
<td>23 (18.7)</td>
<td>40 (40.4)</td>
<td>χ² 12.7 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Alcohol consumers n (%)</td>
<td>35 (28.5)</td>
<td>28 (28.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Comorbidity n (%)</td>
<td>92 (74.8)</td>
<td>61 (61.6)</td>
<td>χ² 4.45 (p &lt; 0.05)</td>
</tr>
<tr>
<td>CV risk factors n (%)</td>
<td>92 (74.8)</td>
<td>81 (81.8)</td>
<td>ns</td>
</tr>
<tr>
<td>Polynicarticular OR n (%)</td>
<td>61 (49.6)</td>
<td>61 (61.6)</td>
<td>ns</td>
</tr>
<tr>
<td>Extraarticular involvement n (%)</td>
<td>17 (13.8)</td>
<td>21 (21.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Positive RF n (%)</td>
<td>89 (72.4)</td>
<td>79 (79.8)</td>
<td>ns</td>
</tr>
<tr>
<td>Positive ACPA n (%)</td>
<td>70 (60.3)</td>
<td>64 (68.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of RA (m) (mean, SD)</td>
<td>96.1 (63.1)</td>
<td>96.0 (73.9)</td>
<td>ns</td>
</tr>
<tr>
<td>MTX toxicity n (%)</td>
<td>47 (38.2)</td>
<td>59 (59.6)</td>
<td>χ² 10.0 (p &lt; 0.01)</td>
</tr>
<tr>
<td>MTX dose (mg) (mean, SD)</td>
<td>15.6 (3.02)</td>
<td>17.8 (3.07)</td>
<td>OR 4.52 (p &lt; 0.0001)</td>
</tr>
</tbody>
</table>

### Conclusions:

The initial treatment of RA with MTX is an effective and safe option, with a high drug survival. MTX response was not associated with antibody positivity (RF or ACPA), but it was significantly better in non-smokers patients and RF < 100. Smoking cessation could significantly improve the response to MTX of RA patients.

### Disclosure of Interest:

None declared

DOI: 10.1136/annrheumdis-2017-eular.1109

### AB0213

**HIGH POWER DOPPLER SIGNALS SEEMS MORE IMPORTANT THAN SYNOVITIS SCORES IN ESTABLISHED RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by synovial inflammation, potential cartilage and bone damages. Evaluation with ultrasound (US) has come into prominence due to its usefulness in soft tissue inflammatory changes and early bone erosions (1,2).

**Objectives:** The value of US has been shown in early arthritis, but is not well known for established RA. The aim of this study is to determine the relation between US signal, disease activity, articular damage and disability in established RA patients.

**Methods:** Forty-four RA patients (21 women, 23 men) were enrolled to the study. Age and gender, duration of disease, morning stiffness, disease activity score 28 (DAS28), The Rheumatoid Arthritis Articular Damage (RAAD) score, Hand disability index (HDI), DASH (Disabilities of the Arm, Shoulder and Hand) scale, and grip strength values were recorded. Wrist, I-III metacarpophalangeal and proximal interphalangeal joints of dominant hand were examined by both B mode (BMOD) and Power Doppler US (PDUS).

**Results:** All of the 44 patients were established RA. The median of disease duration was 12 years (IQR 7 to 18). RA patients were divided into two groups according to their Hand disability index (HDI). In HDI < 20 group, the most important parameters were Power Doppler US signal and Hand disability index (HDI), in HDI ≥ 20 group, the most important parameters were Power Doppler US signal and Morning stiffness. When we take the HDI < 20 group, RA patients with Power Doppler US signal ≥ 4 were HDI < 20 (30/34, p < 0.05) and when we take the HDI ≥ 20 group, RA patients with Power Doppler US signal ≥ 4 were HDI ≥ 20 (12/12, p < 0.05).

**Conclusions:** RA patients with Power Doppler US signal ≥ 4 were HDI ≥ 20 (12/12, p < 0.05).
duration was 156 (48–420) months. DAS 28 score was 2.86 (0.68–5.70) and 54.5% of the patients were in remission. BMDQ synovitis, erosion and PDUS synovitis total scores were 20 (6–36); 6 (0–17); 1 (0–14) respectively. Although US findings were not correlated with DAS 28 and grip strength; there was poor correlation between US findings and DASH, RAAD and disease duration (Table 1). Signs of synovitis associated with PDUS score, 63% of the joints assessed. High-grade PDUS signal (grade 3) was found in 10 (22.7%) of the patients. Duration of morning stiffness, HDI and DASH scores were worse in the patients with high-grade PDUS signals (p=0.01, 0.04, 0.01 respectively) Table 1. Correlation coefficients between clinical, ultrasound and functional variables

<table>
<thead>
<tr>
<th>BMDQ synovitis</th>
<th>BMDQ erosions</th>
<th>PDUS synovitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>DASH</td>
<td>0.37</td>
<td>0.02*</td>
</tr>
<tr>
<td>HDI</td>
<td>0.51</td>
<td>0.17</td>
</tr>
<tr>
<td>RAAD</td>
<td>0.33</td>
<td>0.02*</td>
</tr>
<tr>
<td>DAS 28</td>
<td>-0.04</td>
<td>0.78</td>
</tr>
<tr>
<td>MS</td>
<td>0.24</td>
<td>0.12</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.13</td>
<td>0.38</td>
</tr>
<tr>
<td>Lateral GS</td>
<td>0.07</td>
<td>0.64</td>
</tr>
<tr>
<td>Tip GS</td>
<td>0.11</td>
<td>0.49</td>
</tr>
<tr>
<td>Three fingered GS</td>
<td>0.21</td>
<td>0.89</td>
</tr>
<tr>
<td>Mass grasp</td>
<td>-0.08</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Conclusions: US scores in established RA patients are usually high because of synovial hyperplasia. It is considered that high grade PDUS signals are more appropriate for evaluation of long-standing RA patients. Furthermore in this study, grade 3 PDUS signals were found to be a good indicator of synovial inflammation, morning stiffness, and disability. References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2898

AB0214 METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS: A SINGLE-CENTER EVALUATION OF CLINICAL OUTCOME COMPARING TWO STARTING TREATMENT STRATEGIES

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Background: methotrexate (MTX) is the 'anchor drug' in the treatment of rheumatoid arthritis (RA) and it should be part of the first treatment strategy: at 6 months, according with EULAR guidelines. It is considered that high grade PDUS signals are more appropriate for evaluation of long-standing RA patients. Furthermore in this study, grade 3 PDUS signals were found to be a good indicator of synovial inflammation, morning stiffness, and disability.

Objectives: to compare the different starting treatment strategies with MTX in patients with early RA evaluated at our Early Arthritis Clinic (EAC) in order to assess the rate of patients who reaches the target (remission/low disease activity) at 6 months, according with EULAR guidelines.

Methods: patients with RA (disease duration <12 months) evaluated at our EAC between 2005 and 2016 and treated with MTX parenterally and glucocorticoids (GC) were included. Patients followed a treat-to-target strategy to reach low disease activity with bimonthly tight control. Patients included between 2005 and 2009 were initially treated with MTX 10 mg/week + GC (group A) with increase of 10 mg/week in case of failure to reach the target; patients evaluated between 2010 and 2016 were initially treated with MTX 15 mg/week + GC (group B) with possible increase to 20 and 25 mg/week. The DAS28 response was assessed after 6 months.

Results: 260 patients were analyzed: 123 in group A vs 137 in group B. At baseline patients showed differences in DAS28 (5.68±1.15 vs 4.6±1.16, p=0.006) and HAG (1.125 vs 1 IQR IQR 0.75–1.875 0.375–1.85, p=0.006); there were no differences in terms of autoimmunity. After 6 months of therapy there were no differences in clinical response: 32% of patients in the group A reached the DAS28 remission vs 40% in the group B (p=ns), 27% in the group A reached the DAS28 low disease activity vs 24% of the group B (p=ns), 41% of the group A was in moderate disease activity vs 36% in the group B (p=ns). The need to increase the dosage of MTX during the first 6 months was similar: 27.6% of the group A vs 29.9% of the group B (p=ns), conversely, the need to reduce the dosage of MTX due to intolerance and/or adverse event was significantly higher in the group B (group A: 1.6% vs group B: 9.5%, p=0.014).

Conclusions: the use of higher dose of MTX is associated with a higher rate of side effects but does not provide, at short term, a significant improvement in term of clinical outcome. The initial use of MTX 10 mg/week, with a quick dose titration in case of persistent disease activity, seems to be an appropriate option for many patients with early RA, as also recently suggested by the Utrecht Arthritis Cohort Study Group; in spite of this, there is an amount of patients who do not achieve the clinical target at short term regardless of the initial dose of MTX. Our experience suggests that in the early phase of RA treatment, in a context based on early diagnosis, tight control and treat to target, the clinical outcome seems to be linked more to the treatment strategy than to the drug dosage used.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6437

AB0215 A LONGER MEAN SURVIVAL OF BIOLOGIC TREATMENTS IS ASSOCIATED WITH DAS28 REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

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Objectives: to determine factors associated with remission (DAS28<2.6). We specifically considered the association of biologic treatment duration, number of biologic switches and survival of biologic treatment with remission.

Methods: we conducted a retrospective analysis on a monocentric cohort of rheumatoid arthritis patients. Patients included patients who were on biologic drugs at the time of the analysis (31st December 2016). We considered patients starting the first biologic treatment since January 2000 and with a follow-up >12 months. We considered the following variables: demographics, positive rheumatoid factor (RF) and anti-citrullinated peptides (ACPA), disease duration at the start of the first biologic treatment, number of biologic switches, clinical assessment at the last follow-up, concomitant DMARDs, prednisone dose, current biologic treatment.

We also considered the mean survival of biologic treatments, defined as the duration of the biologic treatment of each patient divided by the number of biologics undergone by the patient.

Mann-Whitney test and chi-square test were used to assess the association of continuous and categorical variables with the outcome. Continuous measures are reported as medians and interquartile range. Multivariate regression analysis included all variables reaching a p value <0.2 in univariate analysis.

Results: we collected data of 330 patients. All patients had complete data. One hundred thirty-five patients (40.9%) were in DAS28 remission. Characteristics of the patients are reported in Table I. We considered 609 biologic treatments (abatacept n=61; anti-TNF alpha n=445; anakinra n=43; tocilizumab n=56; rituximab n=6). Total biologic treatment duration in all patients was 9.62 years (5.68–12.53), in patients in remission 8.95 (4.70–12.53) and in patients not in remission 10.12 (6.28–12.62) (p=0.248). Median number of previous biologic switches was 1.00 (0–1.00) in patients in remission and not in remission (p=0.436). Survival for biologic treatments was 5.33 years (2.89–7.72) in all patients, 4.57 (2.54–7.28) in patients in remission and 5.61 (3.49–7.53) in patients not in remission (p=0.013).

All clinical assessments at the last follow-up were significantly associated with DAS28 remission. Mean prednisone dose was significantly lower in patients in DAS28 remission but was negatively associated with remission as a consequence of remission rather than a predictor (Table I). The type of current biologic treatment was not significantly associated with DAS28 remission.

Variables included in the multivariate regression analysis were: BMI, age, disease duration, positive RF/ACPA mean survival of each biologic treatment. All variables included in the model were independently associated with DAS28 remission. A higher BMI, older age, longer disease duration and positive RF/ACPA were negatively associated with remission. A longer mean survival of biologic treatment was associated with DAS28 remission.
EVALUATING THE SWOLLEN JOINTS WITH CLINICAL EXAMINATION AND COMPARISON WITH ULTRASONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS

AB0216

EFFECTS OF ANTI-CITRULLINATED PROTEIN ANTIBODIES ON SYSTEMIC BONE MASS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Bone loss in rheumatoid arthritis (RA) is a key feature both local and systemic. Anti-citrullinated protein antibodies (ACPA) have recently been found to directly induce differentiation and activation of osteoclasts and therefore contribute to periarticular bone loss.

Objectives: The aim of this study was to analyze the effect of ACPA on systemic bone mineral density (BMD) in patients with established RA.

Methods: This is a cross-sectional study with a single-center RA population. BMD was measured with Dual X-ray absorptiometry at lumbar and femoral sites. ACPA were measured with ELISA. Multivariate analysis was performed adjusting for the main confounding variables.

Results: One hundred twenty-seven RA patients were enrolled. In univariate analysis ACPA-positive patients showed lower BMD T-score (SD below the age-and-gendermatched normal value) at femoral sites (p<0.01). A negative correlation between ACPA titers and BMD Z-score at all sites was observed (p<0.01). The multivariate analysis adjusted for the main confounding variables confirmed the negative effect of ACPA at femoral sites (p<0.05); but not at lumbar spine BMD. No significant effect of rheumatoid factor has been observed.

Conclusions: ACPA have a negative titer-dependent effect on BMD at femoral sites, mainly constituted by cortical bone. ACPA-positive patients, especially if at high titer, should undergo bone investigations and be treated with bone protecting agents. Disease-modifying anti-rheumatic drugs lowering ACPA titer might have positive effects on systemic bone mass.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4842

AB0217

THE PROGNOSTIC VALUE OF IgA AUTOANTIBODIES (RHEUMATOID FACTOR AND ACPA) FOR PREDICTION OF THERAPEUTIC RESPONSES TO ANTI-TNF THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) are important diagnostic markers in rheumatoid arthritis (RA). These antibodies are predominantly of the IgM (RF) or IgG (ACPA) isotype. The added diagnostic and prognostic value of IgA autoantibodies is being debated.

Objectives: To determine the prevalence of IgM-RAF and IgG-ACPA in patients with RA and to investigate their potential predictive value regarding response to treatment with methotrexate (MTX) and TNF inhibitors.

Methods: A total of 255 patients were tested for the presence of IgM-RAF, IgG-ACPA and IgA-ACPA by EIA (Thermo Fisher Scientific). IgM-RAF was measured by nephelometry. Therapeutic responses to MTX and TNF blocking biologicals were calculated in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses simplified disease activity index (SDAI) 50 and American College of Rheumatology (ACR) 20 responses were calculated.

Results: Among the 255 patients tested 125 (49%) had at least one type of IgA autoantibody: 114 (44.7%) were found to be IgA-RAF positive and of these 10.5% were negative for IgM-RAF and 5.2% were double negative for both IgM-RAF and IgG-ACPA; thus, in these patients IgA-RAF was the only detectable antibody. IgA-ACPA were detected in 79 (31%) patients and apart from one exception all of them had also IgG-ACPA. Remarkably, the percentage of patients showing a SDAI50 response to TNF inhibitors was significantly lower in patients positive for IgA-RAF and/or IgA-ACPA (p<0.0001) compared to IgA negative patients. Thus, 58% of IgA negative (but IgM-RAF and/or IgG-ACPA positive) patients showed a SDAI50 response whereas only 25% of the IgA-RAF and/or IgG-ACPA positive ones were responders. Interestingly, while the presence of both IgA specificities did not further change the percentage of responders, patients positive for IgA-ACPA but negative for IgA-RAF showed the lowest response rate to anti-TNF treatment. Completely seronegative patients also showed a significantly lower SDAI50 response (p<0.0001) to TNF inhibitors compared with those with the positive ACPA but negative for IgA-RAF. Similar results were obtained when ACR20 was used as response criteria. No differences between the various serological groups were seen with respect to treatment with MTX.

Conclusions: While the added diagnostic value of IgA antibody measurement was moderate, IgA-RAF and particularly IgA-ACPA appear to be associated with poorer therapeutic responses to TNF inhibitory biological drugs and therefore may help in further stratification of RA patients and therapeutic decision making.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5210

AB0218

CORRELATION OF GRAY SCALE AND POWER DOPPLER ULTRASONOGRAPHY WITH CLINICAL EVALUATION IN RHEUMATOID ARTHRITIS

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Background: While the added diagnostic value of IgA antibody measurement was moderate, IgA-RAF and particularly IgA-ACPA appear to be associated with poorer therapeutic responses to TNF inhibitory biological drugs and therefore may help in further stratification of RA patients and therapeutic decision making.

Objective: The objective of this study was to compare the tender joint and swollen joint in patients with rheumatoid arthritis (RA) with gray scale (GS) and power doppler (PD) ultrasonography (US).

Methods: Thirty RA patients were included. Median disease duration was 53.7 months. Demographic and clinical data, C reactive protein (CRP) level and erythrocyte sedimentation rate (ESR) were recorded for each patient. Disease activity was evaluated using the Disease Activity Score in 28 joints (DAS28) with a median score 3.8. The joint tenderness and swelling were assessed for 10 joints (wrists, second and third proximal interphalangeal and metacarpophalangeal) in each patient. These joints were evaluated by GS and PD by ultrasonography. US joint effusion, synovitis and PD signals were graded from 1 to 3 for each joints. The 10-joint GS and 10-joint PD scores were then calculated. Correlations were tested using the Spearman coefficient.

Results: GS: effusion, synovitis scores (r =0.565, p<0.001) and PD signals (r=0.883, p<0.001) correlated highly with the corresponding swollen joints. There was a significant correlation between DAS28 and number of tender joints (r=0.745, p<0.001) but no correlation was found between the tender joints and ultrasonographical effusion, synovitis grade (r=0.073, p=0.001) and the PD signal (r=0.089, p<0.001). There was moderate correlation between 10 joint GS, 10 joints PD and DAS28, but it was not statistically significant.

Table 1. Demographic and clinical characteristics of the patients (n=30)

| Age (years) | (mean) | SD | 53±11.9 |
| RA duration (months) | 42 (67) |
| RA severity factor positive, n (%) | 10 (50) |
| C reactive protein (CRP) mg/L (IQR) | 4.6 (6.5) |
| ESR (mm/h) (IQR) | 23.5 (21) |

AB0219

INTENSIVE COMBINATION THERAPY WITH MEDICATION AND ARTHROPEDEUTIC SURGICAL INTERVENTION FOR TREATING RHEUMATOID ARTHRITIS PATIENTS WITH DETERIORATED JOINTS

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Background: The aim of treatment of rheumatoid arthritis (RA) is achieving and maintaining remission (REM) or low disease activity (LDA) via tight medical control. However, despite remarkable advances in medication, progressive deterioration and/or deformity of the joint sometimes occurs, if adequate medication is not administered in the early stage. Surgical reconstruction is still required in the joints with functional loss caused by structural damage. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and improved mental wellness.

Objectives: The objective of this study was to clarify the effectiveness of intensive combination therapy with medication and orthopedic surgical intervention in patients who have already achieved REM or LDA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4859

AB0219

INTENSIVE COMBINATION THERAPY WITH MEDICATION AND ARTHROPEDEUTIC SURGICAL INTERVENTION FOR TREATING RHEUMATOID ARTHRITIS PATIENTS WITH DETERIORATED JOINTS

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Background: The treatment aim of rheumatoid arthritis (RA) is achieving and maintaining remission (REM) or low disease activity (LDA) via tight medical control. However, despite remarkable advances in medication, progressive deterioration and/or deformity of the joint sometimes occurs, if adequate medication is not administered in the early stage. Surgical reconstruction is still required in the joints with functional loss caused by structural damage. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and improved mental wellness.

Objectives: The objective of this study was to clarify the effectiveness of intensive combination therapy with medication and orthopedic surgical intervention in patients who have already achieved REM or LDA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4859
Methods: A prospective cohort study was performed on 294 sites in 276 patients with functional loss due to RA scheduled to undergo primary elective surgery between October 2012 and September 2014. There were 99 sites in 96 patients (males: 10, females: 86) whose disease activity was REM or LDA just before surgery. In the REM/LDA group, the average age was 63 (29–82) years, and the average disease duration was 7 (2–17) years. The surgical site was the shoulder in 1 patient, elbow in 7, wrist in 21, hand in 24, hip in 5, knee in 10, ankle in 4, and forehead in 27. The procedures performed included 38 arthroplasties, 41 arthroplasties without prosthesis, 19 arthrodesis, and 9 synovectomies. The patient-reported outcome (PRO) was assessed using the Health Assessment Questionnaire (HAQ-DI, EuroQol 5 Dimensions (EQ-5D), Body Mass Index (BMI), Depression Inventory-II (BDI-II), and Patient’s General Health using visual analogue questionnaire (Pt-GH), and Disease Activity Score (DAS28-ESR, DAS28-CRP). All of these items were investigated just before surgery (baseline) and again at 6 and 12 months after surgery.

Results: On the whole, the physical function (HAQ-DI, DASH, TUG), QOL (HAQ-DI, EQ-SD, Pt-GH), mental wellness (BDI-II, Pt-GH), and disease activity (DAS28-ESR, DAS28-CRP) were significantly improved at 6 and 12 months after surgery compared to baseline (p<0.01). In the REM/LDA group, a significant improvement was noted in the physical function (DASH, TUG) and QOL (EQ-SD) at 6 and 12 months after surgery; however, we did not observe any significant changes in any other items (Table 1).

Table 1: Outcome of combination therapy with medication and orthopedic surgical intervention

<table>
<thead>
<tr>
<th>Group</th>
<th>HAQ-DI</th>
<th>DASH</th>
<th>TUG</th>
<th>DAS28-CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.09</td>
<td>13.0</td>
<td>39</td>
<td>10.7</td>
</tr>
<tr>
<td>6 months</td>
<td>0.69</td>
<td>6.3</td>
<td>30</td>
<td>7.8</td>
</tr>
<tr>
<td>12 months</td>
<td>0.39</td>
<td>3.9</td>
<td>38</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Conclusions: Achieving REM or LDA is not the only ultimate goal of treatment for patients with functional loss caused by structural damage. Further “wellness” can be achieved by surgical intervention. Intensive combination therapy with medication and orthopedic surgical intervention is effective in improving the QOL and mental health of the patient as well as the physical function. Such intervention can also ameliorate the disease activity.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2415

AB0221 IMPACT OF SMALL TO MEDIUM DOSE OF PREDNISOLONE ON BONE MINERAL DENSITY AMONG EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent randomized trials in rheumatoid arthritis (RA) using low to medium dose of corticosteroids showed that bone mineral density (BMD) loss over 2 years was not significantly different from that with placebo. Another study in early RA and undifferentiated arthritis even showed a positive correlation between cumulative glucocorticoid (GC) dose with an increase in BMD at the ultradistal forearm. Whether the use of prednisolone (pred) can prevent bone loss in early RA patients remained controversial.

Objectives: The aim of this study was to investigate the impact of small dose pred (<10mg/day) on BMD in early RA patients.

Methods: Data from 107 patients recruited from 5 sites: 53±11.92 years; females: 79 (73.8%), median disease duration at entry: 7-month (IQR, 4–12) from the Hong Kong early arthritis registry (Clinical Rheumatology Systematic Treat to Target in Asia Leadership [CRYSTAL] project)were analyzed. In this register, clinical and treatment information were systematically recorded, including cumulative GC dose. Hip, spine and forearm BMDs were measured by dual-energy X-ray absorptiometry (DXA) at baseline and month 12. Patients were categorized into three groups according to pred use (never/<3/≥3 months) during the first year of follow-up. Patients who ever took ≥10mg/day of pred were excluded. The change in BMD was compared between groups and between the two time points.

Results: The baseline characteristics of patients were shown in Table 1. Patients were randomized into three groups according to pred use (never/<3/≥3 months) during the first year of follow-up. Patients who ever took ≥10mg/day of pred were excluded. The change in BMD was compared between groups and between the two time points.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration of pred use</th>
<th>BMD (g/cm²)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never (n=58)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>50±6.6</td>
<td>48±25</td>
<td>0.044</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22±5.7</td>
<td>22±5.5</td>
<td>0.496</td>
</tr>
<tr>
<td>RF+</td>
<td>46 (83.7%)</td>
<td>4 (80.0%)</td>
<td>0.976</td>
</tr>
<tr>
<td>AntiCCP+ve</td>
<td>41 (83.7%)</td>
<td>4 (80.0%)</td>
<td>0.976</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>14 (24.1%)</td>
<td>2 (25.0%)</td>
<td>0.540</td>
</tr>
<tr>
<td>Disease duration</td>
<td>10.80±11.4</td>
<td>7.49±3.99</td>
<td>0.032</td>
</tr>
<tr>
<td>Tendens joints</td>
<td>67.75±19.1</td>
<td>63.21±17.4</td>
<td>0.218</td>
</tr>
<tr>
<td>Swollen joints</td>
<td>50.43±3.70</td>
<td>4.13±2.85</td>
<td>0.146</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>59.6±35.62</td>
<td>47.05±19.53</td>
<td>0.387</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>15.18±35.12</td>
<td>14.86±19.56</td>
<td>0.260</td>
</tr>
<tr>
<td>WSAS-IR</td>
<td>4.28±1.20</td>
<td>4.09±1.03</td>
<td>0.042</td>
</tr>
<tr>
<td>DAS28</td>
<td>3 (5.3%)</td>
<td>0 (0.0%)</td>
<td>0.436</td>
</tr>
<tr>
<td>Pred</td>
<td>10 (20.0%)</td>
<td>12 (24.0%)</td>
<td>0.850</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>10 (20.0%)</td>
<td>12 (24.0%)</td>
<td>0.850</td>
</tr>
<tr>
<td>DMARDs</td>
<td>30 (54.1%)</td>
<td>4 (25.0%)</td>
<td>0.332</td>
</tr>
<tr>
<td>NSAID</td>
<td>40 (72.7%)</td>
<td>4 (25.0%)</td>
<td>0.766</td>
</tr>
</tbody>
</table>

Conclusion: Ultrasound guided synovial tissue biopsies are feasible in the United States. Based on our recent success using minimally invasive ultrasound guided synovial biopsies, we believe that this procedure coupled with cutting-edge technologies will provide the critical information to rheumatologists to establish precision based medicine as a reality for RA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5488
who required ≥3 months of pred treatment are older, with a shorter disease duration and a higher disease activity. Significant differences in the percentage change of BMD in forearm was found among the groups (Pred never/Pred ≥3 months: -2.99±4.21/1.05±3.10/0.65±3.45, p=0.045). Post-hoc analysis revealed that the percentage reduction of forearm BMD was significantly less in the Pred ≥3 months group compared to the Pred never group (p=0.043). After adjusting for age, gender, disease duration and baseline DAS-CRP, the changes in forearm BMD was still significantly different among the three groups (p<0.015). No significant differences in the changes of hip and spine BMD were observed. Significant changes in forearm BMD were observed between baseline and month 12 only in the Pred never group (0.54±0.08/0.53±0.0 p<0.001, graph1).

Conclusions: Small to medium dose of prednisolone might protect bone loss in forearm among early RA patients. These results need to be further validated.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2842

AB0224 SIMULATION FOR CHOICE OF BDMAARDS AND TSDMARDS IN ORDER TO SUCCESS FOR THREE-YEAR SURVIVAL IN RHEUMATOID ARTHRITIS TREATMENT

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Background: In rheumatoid arthritis (RA) treatment, bDMARDs and tsDMARDs (BiO) perform tremendous disease activity control, however, its effectiveness is uncertain and unstable, because their survival ratio is not good enough to tolerate. If more right choice is done in guided by some simulation.

Objectives: This study aims more than 80% of three-year survival ratio (SR100 of BiO) in simulating risk of BiO by using statistical clinical data and post marketing surveillance (PMS) data with Bayes estimation.

Methods: Infection risk and survival risk were harvested from Japanese PMS data, and our clinical data. All our cases were calculated with last observation carried forward method (LOCF). If BiO was continued for more than three years or discontinued by attaining clinical remission, it was evaluated as success, while other cases were evaluated as failure. Patient’s clinical data and general status was calculated for each case, and SR100 for success was statistically evaluated with Binary Logistic Analysis for success. Evaluation methods for parameters were divided according to general risk and drug specific possibility. If calculated general risk went above 0.2, selection of BiO was discarded. In other case which had gone below, choice of BiO is done in according to point that had been cumulated by drug specific possibility in choosing what took maximum calculated expectation value.

If chosen drug have matched used BiO, it was evaluated as true, if not, it was evaluated as false, while if true case was in success, it was evaluated as true success, and if in failure, it was evaluated as true failure, while false case was in success, it was evaluated as false success, and if in failure, it was evaluated as true failure. Sensitivity in success cases and specificity in failure cases was calculated for each case, and SR100 for success was statistically evaluated with chi-square test.

Results: 188 cases have had enough data for simulating. In these, 108 were success and 80 were failure. In success cases, simulated TNF inhibitor (TNF-i) counted 37, Tocilizumab (TCZ) counted 11, Abatacept (ABT) counted 12, and...
Tofacitinib (TOF) counted 2 while real chosen cases were TNF-α counted 65, TCZ counted 11, ABT counted 21, and TOF counted 11. Overall success ratio was 57.4%. In these cases, true choice had been done in 97 cases of 108. In failure cases, simulated TNF-α counted 44, TCZ counted 16, ABT counted 2, and TOF counted 1, while real chosen cases were TNF-α counted 49, TCZ counted 17, ABT counted 10, and TOF counted 4. True success counted 97, and false success counted 11, while false success counted 37 and true failure counted 54. Then, sensitivity was 89.8% and specificity was 67.5% (0.01).

**Conclusions:** Drug choice of BIO supported with simulation was superior to real choice. If risk management was adequately performed, SR/37Y is expected more than 85%.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6499

### AB0225 CHARACTERISTICS OF MHAQ FOR UPPER AND LOWER EXTREMITY FUNCTION, AND RELATIONSHIP WITH AGE AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENT

**I Yoshih1, T. Chijiwa2, 1Rheumatology, Yoshii Hospital, Shimanto City; 2Rheumatology, Kochi Memorial Hospital, Kochi, Japan**

**Background:** Activity in daily living (ADL) is one of main target to maintain patient's quality of life in rheumatoid arthritis (RA) treatment. Modified Health Assessment Questionnaire (mHAQ) is a most popular index for ADL in routine practice. mHAQ is divided into five function of extremity; namely the first four categories are reflections of upper extremities (mHAQ-UE), while the latter are of lower extremities (mHAQ-LE). If function of each extremity is separately disabled, it should be reflected on each part of mHAQ.

**Objectives:** mHAQ was separately investigated in order to evaluate characteristics of each part of mHAQ.

**Methods:** 964 RA patients since January 2010 had been treated. In these, patients who have been treated consecutively for more than five years at December 2016 were recruited in this study. Patient who had been operated musculoskeletal surgery was excluded. mHAQ-UE and mHAQ-LE, and 28-joint disease activity index with C-reactive protein (DAS28-CRP) were measured every time since first visit. Average value of these parameters including Sharp/van der Heijde Score (SvdHS) were calculated annually. Relationship between each of mHAQ and parameters for each year were evaluated used with multiple linear regression analysis.

**Results:** Predominant extremity in mHAQ was evaluated as in which upper extremity predominant (G-UE), lower extremity predominant (G-LE), same weight (G-EV), and both of them were zero (G-Z). Changes of the evaluation from first to the last was evaluated by interrupted time series analysis.

**Results:** One hundred and two male and three hundred and thirty-three female, totally four hundred and thirty five patients were picked up. Their average value of age, SvdHS, DAS28-2CRP, mHAQ, mHAQ-UE, and mHAQ-LE were 64.65, 52.1, 2.96, 0.439, 0.286 and 0.491 at first consult, and 71.05, 52.1, 1.72, 0.425, 0.344, and 0.505 at last time follow up, respectively. Both of mHAQ-UE and mHAQ-LE have demonstrated significant regression with both age and SvdHS throughout treatment, while not significant with DAS28-CRP however, mHAQ-UE correlated with tender joints joint except of knee, and mHAQ-LE have correlated with swelling of the knee joint significantly.

G-UE had counted for 85 patients, G-LE for 136, G-EV for 49, and G-Z for 165 at first consult. Once evaluation had changed, there have continued to the last in all patients. G-UE resulted in G-UE for 83, while G-LE for 2 at last. G-LE resulted in G-UE for 133, G-Z for 2, and G-EV for 1, G-EV resulted in G-LE for 24, G-UE for 7, and G-EV for 18. G-Z resulted in G-Z for 137, G-EV for 19, G-UE for 4, and G-EV for 5. G-UE to G-EV demonstrated significant higher DAS28-CRP improvement from first to the last than to G-LE, and to G-UE, and G-EV to G-LE demonstrated significant higher DAS28-CRP improvement than to G-LE, although no significant difference demonstrated for mHAQ improvement among groups. G-UE to G-LE demonstrated significant higher DAS28-CRP improvement than to G-U, as well as G-U to G-LE demonstrated significant higher mHAQ improvement than to G-U.

**Conclusions:** From these results, it is suggested that mHAQ-UE and mHAQ-LE might be decreasing function. However, mHAQ-UE and mHAQ-LE showed by upper extremities joint tenderness, while mHAQ-LE can move more sensitively with knee swelling. Tight disease activity control may reduce mHAQ both of them, however, reduces more predominantly with mHAQ-UE than mHAQ-LE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4098

### AB0226 FUNCTIONAL DISABILITY IN RA PATIENTS TREATED WITH BIOLOGICS: HUR-BIO REAL LIFE RESULTS

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**Background:** Rheumatoid arthritis (RA) is a chronic, erosive disorder which may lead to permanent joints damage. Health assessment questionnaire (HAQ) is frequently used for evaluating functional disability in RA patients.

**Objectives:** The aim of this study is to determine the effect of biologic treatment on functional disability in RA patients.

**Methods:** HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, monocentric database of biological treatments including 1219 RA patients by August 2016. 523 patients in whom HAQ assessment before biologics were available, was recruited in this retrospective analysis. HAQ score $>1.0$ was defined as severe functional disability. $^1$ HAQ assessment at last follow-up visit was evaluated. Improvement of HAQ score 0.22 points or more was considered as clinically significant response to treatment.

**Results:** Among 523 patients (80.5% female), mean age was 52.6±12.5 and mean disease duration was 9.4±7.3 years. Seropositivity for RF and/or CCP was present in 67.2% of patients. At baseline visit, HAQ score was $>1.0$ in 288 patients (51.2%). Baseline and last follow-up HAQ scores were 1.07±0.62 and 0.64±0.57. Minimal clinically significant improvement of HAQ score was observed in 238/377 patients (63.1%). Clinically significant response was more frequent in patients with baseline HAQ score of $>1$ (153/195 (78.4%) vs 85/182 (46.7%); p = 0.001). Table 1 represents features of patients according to baseline HAQ score. Mean follow-up time was 16±4±16.4 months. Data of at least one visit was available for 377 (72.0%) patients.

**Table 1. Comparison of demographic an clinical data of patients according to baseline HAQ score**

<table>
<thead>
<tr>
<th>HAQ $&gt;1$ (n=268)</th>
<th>HAQ $\leq 1$ (n=255)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>55.1±12.3</td>
</tr>
<tr>
<td>Disease duration (years), mean ± SD</td>
<td>10.2±6.0</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>31.3±6.4</td>
</tr>
<tr>
<td>High school or college graduate n (%)</td>
<td>68.2 (25.3)</td>
</tr>
<tr>
<td>Smoking (current or previous) n (%)</td>
<td>95 (35.4)</td>
</tr>
<tr>
<td>Hyper tension, n (%)</td>
<td>101 (37.7)</td>
</tr>
<tr>
<td>Patient global assessment VAS, mean ± SD</td>
<td>6.61±1.4</td>
</tr>
<tr>
<td>Fatigue VAS, mean ± SD</td>
<td>7.61±2.0</td>
</tr>
<tr>
<td>Physical function VAS, mean ± SD</td>
<td>7.1±1.6</td>
</tr>
<tr>
<td>Biologic switch, n (%)</td>
<td>63 (23.5)</td>
</tr>
</tbody>
</table>

**Conclusions:** Functional disability was observed approximately half of patients. Clinically significant improvement was more frequent among patients with higher baseline HAQ scores particularly. Biologic treatment seems to be provide significant functional improvement. However significant functional disability persists in one fourth of patients.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4098
immunological approach to the diagnosis of lesions of the nervous system in patients with rheumatoid arthritis

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Background: Although S100 proteins represent 40% of the neutrophil cytoplasmic proteins, their physiological and pathological functions are still unclear. S100 protein concentrations are dramatically enhanced in synovial fluid and synovium of patients suffering from rheumatoid arthritis (RA). Their expression seems to correlate with disease activity and joint damage [1].

Objectives: Improvement of immunological detection of neurological involvement in RA by means of polyclayamide magnetic beads with immobilized S-100 protein.

Methods: The research was carried out in agreement with the principles of the World Medical Association Declaration of Helsinki. The informed consent had been signed by all involved persons, another obligation require was age 18 years or more. The patients were from the rheumatoid wards in Volgograd Municipal Hospital No. 25 and Volzhsky Municipal Hospital No. 1. Diagnosis of RA was established by ACR-EULAR criteria (2010), RA activity was evaluated using DAS28. Serum anti-S-100 protein antibodies were measured by ELISA, with S-100 protein immobilized on polyclayamide magnetic beads as an antigen. The antibody concentrations were expressed as optical density units (ODU) and were considered positive if the cutoff value (2SD of the reference group, 0.050 ODU) was exceeded. The results were expressed as mean±SD, differences were considered significant when p<0.05. Pearson correlation coefficient (r) was also used.

Results: 40 healthy persons (29 men and 11 women), and 95 female patients with RA and the neurological signs, appeared during active phase of the disease, were recruited for this study. Mean age of the healthy controls was 36±7 years, and for the RA group it was equal to 55±11 years. Mean RA duration was 4.2±2.9 years. 13 patients had low, 52 – moderate, and 8 – high disease activity. The most common types of neurological involvement were mononeuropathy (n=29), polyneuropathy (n=65), radiculopathy (n=80); cervicocranialgia (n=51), and trigeminal neuralgia (n=14). The symptoms of central nervous system damage (TIA, seizures, cerebellar ataxia, dysarthria) were found in 21 patients. In RA group, anti-S-100 protein antibodies were detected in 51 (32.4%) cases, with mean concentration 0.078±0.028 ODU. The patients with different neurological signs had mean anti-S-100 protein antibody concentration 0.138±0.046 ODU, the subgroup without any neurological signs had 0.060±0.024 ODU (p=0.022). In all cases analyzed index correlated with the degree of activity of the pathological process. High levels of antibodies to S-100 protein in RA associated with central nervous system (CNS) and peripheral nervous system (PNS).

Conclusions: We found an association between neurological involvement in RA and elevation of anti-S-100 protein antibody concentrations. These findings give us an opportunity to improve the diagnosis of minor neurological damage in RA and thus to make more precise adjustment of the treatment.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6481
estimates of reversible findings, irreversible findings, and distress to support clinical management decisions. Estimates of joint damage are higher in OA than in RA, although higher than estimates of inflammation in both RA and OA, in patients in all 4 RAPID3 severity categories.

References:

DOI: 10.1136/annrheumdis-2017-eular.3556

AB0232 MINIMAL CLINICALLY IMPORTANT IMPROVEMENT (MCI) OF RAPID3 (ROUTE ASSESSMENT OF PATIENT INDEX DATA 3), AN INDEX OF ONLY PATIENT SELF-REPORT SCORES, PERFORMS SIMILARLY TO TRADITIONAL RHEUMATOID ARTHRITIS (RA) INDICES, DAS28 AND CDAI

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Background: No single “gold standard” measure is available to assess patients with rheumatoid arthritis (RA) in clinical trials and routine care, as in hypertension, diabetes, and other diseases. Therefore, an index of several measures, such as a DAS28 Disease Activity Score-28 and CDAI (Clinical Disease Activity Index), based on 7 RA core data set measures, is needed. However, the only quantitative data in many (most) patients in routine rheumatology care are laboratory test results. RAPID3 (routine assessment of patient index data), which includes only patient self-report scores, is considerably more feasible than DAS28 or CDAI for routine care, distinguishes active from control treatments in RA clinical trials similarly and is correlated significantly with these indices. A minimal clinically important improvement (MCI) to interpret changes in clinical trials and clinical care has not been established for RAPID3

Objectives: To estimate MCIs of RAPID3, and compare results to MCIs of DAS28 and CDAI

Methods: Post hoc analyses were performed of a reported longitudinal study of 250 patients with active RA (1). All 7 RA core data set measures were collected at baseline and after treatment escalation with prednisone 1 month later or with disease modifying medications or biologic agents 4 months later (1). Patient judgment of improvement in arthritis status was obtained as “improved”, “the same” or “worsened”, and analyzed in relation to changes in RAPID3, DAS28 and CDAI. RAPID3 is the sum of 0–10 measures; physical function on a HAQ recalculated from 0 to 10, pain and patient global estimate on 0–10 VAS (visual analog scales), total=0–30. DAS28-ESR (erythrocyte sedimentation rate) and CDAI were computed as described in the literature. Changes in all indices, standardized response means (SRM), MCIs as changes that had a specificity of 0.80 for improvement based on receiver-operating characteristic curves, and MCI as a proportion of the maximum score were computed.

Results: Among 250 patients, 167 (66.8%) reported improvement. RA activity and SRMs improved similarly per the 3 indices (Table), ROC curve areas were ≥0.77 (Table). MCIs with specificity for improvement of 0.80 were -3.5 for RAPID3, -1.17 for DAS28-ESR, and -12.5 for CDAI. MCIs were in a similar range of 11.6% to 16.8% of maximum score (Table).

Conclusions: MCIs for RAPID3, DAS28, and CDAI were in a similar range. Knowledge concerning MCI thresholds can improve interpretation of data from clinical trials and routine clinical care.

References:


<table>
<thead>
<tr>
<th>Measures (range)</th>
<th>Baseline</th>
<th>Follow-up</th>
<th></th>
<th>Mean (%)</th>
<th>change</th>
<th>MCI (95% CI)</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPID3 (0–30)</td>
<td>16.3±6.3</td>
<td>11.1±6.7</td>
<td>-5.2±6.3</td>
<td>-0.79 (-0.71, -0.88)</td>
<td>0.80 (0.74, 0.86)</td>
<td>-3.5 (2.9, -4.3)</td>
<td>11.6%</td>
</tr>
<tr>
<td>DAS28-ESR (9–49)</td>
<td>6.1±16.2</td>
<td>4.8±13.8</td>
<td>-1.3±1.34</td>
<td>-0.96 (-1.09, -0.70)</td>
<td>0.77 (0.71, 0.82)</td>
<td>-1.17 (-1.36, -0.87)</td>
<td>12.4%</td>
</tr>
<tr>
<td>CDAI (0–76)</td>
<td>36±13.5</td>
<td>23.0±13.6</td>
<td>-13.7±14.1</td>
<td>0.86 (-0.90, -1.08)</td>
<td>0.78 (0.73, 0.84)</td>
<td>-12.5 (-14.7, -10.5)</td>
<td>16.4%</td>
</tr>
</tbody>
</table>

SRM = standardized response mean; CI = confidence interval.
Objectives: We investigated the effects of oral contraceptives (OCs) and menopause on RA in South Korean women using nationwide data.

Methods: We examined the proportion of patients in remission and 3 other disease severity categories according to RAPID3 at 3 sites at which MDHAQ is completed by all patients in routine care.

Results: Similar RAPID3 remission rates were seen at 3 USA sites (about 24%), comparable to results from France and Norway. Low severity ranged from 7–24%, moderate severity from 23–99%, and high severity from 21–46%. Age and sex were similar in the analyses. The proportion of patients in 4 RAPID3 categories, high severity (>12/30), moderate severity (6.1–12), low severity (3.1–6), and remission (<3), was computed. MDHAQ demographic and clinical measures and DOCGL were compiled into a 0–30 RAPID3, as well as scores for fatigue, RADAI (0–48), and DOCGL demographic and clinical measures, and self-report RADAI (0–10) in each site. The analyses included 420 RA patients from the 3 sites that were analyzed. Remission rates according to RAPID3 severity ranged from 23% to 26%, similar to reported rates from France and Norway. Low severity ranged from 7–24%, moderate severity from 23–99%, and high severity from 21–46%. Age and sex were similar in the disease severity categories at the 3 sites (Table). Patients in the moderate and high severity groups at each site had higher scores for fatigue, RADAI self-reported joint pain, and DOCGL.

Table 1. Table (SD) for demographic and clinical characteristic of patients in remission versus other disease severity categories according to RAPID3 at each site.

Methods: Data were collected from the 2008–2012 Korea National Health and Nutrition Examination Surveys. A total of 17,890 eligible participants were included. As there were significant differences in baseline characteristics between the patients on OCs and those not taking OCs, we used propensity score-matching to adjust for such differences. We calculated the odds ratios (ORs) and 95% confidence intervals (95% CIs) of OCs leading to RA development.

Results: The peak incidence of RA was between 50–59 years old. The overall rate of OC usage was 16.5% and mean duration of OC using was 18.4±28.78 (ranged from 0 to 360) months. Before propensity score-matching, using multivariable logistic regression adjusted for traditional risk factors, taking OC was a significantly associated with RA development (OR 1.18, 95% CI 1.19–1.19, p < 0.001). After propensity score-matching, taking OCs was not associated with RA (OR 1.05, 95% CI 0.83–1.34, p < 0.001). Menopausal status showed strongly significant increase in the risk of RA.

Conclusions: There was an association between menopausal status and RA development in South Korean women. However, usage of OCs did not show significant effects on the development of RA.

References:

Disclosure of Interest: None declared.
Conclusions: Pts with CDAL <35–36 at BL achieved sustained LDA more frequently and more rapidly than pts in the higher disease category at BL. In pts with higher disease activity at BL a more robust response was observed with bari 4 mg treatment.

References:

AB0236 ASSOCIATION OF LYVE-1 PROTEIN IN EXOSOME WITH DISEASE ACTIVITY AS A NEW CANDIDATE BIOMARKER FOR RHEUMATOID ARTHRITIS
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Background: Exosomes, membrane-bound vesicles of 40–100 nm in diameter, have protein and lipid composition that depends on the cell origin, the state of activation, interaction and/or transformation of the parent cells. Those proteins and lipids may be a role in mediating inflammatory and autoimmune disease as well. Discovery of inflammatory marker to evaluate appropriate response of treatment could give effective timing to adjust treatment for rheumatoid arthritis patients.

Objectives: The aim of this study was to identify protein candidates in exosome being related with inflammatory parameters.

Methods: The study population consisted of 60 RA patients, in which there were 30 patients of clinical remission (rem) group with DAS28-ESR<2.6 and 30 patients of non-clinical remission (non-rem) group with DAS28-ESR>2.6. By exosome preparation with ExoQuickTM kit and protein identification with tandem mass tags labeling/mass spectrometry between the groups, potent protein markers were selected. Level of the proteins was measured by ELISA.

Results: We identified 6 proteins by proteomics approach. Amyloid A (AA) and lipid vascular endothelial hyaluronic acid receptor-1 (LYVE-1) was identified with different levels in exosome between CR group and non-CR group. AA levels of both serum and exosome were higher in non-CR group than CR group (p value<0.001). Significant positive correlations were found between exosome AA level and CRP as well as between serum AA level and CRP (p=0.614, p value=0.001 and p=0.624, p value=0.001). Though LYVE-1 level of serum was not different between non-CR group and CR group, LYVE-1 level of exosome was lower in non-CR group than CR group (p value<0.01). We found positive correlations between serum/exosome of LYVE-1 and CRP in only non-CR group (serum p=0.376, p value<0.04; exosome p=0.545, p value<0.002).

Conclusions: We suggest that LYVE-1 in exosome can be used as an additional marker of disease activity in RA patients and this study provides the evidence about the role of exosome for RA as the carrier of useful marker.

References:

AB0238 THE INFLUENCE OF FATIGUE IN THE DEFINITION OF REMISSION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOLCILIZUMAB
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Background: Achieving disease remission or low disease activity is the therapeutic goal in rheumatoid arthritis (RA) treatment. Disease activity is defined through established criteria requiring high values of inflammatory markers. Several studies have shown fatigue levels in patients with newly diagnosed malignancy. J Cancer. 2014:5(3):1907–20.

Objectives: To evaluate the relation between PBA and fatigue, and whether fatigue influences disease remission definition in RA patients treated with tocilizumab (TCZ), an anti-IL-6 receptor monoclonal antibody.

Methods: We prospectively recruited 18 consecutive patients with RA (ACR/EULAR 2010 criteria), on TCZ treatment (3 months), from a single referral centre. Disease activity was evaluated by disease activity score for 28-joints (DAS28), and the ACR/EULAR Boolean-based criteria for remission were calculated. Visual Analog Scale for Fatigue (VASF) and Multidimensional Assessment of Fatigue scale (MAF) were used to measure fatigue.

Results: 89% of the patients were female and mean age was 55.5±13.8 years (yrs). Mean disease duration was 8.8±6.8yrs and mean duration of TCZ treatment was 2.3±1.3yrs (50% 1st line). Mean PGA score was 3.3±2.0 (3 best-health) and mean DAS28 C-reactive protein (CRP) was 2.27. According to DAS28-3RD 44% of the patients were in remission, 22% had low disease activity and 33% had moderate activity. 3 patients (17%) fulfilled the ACR/EULAR Boolean criteria for remission. Considering all the composites of the Boolean criteria, PGA was the only reason for not achieving remission in 10 patients (56%). The mean fatigue scores were: VASF 6.6±2.3 (0-best health), Global Fatigue Index (GFI), calculated through MAF scale, 24.3±14.9 (1-best health). Amongst the 18 patients, PGA correlated with higher fatigue scores on VASF (r=0.50, p=0.0095) and on GFI (r=0.49, p=0.037). In the group of patients not fulfilling Boolean remission, a similar correlation between PGA and higher fatigue scores was found (VASF: r=0.54, p=0.036; GFI: r=0.79, p=0.0041). In the sub-group of patients in which PGA was the only factor for not achieving Boolean remission, there was a significant correlation between PGA and fatigue scores (GFI: r=0.79, p=0.009), that was not present in the other patients (GFI: r=0.24; p=0.49).

Conclusions: We found a positive correlation between higher PGA and fatigue
scores in RA patients treated with TCZ. PGA was the major limiting factor for higher PGA and fatigue scores was found, not present in the rest of the cohort. These results enhance the influence of fatigue in patients’ perspectives of disease and reinforce the limitations of using PGA to define RA activity and remission. Furthermore, considering the influence of TCZ in fatigue mechanisms, by blocking IL-6 receptor, we still found high fatigue scores in this cohort, which can enhance the complex physiopathology of fatigue in chronic inflammatory diseases, and the role of several other cytokines (IL-1, TNF-α). This effect and comparison with RA patients treated with anti-TNF-α can be explored further in larger prospective studies.

Disclosure of Interest: None declared


AB0239

DKK1 IS NOT ASSOCIATED WITH INFLAMMATORY ACTIVITY INDEXES IN RHEUMATOID ARTHRITIS, BUT WITH FUNCTIONAL DISABILITY RELATED TO THE LONG EVOLUTION OF THE DISEASE

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Background: Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease characterized by joint destruction, deformity, lower functional status and decrease in life expectancy. Wnt signaling pathway recently it has been implicated in bone homeostasis. Studies suggest that overexpression of inhibitors of the Wnt signaling pathway, like the Dickkopf 1 protein (DKK1) has been implicated in bone destruction.

Objectives: To compare circulating levels of DKK1 in patients with RA to their disease activity and functional status.

Methods: 378 consecutive patients with early and established RA were evaluated at the Hospital Militar Central in Bogotá-Colombia, between March 2015 and November 2016. A complete medical history related to RA was obtained. Disease activity was evaluated by DAS28-PCR, CDAI, SDAI and RAPID3. functional status was measurement using MDHAQ and the Steinbrocker functional classification. DKK1 levels measured by ELISA using an Abcam® kit.

Results: The mean age was 60.7±13.1 years, disease duration 13.1±10.9 years, 80.4% were female. Higher levels of DKK1 were not associated with higher disease activity by CDAI (p=0.70), SDAI (p=0.84), DAS28 with CRP (p=0.80) or RAPID3 (p=0.70). Interestingly higher levels of DKK1 were significantly associated to greater disability and lower functional status according to the Steinbrocker functional grading (p=0.013) and with severe disability by MDHAQ (p=0.004), Table 1.

Other variables associated with joint destruction were osteoporosis, elevated rheumatoid factor, smoking, and hospitalization

Steinbrocker functional grading n (%) DKK1 (pg/ml) P

| Class I-II | 286 (75.2) | 4930.9±6801.5 | 0.013 |
| Class III-IV | 93 (24.5) | 7930.6±10811.8 |
| MDHAQ | | |
| Without or low disability | 334 (88.0) | 3192.0±2729.4 | 0.004 |
| Moderate or severe disability | 45 (12.0) | 4446.6±2821.0 |

Conclusions: Higher levels of DKK1 were found in patients with lower functional status. This association was not found in patients with greater disease activity according to CDAI, SDAI, DAS28 and RAPID3. This could be explained by greater structural damage though more studies would be needed to explore this possibility.

References:

Disclosure of Interest: None declared


AB0240

ASSOCIATION BETWEEN LEPTIN CONCENTRATIONS AND CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: It has been observed that leptin plays a role in the development of cardiovascular risk, independently associated with the development of atherosclerosis, as well as with traditional risk factors such as obesity and arterial hypertension, on the other hand, its participation in carbohydrate and lipid metabolism and in coagulation, makes leptin a promoter of the complications of obesity and therefore increase cardiovascular risk.

Objectives: Identify whether there is a relationship between serum leptin concentrations and cardiovascular risk assessed using the Framingham scale.

Methods: We studied patients with the diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria; the leptin determination was through an enzyme immunoassay (ELISA) with the TECO® Test Kit. Cardiovascular risk was calculated using the modified Framingham score, as reported by EULAR, the result obtained was multiplied by 1.5. We considered as risk values of <1% as low; 1–2.5% moderate and >5% high. Statistical analysis was performed using the SPSS 22.0 package. A p<0.05 was considered a significant result. Categorical variables were compared with Chi square test. Continuous variables were compared with either the Student’s T test or the Mann-Whitney non-parametric test, according the case.

Results: We studied 77 patients. The traditional CVR factors that presented the highest prevalence were age, hyperlipidemia and obesity; with regard to the prevalence of non-traditional factors, hyperleptinemia, glucocorticoid use and positive RF were predominant. More than 1/3 parts of the study population consumed metohexate and hydroxyclooroquine, which have been considered as CVR protective factors. Serum leptin concentrations and CVR factors were compared and found that there was a significant difference between higher leptin values and disease activity (p=0.047), obesity (p=0.038), positive rheumatoid factor (p=0.009), Tobacco (0.009) and metabolic syndrome (p=0.001). Likewise, a significant relationship was found between lower leptin concentrations and hydroxyclooroquine consumption (p=0.023). Framingham CVR was calculated and the result obtained was multiplied by 1.5. The 35.5% of the population studied had a Framingham RCV, 38.3% moderate and 25.9% presented a high risk. We compared the level of CVR and serum leptin concentrations, finding that the highest CVR were the leptin values.

Conclusions: There is a positive association between CVR and serum leptin concentrations. It is also significantly associated with traditional and non-traditional risk factors.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6986

AB0241

RELATIONSHIP BETWEEN LEPTIN AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Increased concentrations of leptin have been observed during infectious processes and inflammation, in such a way that it plays a role in the inflammatory and the immune response.

Objectives: Determine the association between serum leptin and disease activity measured through DAS-28 PCR.

Methods: Patients with the diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria were studied. Leptin was determined by enzyme immunoassay (ELISA) with the TECO® Test Kit, the values higher than 17 ng/mL were considered as hyperleptinemia. Disease activity was assessed by DAS-28 PCR, classifying as remission <2.3, low activity ≥2.3 to <3.8, moderate activity as ≥3.8 to <4.9 and high activity ≥4.9. Statistical analysis was performed using the SPSS 22.0 package. A p<0.05 was considered a significant result. A multivariate logistic regression model was used to determine the association between significant variables and leptin concentrations.

Results: 77 patients were studied, 93.5% were female. The activity of the disease was determined, finding that 40.3% of patients were in remission, 41.6% had low activity, 11.7% had moderate activity and 6.5% had high activity. The 46.8% had obesity, 65.5% were overweight, 18.2% had normal weight and 2.5% were underweight. The 37.7% of the patients studied had metabolic syndrome, being the main factor the presence of an altered abdominal perimeter. The 63.6% had positive rheumatoid factor. The 71.4% had leptin levels ≥17 ng/ml. A multivariate logistic regression was performed with leptin as dependent variable. The results show an independent association between higher concentrations of leptin and disease activity (OR 1.9; 95% CI 1.3–3.8; p=0.045), obesity (OR 3.63; 95% CI 1.1–11.9; p=0.033), the presence of metabolic syndrome (OR 2.74; 95% CI 1.7–10.4; p=0.038), and positive rheumatoid factor (OR 3.5; 95% CI 1.2–11.3; p=0.024). Leptin was also found at higher disease activity, there were higher concentrations of serum leptin. Patients with severe activity had higher leptin media than patients in remission

Conclusions: There is a positive relationship between the activity of the disease and the serum leptin concentration, likewise this hormone is related to other inflammatory processes such as metabolic syndrome and rheumatoid factor.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6722


SERUM LEVELS OF ANGIOGENIC AND PROINFLAMMATORY factors. 

Background: The miRNAs, small non-coding RNA, regulate the genetic expression to posttranscriptional level, inhibiting the translation. The role of miRNAs in the evolution of RA is not clear. 

Objectives: To evaluate the variants rs2910164G/C in the evolution of RA and its extra-articular manifestations (EAM) 

Methods: 133 cases with RA were included (ACR/EULAR criteria 2010) and 430 healthy controls. There were evaluated EAM (rheumatoid nodules [RN], Raynaud phenomenon [RP], cutaneous vasculitis [CV], episceritis, sclerosis, peripheral ulcerative keratitis [PUK], multiple mononeuritis [MP]) and levels of ESR, CRP, RF and CCP. It was performed genotyping of single nucleotide polymorphisms (SNPs) rs2910164G/C in miR-146a, rs11614913C/T of miR-196a-2 and rs3746444A/G of miR-499. The descriptive and inferential statistical analysis was performed with the software SPSS and Finetti. 

Results: Patients with RA, women 126 (94.7%); age Me 48.9 (IQR 40–58); patients with EAM 23 (17.2%); women 22 [95.6%]; RN 14 [60.8%], RP 4 [17.3%], CV 1 [4.3%], episceritis 1 [4.3%], PUK 1 [4.3%], MM 1 [4.3%], MP 1 [4.3%]; ESR Me 37 (IQR 22–45), CRP Me 0.11 (IQR 0.03–0.27); positive RF 125 patients (93.9%, high positive 94.1%, negative 5.9%). The alleles and genotypic frequencies and the association with susceptibility and severity to Rheumatoid arthritis (RA) and its extra-articular manifestations (EAM) were shown in table 1

Conclusions: None of the evaluated variants in miRNAs are associated with susceptibility for RA, however, the SNP rs11614913C/T located in miR-196a-2 is associated with EAM. 


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6500

AB0243 SERUM LEVELS OF ANGIOGENIC AND PROINFLAMMATORY CYTOKINES TO DISCRIMINATE BETWEEN 6 SETS OF REMISSION CRITERIA IN RA

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Background: The ideal definition of remission in RA remains to be agreed. Angiogenic factors and proinflammatory cytokines are key in RA pathogenesis.

Objectives: The aim of this study was to analyze serum levels differences of angiogenic and inflammatory biomarkers between SDAI, CDAI, ACR, DAS28 and sonographic remission in patients with (RA). 

Methods: We selected patients with RA in clinical remission (DAS28-ESR <2.6 for <6 months). PDUS of knees and hands was performed. Serum levels of biomarkers of inflammation/angiogenesis were determined by Quantibody ® Human Array. Patients were classified according to 6 sets of remission criteria: RA with EAM, ACR50, DAS28, SDAI, CDAI, ACR, DAS28 and sonographic remission in patients with RA.

Results: 60 patients with RA were collected. 76% female, aged (mean) 53 years; disease duration 110 months. 47% (76%) patients, 27% (45%) biological therapies. At baseline, 67% of patients had PD signal and 48% fulfilled criteria for previously defined UdAS. Although patients in sonographic remission had lower levels of inflammatory biomarkers such as IL-6, IL-17 or IL-23, no significant differences were found between the 6 sets of remission criteria. Angiogenic biomarkers such as CXCL6 (0.025), ENA78 (0.007), SDF1 (0.047) and VEGF-R1 (0.025) were significantly lower in patients fulfilling CDAI remission. Patients with no PD signal (0.009) and no UdAS (0.006) had significantly lower levels of BFGF. 

Conclusions: RA patients in CDAI remission had significantly-lower levels of angiogenic cytokines. However, no differences in serum levels of proinflammatory cytokines were found between the 6 sets of remission criteria.

Disclosure of Interest: None declared

AB0244 MICROWAVE RADIOMETRY-DERIVED THERMAL CHANGES OF SMALL JOINTS AS POTENTIAL ADDITIONAL BIOMARKER IN RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY

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Background: Microwave Radiometry (MR) is a rapid, non-invasive method that detects local tissue temperatures. Using joint ultrasound as reference method, in a proof-of-concept study, we have found that an increased temperature at the knee joint detected by MR in the absence of relevant clinical signs reflects the presence of subclinical synovial inflammation in rheumatoid arthritis (RA) [1].

Objectives: To test the hypothesis that temperature of small joints assessed by MR correlates to global disease activity levels in RA, a disease in which small joints are primarily affected.

Methods: Ten patients with active, untreated RA underwent clinical and laboratory assessments, joint ultrasound and MR of hand and foot small joints (RTM 01 RF5 microwave computer based system, Bolton, UK) at baseline, as well as 15, 30 and 90 days after treatment onset. Twenty aged-matched healthy individuals served as controls.

Results: Using 1248 separate MR-derived recordings from RA patients we created several thermo-scores involving different small joint combinations and compared them with clinical and ultrasound data. The best performing thermo-score involved the sum of temperatures of 16 small joints (2nd-5th metacarpal and proximal inter-phalangeal joints, bilaterally). This thermo-score correlated positively to DAS28 disease activity score (p<0.001), tender joint count (p=0.002), swollen joint count (p=0.001), patient's visual analogue scale (p<0.001), CRP
1. T. Okano 1, K. Orita 2, Y. Sugioka 3, K. Mamoto 1, T. Koike 3,4, M. Tada 5, correlated independently with the at 1 year. Multiple regression analysis revealed that the baseline MMP-3 level predictive value for baseline MMP-3 level in women in terms of structural damage. There was a weak correlation between the baseline MMP-3 level was performed, with 

**References:**


**Acknowledgements:** None. Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3279

**AB0245 DISTRICT DIFFERENCES BETWEEN THE SEXES OF PREDICTIVE VALUE OF MATRIX METALLOPROTEINASE-3 AT BASELINE REGARDING CHANGES IN MODIFIED TOTAL SHARP SCORE AT 1 YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Matrix metalloproteinase (MMP-3), also known as stromelysin-1, is expressed in inflamed synovium of patients with rheumatoid arthritis (RA). It degrades components of articular cartilage, such as proteoglycans. In Japan, MMP-3 has been used as a clinical biomarker of joint destruction and its predictive value for radiographic progression has been reported.

**Objectives:** W aimed to confirm a relation between baseline MMP-3 and radiographic progression at 1 year and to examine the association of the MMP-3 level with ultrasonography (US) findings.

**Methods:** A total of 259 (213 women) consecutive patients with RA were enrolled. We collected baseline data, that included the patient’s age, sex, disease duration, use of glucocorticoid or disease modifying antirheumatic drugs, Disease Activity Score-28, and modified total Sharp score (mTSS); MMP-3 and, C reactive protein levels;, rheumatoid factor or anti-citrullinated peptide antibody status,; and the power doppler score (PD) of US assessment of digits and wrists. Baseline MMP-3 level was analyzed in association with the baseline PD value and changes (Δ) in mTSS, erosion score (ΔERN), joint space narrowing (ΔJSN) at 1 year from baseline by Pearson’s correlation method. Changes between ΔMMP-3 and ΔmTSS, or ΔPD were also analyzed. Multiple regression analysis was performed, with ΔmTSS as the outcome for baseline variables. Statistical analysis was performed separately by sex because the upper normal limits of MMP-3 differ between the sexes (men: <121 ng/ml, women: <9.7 ng/ml).

**Results:** There was a weak correlation between the baseline MMP-3 level and PD score in men. There was also moderate correlations between baseline MMP-3 level and structural damage at 1 year only in men. There was no predictive value for baseline MMP-3 level in women in terms of structural damage at 1 year. Multiple regression analysis revealed that the baseline MMP-3 level correlated independently with the ΔmTSS only in men (p=0.0031), whereas in the women the baseline PD score was correlated independently with the ΔmTSS (p=0.0003).

**Conclusions:** The baseline MMP-3 level was a good predictor of deterioration of the mTSS at 1 year in male patients with RA, but not in female patients. On the other hand, the baseline PD score was a useful predictor of joint destruction in female patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2431

**AB0246 IMPACT OF TREAT TO TARGET STRATEGY WITH COMPLEMENTARY ULTRASOUND ON REAL WORLD RADIOPHIC OUTCOMES IN EARLY RHEUMATOID ARTHRITIS OVER THE PAST DECADE**

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**Background:** Treatment for rheumatoid arthritis (RA) has changed over the past decade. Early diagnosis and prompt aggressive treatment based on treat to target strategy, as well as complementary ultrasound have been adopted and proven to improve patient clinical and radiological outcomes in clinical trials.

**Objectives:** The aim of this study was to compare radiographic progression of early RA patients starting their first DMARD 10 years ago vs more recently in daily clinical practice.

**Methods:** We reviewed the medical records of consecutive patients with symptom of 3 years duration who fulfilled the 1987 ACR classification criteria or the 2010 ACR/EULAR classification criteria in a single center retrospectively. In the first cohort (2000s), 70 patients (55.3±13.3y.o, Female 77%) who were diagnosed with RA during 2003–2005 were included. in the second cohort (2010s), 71 patients (54.5±17.3y.o,Female90%) who were diagnosed with RA during 2013–2015 were included. Radiographs of hands were assessed at baseline and one year after according to the van der Heijde Sharp score (range 0–280) without clinical information and chronological orders of radiographs in the individual patients.

**Results:** Mean changes in radiographic joint damage for joint space narrowing score, erosion score, total radiographic score were higher in 2010s than 2000s (0.92±2.70 vs 0.28±1.86; p=0.010, 0.54±1.35 vs 0.35±0.99; p=0.390, 1.45±3.54 vs 0.68±2.55; p=0.015, respectively). Radiographic progression defined as total radiographic score >0 and ≤5 were 31.4% and 22.5% and 8.6% vs 8.5% between 2000s and 2010s (p=0.230 and p=0.970, respectively). Methotrexate (MTX) was frequently used for initial treatment in 2010s than 2000s (86% vs65%, <0.001), and initial dose and maximum dose of MTX were higher in 2010s than 2000s (9.1±2.09 mg/week vs 4.67±1.54 mg/week; p<0.001 and 12.0±4.73 mg/week vs 8.13±1.84 mg/week; p<0.001, respectively). The mean duration from symptom onset to diagnosis was earlier in 2010s than 2000s (5.75±5.04 months vs 7.85±6.85 months, p=0.001), CRP at baseline and 1 year after were lower in 2010s than in 2000s (2.74±1.90 mg/dL vs 3.35±9.4 mg/dL; p=0.001 and 0.60±1.19 mg/dL vs 1.20±1.99 mg/dL; p=0.003, respectively). There were no significant differences in sex, age, positive rate of RF and ACRA, the Sharp score at baseline, steroid use, and biological agents use between two cohorts.

**Conclusions:** In recent 10 years, early diagnosis with complementary ultrasound and appropriate MTX use based on treat to target strategy led to prevent joint destruction of RA patients in daily clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5649

**AB0247 EVALUATION OF RHEUMATOID ARTHRITIS CASES WITH HIGH ANTI-CCP ANTIBODY LEVEL**

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**Background:** Anti-cyclic citrullinated peptide antibodies (Anti-CCP Ab) are well-established serological markers that show high sensitivity and specificity in diagnosing early rheumatoid arthritis (RA). Furthermore, Anti-CCP Ab is reported to be associated with bone erosions of RA. Therefore, Anti-CCP Ab positive RA patient can be a candidate for intensive treatment.

**Objectives:** Upper measurement limit of Anti-CCP Ab increased recently up to 1200 units. High level of Anti-CCP Ab may be a predictor of the profound therapy for RA. To understand the importance of Anti-CCP Ab level, we evaluated RA patients with high titer Anti-CCP Ab in relationship to the other activity markers of RA and the intensity of the treatment for RA.

**Methods:** Total of 186 RA patients with Anti-CCP Ab higher than 30 units was included in this study. Baseline markers such as CRP, MMP-3, RF and anti-CCP Ab were measured at the entry of the study. Relationship among these markers were evaluated and examined using statistical significance for the single-factor ANOVA and the multiple comparison test. Among those cases 131 cases were treated conservatively with biologics and/or DMARDS and were followed up more than one year. We graded them from 1 to 4 by the intensity of the treatment.

Grade I: Biological agent. Grade II: Methotrexate (MTX) more than 12mg or combination with more than 3 DMARDS Grade III: MTX 6–11mg or combination
with two recommended DMARDs Grade IV: single use of DMARDs including MTX less than 5mg.

**Results:** There was no relationship between titers of Anti-CCP Ab and titers of RF. We found significant statistical correlation between anti-CCP antibody titers and inflammatory markers such as CRP and MMP-3. There was significant statistical correlation between CRP and MMP-3. In terms of treatment intensity, strong intensity group showed high titer of anti-CCP Ab and CRP. Titer of RF and MMP-3 level did not have any relationship with the treatment intensity. In cases treated with biologics, anti-CCP Ab and CRP were significantly higher compared to non-biologic case group. In 80% of cases treated with biologic treatment of anti-CCP Ab titers was more than 200 units. However, non-biologic treatment was continued in more than 50% of cases with anti-CCP Ab higher than 200 units.

**Conclusions:** Even though we treated cases based on the severity of the symptoms of the patient and response in laboratory data, high anti-CCP Ab titers and CRP at the base line were most associated with the treatment intensity after 1 year. The results of our study suggest that the titer of anti-CCP Ab can be better a predictor of the treatment intensity than MMP-3 and RF.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4989

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**AB0249**

**IDENTIFICATION OF INFLAMMATORY- AND IMMUNE DISORDER-RELATED PROTEINS AS PUTATIVE BIOMARKERS FOR IMPROVING RHEUMATOID ARTHRITIS MONITORING**

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**Background:** Rheumatoid arthritis (RA) is a long-lasting inflammatory autoimmune disorder that ultimately leads to the destruction of joints. Potential biomarkers are needed for an early diagnosis and monitoring the disease.

**Objectives:** Using the DAS28 activity index, 80 RA serum samples (40 with low activity and 40 with high activity) were selected in order to be analyzed by mass spectrometry. The aim of this study was to find possible protein biomarkers that could discriminate patients with different RA activity in the daily clinical routine.

**Methods:** In order to facilitate the complex measurement of these serum samples, a simple, fast and reproducible albumin-specific depletion method using ethanol was optimized and applied to this study. Four independent pools of the 40 high RA activity samples (10 samples per pool) and 4 pools of the 40 low RA activity samples were firstly albumin-depleted, and then the remnant serum proteins were digested and differentially labelled with iTRAQ 8-plex reagents. Subsequently, the 8 labelled pools were combined and cleaned using StageTips-C18. Finally, the pool mixture was fractionated by HPLC (Zorbax-C18) and the resulting fractions were analyzed by nanoLC-MS/MS using two different equipments for validation (MALDI-TOF/TOF and TripleTOF).

**Results:** The mass spectrometry analysis led to the identification of 186 proteins. Among these, Haptoglobin, Kininogen-1, Alpha-2-HS-glycoprotein, Serum Amyloid A, Atamin and Histidine-rich-glycoprotein, exhibited a differential relative abundance depending on the RA activity of the patients (p<0.03) in both analysis. These proteins were also validated by other orthogonal techniques (western blot, ELISA and protein arrays).

**Conclusions:** In this proteomic study, 9 proteins were found to be modulated between patients with high and low RA activity. Most of these proteins are related with the RA process and the effects caused by this type of disease (inflammation and immune disorder in joints). Therefore, these proteins are possible biomarker candidates for improving RA monitoring. Future validation experiments and prospective studies are needed to facilitate their implementation in the clinical routine.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4912

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**AB0250**

**THE ADIPOSE TISSUE AS PREDICTIVE FACTOR OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS: EVALUATION OF BODY FAT COMPOSITION BY BIOELECTRICAL IMPEDANCE ANALYSIS AND ULTRASONOGRAPHY**

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**Background:** Adipose tissue (AT) is an endocrine organ able to secrete the adipokine" molecules that contribute to the low-grade inflammatory state in obese subjects and to the local inflammation that affects joints and bone (1,2). High-grade inflammation, in course of RA, leads to an altered body composition (3,4), characterized by the increasing of fat mass and the decreasing of lean mass, mostly not associated to body mass index (BMI) variations (3,5). The BMI is not able to differentiate visceral (VTH) and subcutaneous (STH) fat tissue and to distinguish between muscle mass and fat mass body composition (BC) (6,7). Alternative methods proposed for assessment of visceral fat deposition, are described in the present study.

**Objectives:** The aim of the study is to investigate if BC, assessed by BIA and US,
correlates with disease activity (assessed by the Disease Activity Score using 28 joint counts – DAS28) and affects the response to the therapy (DAS 28 variation from first evaluation).

Methods: 87 consecutive RA patients (pts) (72 women and 15 men; aged 52.4±13.2 years; disease duration of 10.7±8.6 years), treated with DMARDs and/or biologics (bDMARDs), were recruited during their regular visit. The inclusion criteria were the 1987 American College of Rheumatology (ACR) or ACR/EULAR 2010 classification criteria. The pts underwent to anthropometric measures (BMI); abdominal US to assess STH and VTH and derived computing of peritonal circumference (PC); and BIA to the indices of body composition (fat-free mass index (FFMI) and fat mass index (FMI)).

Results: We observed increasing values of BMI, FMI, VTH (fig. 1) and CP with the worsening of disease activity phases, evaluated by DAS 28. In particular, pts with DAS28≥5.1 had highest BMI (30.9±2; p=0.036), FMI (11.5±1.6; p=0.05), CP (92.7±12.5 cm; p=0.035) and VTH (24.8±5.8 mm; p=0.046) than pts in less severe disease activity. By linear regression analysis the predictor of higher DAS28 is the BMI (p=0.028). As regard the drug response, the predictors of DAS 28 improvement are higher FFMI (p=0.044) and lower BMI (p=0.015), independently by bDMARDs or DMARDs treatment.

A trend to higher FMI and US AT measures was observed in female with high disease activity, in particular in menopause pts.

Conclusions: An altered fat distribution is observed in active RA phases; in particular, the FMI increasing is attributable just to visceral AT (VTH and CP). An inflammatory hyperactivity of visceral adiposity could be supposed in RA. The body composition, in addition to BMI, seems to predict the disease activity and drug response in RA patients. The evaluation of VTH by US could be useful to not overestimate the disease activity; instead the BIA could be a useful tool to support the clinicians in a more aggressive treatment management.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4260

AB0251 THE IMPACT OF THE RHEUMATOID FOOT ON FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS EVALUATED BY FFI AND LFIS

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Background: The impairment of function in patients with rheumatoid arthritis (RA) is determined by several factors related to the disease including joint damage. The foot, a location frequently affected during course of the disease, has a major impact on the lower limb and could cause functional disability.

Objectives: The purpose of this study is to evaluate the impact of the rheumatoid foot on function of patients with RA.

Methods: Cross-sectional study was conducted in 33 patients with RA. Patients with static lower limb disorder or foot injury from other origin were excluded. Demographic and clinical characteristics were collected: age, sex, BMI, disease duration, tender joint count, swollen joint count, foot pain evaluated on anVAS, foot squeeze test and various podiatric abnormalities observed clinically (forefoot, midfoot and rearfoot). Biological characteristics also collected: sedimentation rate in the first hour, C reactive protein, rheumatoid factor and anti-CCP.

Disease activity was evaluated by DAS28, CDAI, SDAI and DAS44. Functional repercussions were estimated by the French Functional Index (FFI), comprising 23 items, divided into 3 sections: pain, function and limitation of activity. Functional disability was studied by the Leeds Foot Impact Scale (LFIS), which includes 51 items (21 items specific to foot function alteration (LFIS-I) and 30 related to foot disability (LFIS-D)). Statistical analysis was performed using SPSS21 software.

Results: Thirty-three patients followed for RA were included. The mean age of our patients was 49.39±10.52 with a female predominance (87.9%). Mean disease duration was 9.96±7.49 years. In all patients; 21 (95.5%) were seropositive. The mean DAS28 was 5.5±1.38 and the mean HAQ was 1.37±0.83. 93.9% of our patients had bilateral foot pain; 69.7% in the forefoot, 18.2% in the midfoot and 42.4% in the hindfoot. The medial retromalleolar tufefaction was found in 21.2% of the patients and the lateral retromalleolar tufefaction in 45.5% of them.

The squeeze test was positive in 23 (69.7%) patients. Prevalences of Podiatric abnormalities were noted in the following ordre: hallux valgus (48.5%), quintus varus (12.1%), hallux rigidus (6.1%), claw toe (15.2%), triangular forefoot (9.1%), rearfoot valgus (27.3%) and rearfoot varus (27.3%).

Mean FFI was 52.35±25.63 (FFI-pain: 58.69±24.41, FFI-function: 53.63±30.48 and FFI- limitation of activity: 39.33±30.58). Mean LFIS-I was 1136. Mean LFIS-D was 19.96.

Conclusions: Joint destruction over time was more pronounced in the feet than in the hands. Baseline erosions limited to the feet were associated with low disease activity, suggesting that inflammation localized to the feet may not be reflected by DAS28. These observations may have relevance to the evaluating of disease activity and progression in the individual patient. Possibly inclusion of the feet to DAS28 might improve the validity of this disease activity measure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3634
TIPS ON SELECTION OF BIOLOGICS FOR PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON TREATMENT PATTERNS

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Background: The emergence of biologics has led to innovation in the treatment of rheumatoid arthritis (RA). In the clinical setting, biologics are administered with careful consideration of complications and medical history in accordance with the treat-to-target recommendations. However, the progression of joint damage, the costs incurred before finding an effective biologic are serious concerns. It is therefore desirable to use biologics with long-term efficacy and less financial burden from the early stage.

Objectives: Participants were RA patients treated with one of three biologics having different mechanisms of action who achieved therapy targets with long-term treatment patterns were evaluated.

Methods: Between November 2004 and October 2016, 196, 57, and 85 RA patients were treated with etanercept (ETN), tocilizumab (TCZ), and abatacept (ABT), respectively, in first- or second-line therapy. These patients were divided into the continuation group, who underwent therapy with the same agent for ≥3 years without disease flare (DAS28-ESR ≥3.2) persisting 3 months, and the discontinuation group, who experienced primary failure resulting in discontinuation of the therapy within 3 months. Student’s t test or Mann-Whitney’s U test were used to compare therapy continuation rates and reasons for discontinuation among the three biologics. Finally, relative dose intensity (RDI) was calculated to evaluate the treatment patterns of the individual biologics.

Results: The Kaplan-Meier method showed that the 3-year continuation rates of therapy with ETN, TCZ, and ABT were 54.2%, 23.8%, and 35.8%, respectively: the continuation rate of ETN was significantly higher than that of the other two agents. The numbers of patients treated with ETN, TCZ, and ABT were respectively 46, 9, and 14 in the continuation group and 16, 12, and 11 in the discontinuation group. The proportion of patients treated with ETN plus concomitant MTX was significantly higher in the continuation group than in the discontinuation group (P<0.0057). No significant differences were found in patients’ background characteristics (disease duration, rheumatoid or anti-cyclical citrullinated peptide positivity, number of biologies previously used, and DAS28-ESR). Mean RDI values (median value, 95% confidence interval) over a 3-year period were as follows: 0.95 (0.92, 0.83–1.06) for 25 mg/week ETN therapy; 0.78 (0.90, 0.66–0.89) for 50 mg/week ETN therapy; 0.84 (0.84, 0.76–0.89) for TCZ therapy; and 0.76 (0.76–0.85) for ABT therapy. The cumulative costs for 3 years of the respective treatments were 19,700, 32,200, 27,300, and 39,000 euros (1 euro =115 Japanese yen). After targets were reached, the dose of ETN was maintained at 25 mg/week or reduced from 50 mg/week, while the TCZ and ABT therapies were continued over the long term with a longer dosing interval.

Conclusions: Treatment with ETN plus concomitant MTX showed high continuation rates, and long-term achievement of therapy targets was maintained at a lower dosage (and thus, lower costs). It is beneficial to choose this method over non-TNF inhibitors.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1146

AB0254 COMPARISON OF DYNAMIC PEDOBAROGRAPHIC FINDINGS BETWEEN RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY INDIVIDUALS

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Background: Foot involvement happens early in RA patients and situation hadn't happened yet. Since we excluded patients with severe deformities and those who couldn’t walk alone from the study, and our cases were relatively in early stages of disease, we didn't find any significant difference in pressure or force between symptomatic patients with and without radiographic findings. This can be explained by the fact that foot pressure alteration detectable in pedobarography is already begun in all RA patients with foot symptoms but radiologically evident pathologies had not happened yet.

Conclusions: RA has considerable effect on patients’ feet along with other physical and mental issues. While conventional radiological methods has a limited efficacy in predicting and diagnosing the pathologic changes in foot region, pedobarography can easily shows these changes in foot pressure values and can be used to detect RA patients that need simple interventions like using proper insoles to prevent surgical interventions.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4445

AB0255 EVALUATION OF KINESIOPHIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS


Background: Fear avoidance behavior which is caused by painful injury resulting precision and extreme fear is defined as kinesiophobia. Rheumatoid arthritis (RA) is a chronic, inflammatory and systemic disease with symmetrical arthritis and visceral involvement. Ankylosing spondylitis (AS) is a chronic, inflammatory disease with involvement of peripheral or spinal joints.

Objectives: In our study, we aimed to evaluate the relationships between kinesiophobia and disease activity, quality of life (QoL), level of physical activity and emotional status in RA and AS patients.

Methods: We included 80 patients, with RA (8 males-M, 34 females-F) (group 1), 49 patients with AS (34 M, 15 F) (group 2) and 29 healthy controls (9 M, 20 F) (group 3) in our study. The QoL was assessed using the health assessment questionnaire (HAQ), kinesiophobia was assessed with Tampa scale of kinesiophobia (TSK), pain was assessed with visual analog scale (VAS), fatigue was assessed with VAS and emotional status was assessed with Beck depression inventory (BDI). Disease activity was assessed with Bath ankylosing spondylitis disease activity index (BASDAI) and functional status was assessed with Bath ankylosing spondylitis functional index (BASFI) in patients with AS. Disease activity was assessed with patients with RA.

Results: The mean age was 46.2 in group 1, 43.2 in group 2 and 40.17 in group 3. There was no difference among groups with respect to mean age (p>0.05). Kinesiophobia was present in 37 patients in group 1, 22 patients in group 2 and 7 patients in group 3. Statistically significant differences were found among groups.

Table 1. Baseline features of the patients of AS and RA and healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46.2±17.47</td>
<td>43.2±10.73</td>
<td>40.17±7.77</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>35/34</td>
<td>23/15</td>
<td>9/20</td>
</tr>
<tr>
<td>VAS</td>
<td>47.02±24.42</td>
<td>32.44±26.75</td>
<td>7.12±2.68</td>
</tr>
<tr>
<td>TSK</td>
<td>44.73±7.26</td>
<td>36±12.03</td>
<td>29.58±19.7</td>
</tr>
<tr>
<td>Fatigue (VAS)</td>
<td>55.47±24.31</td>
<td>36.93±27.70</td>
<td>37.93±20.79</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.73±0.83</td>
<td>0.43±0.41</td>
<td>0.06±0.10</td>
</tr>
</tbody>
</table>

*P<0.008 between group 1 and 2; p=0.001 between group 2 and 3; p>0.001 between group 1 and 3. **p=0.05 between group 1 and 2; and 1 and 3. ***p=0.039 between group 1 and 2; p=0.021 between group 2 and 3; p<0.001 between group 1 and 3; p<0.001 between group 1 and 2; p=0.004 between group 2 and 3; p<0.001 between group 1 and 3.
with respect to the number of patients with kinesiophobia and to mean scores of pain intensity, fatigue, HAQ and BDI (p=0.05−0.001). Patients with RA had higher rates of kinesiophobia than patients with AS and healthy controls (p=0.001, p=0.001). Patients with RA had worse scores than patients with AS and healthy controls. Patients with AS had worse scores than healthy controls. In patients with RA and AS, kinesiophobia is associated with pain severity, fatigue, emotional status and QoL.

Conclusions: In our study, patients with RA and AS had higher rates of kinesiophobia. We found that kinesiophobia was related with pain severity, fatigue, depression, disease activity and QoL of the patients. The QoL can be improved through controlling kinesiophobia by reducing pain, depression and fatigue.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6163

**AB0256**

SERUM AND SYNOVIAL KYNURENIC ACID CONCENTRATION AND ITS CORRELATION WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: CLINICAL AND ULTRASONOGRAPHIC STUDY

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease. Kynurenic acid has anti-inflammatory effects, because it is the most important agonist of the orphan G-protein-coupled receptor (GPR35) which expressed on various types of cells associated with the immune system. Stimulation of these receptors by kynurenic acid lead to reduction in the synthesis of proinflammatory cytokines, nitric oxide, and reactive oxygen species (1).

**Objectives:** Detection and quantification of kynurenic acid in serum and synovial fluid obtained from the affected joints in patients with rheumatoid arthritis and its relation to different and synovial aspects of disease activity and signs of synovitis and synovial hyperplasia detected by musculoskeletal diagnostic ultrasound.

**Methods:** Thirty RA patients diagnosed according to ACR and EULAR revised criteria and thirty patients of idiopathic knee osteoarthritis as a control group were enrolled in the study. These patients were collected from outpatient clinic of rheumatology department Benha Teaching Hospital. Kynurenic acid was assessed in Serum samples from all patients and controls coupled synovial fluid samples aspirated from knee joint of all RA patients and fourteen OA patients after musculoskeletal ultrasonographic examination of these joints.

**Results:** Serum and synovial level of kynurenic acid was assessed in the studied groups. Comparison between RA and OA patients as regard serum kynurenic acid showed no differences where it’s level was 29.80±13.86 pg/ml in RA versus 30.98±11.03 pg/ml in OA patients), while synovial kynurenic acid was significantly lower in RA (16.38±6.45 pg/ml) than in OA patients (26.22±2.99 pg/ml (p<0.001). Kynurenic acid was significantly lower in synovial fluid (16.38±6.45 pg/ml) than in serum (29.80±13.86 pg/ml) in RA group of patients (p<0.001). Comparison among different grades of synovitis detected by grey scale U/S and by Doppler signals in RA patients as regard serum kynurenic acid showed that it was significantly lower in hypoperfused grade of synovitis (P<0.001). Synovial kynurenic acid level was negatively correlated with grades of synovitis and Doppler signals (p<0.001).

**Conclusions:** The negative correlation between Kynurenic acid concentration in the synovial fluid and both the synovial thickness detected by ultrasonography and the hyperaemia of synovial tissues as represented by the Doppler activity, may support its use as a local marker of the two faces of rheumatoid arthritis (chronicity and activity) at the joint level.

To the best of our knowledge, this is the first study that gives correlation between the serum and synovial levels of kynurenic acid concentrations and the grade of synovitis detected by grey scale and Doppler ultrasonography.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2198

**AB0257**

SCREENING OF DIFFERENTIALLY EXPRESSED SERUM PROTEINS FOR RHEUMATOID ARTHRITIS BY SURFACE-ENHANCED LASER DESORPTION/IONIZATION-TIME OF FLIGHT-MASS SPECTRA

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**Background:** RA is a chronic inflammatory rheumatic disease, and early diagnosis and treatment can improve prognosis.(1) Surface-enhanced laser desorption/ionization-time of flight-mass spectrometry (SELDI-TOF-MS) combines a protein chip and mass spectroscopy technology own the advantages of low dosage of samples, direct point sample detection and high sensitivity.

**Objectives:** SELDI used to profile and compare the proteomes in serum samples of RA patients including complicated with Sjogren’s syndrome (SS), interstitial lung disease (ILD). Using Biomarker Wizard software and Biomarker Pattern Software established diagnostic model, and calculate sensitivity and specificity,which can simplify clinical procedures, save medical costs and explore the pathogenesis.

**Methods:** Using the Biomarker Wizard and Biomarker Pattern software to screen the differentially expressed serum proteins, then establish disease activity prediction model to predict RA disease progression between the following groups, including simple RA patients (n=44) and RA-SS patients (n=18), RA patients (n=44) and RA-ILD (n=22), RA patients (n=44) and RA-ONFH (n=6). Also 96 RA patients and 77 healthy control, which were randomly allocated to the training set (83 RA patients and 56 healthy controls) and test set (14 RA patients and 20 healthy controls) to develop and verify a pattern by means of decision treearoboom. Using the Biomarker Wizard and Biomarker Pattern software to establish the disease diagnosis model to predict RA disease progression between the following groups, including simple RA patients (n=44) and RA-SS patients (n=18), RA patients (n=44) and RA-ILD (n=22), RA patients (n=44) and RA-ONFH (n=6). Also 96 RA patients and 77 healthy control, which were randomly allocated to the training set (83 RA patients and 56 healthy controls) and test set (14 RA patients and 20 healthy controls) to develop and verify a pattern by means of decision treearoboom.

**Results:** 1. Comparison of RA patients and healthy controls: there are 22 up-regulated expression in RA, 36 down-regulated. The diagnostic model of M/23448.857.4716.712.8214.285 and 10645. The sensitivity and specificity is 91.566% and 92.857%, the area under the ROC curve was 0.937, to verify the diagnostic model, we use 95% confidence interval of 0.914−0.950. The diagnostic model of M/212595.86. The sensitivity and specificity is 86.4% and 84.1% and the area under the ROC curve was 0.856. 2. Comparison of the simple RA and RA-SS: The sensitivity and specificity is 77.8% and 78.5% and the area under the ROC curve was 0.794.

**Conclusions:** The serum protein fingerprinting by SELDI-TOF-MS could identify new biomarkers in RA. The biomarkers may play an important role in pathogenesis of RA. We could diagnose RA in early stage, predict disease progression and determine disease activity by these biomarkers.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3698

**AB0258**

AGE AND QUALITY OF LIFE AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC AGENTS

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**Background:** Rheumatoid arthritis (RA) is a common autoimmune disease of unknown etiology which is characterized by symmetric, chronic inflammatory, peripheral polyarthritis. If it is untreated or unresponsive to therapy, inflammation and joint destruction lead to loss of physical function, inability to carry out daily tasks of living.

In addition to problems related to pain and inflammation, patients with RA are also affected by psychological problems such as anxiety and depression. It has been a while since, the biologic agents have let RA patients to early remission, and improved their Quality of life (QOL).

A few studies show relevance between age and QOL among RA patients. Lambert et al. found that age was positively correlated with pain, indicating that increasing age made the situation worse.

**Objectives:** This study aimed to assess the relationship between age and QOL of RA patients who has been treated with biologic agents.

**Methods:** 149 RA patients who treated with biologic agents at Showa University Hospital, Showa University Northern Yokohama Hospital and Showa University Koto Toyo University Hospital were recruited from 2005 to 2016. This study design was retrospective cohort study. Loss to follow-up was eliminated. The patients were divided into two groups, whose age was 65 years old and over (elderly) and under 65 (adults). The primary outcome was the change of QOL in 6 months’. QOL was measured using SF-36, and we use physical component scale (PCS) and mental component scale (MCS). Logistic regression analysis was performed.

**Results:** Among 149 RA patients, the mean age was 57 years old and 85.9% was female. 92 out of 149 patients (61.7%) were adult group and 57 (38.3%) were elderly group. Adjusted with sex, disease duration, DAS28-ESR, HAQ, and with or without complications which are interstitial lung disease, diabetes mellitus, and chronic kidney disease, there was no significant difference in change of MCS in 6 months’. But those of PCS was significantly higher in adult’s group (regression coefficients -7.25; 95% Confidence Interval (CI) -11.7 to -2.77; p=0.0018).

**Conclusions:** There is a possibility that, younger patient who suffers with RA could achieve better quality of life than those of elderly patients after treatment with biologic agents.
from a dual X-ray absorptiometry database. Demographics and other risk factors, as well as fragility fractures, were recorded. Initially, those who had sustained a fracture were compared to those who had not sustained a fracture using chi-squared tests for categorical variables and T-tests for continuous variables. Following that, univariate and multivariable logistic regression models were fitted looking at the predictors of fracture. Variables included age at scan, height, weight, alcohol, smoking, family history, rheumatoid arthritis, secondary osteoporosis as defined by FRAX™, body mass index and steroid exposure, in addition to BMD in the lumbar spine and femoral neck.

Results: Of 2029 female patients were scanned in the referral period. The mean age at scan was 66 (SD 10.46), 356/2029 (17.5%) had sustained a fracture. Results of the univariate analysis are shown in table 1, significant predictors are indicated with an asterisk (*).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4708

AB0261 CLINICAL AND STRUCTURAL RESPONSES OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS (RA) USING STEP-UP DOSAGES OF TOFACITINIB IN A TREAT TO TARGET APPROACH

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Background: Tofacitinib has been shown to reduce the clinical signs and symptoms of some RA patients at an approved dose of 5 mg bid. Studies report that 10 mg bid is an effective dose. This is the first community practice trial to measure the clinical and structural benefits of stepping up the initial dose of 5 mg bid in non-responders to 10 mg bid in order to achieve a clinical response using a treat to target approach.

Objectives: This study evaluates the optimal dose of tofacitinib (5 mg bid VS 10 mg bid) needed to reach treatment target in a cohort of patients with active RA while comparing the corresponding structural findings measured by low field MRI.

Methods: 20 RA patients who were unresponsive to either methotrexate (10–25 mg weekly) or MTX plus up to 2 prior biologics with synovitis, osteitis or erosions on Baseline MRI (Esaote 0.3T) were treated with 5 mg bid tofacitinib with a treat to target goal of Low Disease Activity (LDA) or remission depending on the Clinical Activity Index (CDAI) score at Baseline. If the target was not met and sustained for 3 months, the dose of tofacitinib was increased to 10 mg bid in an attempt to reach target. MRIs of the hand/wrist were blindly read by a musculoskeletal radiologist using a rheumatoid arthritis MRI scoring system (RAMRIS). A CDAl score of >10 was needed at study entry.

Results: Of the 20 enrolled patients, 6 remained at 5 mg bid and 14 were dose escalated to 10 mg bid most at the 12 week period. Of the 5 mg bid group, 3 completed the trial at target and 3 early terminated (ET) for lack of efficacy, relapse and AE. Structurally, there was no change in erosions in all 3 patients; 2 showed regression of synovitis and 1 showed no change; 2 showed regression in osteitis and 1 no change. Of the 14 patients escalated to 10 mg bid, 11 completed the trial with 7 remissions, 2 LDA and 1 MDA. 3 patients missed due to lack of efficacy. In the 10 mg bid group, 9 patients showed no change in erosions, 1 reduction and 5 progression. 5 patients showed no change in synovitis and 6 showed progression, and 7 showed no change in osteitis, 3 showed progression and 1 showed progression. The CRP values correlated with the improvement of

Disclosure of Interest: None declared

AB0259 PREDICTORS OF HIGH DISEASE ACTIVITY IN A COHORT OF GREEK PATIENTS WITH ACPA POSITIVE EARLY RHEUMATOID ARTHRITIS

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Background: In Early Rheumatoid Arthritis, the presence of ACPA positivity is associated with increased disease activity.

Objectives: To investigate possible predictors, for high disease activity (DAS-28 >5.1), in a cohort of Greek patients with ACPA positive early RA.

Methods: From 2000 until December 2016, 156 patients with ACPA positive early RA, were diagnosed and subsequently followed up as outpatients at the Rheumatology Unit of our hospital. Demographic, clinical, laboratory and therapeutic parameters were evaluated during every follow-up. At the end of the study (last visit during 2016), all the above parameters were re-evaluated, considering the high disease activity (DAS-28 >5.1). The used methods were χ², ANOVA, Binary Logistic Regression (BLR) and ROC Curve.

Results: From 156 patients, 25% were males, 37.8% were current smokers, 16% with anemia of chronic disease (ACD). At the time of diagnosis, Univariate ANOVA, Binary Logistic Regression (BLR) and ROC Curve. Based on the previous results the severity of disease can be predicted with sensitivity for smokers 2.95, for RF positivity 3.397 and for CRP 1.066 respectively. Based on the previous abstract and it showed that the use of AIs significantly reduced lumbar spine BMD (p<0.001) compared to untreated RA patients (p=0.001, CI=0.723–0.878) using the ROC curve.

Conclusions: That 10 mg bid is an effective dose. This is the first community practice trial to measure the clinical and structural benefits of stepping up the initial dose of 5 mg bid in non-responders to 10 mg bid in order to achieve a clinical response using a treat to target approach.

References:

Disclosure of Interest: None declared

AB0260 THE PREDICTORS OF FRAILTY FRACtURES IN PATIENTS ON OMAZTATINb: An OBSERVATIONAL STUDY

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Background: The use of aromatase inhibitors (AIs), given after breast cancer, has been associated with a low bone mineral density (BMD) and as a risk factor for fragility fractures. We have reported on the risk factor for low BMD in a previous abstract and it showed that the use of AIs significantly reduced lumbar spine BMD and femoral neck BMD (1). The FRAX™ tool uses the femoral neck BMD to predict fractures on a population basis but ignores the lumbar spine. Some patients who have undergone bilateral hip replacements would not be able to estimate their risk of fractures. In the 20 mg bid group, 3 completed the trial at target and 3 early terminated (ET) for lack of efficacy, relapse and AE. Structurally, there was no change in erosions in all 3 patients; 2 showed regression of synovitis and 1 showed no change; 2 showed regression in osteitis and 1 no change. Of the 14 patients escalated to 10 mg bid, 11 completed the trial with 7 remissions, 2 LDA and 1 MDA. 3 patients missed due to lack of efficacy. In the 10 mg bid group, 9 patients showed no change in erosions, 1 reduction and 5 progression. 5 patients showed no change in synovitis and 6 showed progression, and 7 showed no change in osteitis, 3 showed progression and 1 showed progression. The CRP values correlated with the improvement of

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6753

References:

Disclosure of Interest:


AB0260 THE PREDICTORS OF FRAILTY FRACtURES IN PATIENTS ON OMAZATINb: An OBSERVATIONAL STUDY

N. Meah1, R. Sinha2, M. Bukhari2. 1Lancaster Medical School; 2Rheumatology, Royal Lancaster Infirmary, Lancaster, United Kingdom

Background: The use of aromatase inhibitors (AIs), given after breast cancer, has been associated with a low bone mineral density (BMD) and as a risk factor for fragility fractures. We have reported on the risk factor for low BMD in a previous abstract and it showed that the use of AIs significantly reduced lumbar spine BMD and femoral neck BMD (1). The FRAX™ tool uses the femoral neck BMD to predict fractures on a population basis but ignores the lumbar spine. Some patients who have undergone bilateral hip replacements would not be able to estimate their risk of fractures. In the 20 mg bid group, 3 completed the trial at target and 3 early terminated (ET) for lack of efficacy, relapse and AE. Structurally, there was no change in erosions in all 3 patients; 2 showed regression of synovitis and 1 showed no change; 2 showed regression in osteitis and 1 no change. Of the 14 patients escalated to 10 mg bid, 11 completed the trial with 7 remissions, 2 LDA and 1 MDA. 3 patients missed due to lack of efficacy. In the 10 mg bid group, 9 patients showed no change in erosions, 1 reduction and 5 progression. 5 patients showed no change in synovitis and 6 showed progression, and 7 showed no change in osteitis, 3 showed progression and 1 showed progression. The CRP values correlated with the improvement of

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6753

References:

Disclosure of Interest:

Conclusions: Our results suggest that a significant number of patients treated with the standard dose of 5 mg bid may potentially have improved outcomes including LDA or remission when treated at a higher dose (10 mg bid). As is evidenced by the results in this study, 11 of the 14 patients had significant improved response after treatment with the step up dose. It would appear that this improved result occurs by 3 months of therapy. Furthermore, the structural findings correlate in large part to the clinical findings showing stabilization or improvement in the majority of patients. A larger study is needed to validate these clinical and structural responses as well as to evaluate the safety outcomes using 10 mg bid for intervals of more than 12 months.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1806

AB0262 EVALUATION OF PATIENT REPORTED OUTCOME USING RAPIDS AND HAQ-DI COMPARED TO DAS28: EXPERIENCE FROM ROUTINE CLINICAL PRACTICE IN MALAYSIA

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Background: Patient reported outcome (PRO) is an important measure for physician in management of patient with rheumatic diseases. Health assessment questionnaire disability index (HAQ-DI) is the most widely used PRO tool in rheumatoid arthritis (RA) clinical trials. Previous studies have shown that HAQ-DI correlates well with disease activity score of 28-joints (DAS28). However, routine assessment of patient index data 3 (RAPID3) is much simpler and faster to use.

Objectives: This study aims to evaluate the correlation between RAPID3 and DAS28 compared to HAQ-DI and DAS28 in our population.

Methods: RA patients who received routine treatment in Hospital Tuanku Ja‘afar from March to November 2016 were included in this study. Validated RAPID3 and HAQ-DI questionnaire were made available in other languages; Malay, Chinese and Tamil, for patients who were not English literate. Descriptive analysis were conducted. Pearson correlation was used to measure the correlation between these PRO tools while area under the curve of the receiver operating characteristic (ROC) curves evaluate the sensitivity to detect disease activity. DAS28-ESR and DAS28-CRP were used as the reference variable in ROC analysis to stratified the disease activity into two groups; low (remission and low) and high (moderate and severe)

Results: A total of 400 patients completed PRO assessments were available for analysis. The median age of our cohort was 57 years old (range 22 to 88) and 73.5% were female. Ethnic distribution in this cohort were as follows: 38.5% Indian, 31.8% Malay and 27.8% Chinese. Both RAPID3 (r=0.74,p<0.001) and HAQ-DI (r=0.57, p=0.001) were correlated with DAS28-ESR. The area under the curve was significantly higher in RAPID3 (83%) compared to HAQ-DI (75%) which implied greater performance in discriminating low and high disease activity using DAS28-ESR as reference. We observed similar performance trend between RAPID3 (92%) and HAQ-DI (82%) compared to DAS28-CRP.

Conclusions: In conclusion, RAPID3 is an effective quantitative measure of disease activity compared to HAQ-DI in our population. Furthermore, RAPID3 and HAQ-DI correlates well with disease activity score of 28 joints (DAS28). However, routine assessment of patient index data 3 (RAPID3) is much simpler and faster to use.
Conclusions: MBDA score may be of additional value in predicting DAS28 flares but not in predicting medication escalations or physician-reported flares in RA patients on TNFi in stable low disease activity.

Acknowledgements: We wish to acknowledge all POET investigators and all who gave their contributions to the POET project.


P. Riel: None declared, M. Laar: None declared, T. L. Jansen: None declared.


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**AB0264 THE PERFORIN A91V GENE AND CLINICAL FEATURES ANALYSIS IN CHINESE SO-JIA CASES WITH MACROPHAGE ACTIVATION SYNDROME**

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**Objectives:** Macrophage activation syndrome (MAS) is a severe, potentially fatal complication of rheumatoid disease, especially in the systemic onset juvenile idiopathic arthritis (SoJIA). We aimed to investigate the clinical characteristics of 31 SoJIA cases with MAS and the perforin A91V gene were detected in part context.

**Methods:** gene-specific polymerase chain reaction (PCR) primers were used to analyze the perforin A91V gene polymorphism.

**Results:** 31 SoJIA cases were associated with MAS.25 out of 31 cases (83%) had infections prior to MAS. Serum ferritin was significantly increased in 27 cases (87.10%). High concentrations of triglycerides (23 cases, 74.19%) and lactic dehydrogenase (27 cases, 87.10%) were observed. What is more, Creatine Kinase (CK) increased in all cases that had been checked. Well-differentiated macrophages phagocytosing hematopoietic elements were found in all cases (100%) 6 cases (19.35%) merged with multiple organ dysfunctions (MODS). The perforin A91V (NCBI: SNP rs35947132) variant gene was detected in twenty cases, but no mutation was found. Corticosteroids, immunosuppressant, cell cycle inhibitors, immunoglobulin, Tumor necrosis factor (TNF) antagonist and plasminogen were effective. After treatment, 28cases (90.32%) children were in remission, while 3 out of 31 cases died with mortality of 9.68%.

**Conclusions:** MAS is a life-threatening complication of systemic onset juvenile idiopathic arthritis. Most cases were preceded by infection. Unrelated levetiracetam, progressive hepatosplenomegaly, lymphadenopathy, cytopenias, elevated serum liver enzymes significantly increased serum ferritin are the main feature. Early diagnosis and treatment is the key to improve prognosis. The perforin gene mutations in our patients have not found yet.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2061

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**AB0265 THE SIGNIFICANCE OF EARLY DIAGNOSIS AND PROGNOSTIC EVALUATION OF FOUR KINDS OF ANTI-CCP ANTIBODIES IN VARIOUS TYPES OF JUVENILE IDIOPATHIC ARTHRITIS**

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**Objectives:** To investigate the relationship between immunological parameters AKA, anti-CCP, the RF-FGIG, RF-IGM and the early diagnosis and prognosis in sub-JIA patients.

**Methods:** Collection of 76 JIA patients in our hospital with system treatment and adhere to the follow-up treatment for at least six months, detect the immunological parameters of AKA, anti-CCP, RF-FGIG, RF-IGM in the early diagnosis, compare the Positive rate in different subtypes and prognosis, and make the statistical analysis of sensitivity, specificity and relevant risk, compare to the normal control group of blood of 49 healthy children.

**Results:** There is a significant difference between various types of JIA and general JIA patients in AKA positive rate, relative risk OR is 3.514.

**Conclusions:** The effect of AKA, anti-CCP, RF-FGIG, RF-IGM in the different subtypes of JIA diagnosis are different, it is found that AKA, anti-CCP has good sensitivity and specificity in polyarticular JIA, AKA appears relate with refractory JIA, it is a large sample of the study to be confirmed that whether it can be a serological marker in the early diagnosis and prognosis of Polyarticular JIA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2054

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**AB0266 EFFECTS OF PERIODONTAL BASIC TREATMENT ON PERIODONTAL CONDITION, CLINICAL RESPONSE AND SERUM INFLAMMATORY PARAMETERS IN RHEUMATOID ARTHRITIS (RA) PATIENTS WITH MODERATE TO SEVERE PERIODONTITIS**

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**Background:** Periodontal disease (PD) shares several clinical and pathogenic characteristics with Rheumatoid Arthritis (RA). Some intervention studies have suggested that periodontal treatment can reduce serum inflammatory biomarkers such as C-reactive protein, or erythrocyte sedimentation rate. Periodontal disorders are not only a threat to dentition, but may also be an aggravating factor in patients with RA, its treatment may improve the RA outcomes. In this study we assessed the effect of periodontal basic therapy in relieving the PD symptoms and the clinical signs of RA in order to evaluate the importance of periodontal treatment in the control of inflammation.

**Objectives:** To evaluate the effects of periodontal basic treatment on periodontal condition, clinical response and serum inflammatory parameters in RA patients with moderate to severe periodontitis.

**Methods:** A total of 46 subjects with confirmed diagnosis of RA and moderate to severe periodontitis were included in the study. 18 subjects completing the study received periodontal basic treatment consisting of scaling/root planing and oral hygiene instruction at baseline and at 6 weeks; 28 subjects completing the study received no treatment as control group. Participants continued using their usual disease-modifying medications for RA without any changes in DMARD therapy during the study period. Periodontal indices and RA measurements, such as probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), high-sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), disease activity scale (DAS28) and subjective symptom were recorded at baseline, 6 and 12 weeks for each participant.

**Results:** After periodontal basic treatment, significantly lower PD, CAL and BOP were observed in the treatment group (P<0.01), hsCRP, ESR, DAS28 and patients' subjective symptom improved significantly (p<0.05). Besides, the PD and BOP were statistically significantly between treatment subjects after therapy and controls (P<0.001). Although hsCRP was significantly lower in the treatment group after therapy than controls (P<0.01), there was no significant difference in the DAS 28 level between the two groups after periodontal basic therapy (P>0.05). Visual analog scale (VAS) was used to evaluate patients' subjective symptom, the results show that the improvement was much better in patients received periodontal therapy than controls (P<0.001).

**Conclusions:** Periodontal basic treatment can effectively improve periodontal status, patients’ subjective symptom and circulating inflammatory status.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6098

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**AB0267 TREATMENT PARADIGMS IN REAL-WORLD PRACTICE: BIOLOGIC AGENT USE PRIOR TO AND AFTER DISCONTINUATION OF ABATCEPT IN THE ACTION STUDY**


**Background:** ACTION is a 2-year, observational study of patients (pts) with moderate-to-severe RA who initiated IV abatacept (ABA) in Canada and Europe (NCT02109666).

**Objectives:** To determine pt biologic (b)DMARD use prior to initiation and after discontinuation of ABA overall and by treatment line in ACTION.

**Methods:** Pts with RA initiated IV ABA as first- or second-line therapy were enrolled during three periods between May 2008 and December 2013. Pts could switch administration routes (IV to SC) during treatment. Crude retention rates (Kaplan–Meier) were compared by log-rank test.

**Results:** Of the 2364 pts enrolled, 2350 were evaluable for analysis: 673 (28.6%) were biologic naïve and 1677 (71.4%) biologic failures. Baseline characteristics differed: biologic-failure pts had longer RA duration, higher CRP levels and prevalence of radiographic erosions, and lower rates of chronic obstructive
pulmonary disease and neoplasms vs biologic-naïve pts. Most biologic-failure pts (96.7%) had previously received ≥ 1 TNF inhibitor (TNFi): 48.7% had received 1 and 48.0% ≥ 2 TNFi; 56.6% had received ≥ 2 bDMARDs. The overall 2-year retention rate was 47.9% and was higher for biologic-naïve vs biologic-failure pts (54.5% vs 45.2%; p < 0.001); the most common reasons for ABA discontinuation were inefficacy (61.4 vs 67.7%) and safety (31.3 vs 21.2%). A small proportion of pts started a bDMARD ≥ 6 months after discontinuation (Table), most commonly ABA IV. Mean (SD) days from stopping ABA to starting a bDMARD was similar for biologic-naïve [93.4 [51.3]] and biologic-failure pts [93.6 [46.0]]. Among pts who restarted ABA, 62% (80.5%) biologic-naïve and 158 (85.0%) biologic-failure pts were considered to have discontinued as the time from last dose was ≥ 84 (IV) or > 28 (SC) days, and thus were no longer temporary discontinuations, as predefined in the protocol. Three pts continued for bad compliance, 3 for lack of efficacy, 3 for remission/major improvement, 12 for safety and 15 for other reasons (Table). EULAR moderate improvement and 10% experienced a good response. In all, 20% of pts at the last follow-up before ABA discontinuation and 58.3% at ABA restart; mean (SD) DAS28 (CRP) was 3.2 (1.1) and 3.8 (1.4), respectively.

Conclusions: Prior to abatacept treatment, over half of biologic-failure pts had received ≥ 2 bDMARDs and most had received a TNFi. After initial discontinuation (protocol defined), over one-third of pts restarted abatacept.

Disclosure of Interest: R. Alten Grant/research support from: Bristol-Myers set as 0.05.

Results: We included 63 RA patients (81% of women), with a mean (SD) age of 61 (10) years and a mean disease duration of 19 (10) years, 86% RF-positive and 87% ACPA-positive. Bone erosions were present in 86% of the patients. At baseline, the mean DAS28 was 5.79 (1.55). Combination therapy with methotrexate and with others cDMARDs was used in 48% and 30% of the patients, respectively; RTX monotherapy in 22% of our sample. Thirty percent of patients were previously exposed to other biologics. The magnitude of response was greater in ACPA-positive vs ACPA-negative patients in terms of DAS28 variation at 6, 12, and 18 (median of 1.09 vs -0.08; 2.03 vs 0.35 and 2.10 vs 0.19; p < 0.029, p < 0.039 and p = 0.044, respectively), without significant differences between groups in terms of initial DAS28 (5.91 [1.60] vs 5.00 [0.90], p = 0.051). The presence of ACPA was also significantly associated with EULAR response at 6 months. 18 (64%), 75% and 85% in ACPA-positive patients vs 25%, 16% and 25% in ACPA-negative patients; p = 0.034, p = 0.010 and p = 0.001, respectively.

Outcomes did not differ according FR status. There were no associations between the values of FR, ACPA and IgG at baseline with the clinical response (DAS28 variation). CD19+ cells depletion occurred in all patients (mean of 146.4/mm3 at baseline vs 10.6/mm3 at 6M). An increase of peripheral NK cells was seen at 6M (mean 231/mm3 at baseline vs 289/mm3 at 6M). We only have found a positive correlation between NK cells number at baseline and DAS28 variation at 6 M (r = 0.35, p = 0.023). There were no associations between, neither NK cells, nor CD19+ cells variations at 6M with clinical response to RTX.

Conclusions: Our data suggest that ACPA seroreactivity is associated with a better clinical response to RTX in RA patients. NK cells at baseline may be useful to identify early responders to RTX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4505

AB0239

RAPID RADIOGRAPHIC PROGRESSION PROGNOSTIC FACTORS IN A LATIN AMERICAN COHORT OF RHEUMATOID ARTHRITIS


Background: Rapid Radiographic Progression (RRP) in Rheumatoid Arthritis (RA) patients predicts long-term disability (1), high related economic costs (2) and loss of working time (3). Detection of RRP predictors as a necessary tool for aggressive therapeutic interventions has been proved, but in Latin-American cohorts, no available data had been reported.

Objectives: To determine independent risk factors associated with RRP in a cohort of RA patients.

Methods: A prospective analysis of RA Almenara cohort (January 2015-April 2016), 500 patients followed up with annual evaluations (background clinical/epidemiology, clinimetric, laboratory, health questionnaires and X-rays) who meet ACR 2010 criteria’s, older than 16 years at diagnosis, sign information, treatment, and disease activity were evaluated. A blinded rheumatologist for the RA condition read all films. Associated factors were analyzed (gender, socioeconomic level, smoking, age at diagnosis, time disease, use of biological and non-biological DMARDs, DAS 28, current steroids, HAQ/functionality, RA, sharp/VDH score and CRP). Clinical response delay and CRP were included to analyze risk factors in the RRP group. Statistical analyses were performed using linear regression models with logitlink. SPSS v. 21.0 was used.

Results: 153 patients, 90.8% women, middle low (37.9%) and middle (35.3%) the most prevalent socioeconomic status. Age at diagnosis was 46.06 (12.73) years, time disease 14.25 (10.26) years. DAS28 average: 4.51 (1.33). Basal Sharp VDH:104.53 (90.09), CRP: 9.77 (10.35) UI/L, RF: 352.49 (538.08) UI/L, ACPA: 563.64 (782.2)UI/dL, PR annual rate was 7.64 (2.4 years of follow-under one-third of pts restarted abatacept.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1392

AB0268

ACPA SEROPOSITIVITY AND PERIPHERAL NATURAL KILLER CELLS AS PREDICTIVE MARKERS OF CLINICAL RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS PATIENTS


Background: The efficacy of B cell-depletion therapy confirms the importance of B lymphocytes in rheumatoid arthritis (RA) pathogenesis. Rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) are prognostic factors for a more severe disease. Others immune elements, namely natural killer (NK) cells, seems to influence RA clinical response to rituximab (RTX), but data are lacking.

Objectives: To analyze the influence of baseline status/levels of RF, ACPA and serum immunoglobulin G (IgG) level in RTX treatment. To study the effect of RTX on NK and CD19+ cell populations and their association with clinical response at 6, 12 and 18 months (M).

Methods: An observational retrospective study was conducted, including all the consecutive patients with diagnosis of RA under rituximab, followed at our Rheumatology department. Demographic and clinical data were obtained by using the shared database (ReumaD) and the analysis was limited until December 2016. RF, ACPA and IgG titles were evaluated at baseline. NK (CD56+CD16+) and B lymphocytes (CD19+) absolute counts were assessed by flow cytometry prior to the first RTX cycle and 6 M after. Clinical responses were assessed by DAS28 and EULAR criteria at 6, 12 and 18 M. Correlations were studied using Spearman correlation coefficient (Spearman coefficient 20.0). Significance level was set as 0.05.

Results: We included 63 RA patients (81% of women), with a mean (SD) age of 61 (10) years and a mean disease duration of 19 (10) years, 86% RF-positive and 87% ACPA-positive. Bone erosions were present in 86% of the patients. At baseline, the mean DAS28 was 5.79 (1.55). Combination therapy with methotrexate and with others cDMARDs was used in 48% and 30% of the patients, respectively; RTX monotherapy in 22% of our sample. Thirty percent of patients were previously exposed to other biologics. The magnitude of response was greater in ACPA-positive vs ACPA-negative patients in terms of DAS28 variation at 6, 12, and 18 (median of 1.09 vs -0.08; 2.03 vs 0.35 and 2.10 vs 0.19; p < 0.029, p < 0.039 and p = 0.044, respectively), without significant differences between groups in terms of initial DAS28 (5.91 [1.60] vs 5.00 [0.90], p = 0.051). The presence of ACPA was also significantly associated with EULAR response at 6 months. 18 (64%), 75% and 85% in ACPA-positive patients vs 25%, 16% and 25% in ACPA-negative patients; p = 0.034, p = 0.010 and p = 0.001, respectively.

Conclusions: Our data suggest that ACPA seroreactivity is associated with a better clinical response to RTX in RA patients. NK cells at baseline may be useful to identify early responders to RTX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4505

References:
**AB0260** HOW DOES THE ACTIVITY OF RHEUMATOID ARTHRITIS AFFECT 2-T WAVE OF RECENT ONSET PATIENTS WITH A 5-YEAR FOLLOW-UP?


**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory joint disease affecting 0.5% of Spanish population. This disease results in a significant radiological and functional deterioration, decreasing the quality of life and increasing health costs. RA specific treatment is not well established. Therefore, the radiological and functional deterioration progress slowly during the whole course of the disease, it has been proven that early and aggressive approach to the disease is important in order for its control because the final outcome can be improved with a close, intense and early follow-up.

**Objectives:** To describe the clinical characteristics and evolution during 5 years of disease activity in RA patients derived from a recent arthritis clinic.

**Methods:** A prospective longitudinal study was carried out of 154 patients diagnosed from 2003 to 2012. They included patients over 18 years old diagnosed with RA (ACR criteria 1987) and with 5 years of follow-up. Socio-demographic and clinical variables such as Rheumatoid Factor (RF) antibody, immunoglobulin G (IgG) rheumatoid factor (RF), anti-citrullinated peptide antibodies (ACPA) or disease activity (DAS28- VASG) as well as treatment were assessed in those patients. Mean and standard deviation of quantitative variables and frequencies and percentages of qualitative variables were calculated.

**Results:** Of the 154 patients, 66.2% were females with a mean age at diagnosis of 52.8±14.64 years. Only 18.8% (29) patients were smokers; 67.5% (104) of patients were RF positive and 57% (88) of them were ACPA positive. Clinical remission measured by means of DAS28- VASG (<2.6) was achieved in 84 patients (54.5%), 92 patients (59.7%) and 95 patients (61.7%) after 1, 2 and 5 years, respectively. Mean values of DAS 28 were 2.58 (2.02) at first year, 2.61 (1.99) at two years and 2.59 (2.02) at 5 years. Of the 154 patients, 108 (78.8%) started treatment with monotherapy (mostly methotrexate) and after 5 years only 18 (25.7%) patients were on biological treatment. No differences were found when remission was compared at first, second and 5 years of follow-up.

**Conclusions:** These results suggest that achieving an early control of the disease is of importance, since control of the disease becomes more difficult as the delay of the diagnosis increases.

Reference:

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6878

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**AB0272** THE PERFORMANCE OF A SINGLE CENTRE INTERVENTIONAL CLINIC IN EARLY RHEUMATOID ARTHRITIS


**Background:** In early rheumatoid arthritis (RA), first assessment by a rheumatologist and/or initiation of disease-modifying anti-rheumatic drugs (DMARD) within 12 weeks of symptom onset are associated with a significant benefit in long-term disease outcome.

**Objectives:** Our objective was to determine the proportion of patients with newly diagnosed RA in whom first rheumatologist assessment and/or initiation of DMARD therapy was within the desired time frame.

**Methods:** A retrospective chart review of adult patients diagnosed with RA during 2014 and 2015 was performed at the rheumatology department of an integrated secondary/tertiary teaching hospital that provides rheumatology services for a population of more than 500,000 residents. Potential cases were identified by searching the electronic medical records for ICD-10 codes M05.7 and M06.* Electronic and paper records of patients were then thoroughly reviewed.

In addition to demographic and clinical data, dates were recorded for onset of inflammatory joint symptoms, referral to rheumatologist, initial assessment by a rheumatologist and/or initiation of DMARD therapy. The percentage of patients assessed by a rheumatologist and/or treated with a DMARD within 12 weeks of symptom onset and the median times for delay were then calculated.

**Results:** Between January 1st 2014 and December 31st 2015, 243 new cases of RA were identified at our Department of Rheumatology. Of those, 197 (81.1%) were referred to our early interventional clinic. Of the remaining 46 patients, 37 (80%) were not referred due to the lack of patients. The characteristics of the 111 (45.7%) new RA patients who were examined by a rheumatologist and/or initiated DMARD therapy were as follows: M05.7% and M06.* Time from symptom onset to DMARD initiation, weeks (median) 13.0 (IQR 4.6–27.8) weeks, median time from referral to consultation was 1.0 (IQR 1.3–3) days and median DMARD treatment delay was 15.7 (IQR 8.7–31.9) weeks.

**Table 1. Demographic data, clinical history, and delays**

<table>
<thead>
<tr>
<th>Gender (female/male) (%)</th>
<th>183/60 (75/25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (median)</td>
<td>64.2 (IQR 52.1–75.9)</td>
</tr>
<tr>
<td>Patients fulfilling ACR/EULAR classification criteria for RA, N (%)</td>
<td>228 (93.8)</td>
</tr>
<tr>
<td>DAS28&lt;3 (mean ± SD)</td>
<td>5.3±1.3</td>
</tr>
<tr>
<td>Erosive disease (plain radiographs) at first rheumatologist assessment, N (%)</td>
<td>67 (31.5)</td>
</tr>
<tr>
<td>Time from symptom onset to first rheumatologist assessment, weeks (median)</td>
<td>13.0 (IQR 4.6–27.8)</td>
</tr>
<tr>
<td>Time from referral to first rheumatologist assessment, weeks (median)</td>
<td>0.14 (IQR 0.14–43)</td>
</tr>
<tr>
<td>Time from symptom onset to glucocorticoid initiation, weeks (median)</td>
<td>13.1 (IQR 5.6–26.9)</td>
</tr>
<tr>
<td>Time from symptom onset to DMARD initiation, weeks (median)</td>
<td>15.7 (IQR 8.7–31.9)</td>
</tr>
</tbody>
</table>

**Conclusions:** 46% of new RA patients were assessed by a rheumatologist and 36% were treated with a DMARD within the recommended time frame of 12 weeks. Most of the treatment delay was due to the time elapsed between symptom onset and referral to a rheumatologist. These results substantiate the efficacy of our early interventional clinic in diagnosing and treating patients with early RA; despite the heavily protracted nationwide waiting times for first rheumatologist assessment and significantly (40%) lower number of rheumatologists per capita compared to European Union average, the percentage of timely treated patients was comparable to recent results from international studies.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5276
AB0273

VERY HIGH, BUT NOT LOWER, RADIOGRAPHIC PROGRESSION LEADS TO AN INCREASE IN HAQ-DI. RESULTS FROM THE SWISS SCQM RA COHORT

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Background: Numerous predictors of radiographic progression in RA patients have been identified over the last years. In general, analyses of radiographic progression in RA rather focus on radiographic non-progression or repair. High radiographic progression in spite of therapy has, to our knowledge not been analysed in detail in the last years, neither in RCTs nor in cohort studies.

Objectives: To analyse radiographic, demographical and clinical data in RA patients with high radiographic progression before and after the individual peak radiographic progression.

Methods: We included all RA patients from the Swiss registry SCQM with at least two subsequently scored radiographs. Radiographic destruction was scored using the Ratingen erosion score. To analyse high radiographic progression we selected for the highest (peak) radiographic progression in every individual patient for the analysis. The individual peak radiographic progression was analysed in groups as change of Ratingen scores/year: 0–≤10, 10–<20, 20–≤30, >30 (groups 1–4, follow up 1998–2015). The baseline disease characteristics were compared using standard descriptive statistics (Kruskal-Wallis or Chi-square tests). The change of DAS 28 and HAQ-DI scores before and after peak progression was analysed with the Wilcoxon signed rank tests.

Results: 3 patients were included in the analysis. 3’049 patients had a peak radiographic progression between 0 and <10/year; 773 between 10 and <20, 150 between 20 and <30, and 61 of >30. All patient groups were within the same age range (mean: 56.5 – 60.5 years). Rheumatoid factor and ACPA were more frequent in patient groups with higher peak radiographic progression (RF: 73.6, 80.0, 88.9, 90.0; ACPA: 68.8, 73.4, 74.3, 82.1, groups 1–4, respectively). When the rate of radiographic progression before and after peak progression was analysed, 69.7%, 74.7%, 76.9%, and 93.3% of the patients had a radiographic progression of 25% or lower as compared to peak progression before and 76.1%, 81.8%, 91.1%, and 93.8% after this peak progression, respectively for patients in groups 1 to 4 (Figure A).

The disease activity, as assessed by DAS 28, was significantly higher in all patient groups before peak progression and lower thereafter (Figure B, p<0.001). Average HAQ-DI scores increased after peak radiographic progression in group 4 (Figure C, p=0.005) whereas it is stable or even decreases among the patients of the other patient groups.

Conclusions: These data show that higher disease activity precedes radiographic peak progression, which is, if high, overall rare. Radiographic progression before and after the individual peak radiographic progression was far lower as compared to the time of radiographic peak progression. Only the highest individual peak (change of Ratingen score >30/year) radiographic progression was followed by an increase of HAQ-DI scores.

Disclosure Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4253

AB0274

THE ASSOCIATION BETWEEN REPEATEDLY INFECTION AND DISEASE OUTCOME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Some publications shows some therapies in rheumatoid arthritis (RA) could cause infections and it also can react the disease prognosis. But there was no report about the relationship between the repeatedly infections during the disease duration and its disease outcome.

Objectives: Our study was to evaluate the association between the history of repeated infectious agents that occurred more than three times during the duration of RA and the current disease status of RA, such as disease activity and physical disability.

Methods: 688 pure RA patients were selected from December 2015 to June 2016 in Peking People's hospital and divided into two groups according to their current disease status. Clinical data were collected including DAS28, HAQ, disease duration and therapies. Infectious agents occurred repeatedly during the duration were identified as history repeated infectious agents. T test, ANOVA, chi-squared test and multivariate analysis of covariance were used for analyzing the association between the infections and disease outcome.

Results: 688 RA patients were divided into two groups based on whether their DAS28 reached 3.2 (active or inactive). The HAQ score and the incidence of airway infection has a significant difference among these two groups (P=0.000; P=0.002). Logistic regression analysis shows that smoking, airway infection and age were the risk factor for RA active (OR=4.844, 95% CI (0.193,1.001); OR=1.326, 95% CI (0.655,2.687); OR=1.013, 95% CI (0.989,1.037)), and the disease duration and the therapy were also affect the disease outcome (OR=0.650,OR=1.560). Than we divided these patients into four groups based on their infectious site such as airway, urinary, intestinal and no-infection. After adjusting for the disease duration, only airway infection incidence has statistically significantly different (P=0.000). DAS 28 has statistical different only among the groups whether they have airway infectious agents after adjusting the smoking and therapy (P=0.002; P=0.002). Compared with infection free group, patients with airway infection has a higher DAS28 because they have more swollen or painful joints, while patients with urinary infection perform a higher scores because they have a high level of ESR.

Conclusions: The repeated infectious agents during the disease duration might lead to poor outcome. We should pay more attention to those patients who have repeatedly infectious agents during their disease duration in order to improve their prognosis.

References:

Disclosure Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3976

AB0275

THE CORRELATION OF CARTILAGE OLGOMERIC MATRIX PROTEIN WITH SONOGRAPHIC KNEE CARTILAGE THICKNESS AND DISEASE CHARACTERISTICS IN RHEUMATOID ARTHRITIS

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Background: Cartilage Oligomeric Matrix Protein (COMP) is an extracellular protein which is primarily found in the cartilage and to a lesser extent in ligaments, meniscus, tendons and synovium. Experimental models of rheumatoid arthritis (RA) and osteoarthritis have pointed out that serum COMP levels are reflective of the cartilage turnover rate.

Figure 1. Levels of clinical data include HAQ, abnormal joints number, CRP and ESR were compared among subgroups of infection free (n=469), airway (n=121), urinary (n=173) and inactive infection (n=85). This figure shows that clinical factors contribute to the difference among these two disease groups.

Conclusions: The repeated infectious agents during the disease duration might lead to poor outcome. We should pay more attention to those patients who have repeatedly infectious agents during their disease duration in order to improve their prognosis.

References:

Disclosure Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3976
Objectives: To investigate the correlation of serum COMP levels with the articular cartilage damage based on sono graphical knee cartilage thickness (KCT) and disease characteristics in RA.

Methods: A total of 61 RA patients and 27 healthy controls were recruited in this study. Serum samples were obtained from all subjects to determine the COMP levels. All subjects had bilateral ultrasound scan of their knees performed by a single radiologist; who was blinded to the details of the subjects. The KCT was based on the mean of measurements at 3 sites; the medial condyle, lateral condyle and intercondylar notch (Figure 1). Besides, the RA patients were assessed for their disease activity based on DAS 28.

Results: Serum COMP concentrations were significantly elevated in the RA patients compared to the controls (p<0.001). The serum COMP levels had an inverse relationship with bilateral KCT in RA subjects and the healthy controls. However, the association was statistically insignificant for bilateral knees in the control arm. COMP correlated significantly with disease activity based on DAS 28 (r = 0.299, p = 0.010), disease duration (r = 0.439, p = 0.05) and mean left KCT (r = 0.285, p = 0.014) in RA (Table 1). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) which are the traditional markers of inflammation; demonstrated a significant positive correlation with the DAS 28 scores (r = 0.372, p = 0.003 for ESR; r = 0.305, p = 0.017 for CRP) comparable to the serum COMP. However, neither ESR nor CRP had a significant association with the KCT, as opposed to the serum COMP.

Table 1. Correlation of Serum COMP levels with Clinical Parameters in RA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.214</td>
<td>0.094</td>
</tr>
<tr>
<td>BMI</td>
<td>0.122</td>
<td>0.259</td>
</tr>
<tr>
<td>DAS 28</td>
<td>0.299</td>
<td>0.010</td>
</tr>
<tr>
<td>ESR</td>
<td>0.065</td>
<td>0.311</td>
</tr>
<tr>
<td>CRP</td>
<td>0.027</td>
<td>0.418</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.439</td>
<td>-0.05</td>
</tr>
<tr>
<td>Mean Right KCT</td>
<td>0.177</td>
<td>0.088</td>
</tr>
<tr>
<td>Mean Left KCT</td>
<td>-0.285</td>
<td>0.014</td>
</tr>
</tbody>
</table>

KCT: knee cartilage thickness.

Conclusions: The serum COMP is a promising biomarker in RA which reflects disease activity and damage to the articular cartilage. Serum COMP appeared superior to the traditional markers in RA i.e ESR and CRP in predicting sono graphical cartilage.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5785
response and ACR 70 criteria were determined after 12 weeks of treatment with a fixed schedule methotrexate and prednisone. Physician perceived remission (PhR) was defined as a global assessment of ≤20 on a visual analogue scale, phrased: “How active do you think the RA of your patient is today?”. Patient perceived remission (PatR) was phrased as: “Would you say that, at this moment, your disease activity is as low as it has ever been?”. In patients in PhR, the change in components of the DAS28 and questions of the Rheumatoid Arthritis Impact of Disease (RAID) and Health Assessment Questionnaire (HAQ) were compared between patients in and not in self-perceived remission.

Results: The agreement on remission between patients and physicians was 64% and was dependent of the definition of remission. In Boolean remission, EULAR good response and ACR70 remission agreement was: 86%, 63% and 80% respectively (table). Patients in PhR, the patients in PatR had more improvement on all RAID subdomains. There were no significant differences in clinical outcomes (ESR was significantly different at baseline, but not after 12 weeks; see figure).

Disclosures: None declared DOI: 10.1136/annrheumdis-2017-eular.6406

AB0278 ULTRASOUND EXAMINATION IN DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS

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Background: Fortunately, management of RA at the early stage has become possible thanks to the emergence of new biotherapies and the strategy treat to target. Musculoskeletal ultrasound (US) is a potent tool for the detection of synovitis, effusion and bone erosion in RA.

Objectives: The aim of this study was to assess the contribution of US in diagnosing RA at the early stage of the disease.

Methods: A cross-sectional study was performed during 2 years. Patients with a history of inflammatory joint pain for <6 weeks and <2 years with synovitis of at least one joint were enrolled in this study. All patients underwent clinical assessment, laboratory tests and plain radiography of hands and feet. US was assessed within one week of clinical examination. Synovitis and erosion were defined according to the OMERACT.

Results: One hundred patients were included in this study with an average age of 51 ± 14.6 years old. Female outnumbered male with a sex ratio of 3.8. The mean duration of the disease was 10 ± 7.4 months. When admitted to our department and after clinical examination it was found that 31% of patients presented polyarthritis, 4% had oligoarthritis and 7% suffered from monarthrosis. US findings: US was found to be more sensitive than clinical examination to detect synovitis. Among the 2200 joints assessed by US, a synovitis was detected in 81% patients, an intra-articular effusion in 96% patients and PD signals in 51% patients. Also, flexor tenosynovitis were present in 55% patients and extensor tenosynovitis in 59% patients. Erosions were more detected in plain radiography (70%) than in US (41%). Clinical parameters (VAS, duration of morning stiffness, number of night awakens, TJC) were not correlated with most US findings. Nevertheless, correlation was detected for US effusion (r=0.250, p=0.028) and for US Dopper (r=0.289, p=0.011) with SJC. PDUS examination correlated with CRP results (r=0.302, p=0.023) but not with ESR results. A significant, positive correlation was observed between erosions in X-rays or US assessment (r=0.342, p=0.002). The US detected synovitis in 25% of patients who had no swollen joint at the clinical examination when admitted to our department and had detected erosions in 9% of patients having negative plain X-rays.

Conclusions: Ultrasound appears as a sensitive tool to detect subclinical synovitis (25%) and infra- radiological erosions (9%). It helps us to make an early diagnosis and start appropriate treatment before the onset of irreversible joint destruction.
Results: The mean age of our population was 49.17±11.21 years (age 24–78). The disease average duration was 7.4±4.22 years (4 months - 29 years), 82.71% of RA were women and 17.29% were men. Seropositive RA were 80.24%, and 71.6% of RA have anti CCP positive antibody. Univariate analysis of the presence of anti-CCP antibodies in conjunction with HLA DRB1 and DQB1 was performed. Complete HLA typing of HLA DRB1 0401 and 1501 were significantly associated with the presence of anti-CCP antibodies (p<0.0001). Four DRB1 0401 carriers were homozygotes with three of them having anti-CCP antibodies.

Garriship of HLA DQB1*0201, 0301, 0302,0501 and 0601 was associated with the presence of anti-CCP antibodies and so was HLA-DQB1*0401*, but with a less significant association.

Conclusions: Although no formal conclusions on causality can be drawn from this association study, these findings suggest that anti-CCP antibodies are associated with different phenotypes; which suggest that various pathogenic mechanisms underlie the positivity for anti-CCP in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2924

AB0282 RHEUMATOID ARTHRITIS PATIENTS ACHIEVED BETTER QUALITY OF LIFE THAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AT SUSTAINED REMISSION: THE IMPACT OF DISEASE DIAGNOSIS ON HEALTH-RELATED QUALITY OF LIFE OUTCOMES

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Background: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) impact the health-related quality of life (HRQoL) of the patients. The 2004 update of the Disease Activity Score (DAS28) allows comparison of outcomes among different conditions. Whether remission represents similar status in terms of QoL in RA and SLE patients is unknown. In 2004 and 1999, respectively, recent-onset RA and SLE cohorts were initiated in a referral center for rheumatic diseases in Mexico City; the SF-36 was applied beginning from enrollment.

Objectives: To compare the SF-36v2 scores between patients from both cohorts who achieved for the first time sustained remission (SR) and to define the role of disease diagnosis as associated to SF-36v2 normative data in SR patients.

Methods: First SR was considered when RA and SLE patients achieved at least 12 months of continuous follow-up with either SLE disease activity index 2000 update >0 or Disease Activity Score (28 joints) <2.4, respectively. Up to December 2015, updated data from 172 RA patients and 211 SLE patients with at least one year of follow-up were reviewed. In the SLE cohort, SF-36 was incorporated to routine assessments from 2005 onwards, while in the RA cohort it was applied since the beginning of enrollment. The SF-36v2 license re-scored the SF-36 used in the SLE cohort. In all the cases, Spanish versions were used and scoring was adjusted by gender and age. SF-36v2 scores were available for the majority of RA patients. Logistic regression models were used to investigate factors associated with normative SF-36v2. Written informed consent was obtained from all patients.

Results: Cohorts were integrated primarily by middle-aged females (89%), with recent-onset disease (5.3±3.2 months); at inclusion, RA patients were older and less educated; follow-up was longer in SLE patients (10.6±2.9 vs. 7.5±3.3 years; p<0.001) and a higher number of them died (15% vs. 2%, p<0.001).

A higher proportion of patients achieved SR sooner in the recent-onset RA cohort than in the SLE cohort: 58% vs. 30.6% of the patients, after 30.8±23.9 vs. 59.4±37.5 months, respectively, p<0.001. At SR, RA patients achieved better scores in 6 out of 8 SF-36v2 domains and in the physical health component summary (PHCS) compared with SLE patients; also, a greater proportion of RA patients achieved normed scores in five domains and in the PHCS; SLE patients achieved more frequent roles (physical and emotional) norms and scored higher mental health component summary than their counterpart. Finally, at SR RA patients had greater improvement in the majority of SF-36v2 domains and both summary components, despite having worse SF-36v2 scores at baseline evaluation.

In SR patients from both cohorts, age (β: 1.08, 95% CI: 1.02–1.1, p<0.003) and SF-36v2 score (β: 9.64, 95% CI: 3.61–25.75, p<0.001) were predictors of not achieving normative PHCS.

Conclusions: RA patients who achieved SR had better HRQoL than their SLE counterparts. Age and SLE diagnosis were associated with not achieving HRQoL norms in RA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1187
Results: At baseline the mean scores of HAQ-DI and RAQoL did not differ greatly among patients on csDMARDs and bDMARDs (1.29±0.75SD vs 1.13±0.54SD, p=0.063; 16.31±8.26SD vs 15.03±7.13SD, p=0.219, respectively). However, the mean physical component summary score of SF-36 was significantly higher in bDMARDs compared with csDMARDs (32.98±5.97 vs 31.50±7.82, p=0.039), while in the mental component of this scoring system not such a difference was found (p=0.983). After 6 months subjects treated with bDMARD showed a significant decreasing of the means of the HAQ-DI and RAQoL, as opposed to the other treatment group (0.86±0.55SD vs 1.17±0.76SD, p<0.01; 10.96±6.53SD vs 14.55±7.96SD, p<0.01 respectively). Similar results were obtained for both physical and mental component summary scores of SF-36 (39.49±6.43SD vs 48.8±6.04SD, p<0.01; 43.69±7.96SD vs 59.66±10.19SD, p=0.001 respectively). At month 12 a significant improvement of QoL measured by the three assessment tools was registered in patient receiving bDMARDs compared with the csDMARD treatment group (p<0.001).

Conclusions: Patient treated with bDMARDs showed better results for QoL than on therapy with csDMARDs within a period of 12 months of treatment. Current management strategies should focus on improving the symptoms of activity and maintaining physical function in order to increase QoL in patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3538

AB0284 ASSESSMENT OF DISEASE ACTIVITY BY DAS28-CRP, CDAI, SDAI AND RESPONSE TO TREATMENT WITH CSDMARDS AND BDMARDS AFTER ONE-YEAR FOLLOW-UP IN RHEUMATOID ARTHRITIS PATIENTS FROM BULGARIAN POPULATION

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Background: The assessment of disease activity is an essential component in the selection of therapeutic approach for the prevention of disability of patients with RA.

Objectives: The current study was conducted to evaluate the disease activity in patients on csDMARDs and bDMARDs after 6 months to 1-year of treatment and to determine whether the benefits of different therapies were sustained over time.

Methods: A total of 260 patients for the study were selected 220 patients with a mean age 55.05±10.63SD years, meeting the 1987 ACR classification criteria for RA. Patients were stratified according to the 1987 ACR classification criteria for RA were included in the study. The other treatment group (p<0.001). Unlike results reported in 48 recent onset RA patients and in the serum from 20 healthy control (n=20) at baseline and 6 months after initiation therapy with non-biological disease modifying anti-rheumatic drugs (DMARDS). In the patients Disease activity was calculated by the 28 joint counts (DAS28) and muscleskeletal ultrasonod examination (MSUS) was performed at baseline and after 6 months using a 12-joint score (bilateral elbow, wrist, 2nd metacarpophalangeal (MCP), 3rd MCP, knee, ankle) [2]; immunoglobulin-M rheumatoid factor (IgM-RF) titre, and cyclic citrullinated peptide (anti-CCP) antibodies titre and C-reactive protein (CRP). Levels were measured and the health assessment questionnaire (HAQ) scores were recorded.

Results: Serum and SF GITRL levels were highly significantly increased in RA (39.38±16.78 ng/mL and 30.6±16.79 ng/mL respectively) compared to serum level in the healthy controls (10.3±5.46 ng/mL, p<0.001). In RA patients, baseline serum and SF levels of GITRL significantly correlated with DAS28 (r=0.52 and 0.56 respectively, p<0.05). anti-CCP titres (r=0.46 and 0.51 respectively, p<0.05), grey scale (GS) (r=0.5 and 0.52 respectively, p<0.05) and power Doppler (PD) (r=0.65 and 0.88 respectively, p<0.001) synovitis scores. Also, serum and SF levels of GITRL at 6 months follow up significantly correlated with the DAS28 (r=0.42 and 0.48 respectively, p<0.05), GS score (r=0.46 and 0.51 respectively, p<0.05), PD signal (r=0.43 and 0.45 respectively, p<0.05). Logistic regression analysis showed that baseline serum levels of GITRL were predictive of follow up DAS 28 and PD synovitis score (p=0.009 and 0.03 respectively).

Conclusions: Rheumatoid arthritis patients have significantly increased serum and synovial levels of GITRL that remarkably correlated with the DAS28 and MSUS parameters of inflammations suggesting that it could be a useful marker to reflect RA disease activity. GITRL could be a useful biomarker to predict treatment outcome in RA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5476

AB0296 14 CASE STUDY OF MACROPHAGE ACTIVATION SYNDROME (MAS) IN SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS

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Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening syndrome.

Objectives: We aim to review the precipitating events,clinical features, treatment, and outcomes of macrophage activation syndrome (MAS). Part patients were analysed the Polymorphisms of Perforin A191V (NCBI:SNP rs35347132) using special primers by polymerase chain reaction (PCR).


Results: Fourteen patients (10 girls, 4 boys) were concluded to have evidence of MAS. The primary diagnosis was systemic onset juvenile idiopathic arthritis, with age ranged from 5 months to 12 years. No medication was identified as trigger. Eleven had infections prior to MAS,specific infectious agents were identified in four. High grade fever, new onset hepatosplenomegaly, lymphadenopathy, dysfunction
of liver, abnormal fat metabolism and hemophagocytosis were common clinical features. Two cases were with ARDS and MOF in three and three died. The perforin A91V (NCBI:SNP rs35947132) gene was detected in seven systemic onset juvenile idiopathic arthritis complicated with MAS cases, but no mutation were found. Glucocorticoid, intravenous immunoglobulin, immunomodpressive therapy were effective and HP (Plasmodiapheresis) used in one serious case was also effective.

**Conclusions:** MAS is a rare and potentially fatal complication of childhood rheumatoid diseases, especially systemic onset juvenile idiopathic arthritis. Most of our patients were male, and most cases were preceded by infection. Bone marrow studies support the diagnosis. MOF may be a poor prognostic sign. Aggressive early therapy is essential.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1791

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**AB0287**

**MUTUAL ASSENT TOWARDS COMPREHENSIVE DISEASE CONTROL: THE RELATIONSHIP BETWEEN US MEASURES AND PATIENT REPORTED OUTCOMES IN EARLY RHEUMATOID ARTHRITIS**

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1Rheumatology, Darent Valley Hospital, Dartford, United Kingdom; 2Community and Public Health; 3Rheumatology and Rehabilitation; 4Radiology, Ain Shams University, Cairo, Egypt

**Objectives:** Assessment of the relationship between US measures of joint inflammation/damage and patient reported outcomes (PROs): HAQ, pain and patient global assessment in early rheumatoid arthritis (early RA) patients over 5-years follow up period.

**Methods:** This longitudinal cohort of 261 patients with early RA was derived from the US monitoring study [1]. Adopting OMERACT definitions; correlations between total US scores (synovial hypertrophy, synovial fluid, Power Doppler, bone erosion and tenosynovitis) and PROs [2] namely functional disability (HAQ), pain and 5-years was not associated with changes in PROs. Radiological damage was assessed using modified Total Sharp score (mTSS). Univariate correlations as well as correlations between interval changes were assessed. Multivariable regression models were used to evaluate the associations across all time-points and their relationship to clinical disease activity measures.

**Results:** There were significant correlations (p < 0.01) between total US score and HAQ (r=0.71), pain (r=0.69) and patient global scores (r=0.66) at all timepoints. Correlation 0.12 at baseline, 0.22 at 1-year and 0.41 at 5-years). Change in mTSS HAQ (r=0.71), pain (r=0.69) and patient global scores (r=0.66) at all timepoints.

**Conclusions:** There were significant correlations (p < 0.01) with the US score of the affected joints. US total score at 1-year predicted subsequent 5-year HAQ score (R2=0.17). At 0, 1- and 5-years, total US scores were higher in patients whose HAQ score was > 1 (9.26) compared to those below 1 (4.16, p < 0.01). The link between joint inflammation/structural damage and PROs is of critical importance to the care of patients with inflammatory arthritis. US measures of inflammation and structural damage correlated independently with functional physical, pain and patient global assessments. A clear relationship between radiographic structure damage and the patient's perceived remission/flare and in each of the two groups, the levels of CRP and ESR were determined. Patients with elevated levels of Nampt had the following laboratory parameters (Mm): ESR – 37.8±5.1, CRP – 56.0±9.37 (rate - less than 5.0 mg/l). The second group had following data: ESR 22.4±5.56, CRP 21.65±1.38. Thus, patients with elevated levels of nicotinamide phosphoribosyltransferase had significantly higher concentrations of ESR and CRP (p < 0.001). There is the relationship between the level of nicotinamide phosphoribosyltransferase serum and laboratory markers of inflammation in RA (CRP and ESR). The data indirectly confirm the hypothesis that increased levels of nicotinamide phosphoribosyltransferase in RA patients is associated with disease activity.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1956

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**AB0289**

**PREDICTOR OF THE SIMPLIFIED DISEASE ACTIVITY INDEX 50 (SDAI 50) AT MONTH 6 DURING BDMARDS TREATMENT IN PATIENTS WITH LONG-ESTABLISHED RHEUMATOID ARTHRITIS: A SINGLE-CENTER, RETROSPECTIVE STUDY**

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**Background:** The simplified disease activity index (SDAI) 50 has good agreement with the EULAR response measures for early rheumatoid arthritis (RA). Although there are reports on early RA, there have been no reports on long-established RA.

**Objectives:** In this study, we analyzed the relationships between various baseline factors and SDAI 50 after six months of biological disease-modifying antirheumatic drugs (bDMARDs) treatment to determine the prognostic factors for long-established RA.

**Methods:** The subjects were 332 RA patients who had been treated with bDMARDs for 6 months. The following characteristics were investigated: age, gender, disease duration, smoking history, body mass index, steroid and methotrexate dosage, previous bDMARDs use, combined csDMARDs use, ESR, CRP, serum matrix metalloproteinase-3 levels, SDAI score, health assessment questionnaire disability index score (for daily living activities) and short-form 36 score (for quality of life). As a primary outcome index, SDAI response was defined as a 50% reduction in SDAI score between baseline and 6 months (SDAI 50).

**Results:** The group of RA patients who achieved SDAI 50 (Group A: 204 patients) had a higher tender joint count (p = 0.041), swollen joint count (p = 0.001), evaluator’s global assessment (p = 0.027) and SDAI (p = 0.006) than did those who did not achieve SDAI 50 (Group B: 152 patients). Before the start of the treatment, steroid dosage (p = 0.018, odds ratio: 1.119, 95% CI: 1.029–1.229) and SDAI (p = 0.0003, odds ratio: 0.953, 95% CI: 0.928–0.978) were determined based on logistic regression analysis. Comparisons were performed between Groups A and B and between before treatment and after 6 months of SDAI. Group A showed a significant improvement compared to Group B by repeated measure analysis of variance (ANOVA) (Interaction: p = 0.000, Group A vs. Group B: p = 0.000, before vs. after treatment: p = 0.000). Our study demonstrated that RA patients with a lower steroid dosage and higher SDAI baseline are more likely to achieve SDAI 50 with bDMARD treatment.

**Acknowledgements:** ASHURA Registry Groups


**DOI:** 10.1136/annrheumdis-2017-eular.1818

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**AB0288**

**LABORATORY MARKERS OF INFLAMMATION AND SERUM NICOTINAMIDE PHOSPHORIBOSYLTransFERASE LEVEL IN RHEUMATOID ARTHRITIS PATIENTS**

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**Objectives:** To study relationship between serum levels of nicotinamide phosphoribosyltransferase and laboratory markers of inflammation in patients with rheumatoid arthritis (RA).

**Methods:** We determined nicotinamide phosphoribosyltransferase level in sera of 140 patients with RA (96 women and 44 men) by indirect enzyme-linked immunosorbent assay (RaiBiotech, cat No. EIA-VIS-1). The control group consisted of 20 women and 10 men aged 22 to 55 years without complaints of pain in the joints throughout life. The mean duration of disease was 5.9±0.37 years.

**Results:** We divided all RA patients into 2 groups: one group (118 patients) with elevated levels of nicotinamide phosphoribosyltransferase serum (more than 3.9 ng/ml) and second group (22 patients) - with normal range.

In each of the two groups, the levels of CRP and ESR were determined. Patients with elevated levels of Nampt had the following laboratory parameters (Mm): ESR – 37.8±5.1, CRP – 56.0±9.37 (rate - less than 5.0 mg/l). The second group had following data: ESR 22.4±5.56, CRP 21.65±1.38. Thus, patients with elevated levels of nicotinamide phosphoribosyltransferase had significantly higher concentrations of ESR and CRP (p < 0.001).

**Conclusions:** There is the relationship between the level of nicotinamide phosphoribosyltransferase serum and laboratory markers of inflammation in RA (CRP and ESR). The data indirectly confirm the hypothesis that increased levels of nicotinamide phosphoribosyltransferase in RA patients is associated with disease activity.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4485

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**AB0290**

**PULMONARY AMYLoidOSIS IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS**

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**Background:** AA amyloidosis (AAa) is one of the most insidious systemic complications (RAa) of rheumatoid arthritis (RA), which fortunately may lead to death [1].

**Objectives:** The aim of this study was to determine the prevalence and location of amyloid A deposition in the lungs of RA patients at the time of death.

**Methods:** A randomized autopsy population of 161 in-patients with RA was studied. AAa complicated RA in 34 (21.1%) cases [1].
At least four tissue samples of lungs (from apical and basal regions of both lungs) were available for histologic evaluation in 33 of these 34 patients. RA was confirmed clinically according to the criteria of the ACR. The presence of amyloid A deposits in various structures of the lungs was determined histologically by amyloid specific Congo red staining, according to Romhányi [2]. The extent of amyloid A deposition was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [1]. "0": no amyloid deposits, "1": sporadic, minimal amyloid deposits on different tissue structures, "2": less than five, "3": five or more involved tissue structures per microscopic field at objective magnification of x20.

Results: Amyloid A deposition in the lungs was detected in 24 of 33 (72.2%) patients. Amyloid deposition in various structures does not begin at the same time. In the early stage of systemic amyloidosis there were histologically detectable amyloid deposits only in a few structures (arterioles, interstitial collagen fibers, peribronchial and perilobular basement membranes). In other structures (small and medium size arteries, peribronchial basement membranes, small veins, collagen IV reticulin fibers, venules, medium size veins and nerves) deposits were seen only in late stages of amyloidosis (with massive involvement of the mentioned structures).

Conclusions: Amyloidosis is a progressive, cumulative process, involving in its early stage only a few structures in some organs, and increasingly more in the later stages of the disease [1]. Amyloid A deposition starts in the most frequently involved structures of the most frequently involved organ [1].

In the lungs amyloid A deposition starts in the wall of arterioles and in interstitial collagen fibers. As time progresses, basement membranes of peribronchial and peripheral regions of lobules, small and medium size arteries become involved. Still later panlobular deposition of basement membranes, small veins, reticulin fibers (collagen IV) of subpleural fat tissue, venules and medium size veins become involved. The involvement of nerves indicates advanced stages of amyloid deposition in the lung. This chronology of amyloid A deposition allows an indirect assessment of the stage of amyloidosis. Based on the involvement of structures in lung biopsy specimens the pathologist may be able to estimate involvement of the other structures, even if not present in the sections. Involvement of arterioles alone (without involvement of small arteries) indicates an early stage of amyloidosis, whereas amyloid A deposits in veins or peripheral nerves suggests an advanced stage with massive involvement of other pulmonary structures.

References:
[1] Bély M, Apáthy Á: Clinical pathology of rheumatoid arthritis: Cause of death, stage with massive involvement of other pulmonary structures. Whereas amyloid A deposits in veins or peripheral nerves suggests an advanced stage of amyloidosis. Based on the involvement of structures in lung biopsy specimens the pathologist may be able to estimate involvement of the other structures, even if not present in the sections. Involvement of arterioles alone (without involvement of small arteries) indicates an early stage of amyloidosis, whereas amyloid A deposits in veins or peripheral nerves suggests an advanced stage with massive involvement of other pulmonary structures.

AB0291 EPIDEMIOLOGY AND COMORBIDITY OF RHEUMATOID ARTHRITIS IN UPPER EGYPT, A HOSPITAL BASED STUDY
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Background: Rheumatoid arthritis (RA) is one of the commonest autoimmune diseases. It affects about 1% of the population worldwide (1). The prevalence of RA varies widely between different countries (2). Not only the prevalence of the disease which differs among different continents, races, ages and socioeconomic levels but also the disease pattern. Studies explaining the epidemiology of RA in Egypt in general and in upper-Egypt, in particular, are very limited (3).

Objectives: To estimate the comorbidity of rheumatoid arthritis and its relation to disease activity, duration, disease pattern and demographic features of RA patients in upper Egypt.

Methods: This study was carried out on 923 patients who fulfilled ACR/EULAR criteria 2010. All of them live in Sohag governorate and aged 18 years or older DAS28-ESR score, first involved joint, joint distribution, disease pattern, extra-articular comorbidities including gastrointestinal, urinary, cardiac, haematological and neurological were estimated. The activity of daily living was valued by Erlangen score (E-ADL).

Results: The mean age of the participants was 45±10.9 years, with a range (19–70). The median of the disease duration was 5 years, with a range (0.5–40 years). Most of the participants were female (691, 74.9%). Disease onset was gradual or insidious in 94.3% of cases and acute in 5.7% of them. First joint group affected were the small joints of the hands (MCPS and MPJs), recorded in 48.9% of cases, followed by wrist joints (29.3% of cases), then knees (9%), ankles and small joints of the foot (6%) and lastly other joints collectively recorded in only 6.8%. The commonest extra-articular comorbidities were haematological, seen in 323 cases; 35%, followed by gastrointestinal in 290 cases (31.4%), then ophthalmological in 31%, entrapment syndromes in 29.4%, pulmonary in 21.7%, urological in 12.4%, rheumatoid nodules in 11.4%, liver cirrhosis in 8.7%, renal impairment in 8.5% and cardiovascular diseases in 6.5%. The activity of daily living (E-ADL) showed that most of the cases fell in score 4 (58.2%). Regarding DMARDs treatment of the study population, Methotrexate (MTX) was used regularly by 78.3% of cases, hydroxychloroquine (HCO) by 78.1%, followed by Leflunomide (LEF) by 26.4% and sulfasalazine (SSZ) by 13.1%. The majority of cases used combination therapy of either MTX+HCO, MTX+SSZ, MTX+HCO+SSZ or MTX+LEF. Regarding other drugs, 99% of cases used NSAIDs (regularly in 30.2% and on demand in 68.8%). Steroids were regularly used by 26.8% of cases.

Conclusions: The commonest comorbidities were haematological, gastrointestinal, ophthalmological and neurological ones; respectively. Erosion, deformity and DAS28-ESR score have a great impact on E-ADL score.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1225

AB0292 CLINICAL FEATURES OF RHEUMATOID ARTHRITIS AT 75 YEARS OF AGE AND OLDER IN JAPAN – COMPARISON WITH POLYMYALGIA RHEUMATICA IN THE SAME AGE GROUP
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Background: As Japan is a super-aged society, we have many chances to care for elderly patients in our hospital. Elderly-onset rheumatoid arthritis (RA) (onset age >60 years) may present similar symptoms to those of polymyalgia rheumatica (PMR). We consider that differential diagnosis of RA and PMR is more difficult in patients over 75 than those under 74 in clinical practice. Anti-cyclic citrullinated peptide antibody (ACPA) was reported to be a helpful tool in the differential diagnosis of EORA from PMR. However, when elderly patients with negative ACPA complained of bilateral shoulder and/or girdle pain, it was difficult to differentiate PMR from RA.

Objectives: The study aimed to explore clinical features of RA and PMR at onset age 75 years. For the present investigation, we used a novel diagnostic
tool to distinguish ACPA-negative elderly RA patients from PMR patients at initial presentation.

Methods: From April 2011 to December 2016, 21 RA patients and 24 PMR patients in our hospital, whose onset age was over 75 years, were recruited for this study. PMR patients did not have any evidence of giant cell arteritis. The diagnosis of RA was made based on 2010 ACR/EULAR RA classification criteria. The diagnosis of PMR was made based on 2012 EULAR/ACR classification criteria or Bird’s criteria. Data were obtained from medical records under informed consent. Statistical analysis was performed using the Mann-Whitney U-test to compare median values and Fisher’s exact test to compare frequencies (IBM SPSS version 24). P < 0.05 indicated statistical significance.

Results: RA patients (6 men and 15 women) consisted of fifteen ACPA+ (11 RF+, 4 RF–), six ACPA– (1 RF+, 5 RF –). PMR patients consisted of 12 men and 12 women. All of them were ACPA–RF– and did not meet 2010 RA criteria. Twenty patients (10 RA, 10 PMR) had a 7-year follow-up. No bilateral shoulder pain met Bird’s criteria. Clinical features and statistical results are shown in the Table. Sixty-seven percent of RA patients and 13% of PMR patients had left-right differences in joint pain.

Scoring was performed based on clinical findings. Tenderness and/or swelling joint counts among wrists, fingers, ankles, and knees – each 1 point, left-right difference = 1 point, no bilateral shoulder pain = 1 point, no girdle pain = 1 point, no fever = 1 point; the maximum score was 8. The mean score in RA patients was 4.8 (SD = 1.44), whereas in that PMR patients was significantly lower at 1.5 (0.98) (P = 0.001). Receiver operating characteristic (ROC) curve analysis was used to determine the most suitable cut-off level to find RA. The area under ROC curve score over 3 was 100% sensitivity and 87.5% specificity. All 6 ACPA-negative RA patients showed a score over 4.

Table: Clinical features in patients with rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR)

<table>
<thead>
<tr>
<th>Age at onset of RA or diagnosis of PMR</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from onset to start of treatment</td>
<td>20.3 (8.3)</td>
<td>20.3 (8.3)</td>
<td>13.9 (9.7)</td>
<td>13.9 (9.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Joint/muscle pain at onset</td>
<td>14.7 (7.4)</td>
<td>14.7 (7.4)</td>
<td>14.7 (7.4)</td>
<td>14.7 (7.4)</td>
<td>0.96</td>
</tr>
<tr>
<td>Systemic symptoms</td>
<td>13.1 (7.1)</td>
<td>13.1 (7.1)</td>
<td>13.1 (7.1)</td>
<td>13.1 (7.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>Rheumatoid factor positive</td>
<td>12.5 (7.3)</td>
<td>12.5 (7.3)</td>
<td>12.5 (7.3)</td>
<td>12.5 (7.3)</td>
<td>0.22</td>
</tr>
<tr>
<td>Anti-CCP antibody positive</td>
<td>13.5 (7.1)</td>
<td>13.5 (7.1)</td>
<td>13.5 (7.1)</td>
<td>13.5 (7.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>CRP (mg/dl) at onset</td>
<td>2.6 (1.5)</td>
<td>2.6 (1.5)</td>
<td>2.6 (1.5)</td>
<td>2.6 (1.5)</td>
<td>0.96</td>
</tr>
<tr>
<td>Matric metalloproteinase 3 (ng/ml) at onset</td>
<td>381 (336.7)</td>
<td>381 (336.7)</td>
<td>381 (336.7)</td>
<td>381 (336.7)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

SO, standard deviation; IQR, interquartile range; CCP, cyclic citrullinated peptide

Conclusions: Pease et al studied RA at onset 60 years and over and PMR, and reported that arthritis of wrists and fingers was suggestive of RA1. However, in our study, small joint swelling was rare in RA patients 75 years and older. The scoring system we made might be useful for the differential diagnosis of ACPA-negative RA and PMR in elderly patients 75 years and older.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1320
The average pregnancy length was 36.36 weeks and the mean birthweight was 2878.90 grams. Growth restriction was identified in several patients, even in those with a normal body mass index.

13 patients never had new flare postpartum and in the others the mean time of postpartum flare was 12.1 weeks.

Objective: Patients with RA have a high risk of postpartum flare, and in every center, the local rheumatologists provided RA pts to be examined by US. All the US machines were identical both for type and controlateral sonographers (rheumatologists with a special interest in US that were performing US as their usual activity for many years). In every center, the local rheumatologists provided RA pts to be examined by US. All the US machines were identical both for type and US examination was performed bilaterally on wrists, MCP and MTP joints, looking for synovitis, effusion, synovial proliferation and PD signal and bone erosions. The positive findings were scored according to a 0–3 score for synovitis components and presence/absence for erosions; the number and size of the largest erosion was also recorded.

Results: Descriptive and demographic data of the 433 pts examined are reported in Table 1. Pts were divided on the basis of the DAS28 result. Statistically significant differences in age and disease duration were registered between the group in CR and the group with DAS28 >3.2 (p=0.019 and p=0.012, respectively), while no differences were found for HAQ or MTX use. Disease activity was assessed by the disease activity score of 28 joints (DAS28), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and visual analog scale (VAS). Disease activity, lipid profile and intra-media thickness (IMT) of common carotid arteries were measured before and after 85 days (6 months) of treatment.

Methods: The study included 82 patients in the Specialized Course Out-patient Therapy Department of the 1st Clinic of Tashkent Medical Academy of age group between 44 and 65 years (mean 52±8.4), predominantly female gender (n=57, 69.5%), with early RA (mean disease duration 9.2±2.4 months).

Objectives: To investigate the US characteristics of RA pts presenting either CR or low disease activity (LDA).

Methods: In 2015 an educational event focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy. After a brief presentation on the evidence of US added value for the clinician given by expert sonographers (rheumatologists with a special interest in US that were performing US as their usual activity for many years), in every center, the local rheumatologists provided RA pts to be examined by US. All the US machines were identical both for type (Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe) and settings (both for grey-scale and power Doppler (PD)). Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). The US examination was performed bilaterally on wrists, MCP and MTP joints, looking for synovitis (effusion, synovial proliferation and PD signal) and bone erosions. The positive findings were scored according to a 0–3 score for synovitis components and presence/absence for erosions; the number and size of the largest erosion was also recorded.

Results: Descriptive and demographic data of the 433 pts examined are reported in Table 1. Pts were divided on the basis of the DAS28 result. Statistically significant differences in age and disease duration were registered between the group in CR and the group with DAS28 >3.2 (p=0.019 and p=0.012, respectively), while no differences were found for HAQ or MTX use. Disease activity was assessed by the disease activity score of 28 joints (DAS28), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and visual analog scale (VAS). Disease activity, lipid profile and intra-media thickness (IMT) of common carotid arteries were measured before and after 85 days (6 months) of treatment.

Methods: The study included 82 patients in the Specialized Course Out-patient Therapy Department of the 1st Clinic of Tashkent Medical Academy of age group between 44 and 65 years (mean 52±8.4), predominantly female gender (n=57, 69.5%), with early RA (mean disease duration 9.2±2.4 months), divided into 2 groups: Group 1 (n=40) received methotrexate (MTX); 7.5 mg/week; plus prednisolone with the same previous doses plus rosuvastatin (40 mg/day). Lipid profile assessment comprised triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C). Disease activity was assessed by the disease activity score of 28 joints (DAS28), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and visual analog scale (VAS). Disease activity, lipid profile and intra-media thickness (IMT) of common carotid arteries were measured before and after 85 days (6 months) of treatment.

Results: 4 patients receiving rosuvastatin were excluded due to abnormal liver function test parameters (De Ritis ratio >9), further assessment was thus performed on 78 (Group 2, n=38) early RA patients. Overall ESR (Group 1: 24.4±7.26; Group 2: 37.4±12.3) and CRP (Group 1: 5.5±6.05; Group 2: 25.8±23.4) were significantly lower during the treatment. The mean DAS28, unconditionally considered as the most important index of clinical disease activity in RA, was found to be lower (p=0.05) in the adjunct statin-treated group (Group 2: 3.68±0.77) than that of the conventional DMARD treated group (Group 1: 4.5±1.08). Statin significantly reduced LDL-C (0.9±2.1 mmol/l to 3.3±0.6 mmol/l; p<0.05) and increased HDL-C (1.3±0.6 mmol/l to 2.0±0.4 mmol/l; p=0.06) after 6 months of treatment. However, rosuvastatin therapy showed no significant improvement in VAS score (6.7±1.5 to 6.9±0.6; p=0.41) and IMT (1.04±0.09 to 1.08±0.07; p=0.05).

Conclusions: Statins ameliorate RA activity, reduce potential cardiovascular risk in the context of atherosclerosis and mediate clinically apparent anti-inflammatory effects, but long-term effects and benefit-risk profile should be addressed in the management of elevated risk of cardiovascular events in RA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6605
low-dose glucocorticosteroids did not influence altered body composition during the first year of eRA therapy.

References:

Disclosure of Interest: None declared

Abbreviations: Rheumatoid Arthritis, HAQ, AAS, ACCP, AMCV, CRP, ESR, RF, anti CCP, ACR, ACR criteria, EULAR, IT, DAS28, VAS, L-thyroxine, medikal euthyreose, thyrotoxicosis, thyroiditis.

1. V. Odin1, O. Inamova2, V. Tyrenko1, M. Toporkov1. Faculty therapy, Military Medical Academy Named After S.M. Kirov; 2Clinical Rheumatic Hospital No. 25, St. Petersburg, Russian Federation

Background: Specific antibodies, including antibodies to cyclic citrullinated peptide (ACCP) and modified citrullinated vimentin (AMCV) are markers of severe course of rheumatoid arthritis (RA). At the same time, rheumatoid arthritis often associated with autoimmune thyroiditis (Hashimoto’s thyroiditis, HT).

Objectives: Evaluate the role of antibodies to ACCP and AMCV on the clinical and laboratory features of rheumatoid arthritis in association with autoimmune thyroiditis.

Methods: The study included two groups of patients. The first group of patients included 16 patients (14 men and 2 women, mean age - 62.37±2.12 years) with RA in combination with HT and detection in the blood only ACCP (group 1).

The second group also included 16 patients (14 men and 2 women, mean age – 52.31±4.94 years) with RA in combination with HT and detection of ACCP and AMCV in the blood (group 2). In the first group of patients 10 patients had euthyreose, from 5 - hypothyroidism, compensated reception L-thyroxine, 1 patient - thyrotoxicosis ongoing medical euthyreose. In the second group of patients was observed in 14 patients euthyreose, from 2 - hypothyroidism, compensated reception L-thyroxine.

Results: Both groups of patients differed on the following parameters studied: erosion detected in 68% in group 1 and 50% in group 2 (p<0.05), in the first group of patients predominated (62%) the high degree of activity of RA by DAS-28, in while in group 2 - the average (56%, p<0.05).

By using correlation analysis Spearman correlation relationships among the studied attracted attention significant (R=-0.62, p<0.05) relationship between erosions and detection in the blood of antibodies to ACCP in the second group of patients (a combination of RA and HT and identifying in blood ACCP and AMCV), which was repeatedly weakened and unreliable in group 1 (combination of RA and HT and only detection of ACCP) in the blood.

Conclusions: Second group patients (a combination of RA with HT and detection in blood ACCP and AMCV) are closer correlations with indicators of joint destruction than group 1 patients, that in the future may use as a prognostic marker of a more severe course of RA in combination with HT.

Disclosure of Interest: None declared


AB0299

ATLANTOAXIAL SUBLUXATION AS A PROBLEM IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Atlantoaxial subluxation (AAS) is important and potentially life threatening complication of Rheumatoid arthritis (RA). It is defined when the space between odontoid process from C2 and arch of the atlas exceeds more than 3 mm. Instability in atlantoaxial joint may result with numerous neurological symptoms, compression of spinal cord and ultimately quadriparesis or quadriplegia.

Objectives: Aim of the study was to determine the frequency and the characteristics of atlantoaxial instability among our patients with RA and its dependence on the nature of the disease.

Methods: 92 outpatients from University Rheumatology Clinic in Skopje, with classical RA (ACR criteria 1988) were examined for the AAS. In all cases were analysed the duration of the disease, haematological and serological tests, disease activity (DAS 28), visual analogue scale (VAS) for the degree of articular pain and verbal rating scale (VRS), for cervical-occipital pain. All patients underwent native and functional x-ray, CT scan and MRI of cervical spine. A complete neurological examination was obtained, with SEP of the n. medianus et n. tibialis. Results: Atlantoaxial instability, with expressed cervical-occipital symptomaticology, occurred in 54 from 92 (58.69%) patients with RA. AAS appeared significantly more often in patients with longer duration of the disease (p<0.0001), in cases with significant cervical-occipital pain (VRS p<0.0001), with stronger joint pains (VAS), with higher values of SR (p=0.002), CRP (p=0.023), RF (p=0.000005), anti CCP (p=0.000003), and DAS 28 (p=0.0001). Anemia and thrombocytosis (p=0.0008) appeared significantly more in cases with AAS. Anterior AAS, (mostly combined with other types) was the most frequent type, presented in 41 participants (75,92%). In one case posterior AAS was detected, what is very rare finding. Positive SEP was significantly higher in the group with AAS.

Conclusions: AAS is serious extra-articular manifestation of RA. Cervical subluxation may be a general anesthetic risk and risk for a neck injury. Routine cervical radiographs with the head in flexed position should be recommended in need of general anaesthesia and in situations with risk for a neck injury.

Acknowledgements: Rheumatoid arthritis, atlantoaxial subluxation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5033

AB0300

ASSOCIATION OF VITAMIN D STATUS WITH RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND UV INDEX

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Background: Lower serum vitamin D levels have been shown to be associated with various autoimmune disorders, including Rheumatoid Arthritis (RA). Vitamin D deficiency is common in RA patients, despite profiling from a sunny country.

Objectives: The aim of the study is to evaluate (1) – the association between vitamin D serum levels and disease activity in patients with RA; (2) – seasonal distribution of vitamin D levels.

Methods: Patients fulfilling the 2010 EULAR/ACR Rheumatoid Arthritis Classification Criteria, which had serum vitamin D [25(OH)D3] levels measured between January 2013 and December of 2016 were included. Demographic data, disease activity scores, including DAS28v-CP and DAS28v-ESR, vitamin D supplementation with cholecalciferol and other therapeutic approaches were recorded. Vitamin D insufficiency was considered between 25–75 nmol/L and deficiency if <25 nmol/L. Radiographs of the cervical spine, chest, knees and hands were utilized to assess erosive damage.

Results: A sample composed by 95 patients, 79 females (83.16%), with an average age (SD) of 68.57 (11.92) years within 40–88 years range were included. Average disease duration was 13.46 (11.41) years. The average age at diagnosis was 57.10 (14.25) years. The average vitamin D levels were 78.13 (60.98) nmol/L in a range between 20–400 nmol/L. Vitamin D levels were not significantly different in male v.s. females patients. The prevalence of vitamin D insufficiency and deficiency was 53.68% and 8.42% respectively, despite 57.89% of the patients taking supplementation (average 6141 (4800) UI/week). The univariable analysis showed that although vitamin D levels presented a negative poor correlation with DAS28v-CP (rho=-0.348, p-value<0.001) and DAS28v-ESR (rho=-0.271, p-value<0.0001), there was a direct reduction in dispersion of the vitamin D values for increasing values of DAS28v-CP and ESR. It was observed that vitamin D levels increase with patient age and decrease with disease duration. Sazonality and supplementation didn’t affect vitamin D levels in our population.

Correlation between vitamin D and DAS28v-CP

Conclusions: Vitamin D insufficiency/deficiency was frequent among RA patients (62.1%), independently of seasonality or supplementation. An interesting pattern
behavior was observed in this study, which indicates that the likelihood of encountering a very narrowband of vitamin D values for patients with high disease activity is very high, and thus, the forecast capability of vitamin D values for patients with increasingly active disease is quite good. Future research will aim at strengthening the statistical parameters of relevance, identifying and characterizing the driving factors of the effects of the global pattern.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4062

AB0301 CARDIOVASCULAR RISK AND END ORGAN DAMAGE IN AN ITALIAN GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The elevated cardiovascular burden of rheumatoid arthritis is well known and the recent update of EULAR recommendations for cardiovascular disease management (1) establish as overarching principle that the rheumatologist is responsible for CVD risk management in patients with RA. They highlight the need of optimal disease activity control, regular CVD risk assessment, lifestyle counseling, appropriate prescription of NSAIDs, corticosteroids, antihypertensives and statins. Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasonography is also suggested: the presence of carotid plaques is associated with poor CVD-free survival and is strongly linked to future acute coronary events in RA patients.

Objectives: We performed an overall cardiovascular assessment to evaluate the presence of end-organ damage in a group of RA patients.

Methods: We carried out non-invasive 24 hours ambulatory blood pressure monitoring, echocardiography, carotid doppler ultrasound and pulse wave velocity (PWV) in a group of RA patients to optimize non-DMARDs therapy and to evaluate end-organ damage.

Results: 55 RA patients, 76.4% female, mean age 62.8±9 yrs were examined. The median disease duration was 12 yrs. 84% were RF +, 80% ACPA + and 51% had erosions. Mean DAS 28 CRP was 2.8±1.23 and HAQ 0.54±0.6. All pts were treated with cDMARDs and/or bDMARDs (54%) and Pd mean dosage was <5 mg/day. Only 3 patients had previous CV event. 49% were hypertensive, 25% had high cholesterol, 13% diabetes and 16% were smokers: median BMI was 25. MAP monitoring revealed that 43/55 (78%) pts were hypertensive: 13 of them had unknown or not/under treated hypertension: 63% had dipper profile and only 12% were reverse dipper. We did not find increased left ventricular mass and wall thickness, but left ventricular diastolic dysfunction grade I-II was found in 26/55 pts, not related to hypertension nor to RA activity. The IMT median value was 655 mm; only in 3 pts was >900 mm: no relation with disease activity was found. In 11 pts carotid plaques were present and related with age, BMI and ambulatory mean pressure values, but not with RA activity or duration. In one patient the plaque required carotid endarterectomy. The PWV median value was >10m/s in 16 pts, all hypertensive.

Conclusions: The accurate evaluation of cardiovascular involvement of this small group of RA patients shows that hypertension is frequent and often not appropriately treated and seems to be the main cause of the increased PWV. Low grade LV diastolic dysfunction was found in half of patients, with no relation with hypertension or RA features, except for CCP presence, but the small numbers do not allow any speculation. Carotid artery involvement was present in 20% of pts, but only in 1 was clinically significant. Once again no relation with RA features was found: the small number of patients, the low disease activity and the tight and overall clinical control could be partial explanations. The clinical tight control of patients with RA is an unique opportunity to fulfill EULAR recommendations.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4127

AB0302 WORKABILITY IN PATIENTS WITH SEROPOSITIVE RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) and other rheumatic conditions can lead to work disability, and temporary or permanent exit from the labour market. The indirect costs related to work disability are higher than direct treatment costs, and pose an economic burden on patients and society. Workability in RA is influenced by many factors, including symptoms, such as pain, swelling and stiffness, muscle strength, or physical or mental exhaustion, which are components of the frailty syndrome.

Objectives: This study aimed to determine the association of workability with disease activity, pain, functional disability and frailty in patients with seropositive rheumatoid arthritis.

Methods: We conducted a monocentric cross-sectional study at a rheumatologic outpatient clinic and day hospital including 100 seropositive RA patients (according to 2010 EULAR classification) in the working age (<65 years). Workability was assessed with the self-administered Work Ability Index questionnaire. For disease activity, we used the Clinical Disease Activity Index (CDAI), a Visual analogue scale for pain assessment and functional impairments, and the Work Ability Index (WAI). The self-administered Health Assessment Questionnaire Disablement Index (HAQ-DI) and for the degree of frailty the SHARE Frailty Instrument (SHARE-FI). After testing for normal distribution, bivariate correlations between workability and associated variables were calculated using Spearman’s correlation coefficients.

Results: Of 100 patients for 58 the workability index could be assessed. The remaining 42 were either unemployed, on disability pension, or employed but currently not working. These 58 patients, 37 women and 21 men, had an average age of 64.8 years (min-max=22–59, SD=9.3) and an average disease duration of 12 months (range: 0–123 months, SD=60.9). 83% of patients reported moderate workability, 27 good workability, 16 moderate workability and 7 poor workability. The workability was weakly correlated with age (rs=−0.37, p<0.004), and moderately correlated with pain intensity (rs=0.42, p<0.001), disease activity (rs=0.40, p<0.002), functional disability (rs=0.64, p<0.000) and frailty (rs=0.632, p<0.000). The workability was not significantly related with sex and country of origin.

Conclusions: A considerable portion of employed RA patients reported poor or moderate workability, which is significantly associated with disease activity but also with other the parameters assessed. An adequate therapy may therefore not only improve well-being and state of health in RA patients but also provide socioeconomically advantage by maintaining patients’ workability.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3567

AB0303 DOES COMORBIDITY ADVERSELY IMPACT ON TREATMENT RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The burden of comorbid illness in Rheumatoid Arthritis is high. Whilst there can be coincidental existence of comorbidity, it can be attributed to the disease process itself or therapeutic agents. Recent EULAR guidelines recommend reporting, screening and prevention of six common comorbidities (cardiovascular, malignancy, infections, gastrointestinal, osteoporosis, depression). Limited research is available evaluating the impact of comorbidity on disease response following biologic treatment.

Objectives: To analyse retrospective data from the King’s College Hospital (KCH) Virtual Biologic Clinic (VBC) to assess the impact of comorbidity on disease response following treatment with biologics.

Methods: Retrospective patient note review data was collected for patients referred to the VBC from May 2013 to July 2016. The following data was recorded: age, sex, disease duration, smoking status, BMI, presence or absence of Anti CCP antibody +/- Rheumatoid factor and the six specified comorbidities. Disease Activity Score in 28 joints (DAS28) at time of referral for biologic and within 6 months of commencing treatment was also recorded in order to calculate treatment response.

The impact of comorbidity and disease variables on 6 month EULAR response were analysed using logistical regression (SPSS version 23).

Results: The database contained 150 patients. 18 patients were excluded due to no follow-up DAS28, leaving 132 for analysis. Mean age and disease duration were 58 years and 10.45 years respectively. Comorbidity was present in 70% of patients. 70% of patients achieved a EULAR moderate response (improvement of >1.2 of DAS28) and 36% of this group achieved EULAR good response (DAS28<3.2). The most prevalent comorbidities were infection, cardiovascular disease and depression.

Logistic regression analysis was run analysing EULAR moderate response against presence of comorbidity and dataset variables (age, gender, serumostatus, baseline DAS, HAQ and polypharmacy). The resulting model was not statistically significant (p=0.975).

Logistic regression analysis looking at EULAR good response against presence of comorbidity was also not statistically significant (p=0.149). Analysis looking at EULAR good response against three variables (HAQ, baseline DAS and serumostatus) was found to be statistically significant (p<0.001)

Conclusions: Comorbidities were present in the majority of patients assessed
AB0304 SERUM LEVELS OF SCLEROSTIN AND DICKKOPF-1, AND THEIR CORRELATION WITH BONE MINERAL DENSITY AND BONE MARKERS IN RHEUMATOID ARTHRITIS


Background: Sclerostin (SOST) and dickkopf-1 (DKK1) are involved in the development of primary osteoporosis. Although to date, it is controverted does exist about if serum levels of these molecules may reflect adequately a subgroup of patients with decrement of Bone Mineral Density (BMD) being useful as clinical biomarkers. Some non-conclusive observations made in postmenopausal osteoporosis have shown abnormalities in serum levels. To date, there is a lack of information about if serum molecules are associated with decrement of BMD in RA. This information is relevant for if the measurement of these serum molecules could be useful in the clinical care to identify a subgroup of patients with low BMD.

Objectives: To evaluate if serum levels of SOST and DKK1 correlate with bone mineral density and other bone markers in RA.

Methods: In this cross-sectional study, we included 115 women with RA ≥40 years old. All patients were assessed for clinical characteristic disease activity (DAS28) and functioning (HAQ-DI). BMD was measured in lumbar spine, hip and forearm using DXA. According to Pearson's results, osteoporosis was identified if the BMD in a patient had a T-score with a decrement of ≤−2.5 standard deviation (SD). According to their results we classified these patients in two groups: a) low BMD (T-score<−1SD on lumbar spine or total hip) and b) normal BMD (T-score≥−1SD). Serum SOST, DKK1, including serum Receptor Activator of NF-κB Ligand (sRANKL) and osteoprotegerin (OPG) were quantified by ELISA. We compared serum levels between the groups using Student t-tests. For comparisons between proportions we performed Chi-square test (or Fisher exact test if required). Correlation between serum levels of SOST, DKK1, with BMD, clinical variables, sRANKL, and OPG were performed using Pearson correlation tests.

Results: From the 115 women with RA, 58 patients had low BMD (50.4%), from them 44 patients (38.3%) had osteoporosis. Patients in the group with low BMD had higher age (63.8±14.9 vs 53.9±1.6, p<0.0001), DAS28 (4.1±1.5 vs 3.3±1.4, p<0.001), and HAQ-DI score (0.69±0.53 vs 0.36±0.47, p<0.001) compared with normal BMD; whereas lower serum levels of sclerostin was observed in the low BMD group (128.5±75.0 vs 178.2±103.3, p=0.004). SOST levels were correlated with BMD in hip or lumbar spine (r=0.393, p<0.0001), DAS28 (r=−0.311) and seronegativity, and low baseline DAS28 and seronegativity contribute towards good treatment response. The limitations of this study include gaps in clinical records, absence of patient reported questionnaires, and small size of database.

Disclosure of Interest: None declared

AB0305 FACTORS CONSIDERED BY RHEUMATOLOGISTS TO DECIDE TREATMENT DURING RHEUMATOID ARTHRITIS PATIENT’S FOLLOW-UP

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Background: Disease activity (DA) is the most important factor in the treatment decision during rheumatoid arthritis (RA) patient’s follow-up. In routine clinical practice, it is recommended to regularly evaluate DA and musculoskeletal ultrasound has been suggested to add value to establish the level of DA. Nevertheless, the final treatment proposal also requires considering additional factors. In a previous clinical study performed in the setting of an early arthritis clinic, we found that in 20% of the clinical scenarios evaluated, the German ultrasound score of 7 joints (GUS-7) (1) findings impacted the rheumatologist is treatment proposal; the impact was more frequent among the trainee in rheumatology (TR) than among the senior rheumatologist (SR).

Objectives: To determine and rate, which among the following factors were determinant to recommend a treatment in the same population of RA patients above described: the clinical assessment, the GUS-7, comorbidities, treatment-related adverse events, DMARDs costs/availability, patient’s preference and DMARD maximum dose. We also compared if factors differed between both physicians.

Methods: Eighty-seven consecutive and randomly selected RA outpatients were invited to participate; 2 patients denied and 85 patients underwent 170 assessments (85 each by the SR and the TR). At first, both physicians (blinded to each other) performed a clinical evaluation that included DAS28 scoring and recommended a RA-treatment. Then, patients underwent GUS-7 by a blinded (to clinical evaluations) rheumatologist. In the final step, the TR and the SR integrated the US findings to their previous evaluation and reviewed their prescription; also, both physicians recorded and rated on a standardized format which of the factors above described were determinant in the final treatment proposal. Patients signed informed consent and were instructed about the process. Only the SR met each patient’s prescription. Descriptive statistics are reported as frequencies (percentages) and 2-tailed p-values. Clinical assessment (DAS28) was rated as determinant in the majority of the clinical scenarios (100%), followed by GUS-7 in 84.7%, DMARD maximum dose in 41.2%, comorbidities in 23.5%, DMARD cost/availability in 21.2%, treatment-related adverse events in 20% and patient’s preference in 14.1% of them. The SR and the TR differed in their selection: GUS-7 and treatment-related adverse events were more frequently considered determinant for the TR (45.9% vs. 38.8%, p<0.01 and 12.9% vs. 7.1%, p=0.08), meanwhile the opposite figure was true for DMARD cost/availability (4.7% vs. 16.5%, p<0.001) and DMARDs maximum doses (17.1% vs. 24.1%, p=0.08).

Conclusions: In a real clinical setting, DA assessed by DAS28 and by musculoskeletal ultrasound were the most important factors to determine the treatment of RA outpatients; additional factors were considered and differently rated by TR and SR.


DOI: 10.1136/annrheumdis-2017-eular.1103

AB0306 CAPLAN’S SYNDROME, CADMIUM AND CHINA CLAY: COULD OCCUPATIONAL KAOLIN INHALATION ENHANCE CADMIUM EXPOSURE TO EXPLAIN THE SIXTY YEAR CONUNDRUM OF CAPLAN’S SYNDROME FIRST REPORTED IN COAL MINERS?

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Background: Caplan’s syndrome was first described in the coal miners of South Wales (UK). The specific cause for rheumatoid pulmonary nodules associated with coal dust exposure remains unknown. Coal dust exposure alone does not appear to explain Caplan’s syndrome as almost all of these men were also smokers. Cigarette smoke is the most important environmental cause of cadmium exposure. We describe Caplan’s syndrome in an ex-smoking kaolin worker associated with a significantly raised urinary cadmium level.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5652

References:

AB0307 TREATMENT DURING RHEUMATOID ARTHRITIS PATIENT’Socupation ever reported. Elevated cadmium levels of 11.2–15.9 mg/kg have been observed in kaolin.2 Fifty fold higher than those reported in coal.4 Cadmium contains variable amounts of clays and minerals such as kaolinite. Cadmium content in coal is strongly associated with levels of kaolinite contamination.4 Cadmium
nanoparticles have been observed to cause lung parenchyma inflammation and granuloma formation in an animal model.5

Conclusions: Kaolinite mineral capacity for adsorption of heavy metals, in particular cadmium, could explain the scale and pattern of Caplan’s syndrome incidence seen in Welsh coal miners and Cornish kaolin workers, and further explains the interactive risk seen in sequential dust and cigarette smoke exposure.

References:

Acknowledgements: Cornwall Arthritis Trust.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3727

AB0307 DIFFERENTIAL ASSOCIATION OF AGE AND DISEASE ACTIVITY WITH CAROTID INTIMA-MEDIA THICKNESS IN MEN AND WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory condition and is characterized by an increased risk in cardiovascular (CV) disease. Carotid intima-media thickness (cIMT) is a surrogate marker of CV disease and many studies have evaluated the relationship between cIMT and RA disease activity with contradictory results.

Objectives: To evaluate in RA patients the association between both cIMT and carotid plaque presence and clinical RA features and analytical measurements.

Methods: We selected 214 RA patients according to the American College of Rheumatology criteria. Conventional clinical evaluation and analytical measurements were performed, including a standard lipid profile. We used My Lab 50 X-Vision sonograph to measure cIMT and atherosclerotic plaque presence.

Results: No differences between men and women regarding age, body mass index, glycemia, LDL-C and TG were observed. However, men had a significantly higher waist circumference, systolic and diastolic BP and lower levels of HDLC. On the other hand, women had significantly higher values of DAS28 (3.7 vs 2.99), HAQ, and VSG with no differences in other inflammatory variables (rheumatoid factor, ACPR, CRP or fibrinogen). Moreover, 74% of patients had pathological cIMT without gender differences and 43% had plaque presence in the carotid artery with a significant higher percentage in men (57%) than women (36%). Overall, men had significantly higher cIMT (0.678 vs 0.627 mm) but when disease activity (DAS28) was considered, we observed that such difference was due to patients that were in remission or in low activity. Men and women with moderate and high disease activity had no statistical differences in cIMT. Furthermore, across women cIMT was significantly higher in those with high disease activity compared to women with remission. This effect was not observed in men. Multivariate linear regression with cIMT showed a significant interaction between age and gender, so that the effect of age on cIMT was significantly more pronounced in men than in women.

Conclusions: We have described that in our RA cohort, disease activity measured with DAS28 and age are differentially associated with cIMT in men and women. Our results could explain the contradictory results published in the literature and it can be justified by a higher incidence of RA in women and by the hormonal-genetic status.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3727

AB0308 DISEASE ACTIVITY, GRIP STRENGTHS AND HAND DEXTERITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting hand joints, and leading impairment in hand functions. To date many studies have evaluated the disease activity of patients with RA, but little attention has been carried out to assess hand functions, and dexterity (1–2).

Objectives: The purpose of this study was to determine the clinical relevance of the Quick Disabilities of Arm, Shoulder and Hand (QuickDASH), hand dexterity with the Purdue Pegboard Test (PPT), and grip and pinch strengths of RA patients.

Methods: Eighty-two women with a diagnosis of RA according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criterion were recruited to the study. The disease activity scores were determined by using Disease activity score-28 (DAS-28). Grip strengths were measured with a Jamar dynamometer, and pinch strengths were measured by the Purdue Pegboard Test (PPT). Multivariate linear regression with the PPT, and functional outcomes were assessed with the QuickDASH questionnaire.

Results: The mean age of the study group was 49.27±10.69 years. Average values of DAS-28, the QuickDASH values were found to be 4.22±1.28, 38.33±18.76, respectively. High correlation was observed between DAS-28 and the QuickDASH values (p<0.001). The mean grip strengths were significantly correlated with the QuickDASH and DAS-28 values (p<0.01) (Table 1). The mean lateral pinch strengths were correlated significantly with DAS-28 and the QuickDASH scores (p<0.001). DAS-28 was correlated with PPT performance just in women with remission hand (p<0.05). The QuickDASH values were not correlated with all PPT performances (p<0.05). Grip strengths were positively correlated with the PPT performances (p<0.05).

Table 1. Showing the correlation coefficients of DAS 28 and QuickDASH scores between other parameters

<table>
<thead>
<tr>
<th>Correlation coefficients (r)</th>
<th>DAS 28</th>
<th>QuickDASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grip strength (dominant hand)</td>
<td>-0.412***</td>
<td>-0.409***</td>
</tr>
<tr>
<td>Grip strength (nondominant hand)</td>
<td>-0.329***</td>
<td>-0.494***</td>
</tr>
<tr>
<td>Lateral pinch strength (dominant hand)</td>
<td>-0.320***</td>
<td>-0.327***</td>
</tr>
<tr>
<td>Lateral pinch strength (nondominant hand)</td>
<td>-0.276*</td>
<td>-0.310**</td>
</tr>
<tr>
<td>Palmar pinch strength (dominant hand)</td>
<td>-0.215</td>
<td>-0.15</td>
</tr>
<tr>
<td>Palmar pinch strength (nondominant hand)</td>
<td>0.190</td>
<td>0.165</td>
</tr>
<tr>
<td>Tip pinch strength (dominant hand)</td>
<td>-0.248*</td>
<td>-0.237*</td>
</tr>
<tr>
<td>Tip pinch strength (nondominant hand)</td>
<td>-0.257*</td>
<td>-0.237*</td>
</tr>
<tr>
<td>Dexterity (dominant hand)</td>
<td>-0.277*</td>
<td>-0.303</td>
</tr>
<tr>
<td>Dexterity (nondominant hand)</td>
<td>-0.128</td>
<td>-0.098</td>
</tr>
<tr>
<td>Dexterity (both hands)</td>
<td>0.004</td>
<td>0.059</td>
</tr>
<tr>
<td>Dexterity (PPT assembly)</td>
<td>-0.084</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Spearmann correlation analysis used for all parameters. *p<0.05, **p<0.01, ***p<0.001.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3541

AB0309 LIPID-LOWERING INTERVENTION OF A PREVENTIVE CARDIO-RHEUMA CLINIC IN MEXICAN MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have a significantly increased risk for cardiovascular (CV) morbidity and mortality when compared to general population (1). Preventive cardio-rheuma clinics have been created in recent years and proven to be effective to manage CV risk in patients with inflammatory joint diseases around the world (2).

Objectives: To evaluate the need for lipid-lowering intervention in Mexican mestizo patients with RA.

Methods: We initiated a preventive cardio-rheuma clinic for appropriate CV disease prevention in patients with RA in our population. A complete evaluation and CV risk stratification was performed to our patients, including blood tests and ultrasound examination of both carotid arteries. Each patient was classified to lifestyle changes only, a lifestyle improvement plus lipid-lowering treatment, or to have a low risk with no need for intervention, in accordance to the 2012 European Guidelines on cardiovascular disease prevention in clinical practice and the 2016 ESC/EAS Guidelines for the Management of Dyslipidemias.

Results: A total of 100 patients were evaluated, patient characteristics and intervention group distribution are shown in Table 1. Among these patients, 49 were found not to need any intervention. The remaining 51 were classified into lifestyle change (n=18, 35.3%) or lipid-lowering drug regimens (n=33, 64.7%). A significant difference between intervention groups was only found regarding age (p<0.001). A multiple regression analysis was performed to predict the kind of intervention needed from age, disease duration, disease...
activity and autoantibody levels, only age added statistically significantly to the prediction.

Conclusions: There was indication for preventive intervention in more than half of our patients. Age is a determinant factor that increases CV risk in RA patients independently from disease-specific factors. Treatment to lipid targets is essential to reduce their risk of CV morbidity and mortality (3). A prospective study evaluating treatment success rate is needed to further evaluate the intervention of the clinic.

References:

Disclosure of Interest: None declared


AB0310 PREVALENCE OF COMORBIDITIES OF RHEUMATOID ARTHRITIS IN A MEXICAN MESTIZO POPULATION

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of developing comorbid conditions which are associated to increased mortality, hospital admissions, higher costs of care and inability to work (1, 2).

Objectives: To evaluate the prevalence of comorbidities in a Mexican mestizo population of RA patients.

Methods: We performed a cross-sectional study in which RA patients who were admitted to our outpatient clinic between August 2014 and December 2016 were consecutively enrolled. We collected data regarding demographics, disease characteristics (activity, severity, treatment), comorbidities (cardiovascular, infections, cancer, and osteoporosis), and performed blood tests at the time of the patient’s visit to the clinic.

Results: We analyzed 225 patients. Their characteristics are shown in Table 1. Age, 55.7±8.3 years (mean ± SD); disease duration, 9.5 (4 – 15.5) (median (IQR)); female gender, 93.7%; Disease Activity Score using 28 joints – C-reactive protein (DAS28-CRP), 3 (2 – 4) (median (IQR)); past or current use of any other conventional disease modifying anti-rheumatic agents.

Conclusions: This study confirms the high prevalence of comorbidities in RA patients. Among our cohort, 63.5% had at least one comorbidity, being those associated with cardiovascular disease the most common. With a systematic assessment (3) including a thorough physical examination, vital signs and laboratory tests, it is possible to detect comorbid conditions that would otherwise remain unrecognized.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1523

AB0311 RESULTS OF SCREENING FOR TUBERCULOSIS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE AND ON TREATMENT WITH BIOLOGICAL DMARDS

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Background: The prevalence of tuberculosis infection in Russia is much higher than in Western Europe. Therefore, screening for TB infection in patients with RA before therapy with biological agents is of particular importance. At the same time, reliable information on the results of screening are very few.

Objectives: Explore the results of the application of different methods of diagnosis of tuberculosis infection in RA patients before and during treatment with biological agents.

Methods: We used the data from the Russian register “Observational REgister of arthritis in Clinical practice” (OREL). 1471 RA patients were screened for TB infection before prescribing biologics, of whom 829 patients were exposed to TB infection monitoring on therapy by biologics. The group included 21.1% men, 78.9% women; at the time of initial screening age was 50.0±5.4 years, the duration of the disease 8,5±3.8 yrs, 68.3% RF +, 85.1% anti-CCP +, DAS28-ESR 5.7±7.1, 95.7% used synthetic DMARDs, 60.1% used systemic steroids.

We used PPD ( Mantoux) test, Diaskin test (intradermal test with tuberculosis antigens CFP10-ES38) and QuantiFeron-TB Gold (QFT) test (in some patients), chest X-ray, chest CT scan (if needed), all the patients were consulted by phthisiatrician. PPD and Diaskin test results were considered positive if the papule was ≥ 5 mm. Duration of treatment with biologics (anti-TNFs and others) varied widely (2–154 months), making a total of 2552 patient-years.

Results: At screening, we got 40.3% positive results of PPD test (significantly more in younger patients and patients who did not receive steroids), 16.5% positive results of Diaskin test (with no significant correlations with age and steroids). Positive results matched in 19.9% of cases, negative - in 51.9%. Discordant results in 217 patients were in 92.2% cases related to negative results of Diaskin in PPD-positive persons. Active TB was found after additional examination in 3 (0.2%) patients, inactive TB-related changes were revealed in 124 (8.8%) patients. Positive PPD and Diaskin results, but not QFT, correlated with signs of inactive TB lesions. Positive results of PPD and QFT tests matched in 36.5% of cases, negative - in 18.7%. Diaskin and QFT – in 33.6% and 41.1% of cases resp. As a result of screening, 224 pts were treated by isoniazid or combination of anti-TB drugs before initiation of biologics. On treatment with biologics, 114 (13.7%) pts became PPD-positive and 56 (6.8%) Diaskin positive, active TB was diagnosed in 8 (0.97%) pts.

Conclusions: In carrying out TB screening before prescribing biologics in high-
risk population of TB infection it is reasonable to use both PPD and Diaskin tests, and repeat them every 6 months on treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6988

U83 SCORING SYSTEMS FOLLOW-UP 48 WEEKS TNF-A ANTAGONISTS PLUS MTX TREATMENT FOR HIGH DISEASE ACTIVITY REFRACTORY RHEUMATOID ARTHRITIS

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Background: US7 score is the ultrasound scoring system for rheumatic ailments (RA). This scoring system has shown good evidence so far. Several reports accessed its inter-rater, intra-rater agreement, its specificity, sensitivity and practical possibility compared to more complex scoring systems such as 72-joints scoring systems, which showed it is an convenient tool for clinical use. Our goal is to explore U83 to investigate the ultrasonic changes during biological agents plus MTX treatment in high disease activity refractory RA patients in Yellow people.

Methods: All cases were diagnosed as RA fulfilling 2009 ACR/EULAR classification criteria and evaluated as high disease activity for DAS28≤5.1 with MTX+HCO=SSAP or MTX+LEF invalid therapy for more than 3 months before baseline. Biological TNF-a antagonist or IL-6 antagonist plus with MTX 10mg qw were then given and ultrasound was performed by 2 observers blinded to physical examination and blood test results at 0, 12, 24, 48 weeks. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w.

Results: 1) 26 subjects were enrolled in the program up to now. 22 were given TNF-a antagonists and 4 were given IL-6 antagonists. 17 finished 24 weeks follow-up. 1 withdrew for TB infection at 12 week and 1 withdrew for fungi pneumonia at 8 weeks. Mean age of 17 was 44.3±11.8 years old, female-male ratio was 15:2, and disease duration was 71 months. All were RF and ACPA positive.

Conclusions: Only 42.8% of the sample had all CV risk factors requested and registered in the clinical record, so should promote improvement in the health team to increase this. The average 10-year CV risk in all people with RA was 12.42%, and in patients who met the criteria to be multiplied by the factor 1.5 increased to 13.03%, which means that these patients should be reported this and followed up. In addition, the questionnaire regarding obesity and cholesterol levels. Despite population receiving biologics are younger, they had lower CV risk. We need more research to confirm this results

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4645

HIGH INFLAMMATORY ACTIVITY AS A PREDICTOR OF INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) have a high risk of cardiovascular (CV) morbidity and mortality. Arterial stiffness (AS) is a known predictor of CVD. Relationships between inflammation and arterial stiffness in patients with RA are not well understood.

Objectives: The aim of the study was to evaluate parameters of AS and their associations with inflammatory activity in patients with RA.

Methods: 62 patients with RA (EULAR 2010) without known CV events were examined (73% females, age 58.5±15.4 (M±SD) years, 13% smokers, 61% with AH, 34% with dyslipidemia). Median duration of RA is 8 years (IQR 3–17). Seropositive RA was found in 69% of patients compared with 58% in our controls. Mean CIMT 0.7±0.2 mm), p<0.05, except 0w:4w, sig<0.05), synovitis Power Doppler scores (0w:4w:12w:24w = 8.5±4.9:3.8:2.7, all sig<0.05, except 4w:12w:24w, 12w:23w, sig=0.361,0.227,0.235), tenosynovitis grey scale scores (0w:4w:12w:24w = 0.63±0.25:0.25:0.07, all sig<0.05, except 4w:12w:24w:12w, 4w:24w, 12w:24w, sig= 1.0, 0.26, 0.26), tenosynovitis Power Doppler scores (0w:4w:12w:24w = 1.00±0.19:0.00 all sig<0.05, except 4w:12w:24w:12w, 4w:24w, 12w:24w, sig< 0.18, 0.18, 1.0), bone erosion scores (0w:4w:12w:24w = 1.2±0.1:0:94:0.53, all sig<0.05 except 0w:4w:12w:4w:24w, 12w:24w, sig< 0.083, 0.317, 0.102, 0.102). The above data showed the scores found biological agents improved thoroughly the whole course as Dass8 did. Synovitis seemed to be eliminated faster than tenosynovitis and the repair of bone erosion was the latest event compared to decreased synovitis and tenosynovitis.

Conclusions: It is recommended U83 used in clinic for US7 scoring system could reflect more excessively than Dass8 in more refined aspects including the changes of tendon, joint, bone at different phases during biological agent treatment for RA. However, more samples and those with positive and negative anti-cyclic citrullinated peptide (anti-CCP)

Methods: We conducted an observational descriptive study of patients who attended a specialized rheumatology clinic in Bogotá, Colombia from 2010 to 2015. Patients with RA were enrolled who had completed at least 5 years of follow-up. The information required to estimate CVD risk was obtained from medical records. Other variables included were biological therapy and test result of anti-CCP. For the calculation of CVD risk, the Framingham estimator was used and adjusted for the Colombian population. Additionally, patients who had 2 or more of these criteria: More than 10 years of evolution of RA, positive rheumatoid factor and/or extra-articular compromise, the risk was adjusted by multiplying by 1.5. Nonparametric statistics (Mann-Whitney U test) was used.

Results: We identified 273 eligible patients with RA with mean age 61, 66% women. Only 117 (42.8%) had recorded in their charts all variables to calculate CVD risk. We found that 32% had high blood pressure, 7% type II DM, 11% Obesity and 13% smoking. The population evaluated, 10-year CVD risk median was 12.42% and for Colombia was 8.69%, adjusting this risk according to the disease in Colombia, increased to 13.03%. When we compare the 10-year CVD risk in anti-CCP positive patients (median: 11.15) and anti-CCP negative (median: 12.42) we found not find differences. However, we found differences in the 10-year CVD risk median 9.04 vs. 23.25, 10-year CVD risk adjusted to Colombia median 6.32 vs. 16.31 and 10-year CVD risk adjusted to Colombia and RA median 6.81 vs. 13.39 between patients using biological therapy versus patients without receiving respectively (p<0.001).

Conclusions: Only 42.8% of the sample had all CV risk factors requested and registered in the clinical record, so should promote improvement in the health team to increase this. The average 10-year CVD risk in all people with RA was 12.42%, and in patients who met the criteria to be multiplied by the factor 1.5 increased to 13.03%, which means that these patients should be reported this and followed up. In addition, the questionnaire regarding obesity and cholesterol levels. Despite population receiving biologics are younger, they had lower CV risk. We need more research to confirm this results

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2640

CARDIOVASCULAR RISK, BIOLOGICS AND ANTI-CYC KLITULATED PEPTIDE POSITIVITY IN RHEUMATOID ARTHRITIS

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Background: Co-factors and traditional cardiovascular disease (CVD) risk factors contribute to atherosclerosis in rheumatoid arthritis (RA). Several records since 1984 have reported an increase of 4 to 5 times the CVD risk and mortality in RA patients. Physicians who evaluate these patients forget to perform or record this assessments in medical records. Since 1948, the Framingham Heart Study became an ambitious project in health research, to identify the general causes of this assessments in medical records. Since 1948, the Framingham Heart Study became an ambitious project in health research, to identify the general causes of...
Objectives: To describe hospital admissions and contributing factors in patients with rheumatoid arthritis (RA) treated biological DMARD (b-DMARD) and conventional synthetic DMARD (cs-DMAR).

Methods: We systematically searched literature (via Pubmed, Cochrane and abstracts from recent ACR and EULAR congresses) up to March 2016 for observational studies providing data concerning the presence of a traditional cardiovascular risk factor. For each cardiovascular risk factor, results were described with the relative risk (RR) and 95% confidence interval (CI) and with p-value. The RR were calculated for both RA patients and for patients with RA in the control group. A random effect model was used to pool the results.

Results: Out of 5714 screened references, 13 studies were included. Due to lack of data, atherosclerosis studies could not be included in this meta-analysis. For hypertension and diabetes, an increased risk was observed: RR =1.35 [95% CI 1.27–1.45], p<0.0001 and RR=1.11 [1.04–1.19], p=0.001, respectively. On the contrary, hypertension was not associated with dyslipidemia (RR=0.93 [0.77–1.2], p=0.63) and diabetes with dyslipidemia (RR=0.93 [0.92–0.94], p=0.0003).

Conclusions: This meta-analysis highlights a moderate excess risk of hypertension and diabetes among patients with RA relative to the general population. A comprehensive identification of cardiovascular risk profile of RA is an opportunity to improve health management of these patients. Future research is crucial in order to establish to what extent the control of modifiable risk factors can improve cardiovascular outcome of these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5432

**AB0316**

HOSPITAL ADMISSIONS OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH DMARD

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Objectives: To describe hospital admissions and contributing factors in patients with rheumatoid arthritis (RA) treated biological DMARD (b-DMAR) and conventional synthetic DMARD (cs-DMAR).

Methods: Retrospective observational study of RA patients admitted to the hospital for any cause from 2010 to 2015. Demographic, clinical and therapeutic characteristics were collected from the medical charts. Multivariate and univariate models were used to identify variables associated with admissions for any cause, major adverse cardiovascular events (MACE), and infection. The statistical program Stata 14.0 was used for the analysis.

Results: In the period 2010–2015, 26% of all RA patients were treated with b-DMARD. There were a total of 1251 hospital admissions for any cause in 600 patients; 1055 admissions in 477 patients treated with cs-DMAR and 196 admissions in 123 patients treated with b-DMARD. Of the 1251 admissions, 251 were due to infections and 60 to MACE. Demographic, clinical and therapeutic characteristics were collected from the medical charts. Multivariate and univariate models were used to identify variables associated with admissions for any cause, major adverse cardiovascular events (MACE), and infection.

Conclusions: infections and MACE are a significant cause of hospital admission in patients with rheumatoid arthritis. Comorbidities as diabetes, hypertension and dyslipidaemia but not b-DMARD are significantly associated with admission for infection or MACE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6769

**AB0315**

THE POTENTIAL ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND TRADITIONAL CARDIOVASCULAR RISK FACTORS: A META-ANALYSIS OF CONTROLLED STUDIES

E. Fitoh, C. Gaujoux-Viala, B. Combe, J. Morel, C. Hua, A. Nutz, C. Lukas, F. Fräsière, Lapeyronie Hospital, Montpellier, Nîmes Hospital, Nîmes, France

Background: Systemic inflammation is the cornerstone of both rheumatoid arthritis (RA) and atherosclerosis. RA is currently considered as a cardiovascular risk factor.

Objectives: The aim of this systematic review was to assess the association between RA and the traditional cardiovascular risk factors (hypertension, dyslipidemia, diabetes mellitus, and atherosclerosis) in RA patients in comparison to the general population.

Methods: We systematically searched literature (via Pubmed, Cochrane and abstracts from recent ACR and EULAR congresses) up to March 2016 for observational studies providing data concerning the presence of a traditional cardiovascular risk factor (among hypertension, dyslipidemia, diabetes mellitus, atherosclerosis) in patients with RA and in a control group. A meta-analysis of the relative risk (RR) concerning patients with RA in relation to the control group was performed for each cardiovascular risk factor.

Results: Out of 5714 screened references, 13 studies were included. Due to lack of data, atherosclerosis studies could not be included in this meta-analysis. For hypertension and diabetes, an increased risk was observed: RR =1.15 [95% CI 1.07–1.24], p=0.0003 and RR=1.11 [1.04–1.19], p=0.001, respectively. On the contrary, not any association was found with the dyslipidemia (RR=0.93 [0.77–1.2], p=0.43).

Conclusions: This meta-analysis highlights a moderate excess risk of hypertension and diabetes among patients with RA relative to the general population. A comprehensive identification of cardiovascular risk profile of RA is an opportunity to improve health management of these patients. Future research is crucial in order to establish to what extent the control of modifiable risk factors can improve cardiovascular outcome of these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5432
RHEUMATOID ARTHRITIS IN BRAZIL – THE “REAL “ STUDY:
COMORBIDITIES IN ECUADORIAN PATIENTS WITH
1, A.B. Vargas-Santos1, C. Albuquerque2, R. Amorim 1,
progress. Ninety-four (41.4%) obstetricians participated in
this survey. They had 22±6.16 years of practice. Thirty-nine
(90.7%) rheumatologists participated in this survey. They
had 26±12.8 years of practice. Figure 1 displays the
percentage of physicians who consider the selected RD medications detrimental
to/not compatible with fertility, pregnancy and breastfeeding.
Average score in accordance with EULAR/BSR guidelines was
0.65±0.154 and results were significantly different between specialties (p<0.001):
rheumatologists scored between 0.41 and 1, with an average of 0.777±0.152
and obstetricians scored between 0.36 and 1 with an average of 0.603±0.124.
Multivariable analysis showed that the scores reflecting adherence to recommen-
dations were significantly associated with type of specialty (rheumatology vs obstetrics) and number of pregnant patients with RD seen per month.

Conclusions: Advices given to RD patients who plan on becoming pregnant in
Lebanon vary largely, especially among the physicians’ specialty and experience in
RD, which highlights the urgency of disseminating the EULAR/BSR guidelines
among rheumatologists and obstetricians alike.

References:

Acknowledgements: Sponsor: Newbridge Pharmaceuticals. MW support: KBP-
Biomar.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3430

AB0318 CLINICAL AND SEROLOGIC CHARACTERISTICS OF A COHORT OF ECUADORIAN MEN WITH RHEUMATOID ARTHRITIS
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Guayaquil; 3Universidad Católica Santiago de
Guayaquil; 4Universidad Espíritu Santo; 5Centro de Reumatología y
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Background: Rheumatoid arthritis (RA) is an inflammatory and disabling disease whose expression and clinical course is influenced by gender. In developed countries the prevalence of RA is 0.5–1%, with a ratio 3:1 female:male.

Comparative gender studies have shown that women have greater functional
disability, disease activity and pain than men1.

Objectives: The purpose of this study is to describe and compare the clinical and serological characteristics of a cohort of men with RA.

Methods: A cross-sectional study was conducted in patients with established RA in 2013 in 2 hospitals (Vernaza Hospital and a private rheumatology center (CERER). The data included demographics, comorbidities, habits, treatments, laboratory exams, number of swollen and tender joints, Visual Analog Scale (VAS), activity and disability index (DAS28 and HAQ-DI) and PHQ-9 for depression. The statistical program SPSS V. 22 was used to analyze the data and calculate frequencies, percentages, means, ranges, Spearman correlation and ANOVA coefficient. Statistical significance used was 0.05, with a 95% reliability.

Results: 402 patients with a mean age of 50 years were included, 67.8% (353) women and 12.2% (49) men. 93.8% (377) were mestizos, 3.5% (14) White, 1.5% (6) indigenous and 1.2% (5) Afro-Ecuadoreans. As for comorbidities, 55.5% (223) were married, 15.4% (62) cohabiting, 12.4% (50) divorced, 8.5% (34) singles and 8.2% (33) widowers. 9.7% (39) of the patients smoked, 7.5% (30) ingested alcohol and 0.5% (2) drugs. The average age of onset of the disease was 41 years, with a median time from onset of symptoms and the first rheumatology visit of 28.7 months, median follow-up time of 51.8 months and average disease duration of 11 years. For comorbidities, 54.8% (147/269) had dyslipidemia, 28.4% (114) gastric ulcer, 23.6% (95) hypertension, 20.1% (81) obesity, 19.6% (79) depression, 15.2% (61) thyroid disease, 12.4% (50) of the sexual involvement, 10.7% (43) allergies, 10.4% (32/307) hypertransaminasemia, 9.3% (21/225) anemia, and 6.7% (27) diabetes mellitus. 32.3% (114) of women had at least one abortion. The PHQ-9 medium was 5.3; according to this 11.2% (45) corresponded to mild depression, 4.5% (18) moderate depression, 3.2% (13) moderately severe depression and 0.7% (3) severe depression. As for the other indicators of disease activity, the average for the number of painful joints was 5 (0–28), swollen joints 4 (0–26), patient VAS 3.9 (0–10) and doctor VAS 3.4 (0–10). In laboratory data, 67.4% (215/319) had positive ESR, 64.8% (149/230) C-reactive protein, 90.5% (182/201) anti CCP positive, and 94.4% (286/307) RF.

Conclusions: This is the first study of comorbidities in patients with RA in Ecuador. Patients with RA have a high prevalence of comorbidities and risk factors, which is why physicians should be prepared to prevent them and offer an early treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1408

AB0320 RHEUMATOID ARTHRITIS IN BRAZIL – THE “REAL” STUDY: A NATIONWIDE PROSPECTIVE STUDY

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Background: Early diagnosis and immediate treatment are critical in achieving optimal outcomes in rheumatoid arthritis (RA). However, anecdotal evidence suggests that in Brazil there is still a significant delay in patient referral, RA diagnosis and DMDAR initiation. The lack of national data hinders effective advocacy for proper public health policies, which led the RA commission of the Brazilian Society of Rheumatology to create a nationally-representative multicenter RA cohort to provide the necessary data.

Objectives: To describe the development process and baseline characteristics of a large, nationally-representative multicenter cohort of RA patients in Brazil.
Methods: Twelve public rheumatology centers from all of the 5 regions of Brazil enrolled ~100 consecutive RA patients each (1987 ARA or 2010 ACR-EULAR). This cohort is being followed prospectively for 1 year, with systematic data collection at time 0, 6±1 months and 12±1 months, and registration of all other visits during this 1-year period. Data collection began in 08–2015, using a single online electronic medical record, and included demographic, socioeconomic, clinical, laboratory, radiographic and therapeutic characteristics, along with functional status, quality of life and adherence to treatment information.

Results: 1125 patients were enrolled (Table). -90% were female, with a mean age of 56 years and median disease duration of 13 years. Median BMI was 27 kg/m², with 64% of the patients classified as overweight or obese. The interval between symptoms and diagnosis varied from 1 to 457 months (median 12 months). Almost half of the patients were on glucocorticoids, 96% on DMARDs, with 36% on biologics. Only 7% were seronegative for both rheumatoid factor and ACPA. Median HAO-DI was 0.075 and median DAS28-ESR was 3.5, with 58.6% of patients presenting moderate or high disease activity.

Table 1. Patient baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Median (IQR)</th>
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<tbody>
<tr>
<td>Age, years</td>
<td>1125</td>
<td>56.7 (22.1–88.8)</td>
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<tr>
<td>Female</td>
<td>1125</td>
<td>89.5%</td>
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<tr>
<td>Current or former smoker</td>
<td>1125</td>
<td>39.6%</td>
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<tr>
<td>BMI, kg/m²</td>
<td>1065</td>
<td>26.6 (15.9–56.2)</td>
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<tr>
<td>Disease duration, years</td>
<td>1124</td>
<td>12.7 (5.7–56.7)</td>
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<tr>
<td>Rheumatoid factor</td>
<td>1105</td>
<td>78.7%</td>
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<tr>
<td>ACPA</td>
<td>479</td>
<td>76.8%</td>
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<tr>
<td>Erythrocyte sedimentation rate (ESR), mm/1st hour*</td>
<td>933</td>
<td>21 (1–140)</td>
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<tr>
<td>Glucocorticoids</td>
<td>1125</td>
<td>47.0%</td>
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<td>NSAIDs</td>
<td>1125</td>
<td>9.0%</td>
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<tr>
<td>Synthetic DMARDs</td>
<td>1125</td>
<td>90.8%</td>
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<tr>
<td>Metformin</td>
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<td>66.5%</td>
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<tr>
<td>Biologic DMARDs</td>
<td>1125</td>
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<td>Erythrocyte sedimentation rate (ESR), mm/1st hour*</td>
<td>933</td>
<td>21 (1–140)</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>1125</td>
<td>47.0%</td>
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<tr>
<td>NSAIDs</td>
<td>1125</td>
<td>9.0%</td>
</tr>
<tr>
<td>Synthetic DMARDs</td>
<td>1125</td>
<td>90.8%</td>
</tr>
<tr>
<td>Metformin</td>
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<td>66.5%</td>
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<tr>
<td>Biologic DMARDs</td>
<td>1125</td>
<td>36.1%</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (ESR), mm/1st hour*</td>
<td>933</td>
<td>21 (1–140)</td>
</tr>
</tbody>
</table>

Conclusions: The delay in diagnosis may explain the high percentage of patients with moderate or high disease activity and erosive disease. The low level of physical dysfunction observed in this established, predominantly seropositive RA population may be explained by the large proportion of patients on glucocorticoid and biologic therapy. Our findings suggest that, despite current treatment concepts being well known and accepted by Brazilian rheumatologists, there is still a gap in early diagnosis and management of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1740

AB0321 RELATIONSHIP OF CAROTID FEMORAL PULSE WAVE VELOCITY WITH AGE AND TIME OF EVOLUTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Early vascular aging occurring in Rheumatoid Arthritis (RA) may be a consequence of chronic inflammation. The measurement of Carotid-femoral pulse wave velocity (cfPWV) is the gold standard to evaluate arterial stiffness. Early vascular aging occurring in Rheumatoid Arthritis (RA) may

Objectives: The aim of this study was to evaluate variations in the Carotid-Femoral Pulse Wave Velocity (cfPWV) and its association to age and time of disease evolution in patients with rheumatoid arthritis.

Methods: RA patients were matched for age and sex with healthy controls. Subjects with a history of smoking, cardiovascular disease, hypertension, diabetes mellitus, cancer, liver disease, thyroid disease and kidney disease were excluded. The cfPWV was calculated using the PulsePen® (Diatrace, Italy) device.

Results: We included 76 women with RA and 28 healthy women, mean age (44.3±10.92 vs. 43.0±16.26, P=0.654). cfPWV demonstrated good correlation with age (r=0.459, P<0.01), disease evolution time (r=0.311, P<0.008), triglycerides (r=0.289, P=0.03), total cholesterol (r=0.421, P<0.001) and atherogenic index (r=-0.320, P=0.02). No association with disease activity was found. cfPWV was higher in those patients with RA >10 years evolution compared to patients with <10 years of disease evolution and to controls (P<0.05).

Conclusions: A significant association between cfPWV was seen in patients with RA, and was also correlated to age and to a disease evolution >10 years long without finding a significant association with increased disease activity.

References:
was significantly higher compared to patients in GCPT group – 7 (10.3%) and 6 (8.8%) respectively (p < 0.038 and p < 0.049). Baseline C-peptide was elevated in patients who developed IGT after a course of GCPT (850 pmol/l before GCPT, 4099 pmol/l 4–6 hours after GCPT and 1904 pmol/l after a 3-days course of GCPT) or DM (1050 pmol/l, 3170 pmol/l and 1796 pmol/l before GCPT, at peak blood glucose level and after a 3-days course of GCPT, respectively) (p < 0.05). C-peptide remained normal in the absence of CMD and in IGT patients. Baseline HOME-IR index was elevated in patients with IGT (4.52, 17.47, 9.67 before GCPT, at peak blood glucose level and after a 3-days course of GCPT, respectively) and DM (5.04, 15.2, 10.4 respectively) (p < 0.05), and normal in patients without CMD (2.5, 5.84 and 4.01 respectively) and patients with impaired fasting glucose (IFG) (2.46, 7.08 and 5.46).

HOME-iel anti index analysis revealed that in the absence of CMD and at earlier stages of CMDs (IFG, IGT) insulin resistance is compensated via an increase of β-cell secretory activity, which is associated with a significant decrease of HOME-iel index to 64.6 at peak blood glucose levels after GCPT compared to baseline level (170) (< 0.05). C-peptide, HOME-IR and HOME-iel index levels in OGCT patients demonstrated same trend as in GCPT patients. Significant differences were observed in patients with IGT and DM before and after oral glucose tolerance test (OGTT) on C-peptide (1042 pmol/l vs. 1978 pmol/l in IGT; 1306 pmol/l vs. 2286 pmol/l in DM) and HOME-IR (4.53 vs. 9.81 in IGT; 5.6 vs. 11.27 in DM patients), whereas in patients without CMD and in patients with IFG, C-peptide before OGTT was 489 pmol/l vs. 742 pmol/l, after - 1295 pmol/l vs. 1488 pmol/l, HOME-IR was 3.9 vs. 2.88 before OGTT and 2.88 vs. 5.85 after the test in the absence of CMD and in IFG patients, respectively. A significant decrease of β-cell function was observed in DM patients, reflected by a decrease of HOME-iel after OGTT compared to baseline (147 vs. 78.4).

Conclusions: C-peptide in IGT and DM in patients with increased IR both during GCPT and long-term OGCT. Long-term OGCT is associated with more CMDs compared to GCPT.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5748

AB0324 IS LOW SERUM VITAMIN D LEVEL ASSOCIATED WITH INCREASED NEUROPATHIC PAIN IN RHEUMATOID ARTHRITIS PATIENTS? A CROSS-SECTIONAL STUDY


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Background: Rheumatoid arthritis (RA) is a systemic, autoimmune, progressive condition characterised by progressive synovitis with resultant joint destruction, functional disability and significant pain. Recent experimental data indicates that there may be a neuropathic component of pain perception in RA.

Objectives: The aim of this study was to examine the development of neuropathic pain (NP) in patients with RA and its relationship with vitamin D.

Methods: We used the Leeds assessment of neuropathic symptoms and signs (LASNSS) questionnaire to evaluate NP in 93 patients with RA. Clinical parameters included general demographics, and disease activity scores were evaluated. The patients also completed Short form-36 survey, and Health Assessment Questionnaire.

Results: Of all the patients who were eligible for the study, 75 were female (80.6%). Mean serum vitamin D level of the participants was calculated to be 22.8±11.9 ng/ml. According to the LANSS questionnaire 31 patients (33.3%) were classified as having NP. There was a negative correlation between vitamin D levels and LANSS value (p<0.001). We have determined that vitamin D serum levels below 20 ng/ml have significantly higher NP positivity rate (p<0.012), besides they have 5.8 times more risk of developing NP when compared to patients with vitamin D serum levels ≥30 ng/ml.

Conclusions: We conclude that Vitamin D deficiency is prevalent in RA patients with NP. However, it is the right diagnosis, Vitamin D deficiency treatment is relatively easy, safe, inexpensive and with satisfactory outcomes; therefore, an underlying vitamin D deficiency should be explored in the etiology of NP in patients with RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4395

AB0325 TREAT TO TARGET AND THE REAL LIFE EXPERIENCE – DATA FROM A COHORT OF RHEUMATOID ARTHRITIS PATIENTS IN SOUTH EAST ROMANIA (CONSTANTA COUNTY)

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Background: Treatment target in rheumatoid arthritis (RA) is remission or low disease activity. Considering that there is no quantitative “gold standard” for measuring disease activity, monitoring and evaluation of RA patients is made through composite scores, which have an important subjective component. Moreover, the laboratory investigations used (ESR and CRP) are commonly discordant with the clinical findings.

Objective: To evaluate patient disease activity and establish relations between disease activity scores and their components in RA patients.

Methods: We performed a transversal study which included 447 RA patients (aged 18 to 86-years-old) admitted to our Rheumatology Department between January 2014 and December 2015. Patients’ evaluation was performed by the rheumatologist. All the data obtained from the medical history, clinical examination, laboratory tests and imaging studies was recorded at the same date. All patients signed a dated informed consent at the time of admission.

Results: The study included 447 patients, mean age 62.13±11.44, 85% women, accounting for a female: male ratio (F:M) of almost 6:1 (5.7:1) with an average disease duration of 49% of 10.75±9.85 years. 48% of our patients presented with normal CRP values (<0.5mg/dl) and values of ≤1mg/dl for CRP; compatible with Boolean remission, were present in 66.6% of the patients. A significant percentage of our sample population (194 patients: 43.4%) registered normal ESR values (<28 mm/h).

Remission and LDA were registered in 18.1% up to 29.8% of the patients, depending on the score used. The lowest rate of remission and low activity is registered through the DAS28 ESR evaluation (18.1%). The other three scores outline similar percentages for T27 group of patients: 27.1% (SDAI), 29.7% (SASSA) and 29.7% (DAS28 4.4). The DAS28 ESR score is characterized in our study by a small number of swollen joints (<1), medium-normal ESR values (<30mm/h) and CRP values ≤1mg/dl (with the exception of SDAI). Consequently, patients with low activity based on the afore mentioned scores meet remission according to Boolean definition.

Conclusions: The disease activity and implicitly the remission rate are appreciated differently depending on the scale used. The limit between remission and low disease activity is fragile, influenced mainly by the purely subjective components of the assessment instruments. The important differences between the subjective and objective components of the evaluation scales recommend the supplementation of methods used in order to emphasize the real degree of joint inflammation.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8320

AB0326 INFLUENCE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS ON ARTERSINAL STIFFNESS IN PATIENTS WITH RHEUMATIC DISEASES

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Background: The association with adverse cardiovascular (CV) events and NSAIDs has been the topic of much debate.

Objectives: The aim of the present study was to investigate the effects of continuing NSAIDs therapy on predictable parameters for CV events.

Methods: We enrolled 155 patients with variable rheumatic diseases (95 rheumatoid arthritis, 49 systemic lupus erythematosus, 3 behceth’s disease, 3 gout, 5others.) who were free from established CV diseases and had taken cardiovascular function tests from June 2015 to June 2016. They were divided into two groups depending on whether or not to have taken NSAIDs therapy for at least 5 years: NSAIDs taking group (91 patients) vs. non NSAIDs taking group (64 patients). For evaluating heart function, thoracish echocardiography was used. Arterial stiffness was assessed using brachial-ankle pulse wave analysis.

Results: There were no significant differences in blood pressure, serum creatinine, serum hemoglobin, total cholesterol, erythrocyte sediment rate, C-reactive protein, disease duration, age, and smoking history between the groups. The NSAIDs
taking group had a higher median (95% CI) baPWV (brachial-ankle pulse wave velocity) and median (95% CI) mean pulmonary artery pressure (mPAP) than non-NSAID taking group: baPWV 13.72 (12.77–15.52) vs. 15.29 (13.93–17.63) m/s, p=0.005; mPAP 26.5 (22.8–30.5) vs. 30.5 (27.3–32.3) mmHg, p=0.011. But baPWV and mPAP were not significantly different between selective cyclooxygenase-2 inhibitor (22 patients) and nonselective NSAIDs (69 patients): baPWV 15.33 (13.98–17.63) vs. 14.83 (13.82–17.39) m/s, p=0.191; mPAP 29.0 (24.5–34.5) vs. 30.0 (26.0–33.0) mmHg, p=0.960.

Conclusions: Our study suggests that continuing NSAIDs therapy is associated with increased arterial stiffness in patients with rheumatic diseases, independently noted to increase the incidence of cardiovascular disease.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2403

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**AB0327**

**FEAR OF FALLING AND FOOT PAIN, IMPAIRMENT AND DISABILITY IN RHEUMATOID ARTHRITIS**

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**Background:** Fear of falling, foot pain and functional disability are commonly reported in rheumatoid arthritis. Moreover, the relationship between the fear of falling and foot pain, impairment and disability has rarely been studied.

**Objectives:** To evaluate the relationship between fear of falling and foot pain, impairment and disability in patients with established RA.

**Methods:** A cross-sectional study that included patients with rheumatoid arthritis. We collected the following data: age, sex, duration of disease, foot pain assessed by the Visual Analogue Scale (VAS), Disease activity assessed by DAS 28, HAQ disability index (HAQ-DI). Fear of falling was assessed by Falls Efficacy Scale-International (FES-I) which consists of 16 different activities, scored using a four point scale (1=not at all concerned, 2= somewhat concerned, 3=fairly concerned and 4=very concerned). The summed scores for the 16 activities for each participant were calculated. Scores of ≥23 indicated a significant fear of falling. Foot disability and impairment were measured using the Leeds Foot Impact Scale (LFIS), Foot disability was represented by the total score of the LFIST; range 0 to 51) of the LFIS and foot impairment by the first subscale (LFISIF; range 0 to 21). Correlations were used to assess the relationship between fear of falling and foot pain, impairment and disability.

**Results:** Thirty-three patients were included. The mean age was 49.3±10.5 years with female predominance (n=29 (87.9%)). The mean disease duration was 9.9±7.5 years. The mean HAQ-DI was 1.02±1.7 and the SDCI was 1.86±2.7. The mean FES-I score was 37.4±15.1 and 69.7% (n=23) of patients had significant fear of falling. The mean VAS pain was 5.3±2.5, the PGA was 6.2±2.1 and the EGA was 5.7±1.7. The mean DAS28 score was 5.5±1.3. The mean CDAI was 29.9±13.6 and the SDI was 31.6±13.7.

Fear of falling was significantly correlated with TJC28 (r =0.52, p=0.001), PGA (r=0.56, p=0.001), EGA (r =0.39, p=0.025), HAQ-DI (r =0.40, p=0.001), DAS28 (r ≥0.38, p=0.029), CDAI (r =0.48, p=0.005) and SDI (r ≥0.52, p=0.002).

**Conclusions:** Our study suggests that continuing NSAIDs therapy is associated with increased arterial stiffness in patients with rheumatic diseases, independently noted to increase the incidence of cardiovascular disease.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5912

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**AB0329**

**DO ANXIOUS OR DEPRESSIVE RHEUMATOID ARTHRITIS PATIENTS ON BIOTECHNOLOGIC THERAPY HAVE WORSE DISEASE ACTIVITY, FUNCTION AND QUALITY OF LIFE?**

J. Borges 1, N. Madeira 1, A. Cardoso 2, L. Cunha-Miranda 1, F. Barcelos 1, C. Miguel 1, C. Silva 1, S. Fernandezes 1, R. Trinca 3, D. Medeiros 1, A. Manelino-Marques 1, H. Santos 1, R. Leitão 1, A. Faustino 1.

Rheumatology; 2Nutrition; 3Nursing, Instituto Portugues de Reumatologia, Lisboa, Portugal

**Background:** Depression, anxiety and fatigue are common symptoms in rheumatoid arthritis (RA) patients, and seem to influence disease activity, pain, quality of life (QoL), and treatment response.

**Objectives:** To assess disease activity, function and QoL in RA patients with symptoms of anxiety/depression.

**Methods:** Observational, cross-sectional study including RA patients on bDMARD followed at our centre, registered at Reuma.pt with ≥1 evaluation from 2015/11 to 2016/07. Clinical data including DAS28, CDAI, SDAI, TJC, SJC, patients’ and physicians’ pain/global assessments (VAS), ESP, CRP, HAQ, EQSD. HADS score (anxiety and depression domains, cutoff >8) and FACIT-F were collected. Data were analyzed using Mann-Whitney, Qui-Squared and Spearman correlation, p<0.05.

**Results:** 182 patients enrolled, 84.6% female, mean age: age at 1st bDMARD 53.8±11.1; time since diagnosis 16.2±9.3 years; DAS28 3.5±1.3; CDAI 10.2±9.6; SDI 11.2±10.4; HAQ 0.97±0.6; HADS-Anxiety 7.1±3.5; HADS-Depression 6.62±4.54, FACIT -F 35.1±9.2, EQ-5D 0.36±0.2. 77 (44.5%) patients scored ≥8.1 evaluation from 2015/11 to 2016/07. Clinical data including DAS28, CDAI, SDAI, TJC, SJC, patients’ and physicians’ pain/global assessments (VAS), ESP, CRP, HAQ, EQSD. HADS score (anxiety and depression domains, cutoff >8) and FACIT-F were collected. Data were analyzed using Mann-Whitney, Qui-Squared and Spearman correlation, p<0.05.

**Results:** Thirty-three patients were included. The mean age was 49.3±10.5 years with female predominance (n=29 (87.9%)). The mean disease duration was 9.9±7.5 years. The mean HAQ-DI was 1.02±1.7 and the SDCI was 1.86±2.7. The mean FES-I score was 37.4±15.1 and 69.7% (n=23) of patients had significant fear of falling. The mean VAS pain was 5.3±2.5, the PGA was 6.2±2.1 and the EGA was 5.7±1.7. The mean DAS28 score was 5.5±1.3. The mean CDAI was 29.9±13.6 and the SDI was 31.6±13.7.

Fear of falling was significantly correlated with TJC28 (r =0.52, p=0.001), PGA (r=0.56, p=0.001), EGA (r =0.39, p=0.025), HAQ-DI (r =0.40, p=0.001), DAS28 (r ≥0.38, p=0.029), CDAI (r =0.48, p=0.005) and SDI (r ≥0.52, p=0.002).

**Conclusions:** This study suggests that fear of falling is frequent in patients with rheumatoid arthritis and demonstrated that fear of falling is significantly correlated with disease activity.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6029
Conclusions: Anxious or depressive patients showed higher disease activity, especially in measures with some subjectivity (such as TJC and PGA) but not regarding ESR or CRP and worse function and QoL. This fact must be taken into account when evaluating therapeutic efficacy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8345

AB0330 RHEUMATOID FACTOR AND RO52kDA ANTIBODIES ARE INDEPENDENT PREDICTORS OF INSULIN RESISTANCE IN RHEUMATOID ARTHRITIS

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Background: The rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) autoantibodies in rheumatoid arthritis (RA), have been used as diagnostic and prognostic tools [1]. However, this traditional perspective has changed toward a major role in RA pathogenesis. Several studies have demonstrated that FR and ACPA autoimmune positivity beyond its level, might influence disease activity, bone erosions and development of comorbidities. Anti-Ro52kDa antibodies have also been associated with disease severity in RA and might influence the development of comorbidities such as insulin resistance (IR) in RA.

Objectives: To evaluate the association between RF, ACPA and anti-Ro52 kDa and IR in RA patients.

Methods: We included 83 RA patients classified according to ACR 1987 and ACR/EULAR 2010 criteria and 90 controls matched for age, gender and body mass index (BMI). Homeostasis Model Assessment-Insulin Resistance (HOMA-IR), anthropometric parameters and antibody positivity (RF, ACPA, Ro52 kDa) were evaluated. Multivariate regression analysis was used to assess the contribution of autoantibodies, adiposity and disease activity to insulin resistance in RA.

Results: Patients positive for RF or anti-Ro52 kDa showed higher levels of basal insulin (P=0.009, P=0.006) and HOMA-IR. DAS-28 ESR was correlated with basal insulin (r=0.31, P=0.01) and HOMA-IR (r=0.29, P=0.02). We also observed positive correlations between serum triglycerides (r=0.47, P=0.01) and HDL-c (r=-0.38, P=0.02) and basal insulin. Multivariate analysis showed that Triglycerides, HDL-c, DAS-28, RF and anti-Ro52 kDa were independent predictors of basal insulin and HOMA-IR in patients with RA.

Conclusions: In RA, RF or anti-Ro52 kDa are independent predictors of IR. This phenomenon might be linked to the network of inflammation, adipokine secretion, since disease activity was also precipitous of higher basal insulin. Both RF and anti Ro52 kDa, along with disease activity are independent predictors of IR in RA patients without comorbidities.

References:
[4] Matsudaira R, Tamura N, Sekiya F, Ogasawara M, Yamanaka K, Takasaki Conclusions: The value of RDW does not appear to significantly change its value regarding ESR or CRP and worse function and QoL. This fact must be taken into account when evaluating therapeutic efficacy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7003

AB0331 BEHAVIOR OF THE VALUE OF RED CELL DISTRIBUTION WIDTH IN PATIENTS WITH RHEUMATOID ARTHRITIS IN TREATMENT WITH DAILY DOSE OF METOTREXATE

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Background: Recently the relationship between inflammatory biomarkers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) has been found, with the increase in the percentage of red cell distribution width (RDW) events related to increase in cardiovascular risk in patients with rheumatoid arthritis (RA). RDW is a parameter that represents the heterogeneity of erythrocyte size and is calculated by an automatic blood analyzer, translates anisocytosis and in turn is related to atherosclerosis, is a predictor of mortality in patients with cardiovascular diseases such as acute myocardial infarction (AMI) and Congestive Heart Failure (CHF) plus it has the advantage of being very cheap. In patients with RA who receive treatment with methotrexate (MTX), particularly those with good therapeutic response with decreased disease activity, the values of ESR and CRP decrease.

Objectives: The aim of this study is to verify if there is a decrease, increase or neither change in the value of RDW in the patients receiving or not MTX comparing the value prior to the start of treatment and the last value measured during their therapy.

Methods: In this descriptive, non-experimental cross-sectional study, men and women older than 18 years of age with a diagnosis of rheumatoid arthritis according to ACR criteria (Aletaha et al., 2010) who were or not treated with methotrexate and other DMARDs. We excluded patients with less than two visits in this unit and the elimination criteria were patients who did not have baseline or last RDW test. The records of all patients included name, age, sex, date of diagnosis of RA, comorbidities, baseline and final laboratory exams during follow-up that included tests with RDW and medications.

Results: A total of 403 all with a diagnosis of RA and an average of 4.62 years of evolution, of which 51 they do not take methotrexate in daily dose and 352 receive treatment and only 4.2% suffered from a cardiovascular event. The comparison was made grouping the patients in whom they received and not treatment with methotrexate and correlated with the value of baseline and final RDW as shown in Table 1.

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<td><strong>Receive</strong></td>
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The results shown in Table 1, do not appear to reveal a significant change in RDW values between the different subgroups; in the figures we compared the median of RDW for each group of patients who take methotrexate from all patients included in this study.

Conclusions: The value of RDW does not appear to significantly change its value when taking methotrexate at a daily dose in RA patients. The value of RDW may have weight in the assessment of the risk of suffering a cardiovascular event in patients with rheumatoid arthritis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3896

AB0332 DOES A COMMUNITY INTERFACE RHEUMATOID ARTHRITIS ANNUAL REVIEW IMPROVE PATIENT CARE?

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Background: Patients with rheumatoid arthritis are known to have a long term disability and increased risk of extra-articular comorbidities. EULAR guidelines suggest annual review of cardiovascular risk in patients with rheumatoid arthritis [1] whilst UK national (NiCE) guidelines suggest a more holistic annual review to look at the impact of the disease on quality of life as well as co-morbidities [2].

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2AB0332
Objectives: Our aim was to look at the annual reviews currently taking place in primary care to see how frequently patient co-morbidities were assessed and documented. We then implemented a formal community rheumatology interface review to assess whether this improved patient care.

Methods: A large primary care practice (16,000 patients) was offered a community rheumatology interface review by a secondary care clinician. A search was undertaken for patients with rheumatoid arthritis who had attended for an annual primary care review between December 2015–2016. Of these 30 reviews were selected and we assessed how frequently the following were recorded: DAS28, HAQ score, FRAX score, Q-Risk2 (CV risk assessment tool) and screening for depression. Once we had analysed these results we implemented a community rheumatology interface review and assessed compliance with the above outcomes had improved compared to standard primary care management.

Results: In patients assessed prior to implementation of interface review, we found that a DAS28 score was recorded in 0%, HAQ score in 0%, FRAX in 13%, Q-Risk2 in 10% and depression screening in 23%. In comparison, patients assessed by a community rheumatology interface clinician recorded DAS28 in 100%, HAQ score in 100%, FRAX in 100%, Q-Risk2 in 100% and depression screening was recorded in 100%. Based on improved interface review 7 patients (23%) were sent for DEXA scanning or started on a bisphophonate, we discussed cardiovascular risk and starting a statin in 8 patients (26%) and 7 patients (23%) required follow-up for mental health. Of the 30 patients in this cohort all patients reported full adherence to their anti-rheumatic regime.

Conclusions: 1. An annual review with a rheumatology interface practitioner is of benefit in holistic patient care and improved compliance with all domains of the annual review.


Disclosure of Interest: None declared

DOI: 10.1163/1875418X-0001

AB0334 KNEE FUNCTION AFTER TOTAL KNEE ARTHROPLASTY IS INFLUENCED BY DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Several studies reported that development of pharmaco-medicolegal treatment for rheumatoid arthritis (RA) contributed to decreased number of orthopaedic surgery. [1–3] Surgical treatment is, however, still required in many cases, and the impact of orthopaedic surgery on disease activity remain unclear.

Objectives: The aims of current study was to evaluate the effect of total knee arthroplasty (TKA) with capsulosynovectomy on changes of disease activity and knee function after TKA in patients with RA.

Methods: Seventy-seven serial patients with RA (61 female and 16 male) who underwent primary TKA with more than one year of follow-up were retrospectively reviewed to assess postoperative disease activity and knee function. The mean age at the time of surgery was 68.3 years. The disease activity of RA was measured using Disease Activity Score in 28 Joints (DAS28). Clinical outcome was measured by treatment score for RA knee of the Japanese Orthopaedic Association (JOA) score. To evaluate the effects of disease activity on knee function, outcomes at before and one year after surgery were separately investigated following two groups; patients who had remission or low disease activity in DAS28-CRP (good controlled group), and patients who had moderate or high disease activity (poor controlled group) one year after surgery.

Results: The disease activity of RA was significantly decreased in DAS28-CRP one year after surgery. (3.9 vs. 2.7, p < 0.01) Postoperative knee function was significantly improved in JOA scores one year after surgery. (48.9 vs. 86.0, p < 0.01). As for differences of knee function between good and poor controlled group, the mean JOA score in good controlled group was significantly better than in poor controlled group. (90.4 vs. 82.1, p < 0.01) Postoperative knee function was negatively correlated with RA disease activity. (R^2=0.21, p < 0.01)

Conclusions: TKA with capsulosynovectomy improves both knee function and disease activity in patients with RA. Based on the results, knee function after TKA is influenced with disease activity.


Disclosure of Interest: None declared

DOI: 10.1163/1875418X-0001
EFFECT OF TOTAL KNEE ARTHROPLASTY ON MEDICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Harigane 1, 2, Y. Mochida 3, K. Kumagai 2, K. Ishii 1, Y. Miyamae 1, N. Mitsugi 3, Biological Therapy in Severe Peripheral Ulcerative Disease. (3.9 vs. 2.7, p < 0.01) As for difference of the disease activity in same and change groups, DAS28-2CRP was significantly decreased after surgery (same group; 3.7 vs. 3.2, p < 0.01) as well as change group; 3.7 vs. 3.2, p < 0.01) DAS28-2CRP in change group was significantly higher both before and after surgery compared with those in same group. (p < 0.01)

Conclusions: TKA with capsulosynovectomy improves disease activity after surgery in patients with RA. Based on the results, patients with higher disease activity before surgery required further medication after surgery.

References:

Objective: This study evaluated the effect of total knee arthroplasty (TKA) with capsulosynovectomy on changes of disease activity and medication in patients with RA.

Methods: Seventy-seven serial patients with RA (61 female and 16 male) who underwent primary TKA with more than one year of follow-up were retrospectively reviewed to assess postoperative disease activity and drug administration. The mean age at the time of surgery was 68.3 years old. The disease activity of RA was measured using Disease Activity Score 28 joints (DAS28). To evaluate the effects of medication on preoperative and postoperative disease activity, outcomes at before surgery and one year after surgery were separately investigated following two groups; patients who were treated with the same or reduced medication (same group) and patients who were administered with additional or alternative medication (change group).

Results: Seventy-two patients (97.3%) were administered with at least one DMARDs before or after surgery. The mean dose of methotrexate (MTX) was 7.7mg/week before surgery and 8.0mg/week after surgery respectively. The number of patients treated with biological DMARDs was increased after surgery (17 patients vs.21 patients), however there was not significant differences. RA disease activity was significantly decreased in DAS28-CRP one year after surgery (17 patients vs.21 patients), however there was not significant differences.

Conclusions: TKA with capsulosynovectomy improves disease activity after surgery in patients with RA. Based on the results, patients with higher disease activity before surgery required further medication after surgery.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2416

AB0336 MAGNETIC RESONANCE IMAGING-ASSESSED SYNOVIAL AND BONE CHANGES IN HAND AND WRIST JOINTS OF RHEUMATOID ARTHRITIS PATIENTS


Background: Magnetic resonance imaging (MRI) is a sensitive and useful method for the detection of synovitis and joint destruction in rheumatoid arthritis (RA) patients. However, the patterns of MRI-detected bone erosion, bone marrow edema (BME), synovitis, and tenosynovitis have received insufficient attention.

Objectives: Therefore, this study evaluated the patterns of bone erosion, BME, synovitis, and tenosynovitis and calculated the RA-MRI score (RAMRIS) of patients with RA at the carpal and metacarpophalangeal (MCP) joints using MRI.

Methods: MRI datasets from 43 RA patients were analyzed. All patients had undergone MRI of one wrist. In addition, 36 patients had MCP joint images taken, and 5 had also received MRI of the contralateral wrist and MCP joints. The MR images were evaluated for bone erosion, BME, and synovitis in consensus by 2 blinded readers according to the OMERACT RA-MRI score (RAMRIS). The MRI-detected tenosynovitis was evaluated based on Haavardsholm’s tenosynovitis score.

Results: The capitale, lunate, triquetrum, and hamate bones were the most common sites of erosion and BME and showed the highest RAMRIS erosion and BME scores. Moreover, MRI-detected tenosynovitis was present in 78.3% of all patients with RA, and the extensor compartment 4 and flexor digitorum profundus and superficialis were frequently affected.

Conclusions: This study identified the distribution and prevalence of MRI-detected bone erosion, BME, synovitis, and tenosynovitis of the wrist and MCP joints in RA patients. The patterns of the MRI-detected abnormalities may help to select sites for the application of MRI protocols in clinical trials and practice.


AB0337 BIOLOGIC THERAPY IN SEVERE PERIPHERAL ULCERATIVE KERATITIS (PUK). MULTICENTER STUDY OF 27 PATIENTS

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Background: Peripheral Ulcerative Keratitis (PUK) is a severe infection that may lead to ocular perforation. PUK may be primary or associated with systemic conditions. Treatment is based on corticosteroids and conventional systemic immunomodulating drugs.

Objectives: To evaluate biologic therapy in cases with severe and refractory PUK.

Methods: Multicenter study of 9 hospitals. Patients presented inadequate response or intolerance to conventional therapy with corticosteroids and at least 1 systemic traditional immunomodulating drug.

The main outcome measures were visual acuity, signs of inflammation, progression to corneal thinning, central keratolysis and ocular perforation. Comparisons were made between baseline and 1st week, 1st month, 6th month and 1st year. Statistical analysis was performed using the software STATISTICA (StatSoft). Results were expressed as means±SD for variables with a normal distribution, or as median [IQR] when they were not normally distributed. The comparison of continuous variables was performed using the Wilcoxon test and categorical variables with chi-square test.

Results: We studied 27 patients/35 affected eyes (7 men/20 women), mean age, 57.2±16.3 years (range 28–89). PUK was primary in 1 case whereas in the 26 remaining cases, the underlying diseases were Rheumatoid Arthritis (RA) (n=19), Psoriatic Arthritis (n=2), RA+Felty syndrome (n=1), Behçet Disease (n=1), Type I diabetes mellitus (n=1), granulomatous panarteritis (n=1), and microscopic polyangiitis (n=1). They received the following biologic drugs: rituximab (n=16), oral doxycycline (3), azathioprine (3) and ascorbic acid (2). Moreover, 10 patients required surgery: amniotic membrane (n=7), penetrating keratoplasty (n=4), conjunctival resection (n=3), tissue adhesives (n=2), conjunctival flap (n=1) and lamellar keratoplasty (n=1).

Anti-TNFα drugs were the most common biologic agents used in these cases (n=19): Adalimumab (ADA) (n=10; 37%), Infliximab (IFX) (n=8; 29.6%). In the remaining 8 cases the biologic agents were rituximab (n=7; 25.9%) and tocilizumab (n=1; 3.7%). The main outcome measures are summarized in the Table. After a mean follow-up of 23.7±20 months, all objective outcomes had improved with a reduction of the median prednisone dose from 33.7 [17.5–52.5] mg at baseline to 0 [0–2.5] mg (p=0.028). The main observed adverse effects were supraventricular tachycardia (n=1) and pulmonary Tuberculosis (n=1).

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.1507

References:

Acknowledgements: The authors(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2416
Conclusions: In our series, biological therapy, especially IFX and ADA, is effective and relatively safe in patients with PUK refractory to standard systemic treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3576

AB0338 HEADS-UP! SARCOIDOSIS AND RHEUMATOID ARTHRITIS CO-EXIST
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Background: Sarcoidosis and rheumatoid arthritis (RA) uncommonly co-occur. How dual diagnosis affects these patients' clinical phenotype is unknown.

Objectives: To characterize the clinical and comorbid phenotype and to increase awareness of the coexistence of sarcoidosis and RA.

Methods: We searched PubMed from 1980–2016 for relevant articles using key words “sarcoidosis” and “rheumatoid arthritis,” excluding cases with tumor necrosis factor inhibitors. We found 12 cases, omitted 5 lacking clinical detail, and added 2 from our experience at the Cleveland Clinic. Clinical features, laboratory and imaging findings were reviewed and summarized.

Results: Females comprised 7/9 cases (77%). Our cases are the first to describe men with dual diagnosis. Of the 8 cases reporting ethnicity, 4 (50%) were white. The mean age at time of diagnosis was 35.3 years for RA and 51.0 years for sarcoidosis. In 5/9 cases (55.6%), RA preceded sarcoidosis. RA affected the hands in 8/9 patients (88.9%). Of the 8 cases reporting symptoms of sarcoidosis, 5 (62.5%) had dyspnea. All cases (100%) had elevated rheumatoid factor (RF) and, when checked, anti-citrullinated peptide (anti-CCP) antibodies. Angiotensin converting enzyme (ACE) was elevated in 6/9 patients (66.6%). Of the 5 patients with joint imaging, 4 (80%) had inflammatory changes. All sarcoidosis (100%) was biopsy-proven. One case (11.1%) demonstrated concomitant pulmonary RA and sarcoidosis.

Conclusions: Sarcoidosis and RA coexist in seropositive patients, most commonly in women in their fourth through sixth decades of life. RA preceded sarcoidosis about half the time. Hand arthritis and dyspnea were the most common symptoms for RA and sarcoidosis, respectively. Awareness of this dual diagnosis may help identify RA and sarcoidosis earlier and prevent treatment delay.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5401

AB0339 COMORBIDITIES AND RISK FACTORS OF CARDIOVASCULAR DISEASES IN RHEUMATOID ARTHRITIS PATIENTS
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Background: It is well known, that atherosclerosis associated cardiovascular diseases in many cases determine the life expectancy in RA patients. At the same time, risk factors which promote the development of premature atherosclerosis, including comorbidities, remain uncertain.

Objectives: to analyze comorbidity conditions in RA patients under age of 50 years and assess their impact on the vascular wall (evaluated by ultrasound investigation of the carotid arteries).

Methods: The study was conducted at the Department of Family Medicine, Shupyk NMAPE at the Kyiv Regional Clinical Hospital. The study included 128 RA patients, aged from 18 to 49 years (women - 102 (81%), men - 24 (19%), average age 43.8±8.8 years, who provided written consent to participate in research. As a control group 30 persons without any autoimmune diseases (women - 25 (83.3%) men - 5 (16.7%), average age 42.4±8.6 years) were examined.

All RA patients and control group underwent comprehensive clinical, laboratory and instrumental examination to identify comorbid conditions including evaluation of atherogenesis by use of ultrasound examination of the carotid arteries with intima-media thickness (IMT) measurement and atherosclerosis plaques (AP) assessment.

Results: The frequency of identified comorbid conditions and diseases in RA patients and control group are presented in Table 1. The average number of comorbid diseases/conditions per RA patient significantly exceeded its number in controls (4.13 and 1.67 respectively, p<0.05); most frequently among RA patients was determined: dyslipidemia (60.32%), nonalcoholic fatty liver disease (61.1%), chronic cholecystitis (36.51%), cholesteroles of the gallbladder (30.16%), hypertension (37.30%), autoimmune thyroiditis (27.77%), spinal osteoarthritis (33.33%).

The study of lipid metabolism included: determining the level of total cholesterol and triglycerides, HDL and LDL cholesterol. Patients with RA had significantly higher total cholesterol, triglycerides, HDL and LDL cholesterol values (p<0.05) at the same time as in the comparison group had a tendency to decrease. Noted a reduction parameters: CRP (83.3%), ESR (81.3%), GLU (81.3%) and BUN (79.7%). RA patients had a higher frequency of comorbid conditions and diseases than controls without RA; some of comorbidities have significant influence on atherogenesis; RA patients require a multidisciplinary and holistic approach for effective management of their health related problems.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3027

AB0340 CLINICAL EFFICACY OF STATINS IN PATIENTS WITH RHEUMATOID ARTHRITIS
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Background: Cardiovascular disease (CVD) is a major cause of mortality in patients with rheumatoid arthritis (RA), in the literature there are conflicting data on the role of statins in patients with RA, indicated lack of awareness. The study of lipid metabolism included: determining the level of total cholesterol. An analysis of the relationship between the use of statins in the treatment of patients with RA and cardiovascular complications, the influence of statins on atherogenesis; a detailed assessment of the lipid profile. The study of lipid metabolism included: determining the level of total cholesterol, HDL cholesterol and low density (LDL), atherogenic index (AI), triglycerides (TG). The study confirmed the positive effect of statins on atherogenesis; a detailed assessment of the lipid profile. The study of lipid metabolism included: determining the level of total cholesterol, HDL cholesterol and low density (LDL), atherogenic index (AI), triglycerides (TG). The study confirmed the positive effect of statins on atherogenesis; the study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol. The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol. The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol. The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol. The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness).

Method: The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol. The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol. The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness).

Table 1. The frequency of comorbidities in RA patients and control group

<table>
<thead>
<tr>
<th>Diseases and conditions</th>
<th>RA (n=126)</th>
<th>Control (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>12 (9.52%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>47 (37.30%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Neurocirculatory asthma</td>
<td>3 (2.69%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>76 (60.32%)</td>
<td>2 (2.67)</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>6 (4.76%)</td>
<td>1 (3.30)</td>
</tr>
<tr>
<td>Chronic gastritis</td>
<td>29 (23.00%)</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>2 (1.61%)</td>
<td>5 (16.67)</td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease</td>
<td>77 (61.1%)</td>
<td>2 (6.67)</td>
</tr>
<tr>
<td>Cholesterolosis of the gallbladder</td>
<td>38 (30.16%)</td>
<td>1 (3.33)</td>
</tr>
<tr>
<td>Chronic cholecystitis</td>
<td>46 (36.51%)</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Gall stones</td>
<td>8 (8.02%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diabetes mellitus type 2</td>
<td>3 (2.38%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diffuse goiter</td>
<td>5 (3.97%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Autoimmune thyroiditis</td>
<td>35 (27.74%)</td>
<td>1 (3.33)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>5 (3.97)</td>
<td>4 (13.33)</td>
</tr>
<tr>
<td>Osteoarthritis of the spine</td>
<td>42 (33.33)</td>
<td>9 (30.00)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>5 (3.97)</td>
<td>1 (3.33)</td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td>21 (16.76)</td>
<td>4 (13.33)</td>
</tr>
</tbody>
</table>

The difference between groups is significant, p<0.05.
for cervical spine subluxation it was higher patient age. Logistic regression confirmed early final awakening and short sleep respectively (HR 1.109, 95% CI 1.120–1.260, p<0.05) and (HR 1.095, 95% CI 0.991–0.998, p<0.005) as independent predictors of anterior atlanto-axial subluxation. The main risk factors for incident hypervascular atlantoaxial joint active pannus was disease activity score (DAS28) at early follow-up. The frequency of early final awakening and short sleep were higher in relation to cervical spine involvement. Male sex, CRP positivity, and older age were risk factors for incident anterior atlantoaxial subluxation.

Conclusions: Cervical spine involvement is common and may be asymptomatic indicating routine cervical spine imaging is needed in patients with RA specially with patients with sleep disturbances and high disease activity

References:

Disclosure of Interest: None declared

AB0334 THE RHEUMATOID FOREFOOT: WHICH FREQUENT INJURY? WHAT IMPACT ON WALK?

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Background: Foot involvement is the most common cause of disability in patients with rheumatoid arthritis (RA). The forefoot remains the most affected location.

Objectives: Investigate the forefoot injuries in patients with RA and evaluate its impact on walking.

Methods: Cross-sectional study of 33 patients with rheumatoid arthritis. Patients with static lower limb disorder or foot injury from other origin were excluded. Demographic and clinico-biological characteristics were collected: age, sex, BMI, disease duration, tender joint count, swollen joint count, foot pain evaluation on aVAS, percentage of patients with such discordance is not clear. The frequency of early final awakening and short sleep were higher in relation to cervical spine involvement. Male sex, CRP positivity, and older age were risk factors for incident anterior atlantoaxial subluxation.

Conclusions: Cervical spine involvement is common and may be asymptomatic indicating routine cervical spine imaging is needed in patients with RA specially with patients with sleep disturbances and high disease activity

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5536

AB0344 SUBCLINICAL VASCULAR DAMAGE AND ITS ASSOCIATION WITH ACPA AND RF IN PATIENTS WITH RHEUMATOID ARTHRITIS


Background: Accelerated atherosclerosis (AE) and increased arterial stiffness

AB0334 THE RHEUMATOID FOREFOOT: WHICH FREQUENT INJURY? WHAT IMPACT ON WALK?

M. Erraoui, B. Amine, L. Tahiri, I. El Binoune, J. Bahha, S. Fellous, Y. Boujenane, F. Allali, R. Bahiri. Rheumatology, Mohammed V University, Faculty of Medicine and Pharmacy of Rabat, El Ayachi Hospital, SALE, Morocco

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Conclusions: Cervical spine involvement is common and may be asymptomatic indicating routine cervical spine imaging is needed in patients with RA specially with patients with sleep disturbances and high disease activity

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5536
**AB0345** PSYCHIATRIC DISORDERS RELATED TO HYPERLEPTINEMIA AND RHEUMATOID ARTHRITIS: CLINICAL ACTIVITY MEASURED BY DAS28

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**Background:** Leptin is an adipose-derived hormone with a role in depression related to chronic stress, anxiety and pain disorders, disturbs with a high prevalence in RA patients. In previous studies, it has been demonstrated the role of leptin in the pathogenesis of RA, in particular, its association with anti-CCP. The purpose of this study was to evaluate the psychiatric disorders risk related to serum soluble leptin levels with clinical activity in RA patients.

**Objectives:** To evaluate the association between psychiatric disorders and serum leptin (sLep) levels and RA disease activity.

**Methods:** 76 outpatients diagnosed with RA (ACR1987/ ACR/ EULAR2010) were evaluated with clinical, laboratory and image assessment. Disease activity was measured using DAS28 CRP. The Mini International Neuropsychiatric Interview Plus (M. I. N. I. Plus) was used for the psychiatric evaluation. sLep levels were measured by ELISA method.

**Results:** sLep levels were significantly higher in RA patients M.I.N.I. plus (+) (n=46) DAS28 CRP (n=50) compared to M.I.N.I. plus (-) (n=18) DAS28 CRP (n=26). The sLep level was significantly higher in patients with a psychiatric disorder (P=0.006) with an odds ratio of 1.6 [1.04–2.46] P=0.03 for present psychiatric comorbidity. After adjustment with age and years of RA diagnosis, the odds ratio increased to 1.72 [1.08–2.73] P=0.02. Also, DAS28 CRP had a moderate correlation with the number of psychiatric diagnosis present, past and for lifetime r=0.485, P=0.001, IC95% [0.30–0.633].

**Conclusions:** sLep levels and DAS28 CRP were associated with symptoms of depression, such as anxiety and pain disorder in RA patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3245

**AB0347** EVALUATION OF THE IMPACT OF RHEUMATOID ARTHRITIS ON SEXUAL FUNCTION

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**Background:** Rheumatoid arthritis (RA) may affect all aspects of life including sexual functioning. The percentage of arthritic patients who experience sexual problems ranged in various studies from 31% to 76%. The reasons for disturbing sexual functioning are multi-factorial and comprise disease-related factors as well as therapy. It can occur before, during and after sexual activities, and can affect sexual health in different perspectives.

**Objectives:** The aim of our study is to evaluate the impact of the RA in sexual function and its associated factors.

**Methods:** This is a cross-sectional and descriptive study during a period of the year 2016, including 37 patients followed in the department of Rheumatology in Mahdia Tunisia. All patients were diagnosed with RA based in ACR 1987/EULAR 2010. We evaluated for each patient the parameters of activity of the disease, the quality of life by the HAQ questionnaire and the mood disorders using the Hospital Anxiety and Depression Scale (HAD).

**Results:** The age of the RA patients (32 females/5 males) ranged from 21 to 76 years. The mean age was 51.6 years. The mean duration of the disease was 11±10 years [1–34]. The mean number of tender joints was 13.2±9.6 and swollen joint was 5.9±7. The mean DAS28 was 5.5±1.5 [2.9–8.2] and the HAQ was 1.6±0.9 [0–2.8]. 51.3% of patients had specific joint deformations, 83.8% had radiologic involvement and 29.7% had osteoporosis.

The biologic analysis showed that the mean ESR was 45±27.1 and the CRP was 13.7±25.3. Rheumatoid factors were positive in 37.8% of cases, the ACPA were positive in 32.4% of cases. 81.1% of RA patients were treated by methotrexate and 13.5% were treated by biologic treatments.

The average score of depression was 9.2±4.2 [0–20]. 12 patients (32.4%) didn’t have signs of anxiety (score ≥8). 12 patients (32.4%) had probably an anxiety (score between 8 and 10) and 13 patients (35.2%) presented a certain anxiety (score >10). We found a significant correlation between the score of anxiety and the number of tender joints, the anxiety score and the HAQ (Health Assessment Quality).

**Conclusions:** Our study showed that the majority of our RA patients suffered from mood disorders; 67.5% had signs of depression and 65.6% had signs of anxiety. So, it’s important to evaluate the mood disorders in RA patients to ameliorate their quality of life.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5279

**AB0346** MOOD DISORDERS (ANXIETY AND DEPRESSION) IN RHEUMATOID ARTHRITIS

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**Background:** In addition to recurrent pain, fatigue, and increased rates of physical disability, individuals with rheumatoid arthritis (RA) have an increased prevalence of some mental health disorders, particularly those involving affective or mood disturbances. Many researchers have shown that mood disturbance and disability may serve as important pathways through which disease burden contributes to poor health functioning in RA.

**Objectives:** Our aim is to estimate the mood disorders (anxiety and depression) in patients with RA and to evaluate the associated factors.

**Methods:** This is a cross-sectional and descriptive study during a period of the year 2016, including 37 patients followed in the department of Rheumatology in Mahdia Tunisia. All patients were diagnosed with RA based in ACR 1987/EULAR 2010. We evaluated for each patient the parameters of activity of the disease, the quality of life by the HAQ questionnaire and the mood disorders using the Hospital Anxiety and Depression Scale (HAD).

**Results:** The age of the RA patients (32 females/5 males) ranged from 21 to 76 years. The mean age was 51.6 years. The mean duration of the disease was 11±10 years [1–34]. The mean number of tender joints was 13.2±9.6 and swollen joint was 5.9±7. The mean DAS28 was 5.5±1.5 [2.9–8.2] and the HAQ was 1.6±0.9 [0–2.8]. 51.3% of patients had specific joint deformations, 83.8% had radiologic involvement and 29.7% had osteoporosis.

The biologic analysis showed that the mean ESR was 45±27.1 and the CRP was 13.7±25.3. Rheumatoid factors were positive in 37.8% of cases, the ACPA were positive in 32.4% of cases. 81.1% of RA patients were treated by methotrexate and 13.5% were treated by biologic treatments.

The average score of depression was 9.2±4.2 [0–20]. 12 patients (32.4%) didn’t have signs of anxiety (score ≥8). 12 patients (32.4%) had probably an anxiety (score between 8 and 10) and 13 patients (35.2%) presented a certain anxiety (score >10). We found a significant correlation between the score of anxiety and the number of tender joints, the anxiety score and the HAQ (Health Assessment Quality).

**Conclusions:** Our study showed that the majority of our RA patients suffered from mood disorders; 67.5% had signs of depression and 65.6% had signs of anxiety. So, it’s important to evaluate the mood disorders in RA patients to ameliorate their quality of life.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6808
AB0348 SLEEP DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is one of the most common autoimmune diseases known to be one of the leading causes of disability. Sleep disorders have direct influence on patient’s life. But the exact nature of relationship between sleep disorders and Rheumatoid arthritis is not completely understood.

Objectives: The aim of our study is to evaluate the impact of RA in sleep quality and to establish associated factors.

Methods: This is a cross-sectional and descriptive study during a period of the year 2016, including 37 patients followed in the department of Rheumatology in Mahdia Tunisia. All patients were diagnosed with RA based on ACR 1987/EULAR2010. We evaluated for each patient the parameters of activity of the disease, the quality of life by the HAQ questionnaire and the quality of sleep using two scales: Epworth (ESS) and Pittsburg scale (PSQI) which is composed from 7 components rated each one from 0 to 3.

Results: The age of the RA patients (32 females/5 males) ranged from 21 to 76 years. The mean age was 53.1 ±12 years. The mean duration of the disease was 11±10 years [1–34]. The mean number of tender joints was 13.2 ±9.6 and swollen joint was 5.97. The mean DAS28 was 5.51±1.5 [2.9–8.6] and HAQ was 1.60±0.9 [0–2.8]. 51.3% of patients had specific joint deformations, 83.8% had radiologic involvement and 29.7% had osteoporosis.

The biologic analysis showed that the mean ESR was 45±27.1 and the CRP was 13.7±25.3. Rheumatoid factors were positive in 37.8% of cases, the ACPA were found to be associated with high score of HAQ. The biologic parameters of RA.

The mean ESR score was 9±5.7 [0–23]. 56.8% of patients had no sleep debt, 32.4% had a sleep deficit and only 10.8% had signs of somnolence. Our study confirmed a significant correlation between the Epworth score and the number of tender joints, the ESR, the Health assessment questionnaire (HAQ) score. The average of the subjective sleep quality was 1.35, latency to sleep was 1.81, “sleep duration” was 1.24, “habitual sleep efficiency” was 1.08, “sleep disorders” was 1.62, “the use of a sleep medicine” was 0.27 and finally the average of the 7th component about “poor form during the day” was 1.11 out of 3. So the latency to sleep and sleep disorders were the most affected components.

We had a significant correlation between PSQI and the number of swollen joints, the HAQ score. The value of the ACPOA was found to be associated with high score of ESR and CRP.

Conclusions: Our study showed that the sleep disruption wasn’t rare in patients with RA. This can be related to the disability and pain caused by this disease. Further studies with large sample size, as well as more careful tools of sleep disorders, would help to generalize results and suggestions. By providing adequate health care, and recognition of the patients’ pain conditions we would ameliorate sleep quality and increase the QOL of RA patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2040

AB0349 THE SERUM LEVEL OF IRISIN IS DECREASED IN THE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adipokines are proteins that are synthesized by and secreted from both skeletal muscle and adipose tissue, and show their effects through autocrine, paracrine or endocrine pathways (1). Irisin, a novel adipokine, is secreted in association with exercise from the skeletal muscle, and from the white adipose tissue to help the brown fat tissue gain the energy expenditure phenotype (2).

There is evidence that the irisin is associated with metabolic syndrome (MetS) and cardiovascular risk (3,4).

Objectives: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular disease (CVD) and MetS compared with the general population (5,6).

The aims of this study were to assess the serum level of irisin, and the possible relationships of irisin with disease activity in patients with RA.

Methods: Eighty four consecutive RA patients fulfilling the 2010 ACR/EULAR RA Classification Criteria were included in the study. Fifty age- and sex-matched healthy volunteers were enrolled as the control group. Disease duration, medications, history of traditional risk factors of CVD and demographic data of patients were noted. Body Mass Index (BMI) was calculated as “weight (kg)/height (m)²”. HbA1c, lipid profile, insulin were measured. Insulin resistance was assessed with the Homeostasis Model Assessment (HOMA) Index. RA disease activity was assessed by disease activity score based on evaluation of 28 joints (DAS28). Serum irisin level was assessed by ELISA. Measurement of carotid intima media thickness by carotid doppler ultrasonography was performed by a radiologist for cardiovascular risk assessment.

Results: There was no significant difference between the groups in terms of BMI (p=0.20), HbA1c (p=0.15), lipid profiles (p<0.05), insulin resistance (p=0.72) and carotid intima-media thickness (p=0.216). Serum irisin levels were found to be significantly lower in RA patients (20.65 (minimum:16.94- maximum:99.35) ng/mL) than healthy controls (37.56 (18.37–84.70) ng/mL) (p<0.001). There was no relationship between RA disease activity and irisin levels.

Conclusions: This study showed that irisin was significantly lower than controls. Irisin may be responsible for increased cardiovascular risk in RA patients. But before a definite judgment, prospective studies with a larger sample size assessing the exercise behaviour of patients and the presence of CVD are necessary.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5298

AB0350 FUNCTIONAL DISABILITY MEASURED BY HEALTH ASSESSMENT QUESTIONNAIRE (HAQ) CORRELATES WITH DISEASE ACTIVITY IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA)’s prevalence increases with age and the recognition of functional disability related to RA could be challenging in elderly patients.

Objectives: In this study, we aimed to look at the correlation between disease activity and the functional disability by using HAQ score in elderly RA patients.

Methods: Elderly RA patients, ≥65 years old at their routine visits were included to the study. The composite “disease activity score” in 28 joints (DAS-28) and “Physician Global Assessment” (PhGA) were used to determine disease activity. Health assessment questionnaire (HAQ) scores were calculated to describe the functional disability and compared across the disease activity groups according to DAS-28.

Results: Two hundred and fifty eight RA patients with the mean age of 71±5...
(65–90) were included. Seropositivity rate was 71% and 47% of the patients had erosive disease. Joint deformity was seen in 72 (28%) of patients and 28 (11%) patients had undergone total arthroplasty. Lung involvement (8.5%) and Sjogren’s syndrome (7.4%) were found as the most frequent extra-articular manifestations. Hypertension (68%) and osteoporosis (36%) were the common co-morbidities. The proportion of IVRT patients with high and moderate disease activity was found as 70%. HAQ and PhGA scores were significantly correlated with the disease activity (Figure).

Conclusions: We provided a novel data concerning the usefulness of HAQ for prediction of disease activity in RA patients who are elderly as well. In the future, our report will be supported by the studies which suggest that HAQ score improve with effective treatment in elderly RA patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6662

AB0351 PROTEIN ANTIBODIES AND SUBCLINICAL CARDiac AFFECTION IN RHEUMATOID ARTHRITIS PATIENTS
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Background: Cardiovascular disease (CVD) is a major cause of morbidity and mortality in rheumatoid arthritis (RA) patients. It has been postulated that chronic inflammatory activity is important for the development of CVD even after adjustment for traditional cardiovascular risk factors. One of the changes occurring in the context of inflammation is citrullination. Development of anti-citrullinated protein antibodies (ACPA) is implicated in higher frequency of extra-articular manifestations including cardiovascular complications.

Objectives: To assess the relation of ACPA to subclinical cardiac affection in RA patients.

Methods: Thirty RA patients fulfilling the 2010 ACR-EULAR classification criteria for RA with no clinically evident CVD were subjected to full history taking and clinical examination. Disease activity was assessed by 28-joint disease activity score based on C-reactive protein (DAS28-CRP) (4 variables). The levels of ACPA, CRP, total cholesterol, triglycerides, high density lipoprotein cholesterol and low density lipoprotein cholesterol were measured. The patients were subjected to M-mode and colour Doppler echocardiographic examination. Patients were subdivided into two subgroups according to ACPA positivity (ACPA positive patients represented “group A” and ACPA negative patients represented “group B”).

Results: The frequency of subclinical cardiac affection by echocardiographic examination was significantly higher among group A patients (4 patients had valvular lesion and 9 patients had diastolic dysfunction) than in group B patients (3 patients had diastolic dysfunction), (p=0.011). ACPA level showed significant positive correlation with isovolumic relaxation time (IVRT) in group A patients (prolongation of IVRT is a sign of diastolic dysfunction), (p<0.001).

Conclusions: The presence of ACPA is related to development of subclinical cardiac involvement in RA patients and all RA patients with high level of ACPA should be routinely evaluated with echocardiography to assess their cardiovascular status.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2801

AB0352 RISK FACTORS AND SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS FEMALES COMORBID WITH HYPERTENSION

Background: Rheumatoid arthritis (RA) associates with accelerated atherosclerosis and high cardiovascular mortality. Cardiovascular risk management in RA comorbid with HT is of a great importance. Our report will be supported by the studies which suggest that patients with RA comorbid with HT were characterized by higher frequency of subclinical atherosclerosis with unstable atherosclerotic plaques in compare with controls.

Methods: The study included 112 RA females with comorbid HT (mean age of 54 (50.5; 61.5) years) and 105 RA females without HT (control group). All pts received stable therapy of RA for more than 6 months. Pts with coronary artery disease were excluded. The risk of fatal cardiovascular disease was calculated using mSCORE (EULAR 2010); RA disease activity was measured using DAS28 scale. Carotid ultrasound with stiffness indexes detection and endothelial-dependent flow mediated vasodilatation (EDVD) by Celermajer method were performed. The levels of adiponectin, insulin were measured using ELISA kit test, insulin resistance was estimated using HOMA2 index.

Results: Subclinical manifestations of atherosclerosis were established in 88 (78.5%) RA females with HT and 55 (52.4%) control group pts. The majority of main group pts have atherosclerotic plaques - 62 (55.4%), unstable plaques had 26 (23.2%) pts. While only 33 (29.5%) patients were high and very high cardiovascular risk assessed by mSCORE. In compare, 35 (33.3%) control group pts have atherosclerotic plaques, unstable plaques had only 14 (13.3%) control pts (p<0.05). The presence of atherosclerotic plaques in RA females with HT was associated with age, RA disease activity, endothelial dysfunction, carotid stiffness, LDL cholesterol level, insulin resistance, adiponectin level, duration of steroid therapy. AUROC index for adiponectin and HOMA2 were 0.83 (95% CI 0.74–0.95; p<0.05 and 0.75 (95% CI 0.68–0.91; p=0.05 respectively, that indicate a good quality of diagnostic models.

Conclusions: RA females with comorbid HT are characterized by higher frequency of subclinical atherosclerosis with unstable atherosclerotic plaques in compare with controls. Endothelial function, insulin resistance, adiponectin level,
carotid stiffness determination may be useful additional tools for cardiovascular risk evaluating in this pts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5343

ASSOCIATED FACTORS FOR FALLS AND FEAR OF FALLING IN AMBULATORY PATIENTS WITH RHEUMATOID ARTHRITIS: A COMPARATIVE STUDY WITH HEALTHY SUBJECTS

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Background: Rheumatoid arthritis (RA) is a chronic disease that affects the bone and joints. Patients with RA might be considered to be at increased risk of falls and FOF for a variety of reasons, including the presence of muscle weakness and stiffness or painful joints of the lower extremities resulting in impaired physical activity, disability, and postural stability (1,2).

Objectives: The aim of the present study was to compare fall history and fear of falling (FOF) in RA patients with healthy controls, and to investigate their relationships between the demographic features, severity of pain, disability, disease activity, walking velocity, balance and emotional status in patients with RA.

Methods: One hundred-twenty patients with RA and 60 healthy volunteers were included in the study. Their fall history (yes, no) and the number of falls within the last year were questioned. FOF by presence of FOF (yes/no) and by Falls Efficacy Scale-International (FES-I) walking time by 10 Meter Walk Test (10MWT), balance by One-Leg Stand Test (OLST) and Berg Balance Scale (BBS), emotional status by Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were performed in both groups. Pain severity and global assessment (PGA) by Visual Analogue Scale (VAS), disability by the Health Assessment Questionnaire (HAQ), disease activity by Disease Activity Score-28 (DAS-28) were evaluated in patients with RA.

Results: There was no statistically difference between the RA patients and controls in terms of presence of fall history while presence of FOF and FES-I scores were significantly high in patients. PGA, 10MWT, pain VAS, HAQ, BAI, and BDI scores were significantly high in patients. BBS score and OLST were significantly low for fallers compared to the non-fallers in the patients (p<0.05). In the patient group, FES-I score was significantly correlated with pain VAS, PGA, DAS-28, HAQ, BAI, and BDI positively and BBS, OLST negatively (p<0.05).

In regression analysis, the number of falls, HAQ, BBS and BDI scores were detected to be independent risk factors affecting variations in FES-I scores (p<0.001).

Conclusions: According to the results of our study, ambulatory patients with RA have increased FOF, disturbed balance, increased walking time and impaired emotional status compared with controls. On the other hand, walking time, pain severity, disability, scores of emotional status and PGA were higher, while the balance scores were lower in the RA patients with fallers. There were relationships between FOF and increased pain, high disease activity and anxiety level, impaired PGA, increased walking time but the most important factors associated with FOF were impaired balance, increased disability and depression, and number of falls in RA patients. Strategies for preventing falls, maintaining balance, improving emotional status and againts FOF are of the utmost importance in patients with RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2888

PREVALENCE OF SIGNS OF CONNECTIVE TISSUE DYSPLASIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CHARACTERISTICS OF THE COURSE OF COMBINED PATHOLOGY

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Background: Connective tissue dysplasia (CTD) has a common pathogenesis with rheumatoid arthritis (RA). Question of peculiarities in such combination remains little known.

Objectives: To analyze the peculiarities of RA in patients with signs of CTD. Methods: Among the 107 patients with RA, seen in the rheumatology departments in Kazan city, 18 (16.8%) patients (15 women and 3 men, mean age 47.9±12.89 years) with reliable signs of CTD were selected, identified clinically and the agreement of their documentation was performed. By DAS28 low RA activity was detected in 1 (5.6%) patients, average - 13 (72.2%), high - 4 (22.2%). The clinical-laboratory and instrumental methods of diagnosis, standardized and independently developed questionnaire for the presence of CTD in selected group of patients were used

Results: The most frequently following signs of CTD syndrome - vegetative-vascular dystonia - 14 (77.7%), myopia - in 9 (50%), mitral valve prolapse- in 6 (33.3%), small heart abnormalities - in 8 (44.4%), flat feet - 6 (33.3%), scoliosis - in 5 (27.7%), hyperkyphosis - in 2 (11.1%), hypermobility of joints - in 2 (11.1%), anomaly of kidney structure- in 2 (11.1%), rhythm and conduction disturbances- in 7 (38.8%). Osteoporosis was observed in 11 (61.1%) patients. We select two group of patients: the first (n=9) from 1 to 5 CTD signs and the second (n=9) - from 6 to 9 dysplasia symptoms. In the second group RA activity by DAS28 was significantly (p<0.05) higher (4.52±1.20) than in the first (DAS28 =3.95±0.81). Obtained differences in RA activity, depending on the availability of myopia (DAS28 =4.68±0.87) and osteoporosis (DAS28 =3.78±1.06); flatfoot (DAS28 =4.53±1.05) or its absence (DAS28 =4.04±1.02) were evaluated. A significant (p<0.05) difference was found in patients with osteoporosis, the availability for activity (DAS28 =4.68±0.97), pain intensity VAS (1.44±m 6.90), compared with normal bone density tissue (DAS28 =3.36±0.36, pain VAS =5.83±2.22 cm).

Conclusions: Among patients with RA CTD signs occur more frequently than in the population (16.8% versus 10%). The most frequently detected are myopia, vegetative-vascular dystonia, cardiac diseases, osteoporosis. Patients with signs of dysplasia had a trend towards a higher activity of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3968

MUSCLE POWER AND FALL RISK IN RHEUMATOID ARTHRITIS

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Background: One of the serious consequences of aging is the gradual loss of neuromuscular function, such as gait speed, in order to the ability to generate high-velocity movements and current evidence suggests that it declines earlier with advancing age [1] and is more strongly related to functional status than muscle force [2]. A decreased capacity for high-velocity movements in the legs has been linked to delayed responses in maintaining postural stability and thus with age-associated fall risk [3]. People with rheumatoid arthritis (RA) may be at high risk of falling due to disease-related impairments such as pain, joint deformity, muscle weakness, altered gait and decline in postural stability.

Objectives: As role of muscle power in fall-risk assessment of RA patients has not been investigated, so far, the aim of the present study was to determine the association between muscle power, muscle force, functional performance and falls in the last 12 months in RA patients.

Methods: 98 subjects with RA older than 60 years from a cross-sectional study on the prevalence of corticosteroid-induced osteoporosis in Germany (PSIO-B Berlin) and 98 age-matched controls without inflammatory disease, randomly chosen from a cross-sectional study collecting reference values for body composition, were analyzed in this case-control study. Muscle function was determined by muscle power body mass in vertical countermovement jumps (ZUPlm, on a force plate, the chair rise test (CRT), gait speed, grip strength and the Short Physical Performance Battery. Differences in muscle function measures between the RA group and the healthy reference were derived separately by sex with Student-T test or Mann-Whitney-U test. Using logistic regression adjusted for age and the association between muscle function and falls was determined.

Results: In bivariate analysis RA patients showed significantly weaker performance in all muscle function tests compared to controls in both sexes. Applying logistic regression, age (OR 1.10, 95%-CI 1.00–1.24) and female sex (OR 5.99, 95%-CI 1.25–28.57) were significantly associated with retrospective falls in RA subjects but not in controls. Gait speed (OR 0.09, 95%-CI 0.01–0.88) remained a significant correlate for falls independent of age and sex in RA patients. In controls only the CRT (OR 1.13, 95%-CI 1.02–1.26) could differentiate individuals who had past fall events in the age and sex adjusted model. No association was found for the ZUPlm and retrospective falls.

Conclusions: The results of the present study could not confirm an association between fall risk and muscle power in RA patients, but they highlight the importance of monitoring neuromuscular function such as gait speed, in order to decrease falls and consequently to prevent fractures, contributing to a better prognosis of rheumatic disease.

References:

Disclosure of Interest: None declared

**AB0356** ASSOCIATION BETWEEN CARDIOVASCULAR RISK FACTORS AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease which affects 0.5% of adults, especially women. This disorder is associated with increased morbidity and mortality due to atherosclerotic cardiovascular diseases. In addition to traditional cardiovascular risk factors, inflammation plays a key role in this fact. Intima-media thickness (IMT) measured by carotid ultrasound is currently used to detect the presence of atherosclerotic disease and its value could be a predictor of subclinical cardiovascular disease.

**Objectives:** To study cardiovascular risk factors, disease activity and carotid IMT in a RA patients series.

**Methods:** Cross-sectional observational study of patients diagnosed with RA according to ACR/EULAR 2010 criteria. Patients with age under 75 years old and up of 5 years of disease evolution were included. Cardiovascular established disease patients were excluded. During a unique visit, anamnesis, physical examination, laboratory test, electrocardiogram, chest X-ray and carotid ultrasound with Esaote-MyLabClassC equipment. Statistical analyses were performed using software R (version 3.3.2).

**Results:** A total of 31 patients (57.1±9.7 years, 83.6% female, with 19.2±11.2 years of average disease course) were included. In relation to the classic cardiovascular risk factors, 19.4% were active smokers, 41.9% hypertensives and 45.2% had hyperlipidemic treatment (85.7% with a statin), three of the patients were diabetic (9.7%). All patients were treated with monotherapy or combination therapy and 4.8% were also given glucocorticoids at low doses during the last 6 months. The mean of the right carotid IMT was 0.9±0.7mm (1° Q=0.8; 3° Q=1.3) with an average HAQ of 0.88±0.68. As for articular-manifestations, 45.2% had xerophasia, 29% xerostomia, and 19.4% had rheumatoid nodules. The median total cholesterol was 195 mg/dL (174–221) and LDL of 116 mg/dL (96.5–138). The median of the right carotid IMT was 576.13±118.78 mm and the carotid left IMT was 616.32±134.31 mm, resulting in 12 determinations higher than values expected to their age and sex provided by the ultrasound developer (38.7%). Using the SCORE table (modified by EULAR), only 5 patients (16.1%) had moderate-to-high cardiovascular risk. Statistical analysis showed a significant association between an increased IMT and tobacco consumption (Pearson correlation risk factor) (p=0.028) and the modified SCORE (p=0.04). Neither years of evolution disease nor the analytical biomarkers showed a significant association.

**Conclusions:** Our study shows that in patients with good disease control data, classic cardiovascular risk factors are related to increased carotid intima-media thickness. However, these factors may underestimate overall cardiovascular risk over other measures of subclinical cardiovascular disease, such as carotid IMT.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5868

**AB0357** SEXUALITY IN WOMEN WITH RHEUMATOID ARTHRITIS - RESULTS OF A SURVEY

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease which affects 0.5% of adults, especially women. This disorder is associated with increased morbidity and mortality due to atherosclerotic cardiovascular diseases. In addition to traditional cardiovascular risk factors, inflammation plays a key role in this fact. Intima-media thickness (IMT) measured by carotid ultrasound is currently used to detect the presence of atherosclerotic disease and its value could be a predictor of subclinical cardiovascular disease.

**Objectives:** To study cardiovascular risk factors, disease activity and carotid IMT in a RA patients series.

**Methods:** Cross-sectional observational study of patients diagnosed with RA according to ACR/EULAR 2010 criteria. Patients with age under 75 years old and up of 5 years of disease evolution were included. Cardiovascular established disease patients were excluded. During a unique visit, anamnesis, physical examination, laboratory test, electrocardiogram, chest X-ray and carotid ultrasound with Esaote-MyLabClassC equipment. Statistical analyses were performed using software R (version 3.3.2).

**Results:** A total of 31 patients (57.1±9.7 years, 83.6% female, with 19.2±11.2 years of average disease course) were included. In relation to the classic cardiovascular risk factors, 19.4% were active smokers, 41.9% hypertensives and 45.2% had hyperlipidemic treatment (85.7% with a statin), three of the patients were diabetic (9.7%). All patients were treated with monotherapy or combination therapy and 4.8% were also given glucocorticoids at low doses during the last 6 months. The mean of the right carotid IMT was 0.9±0.7mm (1° Q=0.8; 3° Q=1.3) with an average HAQ of 0.88±0.68. As for articular-manifestations, 45.2% had xerophasia, 29% xerostomia, and 19.4% had rheumatoid nodules. The median total cholesterol was 195 mg/dL (174–221) and LDL of 116 mg/dL (96.5–138). The median of the right carotid IMT was 576.13±118.78 mm and the carotid left IMT was 616.32±134.31 mm, resulting in 12 determinations higher than values expected to their age and sex provided by the ultrasound developer (38.7%). Using the SCORE table (modified by EULAR), only 5 patients (16.1%) had moderate-to-high cardiovascular risk. Statistical analysis showed a significant association between an increased IMT and tobacco consumption (Pearson correlation risk factor) (p=0.028) and the modified SCORE (p=0.04). Neither years of evolution disease nor the analytical biomarkers showed a significant association.

**Conclusions:** Our study shows that in patients with good disease control data, classic cardiovascular risk factors are related to increased carotid intima-media thickness. However, these factors may underestimate overall cardiovascular risk over other measures of subclinical cardiovascular disease, such as carotid IMT.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5868

**AB0358** PATIENTS WITH EARLY RHEUMATOID ARTHRITIS HAVE INCREASED CARDIOVASCULAR RISK AT THE TIME OF DIAGNOSIS

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**Background:** Cardiovascular (CV) mortality in patients with rheumatoid arthritis (RA) is up to 50% higher than the general population. Whilst traditional CV risk factors such as smoking, diabetes and hypertension contribute to this increased mortality in RA, they do not fully explain the increase in risk. The British Society for Rheumatology, National Institute for Health and Clinical Excellence and European League Against Rheumatism (EULAR) recommend annual assessment of CV risk in RA patients. Furthermore, EULAR recommends modifying such traditional CV risk scores by 1.5 for RA patients who meet two of three criteria consisting of (1) disease duration >10 years, (2) positive rheumatoid factor or anti-cyclic citrullinated peptide (anti-CCP) serology, (3) presence of severe extra-articular manifestation, to account for the unexplained increased CV risk in RA.

**Objectives:** This study assessed CV risk by QRISK2 score and used carotid ultrasound to determine cardiovascular risk and prevalence of subclinical atherosclerosis at the time of diagnosis of RA.

**Methods:** Patients >18 years-old with early RA, defined by ACR/EULAR 2010 criteria and diagnosis of RA <6 months were recruited from The University Hospital of Wales, Cardiff. Exclusion criteria included definite or autoimmune or inflammatory rheumatic disease, ACR Classification of Functional Status stage IV, previous history of CV disease and diabetes mellitus. Demographic details were collected, blood pressure, body mass index, ESR, CRP and lipid profile were measured. The study was approved by Research Ethics Committee for Wales (11/WA0306).

**Results:** 40 patients, 10 males and 30 females with early RA were recruited. Mean age was 55.7±14.8 years. Rheumatoid factor and anti-CCP antibodies were positive in 62% and 80% of patients respectively. Mean BMI was 27.2±5.9. Twenty-nine percent were current smokers. Mean DAS28 was 3.8±3.1. According to the QRISK2, 54% of patients had >10% risk of CV disease over 10 years. Carotid ultrasound was conducted in 35 patients. Mean CIMT was 0.71±0.19 mm. 10 patients (29%) had carotid plaques. Fourteen patients (40%) had either plaque or CIMT >0.9mm, both considered markers of high CV risk. These patients were termed “ultrasound positive” patients. The sensitivity and specificity of the QRISK2 to predict US positive patients was 82% and 56% respectively. The positive predictive value of the QRISK2 was 63% and the negative predictive value of the QRISK2 was 88%. No patients met >1 criteria for EULAR adjustment of risk as all patients had early RA and none had severe extra-articular manifestations.

**Conclusions:** Many patients with early RA have significant CV disease at the time of diagnosis. This suggests subclinical CV disease may be developing before patients become symptomatic. More than half of the patients with early RA fulfill current NICE guidelines for starting lipid-lowering therapy, although of these, over one-third had no subclinical disease on carotid ultrasound. There is scope to improve the sensitivity and specificity of the QRISK2 calculation in RA patients, perhaps with a biomarker.

**Acknowledgements:** This work was funded by Arthritis Research UK, grant number 20760

**Disclosure of Interest:** None declared

AB0359  
**ASSESSING DEPRESSION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS—HOW DO DIFFERENT APPROACHES COMPARE?**

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**Background:** Depression is common in patients with rheumatoid arthritis and negatively impacts on their quality of life and disease outcomes, including disease activity and treatment response. Several case-finding tools for depression are available, including the PHQ2, which is both valid (1) and easy to use. The presence of depression was assessed in 3 ways a) PHQ2 score b) Self-recorded “ever” depression using the self-administered report comorbidity questionnaire (2) and c) Self report health status using the EQSD - which includes a statement regarding current anxiety/depression (dichotomised into no anxiety/depression vs. slight/moderate/severe/extremely anxious or depressed. Ethical approval was obtained (15-W5-0063).

**Results:** 179 RA patients provided data. Of these 119 (66%) were female and the mean (sd) age was 67.1 (11.7) years. 59 patients (33%) reported they had ever had depression using the self-report comorbidity questionnaire and 25 (14%) indicated they were currently receiving treatment. 68 (38%) indicated they were currently slightly (or more) anxious or depressed when assessed with the EQSD. 37 (21%) scored positively on the PHQ2. There was good concordance between the PHQ2 and EQSD at higher levels of depression, in that all those with severe or extreme anxiety or depression on EQSD also scored positively on the PHQ2. However, of those with moderate anxiety/depression on EQSD, 4/14 patients scored less than 3 using the PHQ2 score.

**Conclusions:** Depression is common in patients with established RA. Use of the PHQ2 case-finding questions in patients with established RA, may help clinicians identify patients who may benefit from more detailed assessment of mood and interventions to improve their outcomes. Reliance should not be placed on a single tool, and exploration of mood should be part of routine assessment of a patient with RA.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5996

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AB0361  
**BODY COMPOSITION AND PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS (AR)**


**Objectives:** To describe the body composition and physical activity of patients with RA.

**Methods:** Design: Observational case-control study. Population: 31 consecutive RA-patients (ACR/EULAR 2010 criteria) selected from a prospective inception cohort (diagnosis of RA between 2005 and 2012), and 31 sex and age-matched voluntary controls. Protocol: We included 62 subjects who were assessed using body-composition measurements obtained with a dual-body X-ray absorptiometry (DESA) for the assessment of body composition at study entry. Other clinical measures were also collected from the onset of the disease. The level of physical activity was assessed according to the abbreviated protocol of the International Physical Activity Questionnaire (IPAQ). Main outcome: Fat mass index (FMI) and fat free mass index (FFMI). FMI was defined as fat mass (kg)/height (m²) and FFMI as lean mass (kg)/height (m²).

**Secondary outcome:** Description of the anthropometric parameters: BMI (body mass index), waist-hip index. Variables: Demographic, treatment, clinical-analytical variables: Disease Activity Score of 28 joints (DAS28-ESR), Clinical Activity Disease Index (CdaI) and Simplified Disease Activity Index (SDAI); Anti-cyclic citrullinated peptide antibody (ACPA), Rheumatoid factor (RF), Health Assessment Questionnaire (HAQ) and erosions. BMI was categorized according to the OMS classification. Waist-hip index (central obesity: 1 for men and >0.8 for women). Statistical analysis: Descriptive and paired T-test or ranks test and Wilcoxon signed rank, as required.

**Results:** We included 62 subjects, 31 RA (50%) and 31 controls (50%). The mean duration of the disease of RA patients was 84.4 months. With a DAS28 mean of 3.04 (0.8), mean HAQ 1.77 (0.6). The majority presented erosions (64.5%) RF (83.3%), and ACPA (77.4%) positive. Differences in clinical and densitometric anthropometric parameters between cases and controls are shown in Table 1. Significant differences were observed in the proportion of overweight subjects between cases and controls (p=0.03). A higher percentage of controls had moderate to high physical activity compared with the patients (65.5% vs. 34.8%). The majority of patients with RA patients had low physical activity (74.2%). These had a mean (SD) of HAQ higher than patients with moderate-high physical activity [1.2 (0.9) vs 0.66 (0.6); p=0.09] Finally, patients performing moderate-high physical activity had less inflammatory activity than those performing low physical activity, with a DAS28 mean of 2.69 (0.7) vs 3.08 (0.9) p=0.03, respectively.

**Conclusions:** Patients with RA compared to controls show more overweight and less physical activity.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5037

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AB0360  
**CLINICAL AND HIGH RESOLUTION CT STUDY OF THE LUNGS IN 96 EGYPTIAN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Lung involvement is a common extra-articular manifestation of rheumatoid arthritis (RA) that confers significant morbidity and mortality. However, this issue has not been sufficiently studied in Egyptian patients.

**Objectives:** To assess the prevalence of pulmonary abnormalities by high resolution computed tomography (HRCT) chest in RA patients and their association with clinical variables.

**Methods:** Ninety-six patients with RA were assessed regarding their age, gender, duration of RA disease, sicca symptoms, presence of subcutaneous rheumatoid nodules, rheumatoid factor, respiratory symptoms, use of medications, disease activity of RA using Disease Activity Score 28 (DAS28), basic laboratory investigations and pulmonary abnormalities in plain x-ray and HRCT.

**Results:** HRCT abnormalities were identified in 25% of the patients: 58.3% had respiratory symptoms while 41.7% were subclinical. Dyspnea and cough were the most frequent symptoms. HRCT abnormalities were interstitial lung disease (ILD) in 11 patients (11.5%), pleural involvement in 8 patients (8.3%), consolidation in 4 patients (4.2%), diffuse alveolar hemorrhage in 3 patients (3.1%), bronchiectasis in 2 patients (2.1%), and apical fibrosis with cavitation in only 1 patient (1%). Patients with dyspnea, cough, chest rales, cutaneous rheumatoid nodules, and who received disease modifying antirheumatic drugs (DMARDs) combination were more likely to have HRCT abnormalities.

**Conclusions:** Pulmonary involvement is not uncommon in RA patients, and HRCT is a sensitive tool in pulmonary evaluation.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5996

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**Image:**

- Chest x-ray shows reduced lung volumes with bilateral reticular opacities.
- HRCT chest shows diffuse reticulo-nodular shadows suggestive of interstitial lung disease.
ANALYSIS OF INSULIN RESISTANCE IN A RHEUMATOID ARTHRITIS INCEPTION COHORT: CASE-CONTROL STUDY

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Objectives: To describe insulin resistance (IR) in patients with rheumatoid arthritis (RA) and compare it with healthy controls and to analyze the association between the accumulated inflammatory burden in patients with RA and IR.

Methods: Design: Observational case-control study. Population: consecutive RA-patients (ACR/EULAR 2010 criteria), > 16 years, selected from a prospective inception cohort (diagnosis of RA between 2007 and 2011). Patients with Diabetes Mellitus (according to ADA 2010 criteria) were excluded. Controls: sex- age and BMI -matched controls were collected from a health center in our hospital area. Protocol: Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity (RA patients), analytical values and oral glucose tolerance test (OGTT) were determined. All participants signed informed consent.

Main outcome: IR measured by the homeostasis model for insulin resistance (HOMA-IR) ([IR-2.29 μU * mmol/ml])/2. Secondary outcome: IR measured by quantitative insulin sensitivity check index (QUICKI) (< 0.3 - < 0.5 μU * mmol/ml) and β-cell function by a homeostatic model assessment of β-cell function (HOMA β). Variables: Demographic, clinical-analytical variables, Disease Activity Score of 28 joints (DAS28-ESR), Health Assessment Questionnaire (HAQ), BMI (according to OMS classification) and glucose in insulin and after OGTT values. Statistical analysis: Descriptive and paired T-test or Chi-square test followed by binary logistic regression in RA patients (Dependent variable: Insulin Resistance).

Results: Sixty-two subjects were studied, 8 of them were excluded after OGTT (4 diabetic patients and their respective controls). Finally, 54 subjects were included: 27 RA and 27 healthy controls. The mean age of patients with RA was 52.2 (12.1) years. Most of them were women (88.9%), with seropositive (FR 81.5% and ACPA 74.1%) and erosive (63%) RA. The mean duration of the disease was 85.6 months (27.1) and mean DAS 28 index since the onset of the disease of 2.98 (0.9).

Differences between clinical characteristics and in relation to IR between cases and controls are shown in Table 1. No significant differences in the proportion of subjects with IR in cases and controls were observed. 33.3% of patients with RA had IR. In multivariate analysis, the only independent variable associated with IR in RA patients was disease activity score (DAS28) (OR [95% CI] = 3.6 [1.0–12.9], p=0.045).

Conclusions: The only predictor of IR in RA patients was the inflammatory activity measured by DAS28. We did not find a higher IR in RA patients than in healthy controls, it could be because the patients were well treated and the inflammatory activity was controlled in the most of them.

Disclosure of Interest: None declared


CHARACTERISTICS OF BLOOD PRESSURE PHENOTYPES IN PATIENTS WITH RHEUMATOID ARTHRITIS - EULAR

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Background: Patients with rheumatoid arthritis (RA) have increased cardiovascular risk. Arterial hypertension (AH) is highly prevalent, and seems to be under-diagnosed and under-treated among patients with RA. Data on ABPM profile in patients with rheumatoid arthritis are lacking.

Objectives: The aim of the study was to evaluate ABPM parameters and characterize phenotypes of blood pressure in patients with RA.

Methods: 82 patients with RA (EULAR 2010) without known cardiovascular disease were examined (73% females, age 58.5±15.4 (M±SD) years, 13% smokers, 61% with AH, 34% with dyslipidemia). Median duration of RA was 8 years (IQR 3–17),. Seropositive RA was diagnosed in 69% of patients. Median CRP was 12.1 mg/dl (IQR 2.2–23.4 mg/dl), median rheumatoid factor (RF) was 32.5 IU/ml (IQR 8.3–173 IU/ml), All patients received disease-modifying antirheumatic drugs (DMARDs), 22% (38%) - biological treatment. Median duration of AH was 6.1 years (IQR 0–10 years). All patients with AH received antihypertensive treatment. 24-hour peripheral and central BP monitoring was performed (BPLab Vasotens, “Petr Telejen” – P<0.05 was considered significant.

Results: Mean office BP was 130±15/80±10 mmHg (peripheral) and 123±21/80±10 mmHg (central), 10 (17%) patients had elevated office BP (>140/90 mmHg), Mean BP values for peripheral and central BP were as follows: 125±15/72±9 and 116±14/75±9 mmHg for 24-h BP; 127±15/74±9 and 117±14/77±3 mmHg for daytime BP. 119±15/69±10 and 112±15/70±10 mmHg for nighttime BP. AH according to daytime BP was found in 15 (24.2%) pts, nighttime BP – in 29 (46.8%) pts, 24-h BP - in 19 (30.6%) pts. Phenotypes of BP were as follows: sustained normotension – in 38 (61.2%), masked hypertension in 15 (23.8%), sustained AH in 10 (16.1%), white-coat hypertension in 2 (3.2%) patients. Isolated systolic AH was observed in 12 (19.4%) pts. 10 (16.1%) patients had isolated elevated central BP. 20 (32.3%) pts had elevated central SBP according to individual reference values; all patients with high office BP had elevated central BP.

Conclusions: Patients with RA free of CVD are characterized by high prevalence of with the satisfactory control of office BP in the majority of patients. Relatively high prevalence of masked and isolated nocturnal hypertension despite antihypertensive treatment is observed in this population. These findings may help to optimize hypertension treatment in patients with RA.
Henoch-Schönlein purpura (HSP) is a non-thrombocytopenic leukocytoclastic acute systemic vasculitis of the small vessels with IgA-immunocomplex deposits, most commonly affecting the skin, joints, gastro-intestinal tract and the kidneys. It commonly affects the children aged between 4 to 10 years. The primary goal of treatment for rheumatoid arthritis (RA) is to maximize health-related quality of life (HRQOL) through symptom and damage control, and normalize function and participation in social and life activities. Although fatigue is recognized as one of the most debilitating symptoms of RA, little is known about how fatigue impacts participation.

**Objectives:**
We hypothesized that fatigue, along with pain, mood, disease activity, and pain medication use would be associated with participation.

**Methods:**
RA patients enrolled in an observational study at an academic center completed PROMIS measures assessing fatigue, physical function, mood (depression and anxiety), pain interference, sleep disturbance, and participation. RA clinical indicators were also collected at the visit. Variance inflation factors were examined to evaluate collinearity among variables. Covariates/confounders independently associated with participation included pain, mood (depression, anxiety), sleep, disease activity (CDAI), and physical function. Multiple regression models that did and did not include pain were compared using likelihood ratio tests with SPPS and R.

**Results:**
Participants were mostly female (82%) and white (83%) with mean (SD) age of 56 (13) years; 24% had ≥ high school, 29% had RA <5 years with 13% ≥ 2 years, and 22% were disabled. Mean CDAI was 7.9 (7.8). Most were in CDAI remission (n=56; 32%) or LDA (n=67; 38%); 39 (22%) were in MDA and 14 (8%) in HDA. Mean PROMIS fatigue was 53.9 (10.0); fatigue increased across CDAI levels from 46.2 (8.6) in remission to 64.0 (9.6). Only those with HDA had mean sleep, depression or anxiety scores ≥ 55 (i.e., above population norms). In the full model, fatigue, depression, CDAl, and physical function were significant independent predictors of reduced participation in social roles and activities (F (2, 169), p < 0.001, adj R2 = 0.55). Contrary to our hypothesis, pain was not associated with participation in univariate or multivariate models.

**Conclusions:**
Our results suggest that in RA patients, high levels or fatigue are common; conversely, depression, anxiety, and sleep disturbance were elevated only in patients with HDA. Disability and fatigue appear to have the greatest impact on participation in social roles and activities. RA treatments and interventions that attenuate fatigue and improve mood in people with active RA may improve their ability to participate in social and life situations restoring a sense of normalcy and improving HRQOL.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5597
AB0368 PREDICTORS OF NEUROPATHIC PAIN IN RHEUMATOID ARTHRITIS
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Background: Significant pain persists in a substantial proportion of Rheumatoid Arthritis (RA) patients in spite of disease remission. Recent evidence indicates that features suggestive of neuropathic pain (NP) are present in RA patients with a prevalence range of 33–38% using the painDETECT questionnaire (PDQ).

Objectives: To estimate the clinical predictors of NP in a cohort of RA patients.

Methods: Observational, cross-sectional study was performed with RA patients followed at our Rheumatology department with unchanged DMARD treatment during the last 3 months. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit. Demographic, clinical and laboratory data were collected and disease activity and functional measures were evaluated. Two questionnaires were applied to assess NP: the Leeds Assessment of Neuropathic Symptoms (LANSS) and the PDQ. Univariate and multivariate logistic regression were performed to identify the predictors of NP. Significance level was set as <0.05.

Results: 112 RA patients were included. 86 (77%) were females, with a mean (SD) age of 55.1 (10.8) years and median disease duration of 13 years (range: 2–41). 84% patients were seropositive for Rheumatoid Factor and/or ACPA. 102 (92%) of RA patients were treated with Current MTX and previous/current Hydroxychloroquine (HCQ) treatment. Number of analgesics and current NSAIDs treatment were excluded because they did not respond correctly to a dominant choice for patients to weigh the pros and cons related to each of the treatment options in order to develop a preference.

Conclusion: The purpose of the study was to define representative patient preference phenotypes to enable patient-physician dyads to effectively incorporate patient preferences at the point-of-care.

AB0370 DEVELOPMENT OF PATIENT PREFERENCE PHENOTYPES FOR RHEUMATOID ARTHRITIS
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Background: Many important treatment decisions for patients with rheumatoid arthritis (RA) are conditional on patient preferences and, according to the U.S. National Academy of Medicine, mandate a shared decision making approach (SDM). Furthermore, SDM is being increasingly recognized as an important quality measure. One of the most common preference sensitive decisions in RA is how to escalate care when response to methotrexate monotherapy is inadequate. However, the number of RA medications currently approved makes it challenging for patients to weigh the pros and cons related to each of the treatment options in order to develop a preference.

Objectives: The objective of this study was to develop representative patient preference phenotypes to enable patient-physician dyads to effectively incorporate patient preferences at the point-of-care.

Methods: People living with RA were invited to complete a Choice-Based Conjoint analysis survey including seven attributes (route of administration, time to onset of action, bothersome adverse events (AEs), serious AEs, extremely rare AEs, duration of time on the market and affordability) developed iteratively based on patient feedback. Each attribute was described across three or four levels using plain language. Preference phenotypes were identified by applying latent class analysis to the conjoint data. Class solutions were replicated five times from random starting seeds. A five-group solution was chosen based on Akaike's information criterion. We calculated the percentage of importance assigned to each attribute and performed simulations to estimate preferences for triple therapy, SC and IV biologics, or tocilizumab.

Results: 1100 U.S. subjects recruited via the CreakyJoints online patient community completed the survey. Of these, 49 were eliminated because they completed the survey in less than 10 minutes and an additional 45 people were excluded because they did not respond correctly to a dominant choice task. The mean age was 51.7 (11.2). The majority were female; (95%) and Caucasian (93%). Preferences (assuming low cost across options), and the reasons underlying each respondent’s preference, clustered into five groups (Figure 1). There were no differences in the distribution of demographic or clinical characteristics across the five groups. Phenotypes were created based on the stated preference data.

Conclusion: Preferences vary and can be categorized into distinct phenotypes. Ongoing research is evaluating whether enabling patients to identify with a preference phenotype facilitates SDM at the point-of-care.

Disclosures of Interest: This research was supported by a grant from the Rheumatology Research Foundation.

DOI: 10.1136/annrheumdis-2017-eular.5024
Disclosures: Achieving REM or LDA is not the ultimate goal of treatment for patients with painful callosity and footwear problems caused by typical forefoot deformity. Recently, patients have expressed a desire to achieve functional REM or LDA just before surgery. The patient-reported outcomes (PROs) were assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), and Patient’s General Health using a visual analogue scale of 100 mm (Pt-GH). The 28-joint Disease Activity Score using C reactive protein (DAS28-CRP), the Japanese Society of Surgery of the Foot (JSSF) standard rating system (JSSF) for the RA foot and ankle scale\(^6\), and the Time Up&Go test (TUG) were also assessed. All of these items were investigated just before surgery (baseline) and again at 6 and 12 months after surgery.

Results: Overall, the physical function (JSSF, TUG), QOL (EQ-5D), and mental wellness (depression) (BDI-II) were significantly improved at 6 and 12 months after surgery compared to the baseline values (p<0.05). In the REM/LDA group, significant improvement was noted in the physical function (JSSF), QOL (EQ-5D) both at 6 and 12 months after surgery; however, we did not observe any significant changes in the Pt-GH or DAS28-CRP (Table 1).

Table 1. Outcome of surgical intervention in the deformed forefoot for the patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th>Category</th>
<th>Baseline</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>JSSF</td>
<td>2.69 ± 0.14</td>
<td>1.69 ± 0.14</td>
<td>1.39 ± 0.14</td>
</tr>
<tr>
<td>TUG</td>
<td>18.6 ± 2.3</td>
<td>13.3 ± 2.1</td>
<td>9.2 ± 1.8</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>0.58 ± 0.15</td>
<td>0.54 ± 0.13</td>
<td>0.52 ± 0.13</td>
</tr>
<tr>
<td>BDI-II</td>
<td>1.3 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.5 ± 0.1</td>
</tr>
<tr>
<td>Pt-GH</td>
<td>60 ± 10</td>
<td>50 ± 10</td>
<td>40 ± 10</td>
</tr>
</tbody>
</table>

Conclusions: Achieving REM or LDA is not the ultimate goal of treatment for patients with painful callosity and footwear problem functional loss. A higher QOL and improved function can be achieved by surgical intervention in the deformed forefoot.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3393

AB0372 ASSOCIATED FACTORS OF CERVICAL AND LUMBAR SPINAL INSTABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Few studies have compared rheumatoid arthritis (RA)-related disorders of the cervical and lumbar spine.

Conclusions: The objectives of this study were to examine the prevalence of and risk factors for cervical and lumbar spinal instability in patients with RA.

Methods: From a total of 1,843 patients registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA), 135 patients [118 women, 17 men; mean age, 68 (41–84) years; mean disease duration, 14 (1–63) years] who underwent a radiographic examination were enrolled in this study. In the cervical spine, we defined instability as one of the following characteristics: (1) atlantodental interval (ADI) > 3 mm, (2) Ranawat value < 13 mm on a neutral plain radiograph, or (3) anteroposterior translation > 3 mm at the subaxial cervical spine on an anteroposterior bending plain radiograph. In the lumbar spine, instability was defined as anteroposterior translation > 3 mm on a neutral plain radiograph.

At the time of radiographs evaluation, demographic characteristics, clinical variables, medical history and current medications were investigated. The patients were classified into two groups: with both cervical and lumbar spinal instabilities and without. The independent risk factors for both cervical and lumbar spinal instabilities were then determined using multivariate logistic regression analysis.

Results: Forty-six (34.1%) patients exhibited cervical spinal instability, and 50 (37.0%) patients exhibited lumbar spinal instability. Twenty-four patients (17.8%) exhibited both cervical and lumbar spinal instability. The presence of both cervical and lumbar spinal instability was significantly and independently associated with disease duration (OR: 1.06; 95% CI: 1.01–1.12).

Conclusions: The prevalence of both cervical and lumbar spinal instability in patients with RA was 17.8%. Disease duration was independent risk factor for presence of both cervical and lumbar spinal instability in this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6649

AB0373 ANALYSIS OF RISK FACTOR FOR LOCOMOTIVE SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM CHIKARA STUDY

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Background: Patients with rheumatoid arthritis (RA) are at a higher risk for sarcopenia due to joint destruction and chronic inflammation\(^1\), which can lead to locomotive syndrome (LS), i.e., being restricted in the ability to walk or lead a normal life owing to a dysfunction in one or more of the parts of the musculoskeletal system\(^2\). The present observational CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis; registration number UMIN000023744) was begun in 2016 to investigate the correlation between RA disease activity and sarcopenia and LS.

Objectives: We investigated the relationship between LS and disease activity at baseline in patients with RA.

Methods: One hundred patients (78% women; average age, 66y) enrolled in the CHIKARA study were examined for body weight, muscle mass, fat mass, predicted bone mass, basal metabolic rate (BMR), leg muscle score, etc., using a body composition analyzer. Laboratory data, disease activity, Health Assessment Questionnaire (HAQ) and treatment were also investigated. LS was diagnosed using a questionnaire called Locomo-5. We investigated the correlation between LS and each status using univariate and multivariate analyses.

Results: Fifty-two percent of the patients with RA that we examined had LS. Mean disease duration was 5.5 years and mean DAS28-ESR was 3.55. Table 1 shows the risk factors for LS. Univariate analysis showed that age, percent body fat, body weight, visceral fat rating, leg muscles score, rheumatoid factor status and HAQ had significant associations to LS. Leg muscle score and HAQ were detected as significant factors by multivariate analysis. Patients whose leg muscle score was less than 90 had a significantly higher prevalence of LS by ROC curve analysis (Odds ratio 3.77, p<0.001). Disease activity and use of glucocorticoids or biological agents showed no significant relationship.

Table 1. Risk factors for locomotive syndrome in patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>p value</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>% body fat</td>
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</tr>
<tr>
<td>% body water</td>
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<td>0.014</td>
</tr>
<tr>
<td>% body water</td>
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<td>Visceral fat rating</td>
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<td>0.019</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
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<td>0.027</td>
</tr>
<tr>
<td>Health Assessment Questionnaire</td>
<td>0.460</td>
<td>-0.001</td>
</tr>
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</table>

Conclusions: Lower leg muscle score and higher HAQ score are independent risk factors for LS among patients with RA.

References:

Disclosure of Interest: None declared
Rheumatoid arthritis - anti-TNF therapy

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Background: Anti-TNF are nowadays widely used for the treatment of Rheumatoid Arthritis (RA), which has dramatically changed the prognosis of the disease, carrying an important healthcare expense. This is why optimisation seems a successful strategy that should not be linked to a worse become of our patients’ clinical evolution.

Objectives: Describe a population of patients with RA under optimised treatment with Adalimumab (Ada) and Infliximab (Ifx). Study the incidence of flares and establish predictive factors of flares at baseline and pre-optimization.

Methods: Observational study of the prospective cohort RA-Paz. All the patients diagnosed of RA under treatment with Ifx and Ada between Jan.2000 and Dec.2016 of the day-care unit of La Paz Hospital, were included. Demographic data, clinical activity and blood sample results were collected at baseline, pre-optimization (pre-op) and at 3, 6, 9, 12, 18 and 24 months. Drug serum trough levels were measured under ELISA in each visit. Optimal range for Ifx was described as drug concentration between 1000-4000 ng/mL and 1500-5000 ng/mL for Ada. Optimisation was defined as drug use below standard dose. Flares were collected from the pre-op visit. Flare was described as clinical worsening which led to a therapeutic change or a DAS28 > 3.2. DeltaDAS28 > 0.6. Predictive factors of flare at baseline and pre-op were evaluated with a univariate and multivariate analysis. Statistical study was performed with the statistical program SPSS.

Results: Of the 271 patients diagnosed of RA, 74 patients were optimised (44 under Ada and 30 under Ifx). Baseline demographic characteristics are shown in the table below. During the 24 months after the pre-op visit, 55.4% (41) of the patients presented at least one flare with an average of 1.38 flares [1–5]. Most of the patients (53.7%, 22/41) were controlled with the adjustment of non biological treatment. Only 39.0% (16) of the patients, had to go back to the previous optimised dose and 7.3% (3) to the standard dose. 88.9% (39/41) were controlled after the dose modification. 104 flares were collected, 33% (34) at the pre-op visit. Flares were described as clinical worsening which led to a therapeutic change or a high DAS28 values in relationship to the MTX dose, statistical differences are observed with use of HD (≥ 20 mg/week) (3.1±1.3 with HD vs 3.9±1.1 without MTX, p=0.001). A least proportion of patients with flares were in supra-optimal range (13.3% with flares vs 26% without p=0.007). At baseline, no clinical factors were predictive of flare. Nor were blood sample results. In contrast, a higher disease activity, measured by DAS pre-op (p=0.004), a worse EULAR answer (p=0.027) and not being in supra-optimal range (p=0.032) were statistically correlated with flares development at the univariate analysis. Time to the optimisation tended to the significance (OR=1.152; p=0.08). In the multivariate analysis, only a higher DAS pre-op (OR=2.00, 1.08–3.73) and being in optimal (OR=5.90, 1.38–25.2) and sub-optimal range (OR=6.05, 1.28–28.7) were independently correlated.

Conclusions: In our cohort of optimised patients, we noted a high proportion of flares. However, flares were controlled with dosage readjustment without needing a treatment change. Independently correlated predictive factors for flares were a higher disease activity measured by DAS and not being in therapeutic range in the pre-optimisation visit.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6859

Rheumatoid arthritis - anti-TNF therapy

1Rheumatology, University Hospital la Paz, Madrid, Spain

Background: Several publications in rheumatoid arthritis (RA) have demonstrated a beneficial effect of concomitant methotrexate (MTX) use with TNF inhibitors (TNFi), mainly because of the MTX effect in reducing immunogenicity. In a previous work in the RA-La Paz cohort, we found that the concomitant use of MTX had a positive effect on the pharmacokinetics of serum TNF levels, decreasing the immunogenicity of these drugs. Furthermore, the MTX effect was dose-dependent, being greater at high MTX dose. Currently, we investigate the effect of concomitant MTX use on the clinical response.

Objectives: To investigate the MTX influence on the clinical response in the RA-La Paz cohort treated with Infliximab (Ifx), Adalimumab (Ada) or Etanercept (Etn) at one year of treatment.

Methods: This is an observational study from a prospective cohort from the Rheumatology Unit of the University Hospital La Paz, Madrid, Spain that analysed a total of 150 RA patients (112 with RA patients. ARA (71 patients) and Etn (110 patients). Patients were grouped according to the MTX dose: no MTX, low dose (LD: ≤2.5 mg/week), intermediate dose (ID: 15–17.5 mg/week) and high dose (HD: >20 mg/week). For this study, the clinical response was evaluated by DAS28-ESR and the clinical improvement by sDAS28. Data were collected at baseline (BL) and 1 and 2 years of treatment. Statistical analysis was performed using GraphPad Prism 6.0 software.

Results: Out of 293 RA patients (pts) under TNFi treatment, 184 (71 with Ifx, 40 with Ada and 73 with Etn) were included. In this cohort, 128 (70%) pts used concomitantly MTX (91% oral administration) and 56 (30%) pts were in monotherapy. No differences in DAS28 were found at baseline between patients with or without MTX (p=0.8). After one year of treatment, pts with TNFi +MTX have a significantly lower DAS28 than patients without MTX (3.3±1.3 vs 3.9±1.1, p=0.004). When analyzing the DAS28 values in relationship to the MTX dose, statistical differences are observed with use of HD (≥ 20 mg/week) (3.1±1.3 with HD vs 3.9±1.1 without MTX, p=0.001) but not with intermediate (3.4±1.2 with HD vs 3.9±1.1 without MTX; p=0.08) or low MTX dose (3.6±1.6 with LD vs 3.9±1.1 without MTX; p=0.4) at 1 year of therapy.

Clinical improvement by sDAS28 was higher in patients with TNFi +MTX than in patients without MTX (1.7±1.4 vs 1±3.0, p=0.007). This effect was observed with all MTX doses (1.7±1.5 with HD vs 1±3.0 without MTX, p=0.01; 1.6±1.3 vs with HD 1±3.0, p=0.03) and being in optimal (OR=1.38–25.2) and sub-optimal range (OR=6.05, 1.28–28.7) were independently correlated.

Conclusions: We demonstrated a positive effect of any MTX dose on the clinical improvement at one year of treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2884
Results: of the 64 patients included in the study, 59 (92.2%) were women and 5 (7.8%) men, mean age 57.5±9.42 years. After 6 months, 7 patients were declared nonresponders, 38 achieved a moderate response and 19 good response.

Following baseline COMP titres and the EULAR response at 6 months, general tests were performed for all patients, the results were compared. Lower baseline titres had predictive value for achieving a good response (746.0±130.095 ng/ml) compared with moderate responders (1032.8±186.671 ng/ml) and nonresponders (1042.2±181.717 ng/ml, p=0.0000).

After 12 months 11 patients achieved moderate response, 44 a good response and just 1 patient was declared nonresponder. At this visit, even if we didn’t find significant differences between baseline COMP titres and the EULAR response (p=0.1430), we observed lower baseline titres for good responders (917.8±219.943 ng/ml) versus moderate responders (1042.7±193.117 ng/ml).

Grouping patients in 2–3 categories (good responders, moderate responders, nonresponders) there were no differences between groups at 6 months (937.2±218.106 ng/ml versus 1042.2±181.717 ng/ml, p=0.227) or 12 months (942.8±219.025 ng/ml versus 896.5±0.000 ng/ml, p=0.9755).

Following the status pretreatment of COMP and EULAR response at 6 months, we identified differences between groups (p=0.0001), all 7 patients declared nonresponders were COMP positive and only 13/19 (68.4%) of good responders were tested positive. At 12 months there were no differences between pretreatment status of COMP and response to treatment (p=0.2085).

Regarding the evolution of serum levels, we noticed a decrease statistically significant from baseline (948.7±215.683 ng/ml) to 12 months (740.8±227.04 ng/ml, p=0.0000).

Conclusions: COMP could be one of the biomarkers for identifying pretreatment the patients who will respond to biologic therapy in Rheumatoid Arthritis.

References:

Disclosure of Interest: None declared


SWITCHING FROM BIO-ORIGINAL ETANERCEPT TO BIOSIMILAR ETANERCEPT SB4: PATIENT ACCEPTABILITY AND OUTCOMES IN THE REAL WORLD

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Background: A number of studies have demonstrated the efficacy of biosimilar therapies including SB4 (a biosimilar-etanercept). However, real world data of the process of switching, acceptability to patients, efficacy and safety is lacking.

Objectives: To obtain real world data of the acceptability and outcomes of patients with severe (eligible for TNFi therapy as defined by UK NICE) rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) who switch from bio-original etanercept (boDMARD-ETN) to the bsDMARD etanercept SB4 (bsDMARD-ETN).

Methods: Adult patients, with RA, PsA & AS, currently enrolled in the SmART study and switching from boDMARD-ETN to bsDMARD-ETN were followed for 6 months. Primary outcome was change in DAS28, PsARC response or BASDI following switching. Additional outcomes included: % change of remission rate, HAQ-DI, CRP or ESR levels, patient satisfaction, PDUS and SAEs leading to discontinuation. All patients had severe disease and were receiving boDMARD-ETN as per local guidelines of UK NICE. Analysis was performed in a similar way to a cross-over RCT trial design where patients act as their own control with respect to treatment.

Results: 462 patients were enrolled and 255 patients completed the study. Mean age was 53.9 (±12.1) yrs; 82.2% of enrolled patients were female; average disease duration was 7.8 (±7.5) yrs. DAS28 decreased from 6.1 (±1.1) at baseline to 2.9 (±0.1) at study end, whereas the mean HAQ-DI from 1.6 (±0.6) to 0.7 (±0.5). The proportion of patients in LDA and REM at study end was 56.0% and 31.1%, respectively. Total SQUASH score increased from 4772 (±4132) to 6104 (±5492), representing 28% improvement in overall physical activity. The largest score improvements were seen in the SQUASH domains of leisure time and sport (by 43%), followed by household activities and activities at work and school (each by 19%). The correlations between the total SQUASH score and its subscores with DAS28 were weak (r=-0.1 to baseline and study end). A significant correlation between the total SQUASH and HAQ-DI scores was seen at baseline (r=-0.30), but not at the study end (r=-0.22). Correlations between SQUASH subscores and HAQ-DI were not significant. The percentage of work disabled subjects decreased from 22% to 17%. According to linear regression analysis, sociodemographic factors did not substantially influence habitual physical activity.

Conclusions: Treatment with adalimumab in clinical practice in CEE resulted in clinically meaningful improvements in disease activity and physical function as well as improvements in physical activity. The correlation between the scores for disease activity, physical function and physical activity were however poor and there was no clear influence of the standard sociodemographic factors on physical activity.

References:

Disclosure of Interest: Funding: The design, study conduct, and financial support for the clinical trial were provided by AbbVie. AbbVie participated in the interpretation of data, drafting, review, and approval of the abstract.

Acknowledgements: To the clinical trial were provided by AbbVie. AbbVie participated in the interpretation of data, drafting, review, and approval of the abstract.
AB0379 EFFICACY OUTCOMES FOR ORIGINATOR TNF INHIBITORS AND BIOSIMILARS IN RHEUMATOID ARTHRITIS AND PSORIASIS TRAILS: A SYSTEMATIC LITERATURE REVIEW

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Background: Regulatory approval of biosimilar versions of innovator biotherapeutics requires that new biological products be highly similar to innovator biologicals, with no clinically meaningful differences in safety, purity, and potency.1,2 Pre-specified margins for equivalence in efficacy have been met in comparative trials of biosimilars of tumour necrosis factor inhibitors (TNFis) in rheumatoid arthritis (RA)1 and plaque psoriasis (PsO).4,5 Supporting biosimilarity, but differences in treatment responses between originator pivotal trials and biosimilar trials have posed some interesting questions.

Objectives: To compare American College of Rheumatology 20% response (ACR20) and Psoriasis Area Severity Index 75% (PASI75) responses to originator TNFis in pivotal trials with those to originator TNFis and TNFi biosimilars in biosimilar trials in RA and PsO.

Methods: Historical data from originator pivotal trials (averaged across trials) were obtained from published systematic literature reviews. Searches were conducted to identify comparative randomized clinical trials of approved or proposed biosimilars of adalimumab (ADA), etanercept (ETN), and infliximab (INF) sourced from the European Union (EU). The databases were Embase®, MEDLINE®, the Cochrane Central Trials Register and Database of Systematic Reviews, and other Cochrane Library databases, and 2015/16 congress abstracts. To reduce variability, only studies conducted in disease-modifying antirheumatic drug-experienced patients treated with the same biologic dosages and assessed at the same time points were selected for analysis.

Results: Of 83 publications initially identified, 16 publications were included for analysis (RA: originators, n=4; biosimilars, n=6; PsO: originators, n=3; biosimilars, n=3). Higher proportions of ACR20 responders were found among RA patients receiving the originator biologics and biosimilars in biosimilar trials, than among patients receiving the originator biologics in pivotal trials (Table). Insufficient data were available from ADA and INF biosimilar studies in PsO; in ETN studies in PsO, a difference was also observed in the proportions of PASI75 responders between biosimilar and pivotal trials.

Table: ACR20 and PASI75 responders in pivotal vs biosimilar trials and differences in response rates

<table>
<thead>
<tr>
<th>Product</th>
<th>RA trial type</th>
<th>Time point (wk)</th>
<th>ACR20 responders (%)</th>
<th>Difference, pivotal vs biosim, (%)</th>
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<tr>
<td>ADA</td>
<td>Infliximab</td>
<td>24</td>
<td>65</td>
<td>-</td>
</tr>
<tr>
<td>ADA</td>
<td>Biosim4</td>
<td>24</td>
<td>72</td>
<td>7</td>
</tr>
<tr>
<td>ADA</td>
<td>Biosim5</td>
<td>24</td>
<td>72</td>
<td>0</td>
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<td>Biosim3</td>
<td>24</td>
<td>75</td>
<td>13</td>
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<td>73</td>
<td>10</td>
</tr>
<tr>
<td>ETN</td>
<td>Pivotal5</td>
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<td>71</td>
<td>-</td>
</tr>
<tr>
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<td>58</td>
<td>10</td>
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</tbody>
</table>

Conclusions: Differences were observed in treatment response rates between originator pivotal trials and more recent trials of originator biologics and their respective biosimilars. Such differences in outcomes may be attributable to fundamental differences in study design and/or baseline patient characteristics, which require further analysis. Additional research is also needed to explore the clinical relevance of these differences.

References:

AB0380 RESULTS FROM A RANDOMIZED, SINGLE-BLIND, SINGLE-DOSE, PARALLEL-GROUP STUDY IN HEALTHY SUBJECTS DEMONSTRATING PHARMACOKINETIC SIMILARITY BETWEEN ABP 710 AND INFliximab


Background: ABP 710 is being developed as a biosimilar with the same amino acid sequence as infliximab, an anti-tumor necrosis factor therapy. Analytical and functional comparisons between ABP 710 and infliximab have been conducted and confirmed no clinically meaningful differences in terms of purity, safety, and potency.1,2

Objectives: This report describes the results of analyses comparing the pharmacokinetics (PK), safety, and immunogenicity of ABP 710 and infliximab sourced from the European Union (EU).

Methods: This was a single-blind, single-dose, parallel-group study among healthy adults, 18 to 45 years of age and with a body mass index of 18 to 30 kg/m². Subjects were randomized to receive a 5 mg/kg intravenous infusion of either ABP 710 or infliximab. The primary objective of this analysis was demonstration of PK similarity of ABP 710 to infliximab based on area under the serum concentration-time curve from 0 extrapolated to infinity (AUC(∞); primary endpoint). PK equivalence was deemed achieved if the geometric mean (GM) ratio and its 90% confidence interval (CI) for AUC(∞) was within the range of 0.80 to 1.25. Secondary endpoints included maximum observed serum concentration (Cmax), area under the serum concentration-time curve from time 0 to last quantifiable concentration (AUC(0-τ)), safety, and immunogenicity.

Results: A total of 49 subjects received ABP 710 and 49 subjects received infliximab. Following a single dose, the adjusted least square (LS) GM of AUC(∞), Cmax, and Cmax for ABP 710 was 33559 μg·h/mL, 31789 μg·h/mL, and 123 μg/mL, respectively. The adjusted LS GM of AUC(∞), Cmax, and Cmax for infliximab was 33706 μg·h/mL, 31847 μg·h/mL, and 121 μg/mL, respectively. Ratios of adjusted LS GMs (90% CIs) between ABP 710 and infliximab for AUC(∞), AUC(0-τ), and Cmax were 0.996 (0.904, 1.096), 0.998 (0.918, 1.086), and 1.021 (0.962, 1.083), respectively.

Safety: There was one subject in the infliximab group who developed polyarthritis that resolved with treatment and the subject completed the study. There were no deaths, other serious adverse events, or treatment-emergent adverse events (TEAEs) leading to discontinuation from the study. The incidence of TEAEs was similar in the two treatment groups (ABP 710: 83.7%; infliximab: 83.7%); the majority of TEAEs were mild or moderate. The most frequently reported TEAEs were somnolence, headache, nasopharyngitis, upper respiratory tract infection, nausea, and leucytosis. Immunogenicity: All subjects tested negative for antidrug antibodies (ADAs) prior to receiving any investigational product.

Conclusions: The study was designed to demonstrate PK similarity between ABP 710 and infliximab sourced from the EU among healthy subjects. The safety and immunogenicity profile were comparable between the two treatment groups.


DOI: 10.1136/annrheumdis-2017-eular.3281
to RTX (6.6). The demographic and response data DAS 28 are shown in Table 1. There are no differences in the years of evolution,% of women, FR or ACPA positive, erosions and disease activity, as measured by DAS 28, before the switch, between the two groups (anti-TNF vs non-anti-TNF). Patients in the anti-TNF group were slightly younger than non-anti-TNF:When the DAS 28 response is evaluated at 3 and 6 months, the modifying treatment is effective (DAS 28 beginning 4.4 vs DAS 28 6 months 2.8 ± 0.001). When assessing the response to change, there is no difference in the DAS 28 response at 3 months or 6 months, if you switched to anti-TNF or non-anti-TNF (3.18 vs 2.52 ± p=0.122).

When comparing the patients with anti-TNF alpha vs TCZ, 62.5% of the patients with TCZ are in remission compared to 38%, 5% (p=0.047).

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong> (n=61)</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Sex ( % M/F)</td>
</tr>
<tr>
<td>Years evolution (years)</td>
</tr>
<tr>
<td>Erosion (%)</td>
</tr>
<tr>
<td>ERA (%)</td>
</tr>
<tr>
<td>ACPAs (%)</td>
</tr>
</tbody>
</table>

Conclusions: In this retrospective study in daily clinical practice, it is evident that the change in treatment after failure of the first biological one, without differences if the change is to an anti TNF or another treatment. The percentage of patients who switched from anti-TNF at 6 months is higher if the change is at TCZ. Given the small number of patients, larger studies would be needed to confirm the results.

References:
[1] Johnston SS et col. Comparison of Biological Disease-Modifying Antirheumatic Drug Therapy Persistence Between Biologics Among Rheumatoid Arthritis Patients Switching from Another Biological, Rheumatol Ther.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3375

AB0382 OUTCOMES OF ETANECOTER THERAPY IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS: AN INVESTIGATION OF THE AKITA ORTHOPEDIC GROUP ON RHEUMATOID ARTHRITIS REGISTRY

H. Anumam, T. Kashiwagura, M. Urayama, M. Kobayashi, T. Aizawa and 24 patients discontinued treatment. The AE and LOE cohorts contained 12 and 7 patients, respectively. The AE cohort had a mean age of 75.5 years at the start of treatment, with a mean disease duration of 20.7 years, 8.3% of patients switching from another biologic agent, 16.7% performing ADL independently, and a comorbidity rate of 100%. Corresponding values for the LOE cohort were: mean age, 71.4 years; disease duration, 12.7 years; switching from another biologic agent, 42.9%; performing ADL independently, 57.1%; and comorbidity rate, 28.6%. Efficacy was noted for 81.8% of all patients with 52 weeks of ETN therapy, achieving good efficacy in 21 cases and moderate efficacy in 24 cases.

Conclusions: Retention rate and efficacy were considered satisfactory in elderly RA patients receiving ETN therapy. The risk of adverse events was suggested to increase with increasing age and the presence of comorbidities. These factors require attention when prescribing ETN therapy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6102

AB0383 SUBCLINICAL BRAIN DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS RELATIONSHIP TO TNF BLOCKER THERAPY

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Background: RA is a chronic disease with a yet unclarified etiology, which causes the activation of pro-inflammatory pathways that bring about joint and systemic inflammations (1). In recent years, the pathophysiology of brain damage that can occur in RA has drawn attention. Emphasis is being put on the possibility that brain damage occurs due to blood-brain barrier (BBB) damage that is linked to chronic inflammation.

Objectives: In this study, we aimed to investigate the peripheral blood levels of brain-specific proteins such as S100 beta and GFAP (glial fibrillary acidic protein), the differences in these proteins in patients who did and did not undergo TNF blocker therapy and their relationship with cranial MR lesions, disease activity and cognitive functions with the purpose of determining CNS (central nervous system) damage in patients with rheumatoid arthritis (RA).

Methods: 59 RA patients (47 (81.0%) females, 11 (19.0%) males) and 34 healthy controls (24 (70.6%) females, 10 (29.4%) males) were included in the study. All RA patients were on synthetic DMARD therapy at the beginning. While 30 patients continued sDMARD therapy, 28 patients with high disease activity were started on TNF blocker therapy. All demographic characteristics of the patients were recorded. Disease activity was evaluated using DAS28. The Mini-Mental State Examination (MMSE) was used to evaluate cognitive functions, and the Fazekas Scale was used to assess the cranial MRI lesions. The peripheral blood S100 beta, GFAP, claudin, IL-17, IL-1 beta levels of the patients were measured at the beginning and on the 6th month.

Results: Demographic characteristics were similar between the two groups and no statistical difference was detected between the patient group and the control group except age. RA patients that was started on TNF blocker therapy, S100 beta and GFAP levels were higher to a significant degree compared to the control group. (p<0.05) In the group that was started on TNF blocker therapy, S100 beta and GFAP levels were detected to have decreased significantly 6 months after treatment compared to the start of treatment. (p<0.05) No difference was found between the RA and control groups in terms of hyperintense lesions seen in the cranial MRI. (p>0.05) As the lesions in the deep white matter seen in the cranial MRI of RA patients increased, their S100 beta levels were also seen to increase. (p<0.05)

Conclusions: In conclusion, next to decreasing disease activity and joint erosions by suppressing inflammation, anti-TNF therapy in RA can also suppress potential brain damage linked to subclinical BBB (blood-brain-barrier) dysfunction. Further studies with broader participation and longer patient follow-up are needed to reinforce this hypothesis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2315

AB0384 CLINICAL AND RADIOLOGICAL EVOLUTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS AFTER DEINTESIFICATE BILOGICS

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Background: RA is the most common chronic inflammatory arthritis. About 30% of patients need treatment with biologic therapy (BT). Deintensification of BT for patients in clinical remission, is a strategy used in clinical practice to reduce side effects and burden.

Objectives: The primary endpoint was evaluate clinical and radiological behavior of the RA in patients receiving BT at reduced doses.
The secondary endpoint was to analyze the characteristics of patients who remain for a longer period of time in an optimized dose regimen.

**Methods:** In our Rheumatology Unit we are treating 271 RA patients with BT, the dose was deintensified for 62 (23%) patients in remission or low disease activity for at least 6 months. We have selected 32 patients with BT reduced for at least 6 years in an observational, longitudinal, retrospective study. Disease activity was measured by the DAS 28 index. Structural damage was evaluated by SENS method.

**Results:** We analyze 32, 20 female, 12, male mean age at diagnosis 42.6 years old; BT was started after RA evolution of 98.63 months. Drug reduction was performed after full BT for 62 months, mean DAS 28 was 2.47.

Patients were 75% FR positive and 56.7% ACPA positive. Etanercept was the BT more commonly reduced 59.4%, followed by adalimumab 21.9%, infliximab 12.5% and certolizumab 6.3%.

For 21 patients remaining on reduced doses, the mean DAS28 at time for analysis was 2.67. BT reduction as different drugs: none infliximab reduced dose patients required return to normal dose. All certolizumab reduced (2 patients) patients needed to back to normal dose. Etanercept in 36.8% and adalimumab 28.6%.

The mean of SENS score before the optimization was 8.78 and at time for analysis 10.67 for both kind of patients, who continued reduced and those who returned to increase BT dose.

For the secondary endpoint 10 out of 12 male continue with deintensificated BT (83%) in the other hand only 11 out of 20 female (55%) maintained reduced dose.

More negative for FR (69.2%) and ACPA (75%) patients keep on reduced dose regimen.

**Conclusions:** We have deintensificated 62 out of 271 RA patients on BT (23%).

All patients were in clinical remission at the beginning of BT dose reduction for more than 6 months.

Most patients (65%) analyzed remain long time with reduced BT in clinical remission.

We have not observed significant X-ray progression for reduced patients, even if they increase disease activity and need to back to the original BT dose.

The increase in disease activity was the main reason to interrupt the optimization regime.

Infliximab was the drug that remained more time optimized.

According to the results of our study, male patients negative for ACPA and FR remain longer with reduced doses.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5273
OBJECTIVES: To investigate and compare etanercept monotherapy versus combination with sDMARDs in RA patients regarding survival on drug, efficacy, quality of life and reason for discontinuation.

METHODS: Observational, open, long-term study of patients from the ATTRGA registry starting the ETN therapy since 2010 either on monotherapy or in combination with sDMARDs (n=406). 461 patients (80.7%) were females. Mean ± SD at baseline was 74.5% ± 15 years. A multidisciplinary team of rheumatologists and clinical pharmacists in a third-level hospital was involved in decision-making on treatment and dose reduction, which invovled the application of protocols and the follow-up of patients at least every hospital was involved in decision-making on treatment and dose reduction, which involved the application of protocols and the follow-up of patients at least every 3 months of duration on November 1, 2013, constituted the cohort of patients who were optimized for 3 years. None of the differences reach statistical significance.

CONCLUSIONS: The strategy of dose reduction of biological therapies in patients with established RA that achieve sustained remission is possible in 37.3% of cases in real clinical practice (CREATE Registry) and it was maintained for 3 years.

The probability of occurrence of relapse decreases after 2 years of treatment with an optimized regimen in those patients who have not relapsed before.

This strategy is possible in patients with persistently controlled disease and in view of our results, it is independent of the drug administered (antiTNF versus non-antiTNF).

After 3 years of follow-up, all patients maintained clinical remission (DAS 28 <2.6) despite relapses, and after resumption of the usual dose, all of them reached the therapeutic goal again.

Patients who maintain clinical remission for 3 years achieve DAS28 values statistically lower than those who did not after 2 years.

DISCLOSURE OF INTEREST: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2583

RESULTS AT 3 YEARS OF AN OPTIMIZATION GUIDELINE OF BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS. CREATE RECORD RESULTS

P. Font1, M.C. Castro2, M. Romero3, R. Ortega3, L. Calvo3, D. Ruiz3, M. Cardenas2, R. Alejandre2, P. Carreto1, E. Collantes2, 1Hospital Reina Sofia - Imibic-Universidad de Cordoba; 2Hospital Reina Sofia - Imibic-Universidad de Cordoba, Cordoba; 3MFyC de Valladolid, Area Este, Valladolid, Spain

BACKGROUND: Dose optimization, such as dose reduction or dose spacing, is nowadays presented as a therapeutic strategy to be followed in patients with rheumatoid arthritis (RA) who have managed to reach and maintain clinical remission for a while. This strategy reduces the frequency of adverse effects and promotes cost savings.

METHODS: Patients with RA (Criteria ACR 1987) of the CREATE registry (patients who were treated in real life conditions) who had clinical remission (DAS28 <2.6) on a 6 months of duration on November 1, 2013, constituted the cohort of patients who were optimized for the dose received. According to the consensus of the Spanish Societies of Rheumatology and Hospital Pharmacy, the optimization of doses meant the reduction of between 20 and 50% of the same. A multidisciplinary team of rheumatologists and clinical pharmacists in a third-level hospital was involved in decision-making on treatment and dose reduction. There are many evidences that Th9 lymphocytes take part to the immunogenicity of biologic agents.

We aimed to evaluate the immunogenicity of branded and biosimilar infliximab by detecting changes in Th9 percentages following an “in vitro” stimulation test.

RESULTS: PBMCs from 55 consecutive RA outpatients (15 drug-free, 20 successfully treated with branded infliximab and 20 failing branded infliximab) and from 10 healthy controls were collected. PBMCs were cultured with/without 50 μg/mL infliximab originator (Remicade®) or 50 μg/mL infliximab biosimilar (Remisima®), 50 μg/mL Human IgG1kappa and 50 μg/mL recombinant Human IgG Fc for 18 hours. Th9 lymphocytes were identified by means of flow cytometry as Pu.1+, INF-γ, IL-9+ CD4+ cells. Furthermore, the markers CCR7 and CD45RA were used to distinguish naive from memory IL-9-producer cells.

Despite the variety of stimuli tested, changes in Th9 percentages were not statistically significant.

CONCLUSIONS: The results are consistent with the findings of previous studies that Th9 lymphocytes are implicated in the immunogenicity of biological therapies. However, further studies are needed to confirm these data.

DISCLOSURE OF INTEREST: None declared.

DOI: 10.1136/annrheumdis-2017-eular.4401

THE IMMUNOGENICITY OF BRANDED AND BIOSIMILAR INFLIXIMAB IN RHEUMATOID ARTHRITIS ACCORDING TO TH9-RELATED RESPONSES

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BACKGROUND: There are many evidences that Th9 lymphocytes take part to the immunogenicity of rheumatoid arthritis (RA), however it is unclear whether these cells are implicated in the immunogenicity of biologic agents.

OBJECTIVES: We aimed to evaluate the immunogenicity of branded and biosimilar infliximab by detecting changes in Th9 percentages following an “in vitro” stimulation test.

RESULTS: PBMCs from 55 consecutive RA outpatients (15 drug-free, 20 successfully treated with branded infliximab and 20 failing branded infliximab) and from 10 healthy controls were collected. PBMCs were cultured with/without 50 μg/mL infliximab originator (Remicade®) or 50 μg/mL infliximab biosimilar (Remisima®), 50 μg/mL Human IgG1kappa and 50 μg/mL recombinant Human IgG Fc for 18 hours. Th9 lymphocytes were identified by means of flow cytometry as Pu.1+, INF-γ, IL-9+ CD4+ cells. Furthermore, the markers CCR7 and CD45RA were used to distinguish naive from memory IL-9-producer cells.

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DISCLOSURE OF INTEREST: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2583

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METHODS: Patients with RA (Criteria ACR 1987) of the CREATE registry (patients who were treated in real life conditions) who had clinical remission (DAS28 <2.6) on a 6 months of duration on November 1, 2013, constituted the cohort of patients who were optimized for the dose received. According to the consensus of the Spanish Societies of Rheumatology and Hospital Pharmacy, the optimization of doses meant the reduction of between 20 and 50% of the same. A multidisciplinary team of rheumatologists and clinical pharmacists in a third-level hospital was involved in decision-making on treatment and dose reduction. There are many evidences that Th9 lymphocytes take part to the immunogenicity of biologic agents.

We aimed to evaluate the immunogenicity of branded and biosimilar infliximab by detecting changes in Th9 percentages following an “in vitro” stimulation test.

RESULTS: PBMCs from 55 consecutive RA outpatients (15 drug-free, 20 successfully treated with branded infliximab and 20 failing branded infliximab) and from 10 healthy controls were collected. PBMCs were cultured with/without 50 μg/mL infliximab originator (Remicade®) or 50 μg/mL infliximab biosimilar (Remisima®), 50 μg/mL Human IgG1kappa and 50 μg/mL recombinant Human IgG Fc for 18 hours. Th9 lymphocytes were identified by means of flow cytometry as Pu.1+, INF-γ, IL-9+ CD4+ cells. Furthermore, the markers CCR7 and CD45RA were used to distinguish naive from memory IL-9-producer cells.

Despite the variety of stimuli tested, changes in Th9 percentages were not statistically significant.

CONCLUSIONS: The results are consistent with the findings of previous studies that Th9 lymphocytes are implicated in the immunogenicity of biological therapies. However, further studies are needed to confirm these data.

DISCLOSURE OF INTEREST: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2583
**AB0390** EFFICACY AND SAFETY OF YISAIPU, A RECOMBINANT HUMAN TUMOR NECROSIS FACTOR-α RECEPTOR II IGG FC FUSION PROTEIN IN CHINESE PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is characterized by chronic autoimmune diseases of progressive synovitis and joint destruction, which can eventually lead to joint deformation and disability. A number of clinical studies showed the effectiveness of tumor necrosis factor antagonist combined with methotrexate in the treatment of RA. Yisaipu used in this study is produced by CPGC Company (Shanghai, China), which was approved to treat RA by Chinese Food and Drug Administration, in 2005, which is biosimilar of etanercept (a soluble recombinant TNF receptor antibody fusion protein, an immunoglobulin molecule which connects two TNF receptors (p75) to the human IgG1 FC division). Etanercept had been confirmed the effectiveness in rheumatoid arthritis already in many clinical trial. However, there is however randomised controlled study published regarding Yisaipu in international journals. We conducted an open-label, randomized controlled study for 24 weeks to evaluate the efficacy and safety of Yisaipu in combination with DMARDs in comparison with low or medium dose of glucocorticoid in patients with moderate to severe RA.

**Objectives:** to evaluate the efficacy and safety of Yisaipu in combination with DMARDs in comparison with low or medium dose of glucocorticoid in patients with moderate to severe RA.

**Methods:** Eighty-four patients with moderate to severe rheumatoid arthritis were randomly assigned into 4 groups: group 1: methotrexate plus Yisaipu; group 2: methotrexate plus medium-dose prednisone (30mg/d, reduced to 15 mg/d after 2 weeks); group 3: methotrexate plus low-dose prednisone (7.5mg/d); group 4: methotrexate alone. Each group was treated with MTX (12.5mg once weekly, the next day with folic acid 10mg) and hydroxychloroquine sulfate (200 mg twice a day) concomitantly. The primary endpoint was ACR20 response rate at week 24. Secondary efficacy endpoints were ACR70, ACR70, DAS-28, Higher Health Assessment Questionnaire (HAQ) and EULAR remission rate at week 4, 12 and 24.

**Results:** At week 24, a higher proportion of patients in group 1 and group 2 than the other two groups met the ACR20 response criteria (85.7% in group 1 and 71.4% in group 2 vs. 62.5% and 58.9% in group 3 and group 4, P<0.05). The reductions of HAQ at week 24 showed significant improvement in group 1 and group 2 compared to group 3 and 4 (-2.96 and -2.69 respectively, P<0.05). Reduction of DAS-28 in group 1 and group 2 were significantly higher than the other two groups (P<0.05). The percentage of EULAR remission rate of group 1 and group 2 is significantly higher than group 3 and group 4 at week 24 (47.6% in group 1, 33.9% in group 2, 23.8% in group 3 and 14.3% in group 4, P<0.05). There were no significant differences of adverse event among four groups.

**Conclusions:** Yisaipu plus MTX or GCs plus MTX in Chinese patients with moderate to severe RA is safe and effective in our study. More studies are needed to compare the long-term safety and cost-effectiveness between Yisaipu and GCs in treatment with RA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1867

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**AB0392** SAFETY AND EFFECTIVENESS OF CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 24 MONTHS NATIONWIDE REGISTRY IN KOREA

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**Background:** CT-P13 is approved in both European Union and United States, and licensed for use in 79 countries around the world as a biosimilar to innovator infliximab (INFx). The independent registries of CT-P13 have been conducted in a number of European countries and Korea [1].

**Objectives:** to evaluate safety and effectiveness of CT-P13 when administered in a real-life setting in active RA patients.

**Methods:** This study collected data of patients who were treated with CT-P13 from 2013 December to 2016 June. Efficacy was assessed at baseline and every 6 months thereafter using DAS28 (ESR) and/or DAS28 (CRP) and collection of adverse events (AEs) was performed. Infliximab was assessed at baseline, Week 30 and every year during CT-P13 treatment period.

**Results:** Total 125 patients were enrolled; 104 patients started treatment with CT-P13 (Naive group) and 21 patients (8 from INX, 13 from other anti-TNFs) switched treatment to CT-P13 (Switched treatment group). The mean (SD) duration since RA diagnosis was 6.5 (±6.85) years for all patients. Of all patients treated with CT-P13, only 4.8% (6/125) of patients changed to other RA diagnosis was 6.5 (±6.85) years for all patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3507

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**AB0391** SIMILAR PHARMACOKINETICS, SAFETY AND TOLERABILITY OF THE ADALIMUMAB BIOSIMILAR CANDIDATE BI 695501 ADMINISTERED SUBCUTANEOUSLY VIA PREFILLED SYRINGE (PFS) OR AUTOINJECTOR (AI) (VOLTAIRE®-AI)

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**Background:** PK bioequivalence of BI 695501, an adalimumab biosimilar candidate, and the adalimumab originator was demonstrated previously (VOLTAIRE®-PK). Wynne et al., Expert Opin Investig Drugs 2016;25:1361–70). Administration of appropriate terminal phase (only one non-BLQ [below the limit of quantification] value in the elimination phase).

**Methods:** in a real-life setting in active RA patients.

**Results:** Seventy-one volunteers were randomised: PFS, n=36; AI, n=35. Key demographic and baseline characteristics were well balanced between the treatment groups. PK end point results are shown in Table 1. Estimates for AI/PFS geometric mean (gMean) ratios were within the standard bioequivalence acceptance range (80–125%). Mean plasma concentration-time profiles and

**Table 1. PK Parameters over All Subjects for BI 695501 via PFS or AI**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PFS</th>
<th>AI</th>
<th>Adjusted gMean*</th>
<th>Adjusted gMean†</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC&lt;sub&gt;0–12h&lt;/sub&gt; (μg·h/ml)</td>
<td>35°</td>
<td>2270</td>
<td>35</td>
<td>2280</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0–24h&lt;/sub&gt; (μg·h/ml)</td>
<td>1960</td>
<td>35</td>
<td>1960</td>
<td>35</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (μg/ml)</td>
<td>306</td>
<td>3.76</td>
<td>36</td>
<td>3.4</td>
</tr>
</tbody>
</table>

*Adjusted for treatment and BMI group as fixed effects; †Based on observed last concentration values; ‡AUC values could not be calculated for one subject (Subject 1001-0110), due to the lack of appropriate terminal phase (only one non-BLQ [below the limit of quantification] value in the elimination phase).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.283
For naïve group, 50% (52/104) of patients had at least one positive anti-drug antibody result and it is consistent to other published study [2]. Overall safety summarized as the percentage of patients with at least one treatment emergent AE (TEAE) was similar or lower after switching to CT-P13 (Table 2). No cases of active tuberculosis were reported. **Table 1. DAS28 in CT-P13 Naïve group over 24 months**

<table>
<thead>
<tr>
<th>Control</th>
<th>Baseline</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>67</td>
<td>62</td>
<td>40</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Mean</td>
<td>5.78</td>
<td>3.61</td>
<td>3.30</td>
<td>3.01</td>
<td>2.42</td>
</tr>
<tr>
<td>SD</td>
<td>1.14</td>
<td>1.40</td>
<td>1.22</td>
<td>1.03</td>
<td>0.74</td>
</tr>
</tbody>
</table>

**Table 2. Safety results in CT-P13 Naïve and Switching group**

<table>
<thead>
<tr>
<th>TEAEs</th>
<th>Naïve group</th>
<th>Switching group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection and Infestation</td>
<td>42.3% (44/104)</td>
<td>33.3% (14/42)</td>
</tr>
<tr>
<td>Related TEAEs</td>
<td>31.7% (33/104)</td>
<td>28.6% (6/21)</td>
</tr>
</tbody>
</table>

Conclusion: The overall safety profile revealed that CP-T13 is well-tolerated in patients with RA and remission rate for 24 months also showed that CP-T13 is efficacious under real world practice.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2413

**AB0393 ADVERSE SKIN REACTIONS IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING TUMOR NECROSIS FACTOR ALPHA INHIBITOR – AN ANALYSIS OF DATA FROM THE SLOVENIAN BIOLOGICAL REGISTRY**

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Background: Paradoxical skin reactions (PSR) are defined as a new onset or worsening of skin conditions during treatment with tumour necrosis factor alpha (TNF-α) inhibitors that generally improve or respond to this therapy. The list of PSR is growing. The most commonly reported are psoriasis skin eruptions. Objectives: To evaluate the frequency of PSR in the group of rheumatoid arthritis (RA) patients treated with TNF-α inhibitor at the time of development of skin eruption. Methods: We conducted the analysis of the data from the mandatory Slovenian national registry of patients treated with bDMARDs (BioRx.si) which includes spontaneous adverse reaction reports between 01.01.2008–31.05.2016. The analyses were limited to patients with RA.

Results: During the observation period, 1,046 RA (82% female; median (IQR) age at initiation of TNF-α inhibitors 56 (49–63) years) patients treated with TNF-α inhibitors for 3,140 person years. We identified 14 cases with PSR (71% female, median age (IQR) 45 (53–62)). There were 6 PSR cases on adalimumab, 4 on etanercept, 3 on certolizumab – pegol, and 1 on infliximab. 10 patients developed psoriatic/psoriasiform eruptions, 2 patient leucocytoclastic vasculitis, one had lichen planus, and one undifferentiated skin changes. The incidence rate of new psoriatic/psoriasiform eruptions, 2 patient leucocytoclastic vasculitis, one had lichen planus, and one undifferentiated skin changes. The incidence rate of new psoriasiorm PSR, which is in line with published data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1934

**AB0394 TAPERING TNF INHIBITORS IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY**

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Background: Increasing evidence suggests the feasibility of biologic DMARD tapering in RA patients after achieving and maintaining good control of disease activity. Current guidelines on RA treatment also recommend tapering of biologic and non-biologic DMARDs for patients in remission. Data on biologic DMARD tapering reflecting real life settings are limited.

Objectives: To collect information on biologic DMARD tapering and its outcome in RA patients who are followed-up in a rheumatology outpatient clinic.

Methods: In this retrospective study we used the hospital administrative database to identify patients with a diagnosis of RA and a first time prescription of a biologic DMARD (TCZ was specifically limited to one of the 3 TNF inhibitors (etanercept, adalimumab, infliximab)) between January 2012 and the end of December 2013. Demographics and information regarding treatment and outcome were taken from the medical charts.

Results: Of the 125 patients identified at the database search, 104 were belonging to our clinic and had available follow-up data until June 2016. Seventy-nine of them were women and 25 were men. Their mean age was 47.7±13 SD years and their mean disease duration was 7.4±6.9 years. 60% were prescribed etanercept, 23% adalimumab, 17% infliximab. After a mean duration of 14.0±7.6 SD months a dose reduction of TNF inhibitors was made in 44 patients (42%). This was in the form of spacing in 39 patients (Etanercept +16, Infliximab +14, Adalimumab +9) and dose tapering in 5 (all Etanercept). All of these were due to good clinical response except for 1 patient’s own request for fear from adverse effects. Following dose reduction increased disease activity was seen in 16 patients (36%) mandating restoration to original dose within a mean of 8.8±9.7 SD months with good response. Twenty-eight patients (64%) preserved their good clinical response during a mean follow-up of 46.1±8.3 SD months which enabled further dose reductions in 20 patients. There was also reductions in the mean number of synthetic DMARD’s (1.4±0.8 SD at the initiation of TNF inhibitors and 0.7±0.8 SD at the end of follow-up) and in the percentage of patients using steroids (78% to 33%). At the end of the follow-up, among the whole group of 104 patients, only 73 (70%) were using biologics (TNF inhibitors +49, non-TNF biologics +24). The reasons for stopping biologics in the remaining 31 patients were ongoing remission (16 patients), pregnancy (1 patient), non-compliance (4 patients), injection site reactions (3 patients), fear from adverse events (1 patient).

Conclusion: Tapering of TNF inhibitors was possible in 40% of RA patients during their routine follow-up. Half of the patients maintained good clinical response after tapering allowing further dose reductions in one third.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1934

**Rheumatoid arthritis - other biologic treatment**

**AB0395 SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: 24 WEEKS RESULTS OF THE FRENCH PHASE II STUDY, TOSCA**


Background: After the two global pivotal studies, which evaluated the safety and efficacy of subcutaneous tocilizumab (TCZ-SC) in combination (como) with conventional synthetic disease-modifying antirheumatic drugs (cDMARDs), it was important to understand the efficacy and safety profile of TCZ-SC both as monotherapy (mono) and in combo with csDMARDs in patients (pts) managed in conditions less strict than those of pivotal clinical trials.

Objectives: To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as mono and in combo with csDMARDs over 24 weeks in adult pts with moderate to severe RA. The primary efficacy criterion was the change in DAS28-ESR from baseline to week 24 (W24).

Methods: TOSCA is a national, multicenter, open-label phase IIb study, part of the international umbrella study (TOZURA). It aimed to enroll TCZ-naïve patients who were csDMARDs inadequate responders (IR) and/or biologic DMARD-IR. Pts received TCZ-SC 162 mg qw for 24 weeks, administered at the investigator’s discretion as mono or in combo with a csDMARD. Stable oral corticosteroids (CCS), ≤10 mg/day prednisone or equivalent (eq.pred), were allowed.
Results: The baseline characteristics of the 139 included patients were: mean age 57.3 years (±13.8), 74.1% female, mean RA disease duration 10.8 years (±9.2), immunonpositivity 85.5%, structural joint damage 65.6%, mean DAS28 5.8 (±1.1). 52.5% of patients were bDMARD-IR. TCZ-SC was initiated in mono TCZ in 30.9% of pts and in combo in 69.1% (79.1% MTX). Oral CCS were used by 50% of pts (mean 7.4 mg/d eq/pred.±2.7). In comparison with mono pts, the mono pts were older (58.7 vs 56.7 years), with a higher mean DAS28 (6.1 vs 5.7), a longer disease duration (11.5 vs 10.6 years), and a higher CCS mean dose (8.3 vs 6.9 mg/d eq/pred.). At W24, the mean DAS28 score variation vs baseline was -3.1 overall (p<0.0001); -3.0 in mono TCZ vs -3.1 in combo TCZ (p=0.07) (Fig.). The proportion of pts who achieved DAS28 remission was 51.1% (41.9% in mono vs 55.2% in combo (p=0.14)). CDAI remission, which does not include acute phase reactants, was achieved in 17% pts, 16% in mono vs 17% in combo (p=0.95). At W24, 27.9% of pts receiving >5 mg CCS at baseline decreased the daily dose of pred. (30.1% in mono TCZ and 26.7% in combo. Out of the 23 pts (16.5%) who withdrew, 13.0% did so for lack of efficacy and 52.1% for safety reasons; one death occurred following a septic shock after surgery for gastric volvulus, not related to TCZ. At W24 95.7% of pts had experienced at least one adverse event (AE) and 10.1% at least one serious AE with similar rates between groups.

Conclusions: TCZ-SC demonstrated at 6 months comparable efficacy, safety and steroid sparing results in mono- and combo therapy consistent with the known profile of TCZ-IV.


AB0396 TOCILIZUMAB I.V. EFFECTIVENESS IN RA PATIENTS IS INDEPENDENT OF SMOKING STATUS


Table 1  Efficacy and safety of TCZ I.V. in RA patients

<table>
<thead>
<tr>
<th>Baseline characteristics, % (n)</th>
<th>WT04 [Total]</th>
<th>Smokers</th>
<th>Non-smokers</th>
<th>Ex-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years], mean ± SD</td>
<td>55.7 ± 12.4</td>
<td>51.8 ± 10.1</td>
<td>56.8 ± 13.6</td>
<td>56.6 ± 11.4</td>
</tr>
<tr>
<td>Duration of RA [years], median</td>
<td>8.0</td>
<td>6.0</td>
<td>8.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Concomitant, % (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMARDs</td>
<td>42.6 (384)</td>
<td>48.7 (85)</td>
<td>41.4 (195)</td>
<td>37.9 (58)</td>
</tr>
<tr>
<td>SCS</td>
<td>61.5 (550)</td>
<td>64.5 (117)</td>
<td>59.7 (283)</td>
<td>62.2 (100)</td>
</tr>
<tr>
<td>Comorbidities, % (n)</td>
<td>72.5 (654)</td>
<td>68.4 (117)</td>
<td>72.4 (343)</td>
<td>74.9 (126)</td>
</tr>
</tbody>
</table>

Effectiveness

<table>
<thead>
<tr>
<th>VAS [mm], median (IQR, Q3)</th>
<th>Exhaustion/Tiredness (Baseline)</th>
<th>(Last visit)</th>
<th>Intensity of pain (Baseline)</th>
<th>(Last visit)</th>
<th>Sleep disturbances (Baseline)</th>
<th>(Last visit)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baxline</td>
<td>(Last visit)</td>
<td>Baxline</td>
<td>(Last visit)</td>
<td>Baxline</td>
<td>(Last visit)</td>
</tr>
<tr>
<td></td>
<td>30.0 (9.0)</td>
<td>30.0 (9.0)</td>
<td>50.0 (19.0)</td>
<td>50.0 (19.0)</td>
<td>20.0 (9.0)</td>
<td>20.0 (9.0)</td>
</tr>
<tr>
<td></td>
<td>30.0 (10.0)</td>
<td>30.0 (10.0)</td>
<td>50.0 (19.0)</td>
<td>50.0 (19.0)</td>
<td>20.0 (9.0)</td>
<td>20.0 (9.0)</td>
</tr>
</tbody>
</table>

Safety (event rate per 100 patient years)

<table>
<thead>
<tr>
<th>Adverse events (AEs)</th>
<th>Smokers</th>
<th>85.1</th>
<th>99.0</th>
<th>74.6</th>
<th>97.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events (SAEs)</td>
<td>19.4</td>
<td>36.4</td>
<td>15.7</td>
<td>22.2</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: TCZ I.V. treatment over two years resulted in improvements of all disease activity parameters. Contrary to csDMARDs and TNF-blockers, the results show that smokers benefit from TCZ I.V. to the same extent as non-smokers and ex-smokers. The similar effectiveness of TCZ I.V. was confirmed by distinctly improved patient reported outcomes (PROs) in all subgroups. On the other hand, smoking seems to coincide with a higher rate of adverse events and an increased risk of infections. However, due to differences in baseline characteristics between the subgroups, this has to be interpreted with caution.

References:

Acknowledgements: This study was funded by Roche/Chugai, Germany. Writing assistance was provided by Eron Acunova GmbH, Germany with support from Roche/Chugai.
AB0397 ABATACEPT SHOWS BETTER SUSTAINABILITY THAN TNF INHIBITORS WHEN USED FOLLOWING INITIAL BIOLOGIC DMARD FAILURE IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF REAL-WORLD OBSERVATIONS FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

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Background: In the absence of biomarkers predicting response to a specific therapy, the choice of second biologic is based mostly on habit and availability of an alternative agent. Traditionally, a second anti-TNF was the preferred option, but recent registry data point to better responses and retention if a drug with a different mode of action is prescribed.

Objectives: Assess the long-term retention of abatacept (ABA) and TNFi following first biologic (b)DMARD inadequate response in RHUMADATA® registry patients (pts) with RA.

Methods: Data from RHUMADATA® pts with RA prescribed either ABA or TNFi as the second DMARD after 1 January 2006 were analysed. Pts were followed until treatment discontinuation or 9 January 2017 cut-off. Pt characteristics were compared using descriptive statistics, bDMARD discontinuation rates using Kaplan-Meier methods, and proportional hazard models were used to identify predictors of treatment discontinuation.

Results: Data for 92 and 194 pts prescribed ABA or a TNFi, respectively; as second-line treatment were examined. No clinically significant differences in baseline characteristics were noted between treatment groups. Most pts were women (76.2%), average age (SD) was 45.1 (13.3) years at diagnosis and disease duration 10.8 (9.0) years. Most pts were stopping an anti-TNF agent: 97% of those who were switched to ABA and 83% of those who were prescribed a second anti-TNF. Overall, 77.6% of pts stopped their first bDMARD after >6 months of treatment (secondary failure). Significant differences in retention between ABA and TNFi groups (log-rank p=0.0002) were observed (Figure). Results remained unchanged for pts treated with TNFi only in first line, and primary/secondary failure of the first bDMARD did not affect sustainability of the second agent. Lack of efficacy (57.7%) and AEs (16.5%) were the most commonly cited reasons for treatment discontinuation.

Conclusions: Abatacept has better sustainability over a second line TNFi in RA patients having failed one prior bDMARD.


DOI: 10.1136/annrheumdis-2017-eular.2379

AB0398 IMPACT OF BODY COMPOSITION ON RESPONSE TO BIOThERAPY IN RHEUMATOID ARTHRITIS

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Background: Biological therapies had greatly improved the treatment of rheumatoid arthritis (RA). The response to biologics may be influenced by many factors. Little is known about the impact of body composition in RA biologics.

Objectives: We aimed to investigate the impact of obesity (BMI≥30) and body composition (lean mass/fat mass) on response to biologics in RA.

Methods: A retrospective study was performed over a period of 11 years (2006–2016). Patients diagnosed RA (according to the ACR 1987 criteria) and treated by biologics were enrolled. Body composition (lean mass/ fat mass) was measured by X-ray biophotonic absorption (DXA). The threshold of significance was set for a value of p<0.05.

Results: Fifty patients were enrolled, including 5 men and 45 women (sex ratio=0.11). The mean age was 66 years [38–79]. The mean duration of RA was 5 years [1–30]. The mean duration of treatment with biologics was 38 months [6–120]. Thirty nine patients were treated by TNF inhibitors (25 etanercept, 7 adalimumab, 6 infliximab and 1 certolizumabpegol), 6 rituximab and 5 tocilizumab. Nine patients had a normal weight (18%), 17 had overweight (34%) and 24 had obesity (49%). The average percentage of fat mass was 44.8% (23–54), with a median of 46. While comparing obese patients with others, we did not notice a significant difference in the mean variation of the DAS28 at 6 months for TNF alpha inhibitors nor for all biotherapies combined (respectively p=0.6 and p=0.9). The same result was observed while comparing the DAS28 according to the body composition (relative to the median of the percentage of the fat mass: for TNF alpha inhibitors (p=0.6) and for all biotherapies combined (p=0.03)).

Conclusions: In our study, there was no change in response to biologics in patients with RA. Further prospective studies with a larger size will be required to confirm or reverse these results.

References:

Disclosure of Interest: None declared


AB0399 RITUXIMAB TREATMENT AND IMMUNOGLOBULIN LEVELS MONITORING

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Background: Rheumatoid arthritis is a well-known inflammatory condition with a prevalence around 1% in females and 0.5% in males in UK (as per NOAR study). In the past decade use of biologic therapy has helped clinicians to treat rheumatoid arthritis more effectively. Rituximab is one of the biologics which is used commonly for treating rheumatoid arthritis. Rituximab is chimeric monoclonal antibody targeting CD20 molecule of B cells. First trial of rituximab in treating rheumatoid arthritis was published in 2004 and since then it has shown promising results in clinical trials and is now the standard of care for treating rheumatoid arthritis. Little is known about the impact of body composition in RA biologics.

Objectives: To assess whether patients receiving Rituximab are appropriately monitored with pretherapy evaluation of immunoglobulin levels
To assess the effects of rituximab on immunoglobulin levels and incidence of infection among patients on rituximab

**Methods:** Data was collected of all (N=105) patients who received Rituximab between May 2014 until April 2015 at the Haywood Hospital where patients attend for Rituximab injections. Data was collected retrospectively from the Diamond System, Medisec system and Clinical Information System and entered onto an excel spread sheet which included following details

- Start date of Rituximab
- IgG levels prior to Rituximab and current IgG levels
- Total doses of rituximab and frequency of IgG monitoring
- Intermittent infections and type of infections.

**Results:** We observed that 82 out of 105 patients were started on rituximab after February 2011 when the BSR guidance was published and 53 out of 105 patients had their immunoglobulin levels checked prior to commencing treatment. 35/76 (46%) patients had 1 or more episodes of infections whilst on Rituximab which required treatment. Of these, 16 (46%) had recurrent infections. 39 patients had dropped their IgG levels after starting rituximab 18 (46%) of these suffered from infections.

17 patients had a drop in IgG ≥20% and 6 of these (36%) had recurrent infections and 1 patient had 1 episode of infection. None of the patients had dropped their IgG levels below 5

**Conclusions:** A significant number of patients (35/76 ≥46%) had 1 or more episodes of infections despite IgG levels being above lower normal limit Among patients who dropped their IgG level, had increased number infections. Also they had more than 1 episodes of infection Patients who dropped IgG levels ≥20% suffered with recurrent infections

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1160

**AB0400 EFFICACY AND SAFETY OF INTRAVENTOUS AND SUBCUTANEOUS TOCILIZUMAB IN A COHORT OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS IN REAL-LIFE**


**Background:** Tocilizumab (TCZ) is a humanized monoclonal anti-interleukin-6 receptor antibody, used for the treatment of moderate to severe rheumatoid arthritis (RA). Although TCZ has been proved to be highly effective and safe in RA patients in large clinical trials, few data are available from real-life practice [1].

**Objectives:** To evaluate efficacy, safety and retention rate of intravenous (IV) and subcutaneous (SC) TCZ in a real-world setting.

**Methods:** We evaluated patients affected by moderate-to-severe RA and treated with IV-TCZ from April 2010 to January 2017. Data of patients treated with IV-TCZ and SC-TCZ from January 2015 were collected retrospectively, while patients treated with either IV-TCZ or SC-TCZ from April 2010 to January 2017. Data of patients treated with IV-TCZ was estimated by Kaplan-Meier method.

**Assessment and paired t test was used for statistical analysis. Treatment retention rate was estimated by Kaplan-Meier method.**

**Assessment:**

- DAS28-CRP, CDAI and SDAI scores were used for disease activity assessment.
- CD3+, CD4+, CD8+ T, CD19+ B, CD20+ B, CD45RA+ B cells, CD69+ T cells and IFN-γ and Th17/Th1 ratio were used to assess disease activity, treatment discontinuation and/or onset of adverse events (AEs).
- Baseline immunoglobulin IgG, IgM, IgA, IgE with baseline the therapy in two group, and clinical adverse events (CRP, ESR, FER, ALT/AST, WBC, Hb, Ht, platelet) were used to assess disease activity, treatment discontinuation and/or onset of adverse events.

**Results:**

- CRP, ESR, FER significantly reduced in IV-TCZ group (P<0.05) at 12 weeks.
- There was no significant difference in frequencies of other risk factors, signs of disease activity, treatment discontinuation and/or onset of adverse events (AEs).
- After 12 weeks, tocilizumab + DMARDs group, CRP, ESR, FER significantly decreased, the most frequently occurring adverse reaction was infection, mostly upper respiratory tract infection, followed by elevated transaminase, cholesterol, low-density lipoprotein High-density lipoprotein triglyceride levels increased; two groups no serious adverse events (three-line reduction, severe infections, etc.).
- The proportion of CD4+ T, CD19 B cells in Tocilizumab group were lower than baseline (P<0.05), CD8, CD3+ T cells were increasing in comparing with baseline, however, no significant change with CD16+ 56-NK cells (P<0.05), and immunoglobulins IgG, IgM, IgA lower than baseline (P<0.05).

**Conclusions:** Tocilizumab can significantly reduce inflammatory markers (CRP, ESR, FER), but affect lipid metabolism and ALT/AST.Blocking IL-6 can be adjusted hyperthyroidism humoral and regulate CD4+ T, CD19 B cells, reduce joint destruction. Tocilizumab can effectively control the development of DMARDs poor efficacy SJIA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2114

**AB0402 RITUXIMAB MAY DELAY THE MOVEMENT OF RHEUMATOID ARTHRITIS PATIENTS ON CARDIORENAL CONTINUUM: RESULTS FROM A PROSPECTIVE OBSERVATIONAL SINGLE-CENTRE COHORT STUDY**

J.R. Gaisin1, L.V. Ivanova2, A.A. Trukchina3, A.A. Tukmacheva4, Y.A. Volkova1, A.A. Tebenkova1, N.I. Maximov1,1, Izhevsk State Medical Academy;2 Clinical Diagnostic Centre of the Udmurt Republic, Izhevsk, Russian Federation

**Background:** Similarities in risk factors, initial stages, progression and final stage of both atherosclerotic cardiovascular disease (CVD) and chronic kidney disease (CKD) allowed formulating a concept of cardiological continuum.1,2 CVD and CKD remain the main causes of mortality in rheumatoid arthritis (RA) patients.

**Objectives:** We aimed to evaluate the effects of rituximab biologic therapy on cardiological continuum of RA patients.

**Methods:** Biologics-naïve RA patients (n=50; age 55.1±10.3) were followed up for 72 months after commencing and continuing rituximab therapy (1–10 standard courses) compared with 30 control RA patients (age 53.2±9.8) followed up for 12 months. Comparing immunoglobulin IgG, IgM, IgA and IgE between baseline and after 12 weeks treatment. Comparing immunoglobulin IgG, IgM, IgA with baseline the therapy in two group, and clinical severe infections, etc.).

**Results:**

- After 12 weeks, tocilizumab + DMARDs group, CRP, ESR, FER were significantly decreased, the most frequently occurring adverse reaction was infection, mostly upper respiratory tract infection, followed by elevated transaminase, cholesterol, low-density lipoprotein High-density lipoprotein triglyceride levels increased; two groups no serious adverse events (three-line reduction, severe infections, etc.).
- The proportion of CD4+ T, CD19 B cells in Tocilizumab group were lower than baseline (P<0.05), CD8, CD3+ T cells were increasing in comparing with baseline, however, no significant change with CD16+ 56-NK cells (P<0.05), and immunoglobulins IgG, IgM, IgA lower than baseline (P<0.05).

**Conclusions:** Tocilizumab can significantly reduce inflammatory markers (CRP, ESR, FER), but affect lipid metabolism and ALT/AST.Blocking IL-6 can be adjusted hyperthyroidism humoral and regulate CD4+ T, CD19 B cells, reduce joint destruction. Tocilizumab can effectively control the development of DMARDs poor efficacy SJIA.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2114
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5704

**AB0403**

**ADHERENCE AND ACCESS TO BIOLOGICAL THERAPY AND TOFACITINIB IN A COHORT OF COLOMBIAN PATIENTS WITH RHEUMATOLOGICAL DISEASES**


**Background:**
Biological disease-modifying antirheumatic drug (bDMARD) and tofacitinib are highly effective, but with different pharmaceutical forms, adverse reactions and cost that could affect adherence therapy and drug access.

**Objectives:**
To determine patient adherence and administrative access to the treatment with bDMARDs and tofacitinib in patients with rheumatological diseases in Colombia.

**Methods:**
A retrospective cohort study, which included all patients in management with bDMARD and tofacitinib initiated between July 1, 2015 and June 30, 2016. A monthly follow-up of the administrative adherence were evaluated by holding or applying the medication, as well as the application of Morisky-Green test. Adherence was better with self-administered oral and subcutaneous therapies (non-adherent patient was considered when at least one doses is lost), other variables such as sociodemographic, comorbidities, and co-prescriptions were evaluated. A descriptive analysis, $x^2$ for comparison and multivariate logistic regression were performed.

**Results:**
Among 1,020 patients were evaluated, with a mean age of 52.8±15.4 years and a female predominance (72.8%). The most frequent comorbidities were hypertension (22.6%) and dyslipidemia (15.9%). The most prescribed drugs studied were adalimumab (31.9%), etanercept (22.2%) and tofacitinib (12.5%). 52.8% use conventional DMARDs and 42.2% use glucocorticoids. Global adherence was 66.3% as measured by Morisky-Green test. Adherence to treatment with bDMARDs and tofacitinib was associated with a greater probability of presenting delays in access after adjustment of variables.

**Conclusions:**
Subcutaneous other applications of bDMARD have better adherence rates compared to oral drug. However, the limitations in access to treatment decreased the adherence. On the other hand, the impact of the adherence could be major in the case of self-administered DMARD when weekly or longer intervals doses are lost, compared with the loss of one daily dose of tofacitinib.

References:

Acknowledgements: To Universidad Tecnológica de Pereira and Audifarma S.A. Disclosure of Interest: J. Machado-Alba Grant/research support from: The authors declare that Pfizer Colombia financed the data collection process in medical records. There was no intervention in the stages of processing, analysis or publication of that data. No non-financial interest of conflict exist for any of the authors., M. Machado-Duque: None declared, S. Granada: None declared DOI: 10.1136/annrheumdis-2017-eular.5823

**AB0404**

**SIMILAR REMISSION RATES AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ANTI TNF AND NON-ANTI TNF THERAPIES: REAL-LIFE DATA**

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**Background:**
Several biological DMARD (bDMARD) therapies have been approved for use in rheumatoid arthritis (RA) and are classified according to their respective therapeutic target: Anti TNF therapies and non-Anti TNF therapies. They are very effective in most of patients but their comparative efficacy in daily clinical is less well known.

**Objectives:**
Our aim was to compare the efficacy of anti-TNF therapies vs non-Anti TNF therapies in a cohort of Colombian RA patients followed in different arthritis clinics under daily clinical practice conditions.

**Methods:**
We conducted a cross-sectional study including with RA patients treated at Medicarte IPS from March 2009 to December 2016. Medicarte is a referral center for the integral medical care and pharmaco-surveillance of patients under biologic therapies in 13 cities in Colombia for inflammatory arthropathies, mainly RA, psoriatic arthritis and spondyloarthropathies. Clinical information was obtained from electronic clinical records and medical claims. Only those patients with disease activity scores (DAS-28) at baseline and at the last visit were included. Remission was defined as DAS-28 <2.6 on the last visit. Patients treated only with conventional DMARD and/or tofacitinib were excluded.

**Results:**
A total of 1,020 patients with RA were identified. 844 patients (88% female) were included in the final analysis, 416 patients with anti TNF and 428 with non-anti TNF therapies (Rituximab 199, Tocilizumab 125 and Abatacept in 104 patients). The mean age was 55.2±11.8 years, with a mean disease duration of 10.4±9.5 years. The percentage of patients with DAS-28 <2.6 was 61% in the anti TNF group and 51% in the non-anti TNF group.

**Table 1. General Characteristics of patients with RA under bDMARD therapy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>(N) (%)</th>
<th>Drug administration route and interval</th>
<th>Morisky-Green test adherence (%)</th>
<th>At least one dose application delay in the year of follow-up (%)</th>
<th>Median dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>251</td>
<td>SC - Every two weeks</td>
<td>74.8</td>
<td>62.7</td>
<td>51.3</td>
</tr>
<tr>
<td>Etanercept</td>
<td>232</td>
<td>SC - weekly</td>
<td>72</td>
<td>72</td>
<td>22.4</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>136</td>
<td>OA - every 12 hours</td>
<td>49.8</td>
<td>52.2</td>
<td>52.2</td>
</tr>
<tr>
<td>Golimumab</td>
<td>54</td>
<td>IC - monthly</td>
<td>64.7</td>
<td>32.0</td>
<td>28</td>
</tr>
<tr>
<td>Rituximab</td>
<td>66</td>
<td>IV - Intermittent and Annual</td>
<td>Not applicable</td>
<td>3.0</td>
<td>3.5</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>98</td>
<td>SC - monthly</td>
<td>81.9</td>
<td>82.8</td>
<td>32.8</td>
</tr>
<tr>
<td>MTX</td>
<td>40</td>
<td>IV - every two months</td>
<td>63.5</td>
<td>39.0</td>
<td>23.5</td>
</tr>
<tr>
<td>Abatacept</td>
<td>62</td>
<td>IV SC - monthly and weekly</td>
<td>42.9</td>
<td>36.7</td>
<td>27.4</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>62</td>
<td>IV SC - monthly</td>
<td>50.0</td>
<td>36.7</td>
<td>23.3</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Features</th>
<th>Rituximab group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factors</td>
<td>Hypertension</td>
<td>50.0</td>
<td>38.3</td>
</tr>
<tr>
<td></td>
<td>Dyslipidemia</td>
<td>44.0</td>
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</tr>
<tr>
<td></td>
<td>Pre-diabetes</td>
<td>52.4</td>
<td>36.3</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome</td>
<td>12.0</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>4.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Anxiety/depression</td>
<td>83.2</td>
<td>41.5</td>
</tr>
<tr>
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<td>Progression Angina</td>
<td>6.0</td>
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<td></td>
<td>Uncompensated systolic heart failure</td>
<td>8.0</td>
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<td></td>
<td>Left ventricular hypertrophy</td>
<td>8.0</td>
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<td></td>
<td>Diastolic dysfunction</td>
<td>48.0</td>
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<td>Albuminuria</td>
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<td>Kidney impairment</td>
<td>6.0</td>
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<td>Heart failure</td>
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<tr>
<td></td>
<td>Acute/chronic renal failure</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>12.9</td>
<td>0</td>
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</table>

**Conclusions:**
Subcutaneous other applications of bDMARD have better adherence rates compared to oral drug. However, the limitations in access to treatment decreased the adherence. The other hand, the impact of the adherence could be major in the case of self-administered DMARD when weekly or longer intervals doses are lost, compared with the loss of one daily dose of tofacitinib.
of 15.2±9.5 years. bDMARD therapy was used for a mean time period of 3.2±2.5 years. Eighty three percent of patients were treated in combination therapy and 80% of patients were seropositive (CCP and/or RF). Both groups did not differ significantly on baseline clinical characteristics (see Table), with 2 exceptions: patients who received Anti-TNF therapies were treated more frequently as first line therapy (79.2% vs 53.2%, p=0.001) and received in a higher proportion combined therapy (90.9% vs 75.0%, p<0.001). A total of 59% of patient achieved remission at the last visit. Three year remission rates were slightly higher but not significant in patients treated with non-anti TNF therapies vs anti-TNF therapies (59.6% vs 53.3%, p=NS). We did not find significant differences in remission rates according serological status.

Conclusions: In real-life setting, a meaningful proportion of RA patients achieved remission on the last visit. Patients treated with anti-TNF and non-anti TNF therapies had similar baseline characteristics and after a mean time period of treatment of 3 years, achieved similar remission rates.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5293

AB0405

SAFETY OF RITUXIMAB THERAPY IN AUTOIMMUNE DISEASES:SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Treatment with rituximab (RTX), a chimeric CD20 monoclonal antibody, has demonstrated efficacy for patients with several autoimmune diseases. There is a growing concern, however, safety evidence of RTX is still lacking.

Objectives: We conducted to evaluate the safety of rituximab (RTX) for autoimmune diseases.

Methods: A literature review was performed based on the randomized clinical trials (RCTs) that assessed adverse events by comparing RTX and placebo or no treatment for autoimmune diseases. The same add-on treatment for both arms were allowed. Study selection and data extraction were independently conducted in duplicate. Meta-analyses were performed for each outcome separately using fixed model and generic inverse variance method.

Results: In the primary analysis, 16 eligible RCTs, with a total of 4147 patients for five autoimmune diseases (n=8: rheumatoid arthritis, n=3: Sjogren syndrome, n=1: systemic lupus erythematosus, multiple sclerosis, ulcerative colitis, Graves orbitopathy, immune thrombocytopenia) were analyzed. The incidence of infection related reactions and the human antichimeric antibody (HACA) were higher in RTX group than placebo/no treatment group (OR 1.49, 95% CI 1.25–1.77 and OR 2.25, 95% CI 1.35–3.76, respectively). However, there were no significant differences the odds of total adverse events, serious adverse events, withdrawal for adverse events, infections, serious infections, malignancy, and all-cause death between two groups.

Conclusions: Our meta-analysis revealed that RTX was not associated with an increased risk of adverse events except for infusion related reactions and the incidence of HACA compared with placebo.

Acknowledgements: Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5643

AB0406

STABLE EFFICACY AND SAFETY AFTER SWITCHING FROM TOCILIZUMAB INTRAVENOUS TO SUBCUTANEOUS IN RHEUMATOID ARTHRITIS: RESULTS OF A COHORT OF 200 PATIENTS

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Background: Intravenous tocilizumab has been used since 2009 in Europe for the treatment of active rheumatoid arthritis. Since 2015, a subcutaneous formulation is available. The switch from a monthly, intravenous, with dose adjusted for bodyweight treatment to a weekly, subcutaneous, fixed dose, leads to various questions about efficacy and toxicity.

Objectives: The objectives were to evaluate the efficacy maintenance (mainte-
nance rate and DAS28 variation), the safety, the dose variation after the switch and the characteristics of patients switching to the subcutaneous form respect to those following with the intravenous tocilizumab.

Methods: A retrospective study was performed from a cohort of 203 patients undergoing intravenous tocilizumab from the rheumatology unit of 7 university hospitals between September 2015 and May 2016. Assessment has been done on the records, effectiveness was assessed using the DAS28, adverse events and reasons for staying on IV form were reported.

Results: On the 203 records analyzed, 3 were secondarily excluded. Of the 200 patients, 77 have switched for the subcutaneous form. Mean age of the 200 patients was 58 years (+/- 13.3) with 155 women (78%) and the mean duration of rheumatoid arthritis was 14 years (+/- 10.4), 72% of patients received a standard intravenous dose (8mg/kg/month) at baseline.

At the first visit after the prescription of the subcutaneous treatment, 58 patients on 65 (99%) maintained the treatment. The mean DAS28 was 1.53 (+/-1.00) at baseline and 1.19 (+/-0.78) at T1 (45 patients). Three patients received a reduced subcutaneous dose of 162mg/2 weeks following a reduced IV dose (<8 mg/kg/month) and maintained the subcutaneous treatment.

About safety, there was on new case of neutropenia.<1000/mm³. One severe adverse effect occurred (gastrointestinal perforation).

Regard to the dose variation, for the 77 patients switching, the mean difference between intravenous and subcutaneous dose was + 29mg/week (+/35mg) with the same previous tocilizumab dose.

Reasons for staying on IV form were essentially: the subcutaneous tocilizumab was not proposed in 55% of the cases and 17% of patients refused the subcutaneous form.

Conclusions: 89% of patients maintained the subcutaneous treatment after 4 months; efficacy was maintained in patients who received a reduced subcutaneous dose. Despite the higher dose after the switch (>28mg/week), there was no new case of neutropenia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6006

AB0407

COMPARATIVE EFFECTIVENESS OF TOCILIZUMAB (TCZ) MONOTHERAPY WITH TUMOR NECROSIS FACTOR INHIBITORS (TNFI) IN COMBINATION WITH VARYING DOSES OF METHOTREXATE (MTX) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Clinical studies have shown that the efficacy of TCZ monotherapy and TCZ in combination with MTX is superior to that of TNFi monotherapy and comparable to that of TCZ in combination with MTX.

Objectives: To compare the effectiveness of TCZ mono vs TNFi plus varying doses of MTX in patients with rheumatoid arthritids (RA) and prior exposure to TNFi in routine clinical practice.

Methods: Eligible participants were TCZ-naïve patients from the Corrona RA registry who had prior exposure to ≥1 TNFi, initiated TCZ mono or a TNFi + MTX between 2010 and 2016 and had a 6-month follow-up visit. The primary outcome was mean change from baseline in Clinical Disease Activity Index (CDAI) at 6 months. Secondary outcomes included achievement of low disease activity (LDA; CDAI ≤ 10) at 6 months. Patients initiating a TNFi + MTX were grouped by MTX dose (<10 mg; >10 to <15 mg; ≥15 to <20 mg; >20 mg); outcomes in each group were compared with those initiating TCZ mono using trimmed populations, excluding patients outside the propensity score (PS) distribution overlap (not on common support). The PS included age, gender, body mass index, smoking status, American College of Rheumatology functional class and baseline modified Health Assessment Questionnaire, CDAI and patient pain scores. As a sensitivity analysis, propensity-matched populations were created (stratified by 1 vs >2 prior biologics, then matched on PS). Linear and logistic regression models were estimated in the trimmed populations, adjusting for the same covariates as in the PS.

Results: Baseline demographics were generally comparable between the TNFi + MTX groups and their matched TCZ mono groups. Overall, the mean age was 54 to 59 years, and the mean disease duration was 10.5 to 15 years. A higher proportion of patients initiating TCZ mono had received ≥3 prior biologics compared with those initiating TNFi + MTX. Patients initiating TCZ mono had significantly longer mean disease duration than those initiating TNFi + MTX ≥15 to <20 mg, ≥20 mg or TNFi + MTX > 20 mg (12.3 vs 9.3 years) and a higher mean baseline CDAI than those initiating TNFi + MTX <10 mg (28.1 vs 25.4). Patients in all groups had improvement in CDAI scores at 6 months. In adjusted models, improvement in CDAI and the likelihood of achieving LDA were similar between the TCZ mono group and all TNFi + MTX groups (Table). Similar results were observed in the PS-matched cohorts.

Conclusions: TCZ mono was as effective as TNFi + MTX, regardless of MTX dose, for improving disease activity in patients with prior TNFi exposure. These data suggest that TCZ mono is an effective treatment option for patients with RA who cannot tolerate or prefer not to use MTX.

Acknowledgements: This study is sponsored by Corrona, LLC. Corrona, LLC, has been supported through contracted subscriptions in the past 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche, Schering-Plough, UCB.

Disclosure of Interest: L. Harold Shareholder of: Corrona, LLC, Grant/research support from: Pfizer, Consultant for: Roche, Employee of: University of Massachusetts Medical School; Corrona, LLC, G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, J. Best Employee of: Genentech, Inc, S. Zlotnick
Results: The 330 pairs of propensity score-matched ABA and TNFi initiators had no substantial differences in baseline characteristics. Both treatment groups had similar mean change in CDAI at 6 months as well as achievement of LDA, remission and aMCR20/50/70 responses (Table). Among the 97 matched biologic-naïve pairs, there was no significant difference in change in CDAI for ABA initiators vs TNFi initiators (p=0.19). However, in the 233 matched biologic-experienced pairs, those initiating ABA had a greater improvement in mean change in CDAI (p=0.033) and were more likely to achieve an aMCR50 response (p=0.014).

Conclusions: Pts with RA who were CCP+ and received either ABA or TNFi had a substantial improvement in clinical disease activity. In the overall propensity score-matched sample, similar outcomes were observed for both treatment groups. However, analysis of the biologic-experienced cohort found that ABA initiators had a greater improvement in disease activity than TNFi initiators.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1643

Comparative Effectiveness of Abatacept Versus TNFi in Patients with Rheumatoid Arthritis Who are CCP+ in the United States Corrona Registry


To compare the effectiveness of ABA vs a TNF inhibitor (TNFi) in pts with RA who are CCP+.

Methods: We included adult pts with RA from a large observational US cohort (1 Dec 2005–31 Aug 2016) who initiated ABA or a TNFi and who were CCP+ (≥20 U/mL) at or prior to initiation. Both groups had to have no prior exposure to other non-TNF biologics or targeted synthetic DMARDs. TNFi initiators were excluded if they had prior use of ABA. Using propensity score matching (1:1) stratified by prior TNFi use (0, 1 and 2+), effectiveness at 6 months after initiation was evaluated. Mean change in CDAI over 6 months following initiation was the primary outcome, with secondary outcomes being: achievement of remission (CDAI < 10), mACR20/50/70 responses and achievement of LDA/remission (CDAI < 10) in pts with moderate/high disease activity at initiation. A subset analysis was performed to consider separately pts who were biologic naïve and those who were biologic experienced at initiation.

Conclusions: Pts with RA who were CCP+ and received either ABA or TNFi had a substantial improvement in clinical disease activity. In the overall propensity score-matched sample, similar outcomes were observed for both treatment groups. However, analysis of the biologic-experienced cohort found that ABA initiators had a greater improvement in disease activity than TNFi initiators.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3295

Corticosteroid-Sparing in Patients with Rheumatoid Arthritis on Tocilizumab: First Experience of BAB-EL-OUED HOSPITAL


Background: Tocilizumab (TCZ) is a monoclonal antibody directed against the IL-6 receptors. This treatment (TRT) allows for the cortisone weaning in preventing of its complications.

Objectives: The goal of this study is to evaluate the corticosteroid sparing in patients with RA treated with TCZ.

Methods: Prospective, descriptive study of patients hospitalized between 2012 and 2016, the diagnosis was made according to the ACR 1987 ACR/EULAR 2010 criteria. Included, are the patients treated with TCZ for at least 3 months associated with corticosteroids.

We have studied the following: the epidemiology, the associated DMARDs, the average DAS28VS, the average dosage of prednisone-equivalent and the percentage of patients with decreased or interrupted corticosteroids at M0, M3, M6 and M12.

Results: 28 patients (sex ratio: 0.7) treated with TCZ and corticosteroids, average age is 43.4 years (range 30–62). Average duration of the development of RA: 9.1±6.4 years. DMARDs was associated in 15 patient. At baseline. 46.2% of patients were on 10 mg/day of cortisone, the average dose of prednisone-equivalent was that 7.7±3.6 mg at M0, 5.3±3.2 mg at M3, 4.6±2.3 mg at M6, 2.6±2.6 mg at M12 with a statistically significant difference (p=0.000003). The average DAS28VS index was 5.6±0.9 at M0, 3.5±1.3 at M3, 3.0±1.2 at M6 and 2.6 ± M6 at M12 with a statistically significant difference (p=0.000001). Corticosteroid treatment was stopped in 12 patients after 1 year of treatment.

Conclusions: Through this study we note that the TRT using TCZ has enabled a significant reduction in the dose of corticosteroids. Stopping prednisone was possible in 50% of patients after 1 year of biotherapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3965
THE INTERPLAY BETWEEN C3 AND C4 AND DISEASE ACTIVITY IN PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS DURING TREATMENT WITH ANTI-IL6 RECEPTOR

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Background: The complement system (CS) is involved in the pathogenesis of rheumatoid arthritis (RA). Evidence reported that high C3 levels C4 in RA patients might reflect a pro-inflammatory status and represent a negative prognostic factor for TNF-inhibitors therapy.

Objectives: We evaluated CS in a cohort of RA patients treated with tocilizumab (TCZ) to explore whether there was any correlation between CS and both disease activity and response to therapy.

Methods: Consecutive outpatients affected by RA who started TCZ treatment i.v. at the Rheumatology Unit of "Policlinico Tor Vergata" in Rome (Italy) were enrolled (n=25) (Table I). We included 25 healthy subjects as controls. Disease activity was assessed by using DAS28 ESR-based while clinical response to therapy by EULAR response criteria. Peripheral blood samples were obtained from all patients at the time of each infusion. Laboratory assessment included ESR, CRP, RF, ACPA, C3, C4, CH50 assay. Clinical and laboratory data were registered at baseline (T0), after 1 (T1), 3 (T3), 6 (T6), 9 (T9), and 12 (T12) months from the beginning of the TCZ treatment.

Results: At baseline, both C3 and C4 were significantly higher in RA than in controls (Table I).

Table 1

<table>
<thead>
<tr>
<th>RA (N=25)</th>
<th>Controls (N=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Controls</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>23/92</td>
<td>23/92</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.4±11.5</td>
<td>60.1±9.3</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>13±6.2</td>
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</tr>
<tr>
<td>DAS28</td>
<td>6.5±3.1</td>
<td>N.A.</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.9±0.8</td>
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</tr>
<tr>
<td>Positive of RF (N/%)</td>
<td>17/68</td>
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</tr>
<tr>
<td>Positivity of ACPA (N/%)</td>
<td>20/90</td>
<td>N.A.</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>58±12.8</td>
<td>N.A.</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>8.5±7.6</td>
<td>N.A.</td>
</tr>
<tr>
<td>C3 (mg/dl)</td>
<td>119±32.2</td>
<td>104±18</td>
</tr>
<tr>
<td>C4 (mg/dl)</td>
<td>26±6.7</td>
<td>22±4</td>
</tr>
<tr>
<td>CH50 (%)</td>
<td>108±24</td>
<td>100±18</td>
</tr>
<tr>
<td>Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDN ≤ 5 mg/die (N/%)</td>
<td>9/36</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

No difference in C3 and C4 resulted between ACPA positive and ACPA negative patients during the follow up. ESR, CRP and DAS28 levels were significantly reduced at T1, T3, T6, T9, and T12 with the respect to T0 (Figure 1-A-C). C3 levels were significantly reduced at T3, T6, T9 and T12 with the respect to T0 while C4 levels were significantly reduced at T3, T6, T9 and T12 with the respect to T0 (Figure 1D-E). The positive correlations resulted between DAS28 and both C3 and C4 at T1 and T3 (Figure 1F-I). C3 and C4 were directly related with ESR at T1 (C3: P < 0.002; C4: P < 0.005), T3 (C3: P < 0.04; C4: P < 0.03), and T6 (C3: P < 0.002; C4: P < 0.002) and with CRP at T1 (C3: P < 0.03; C4: P < 0.01) and T6 (C2: P < 0.001; C4: P < 0.03). When stratifying patients in accordance with the EULAR response to therapy, C3 decreased significantly with no-responders than in no-responders at T1; moreover, responders showed lower levels of both C3 and C4 at T1 and T3 with the respect to T0 (Figure 1L-O).

Conclusions: In RA patients, treatment with TCZ is able to reduce C3 and C4 levels in an early and sustained way. The disease activity is directly related with the reduction of C3 and C4 serum levels. RA patients with a good/moderate clinical response show significantly lower C3 and C4 levels than no-responders patients. Our preliminary data suggest that C3 and C4 can be a reliable marker of both the disease activity and the response to therapy in RA patients treated with TCZ.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4643

COMPARISON OF TUBERCULIN SKIN TEST AND INTERFERON-GAMMA RELEASE ASSAY SCREENING IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING ANTI-TUMOR NECROSIS FACTOR FACTOR THERAPY

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Background: Biologic agents provide clinical benefits in patients with Rheumatoid Arthritis (RA) but they are associated with an increased risk of tuberculosis (TB) infection.

Objectives: We investigated the accordance between the tuberculin skin test (TST) and the interferon-gamma (IFN-γ) release assay (IGRA) for the diagnosis of latent tuberculosis infection (LTBI) in patients with RA. The objective of our study was a direct comparison between the IGRAs and the TST regarding LTBI diagnosis in RA patients before starting anti-TNF agents and at least one year after the initiation of treatment.

Methods: Consecutive patients have been included in the study both before and after 1 year of the initiation of TNF-α antagonist therapy. A standard questionnaire was completed for each patient, including basic demographic data and concurrent immunosuppressive therapy (corticosteroids, disease-modifying anti-rheumatic drugs [DMARDs], synthetic and biologicals). The patients were screened for LTBI using IGRA and TST methods.

All analyses were performed with IBM-SPSS Statistics for Windows (version 21). The kappa coefficient (κ) was calculated to determine the concordance between the two tests: TST and IGRA. The strength of the agreement was considered "poor" for κ ≤ 0.20, "low-moderate" for 0.20 < κ < 0.40, moderate for 0.40 < κ < 0.60, "substantial" for 0.60 < κ < 0.80, and "optimal" for 0.80 < κ ≤ 1.

Results: 78 patients (67 female, 11 male) have been screened with TST and IGRA. The accordance between TST and IGRA was 98.7% (κ = 0.514, p = 0.001). A κ value of 0.514 represents a moderate accordance between the two tests. 6 female patients converted TST (4 became positive, and 2 became negative). No patient developed active tuberculosis.

Conclusions: A moderate accordance between the two methods (TST and IGRA) was obtained. In the absence of a diagnostic gold standard for LTBI, different issues should be taken into consideration regarding the two methods (cost, laboratory expertise and equipment etc). More studies are needed in the field in order to elucidate the cost-effectiveness but also the appropriateness of both methods.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6400

LESS THAN 5% OF REAL-LIFE PATIENTS WHO SWITCH FROM IV TO SC ABATACEPT IN REAL-WORLD CLINICAL PRACTICE SIMULTANEOUSLY SUBSITUTE BACK TO THE IV FORMULATION

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Background: Patients (pts) with RA may be able to switch from IV to SC abatacept without no loss of efficacy or safety concerns, but data are inconclusive.1, 4 In the ACTION [AbataceptIn Rheumatoid Arthritis clinical practice; NCT02109666] study, a 1-year interim analysis showed that switching had no adverse clinical effect.3

Objectives: To examine treatment patterns and explore abatacept formulation switching over 2 years in ACTION.

Methods: ACTION is a 2-year, prospective, observational study of pts with moderate-to-severe RA who initiated IV abatacept in Europe and Canada between May 2008 and December 2013. Assessments in biologic-naïve and biologic-failure pts were: baseline characteristics, rates of and reasons for switching (IV to SC), and re-switching to IV over 2 years. Descriptive data were generated: mean (SD) for continuous variables and n (%) for categorical variables. Rates of switching were estimated by Kaplan–Meier analysis. Cohorts were pooled to analyse further pts who switched owing to low numbers.

Results: In the ACTION cohort, 2350/2364 pts (99.4%) were evaluable for this analysis. 673 (28.6%) biologic naïve, 1677 [71.4%] biologic failure. A total of 729
(43.4%) biologic-failure pts had received 1, and 948 (56.6%) had received ≥ 2 previous biologics. Baseline characteristics in biologic-naïve and biologic-failure pts, respectively, were: mean (SD) age 59.9 (12.7) and 56.9 (12.5) years; RA duration 7.2 (8.22) and 12.1 (9.13 years); 496 (73.7%) and 1379 (82.2%) were women; 621 (92.3%) and 1592 (92.5%) had received prior MTX; and 533 (72.9%) and 1386 (82.6%) had received corticosteroids. Over 2 years, 195 pts switched from IV to SC abatacept (57 biologic naïve, 138 biologic failure; Fig.). Reasons for switching were available for 172 pts (51 biologic naïve, 121 biologic failure; some had > 1 reason): biologic naïve/biologic failure: pt wish 54.9%/82.0%, physician choice 31.4%/19.8%, safety 5.9%/9.9%, remission/major improvement 3.9%/5.0%, poor compliance 0%/4.1%, lack of efficacy 2.0%/3.3%, surgery 2.0%/0.8%, weight adjustment 2.0%/0.0%, other 49.0%/36.4%. Only eight pts (2.6%) re-switched to IV abatacept (2 biologic naïve, 6 biologic failure). Reasons for re-switching were: pt wish (n=4), lack of efficacy (n=4), safety issue (n=1) and other (n=2).

Figure. Patients Who Switched From IV to SC Abatacept Over 2 Years (Kaplan-Meier Analysis)

Conclusions: Less than 5% of pts who switched formulation from IV to SC abatacept in real-world clinical practice re-switched to the IV formulation, suggesting that switching has no clinical adverse impact. A change in formulation was mainly due to pt wish, reflecting their involvement in decision-making.

References:

Disclosure of Interest: R. Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, H.-M. Lorenz Consultant for: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, Astra-Zeneca, Pfizer, Actelion, X. Mariette Grant/research support from: Biogen, Pfizer, UCB, Consultant for: Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, H. Nüdling Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, M. Galeazzi: None declared, F. Navarro Grant/research support from: Pfizer, GSK, UCB, AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, M. Chartier Employee of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, LFB, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1379

AB0413

INDUCTION AND PROGRESSION OF SUBCUTANEOUS NODULOSIS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

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Background: Tocilizumab (TCZ) is a monoclonal antibody (moAb) directed against the IL-6 receptor approved for moderate-to severe rheumatoid arthritis (RA) treatment. Some authors have reported a beneficial effect of TCZ in preventing lung and subcutaneous nodulosis in RA patients. On the contrary, to our knowledge no data concerning the acceleration of subcutaneous nodulosis that considerably worsened during the treatment with tocilizumab. Patients experimented the development of new subcutaneous nodules localized at the fingers, elbows or the inframammary fold, tending to ulceration. The management of this medical event included the tapering of MTX, the administration of steroids, the addition of HCQ, the use of antibiotics and surgery. However, neither pharmacological nor surgical treatment was completely effective, as nodules tended to recur and to increase in number and dimensions.

Results: To our knowledge this is the first report describing an accelerated subcutaneous nodulosis in a small cohort of RA patients treated with tocilizumab.

AB0414

THE USE OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: IN WHICH INFUSION INTERVALS WERE GIVEN AND HOW DID THEY RESPOND? HUR-BIO REAL LIFE RESULTS


Background: Rituximab is one of the treatment options in rheumatoid arthritis (RA) patients and officially recommended as a maintenance treatment given every 6 months after the initial loading of first course.

Objectives: In this real life study, it was aimed to investigate the infusion frequency of rituximab maintenance treatment and possible effects on disease activity.

Methods: The HUR-BIO is a single-center biologic registry of Hacettepe University which is established in Ankara and in which patients have been prospectively recorded since 2012. This database has 1235 RA patient records as of August 2016. Rituximab was prescribed at least once in 273 (22.1%) patients. The residence address of 85 those patients was within the boundaries of center city (Ankara) and they were included in to the study. In our clinic, the dates and the DAS-28 scores at the time of rituximab courses were recorded. Rituximab infusion compliance was classified as: “regular” if there is less than one month delay, “slightly irregular” if less than 3 months delay and “irregular” if more than 3 months delay.

Results: The mean age of the 85 patients (80% female) was 59.1 (10.1), the mean disease duration was 12.9 (8.6) years and 74.1% of patients were seropositive. 39/85 (46%) patients previously used at least one biological agent (46 (54%) patients were biologic naïve before Rituximab therapy). Median rituximab course number was 3 (1–8). A total of 211 rituximab courses were given to 85 patients. Rituximab course number and percentage is shown in figure. The mean interval time between rituximab courses was 7.9 (2.8) months. Total of 102 (52.6%)
courses were admitted at normal times regularly, 60 (30.9%) were slightly irregular and 32 (16.5%) were irregular. There was no significant difference between the mean DAS-28 responses in the time of the courses and the rituximab infusion compliances [in regular group mean DAS-28 was 3.31 (1,19), in slightly irregular group mean DAS-28 was 3.26 (1.35) and irregular group mean DAS-28 was 3.57 (1.34), p = 0.05]. Before rituximab courses, 33.7% of patients had remission, 19.1% had low disease activity, 36.3% had moderate disease activity and 10.9% had high disease activity.

Conclusions: Rituximab administration was approximately 2 months delayed in RA patients who were living in center-city boundaries. The pre-treatment mean disease activity scores were similar, even if there was a delay in rituximab administration. In our center, about 85% of patients were taking RTX courses regular and/or slightly irregular and about half of the patients before treatment were in remission and/or low disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4430

AB0415 TENDENCY TO CHOOSE FIRST BIOLOGIC AGENT THERAPY OF RHEUMATOID ARTHRITIS IN THE ELDERLY: RESULTS FROM JAPANESE MULTICENTER REGISTRY

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Background: Of the treatment of rheumatoid arthritis (RA), biologic agent therapies are chosen, if disease activity remains moderate or high despite csDMARDs therapy. In the elderly, with comorbidity and their less spare ability, safety is often concerned in the choice of biologic agent.

Objectives: We investigated the tendency to choose biologic agent and drug continuation rates in elderly in last decade.

Methods: Records of relevant patients with RA were collected from the Tsurumai Biologic Communication Registry, wherein the department of Nagoya University and 20 affiliated hospitals in Japan are enrolled. A total of 873 biologics-naïve and age 65 and older patients were recruited from January 2004 to December 2014. We studied the choice of the biologic agent year by year, and baseline disease activity and concomitant methotrexate (MTX) among TNF inhibitors, tocilizumab (TCZ) and abatacept (ABT) groups. Drug continuation rates were compared among TNF inhibitors, TCZ, and ABT groups.

Results: From 2005 to 2010, etanercept (ETN) was used the most (2007, 73.5%, 2009; 65.9%). After the advent of ABT, ABT was used the most (2011; 44.3%, 2014; 38.8%). Baseline disease activity slightly decreased as a whole (DAS28-CRP: 4.88 to 4.44). Despite baseline disease activity of TNF inhibitors group decreased (DAS28-CRP: 4.88 to 4.37), that of TCZ group increased (DAS28-CRP: 4.94 to 6.24).

In 2011–2014, baseline disease activity of TCZ group (5.85) was higher than that of TNF inhibitors group (5.11) (p<0.05). Concomitant MTX rate and dose were lower in ABT group (40.2%, 7.6mg) than that of TNF inhibitors group (79.0%, 8.8mg). 2 years drug continuation rate due to all unfavorable causes; ABT group was 82.4%, better than that of TNF inhibitors 77.1% and TCZ 69.2% (p<0.05). 2 years drug continuation rate due to adverse events; TCZ group was 80.8%, lower than that of TNF inhibitors 94.6% and ABT 96.2% (p<0.05).

Conclusions: ETN was used most before the advent of ABT. After the advent of ABT, ABT was used most and ETN decreased. This selection was made for speculation that ABT is lower risk than other biological agents. Baseline disease activity slightly decreased showing that tight control management became also popular among elderly. In 2011–2014, concomitant MTX rate and dose were lower in ABT group, but 2 years drug continuation rate was the highest.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1679

AB0416 WHICH FACTORS PREDICT THE RESPONSIVENESS TO TOCILIZUMAB IN RHEUMATOID ARTHRITIS? THE DIFFERENCE BETWEEN THE USAGE AS THE FIRST BIOLOGIC AND AS THE SECOND BIOLOGIC

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Background: Although recent development of a variety of biologics has dramatically improved treatment for rheumatoid arthritis (RA), it is still unclear which biologics is better for use in each patient. Some previous studies have shown the predictive factors for good response (GR) to tocilizumab (TCZ), including low HAQ, high DAS28, low levels of serum soluble IL-6 receptor5), and low numbers of previous use of other biologics5). However, the consensus is not immediately available.

Objectives: To compare continuation rates (CR) of TCZ by the responsiveness to the therapy and to identify predictive factors for GR to TCZ in RA.

Methods: Patient with RA who newly started receiving TCZ after April 2008 in our hospital, were included in the study. We collected patient records, medication histories, laboratory data, and clinical parameters longitudinally after starting TCZ. Statistical analyses were performed using the chi-square test, binomial logistic regression analysis, Kaplan-Meier method, and the log-rank test.

Results: Ninety-two patients were included in the study. The mean age and disease duration at baseline were 60.0±13.5 years and 8.7±8.0 years, respectively. The seroprevalence of the anti-cyclic citrullinated peptide antibody and the rheumatoid factor were 95.4% and 95.7%, respectively. The rate of metotrexate and prednisolone at baseline were 45.7% and 64.1%, respectively. TCZ was administered as the first biologic in 42 patients, and as the second biologic in 33. DAS28 (ESR) and CDAI revealed high disease activity at baseline (5.2±1.5 and 25.4±14.1, respectively). The mean CR of all patients was 42.1±4.0 months. The CR was significantly higher in patients who achieved GR in EULAR response criteria at 6 months after starting TCZ than those who did not achieve GR (54.0±6.0 months vs 29.0±5.3 months, p<0.004). Multivariate statistical analysis revealed two predictive factors for achieving GR at 6 months after starting TCZ, the low number of previous use of other biologics and the low CDAI at baseline (p<0.018, odds ratio (OR) =0.386, and p=0.011, OR=0.944, respectively). We divided the patients into two groups, patients using TCZ as the first biologic and patients using it as the second biologic. Univariate statistical analyses revealed low usage rate and dose of prednisolone (PSL) and low serum creatinine level at baseline as the predictive factors for achieving GR in patients using TCZ as the first biologic, and low DAS28 (ESR), CDAI and HAQ-DI in the patients using TCZ as the second biologic. By multivariate statistical analysis, we identified the low CDAI as a predictive factor in the patients using TCZ as the second biologic.

Conclusions: RA patients who achieved GR at 6 months after starting TCZ showed higher CR than the others. This study also suggests that low number of biologics usage and low CDAI at baseline are the predictive factors for GR. The history of biologics usage may be important to identify the predictive factors for GR to TCZ.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4059
Rheumatoid arthritis - non biologic treatment

AB0417 Efficacy and Safety of Methotrexate and Leflunomide as a combination therapy in Rheumatoid Arthritis Patients with High Disease Activity: Presenting at a tertiary care setting in Pakistan

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Background: In the management of rheumatoid arthritis (RA), the goal is remission. However, it is not easy to attain this goal in all patients. It's not only the high disease activity, but rather other factors like availability and cost of biologics in developing countries. Therefore various combination therapies of conventional DMARDs are in vogue in such scenarios. Methotrexate (MTX) and Leflunomide (LEF) in combination is an effective option which can be fairly utilized in resource constraint settings to induce remission.

Objectives: To study the efficacy and safety profile of MTX+LEF combination in patients with active RA at 24 weeks.

Methods: This is a quasi-experimental study conducted at Rheumatology department, Fauji Foundation Hospital, Rawalpindi. 95 patients with active RA despite optimal dose (20–25 mg/week) of MTX. Leflunomide 20mg/day was added. Patients underwent clinical and laboratory review at 0, 4, 12 and 24 weeks to note down primary efficacy endpoints and adverse effects.

Results: Ninety five patients were enrolled with a mean age (years) ± SD of 51.7±8.9 and a mean duration of disease (years) of 8.6±7.1. Patients had active disease at baseline with a mean disease activity score (DAS28) of 5.99±0.6. At 24 weeks the mean change in tender joint count (TJC), swollen joint count (SJC), patients pain score on visual analogue scale (VAS) and DAS 28 were all statistically significant (p-value <0.000). The mean change in m HAQ was also statistically significant (p-value <0.000).

At 6 months the most frequent side effects (though mostly mild); were abdominal pain and nausea. 76 patients (79.1%) continued with the combination therapy. Only 3 patients stopped the treatment temporarily (due to raised ALT and vomiting), 14 patients discontinued treatment mainly due to diarrhea, severe oral ulcers and markedly raised ALT.

Table 1. Baseline and clinical demographic features of patients enrolled for MTX+LEF combination therapy

<table>
<thead>
<tr>
<th>Total patients</th>
<th>95 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean ± SD (years)</td>
<td>51.7±8.9</td>
</tr>
<tr>
<td>Gender m/f</td>
<td>2/93</td>
</tr>
<tr>
<td>Duration of disease (SD, years)</td>
<td>8.6±7.1</td>
</tr>
<tr>
<td>RA factor (positive)</td>
<td>72 (75.8%)</td>
</tr>
<tr>
<td>Anti CCP (positive)</td>
<td>61 (64.2%)</td>
</tr>
<tr>
<td>DMARDs</td>
<td>45 (47.4%)</td>
</tr>
</tbody>
</table>

Conclusions: MTX+LEF combination is an effective and safe option in RA patients.

Table 2. Outcome/efficacy measure of MTX+LEF (n=95)

<table>
<thead>
<tr>
<th>Baseline (0 week)</th>
<th>24 weeks</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TJC</td>
<td>14.9±6.4</td>
<td>3.9±2.3</td>
</tr>
<tr>
<td>Mean SJC</td>
<td>4.2±3.3</td>
<td>0.9±2.8</td>
</tr>
<tr>
<td>Mean pain VAS (Patient)</td>
<td>7.1±1.8</td>
<td>2.9±1.8</td>
</tr>
<tr>
<td>Mean ESR</td>
<td>33.3±10</td>
<td>16.7±5.9</td>
</tr>
<tr>
<td>Mean DAS 28</td>
<td>5.9±1.6</td>
<td>3.5±0.6</td>
</tr>
<tr>
<td>MHAQ</td>
<td>1.7±0.6</td>
<td>0.5±0.2</td>
</tr>
</tbody>
</table>

AB0418 COMPARISON OF ANTI-INFLAMMATORY DRUGS WITH GLUCOCORTICOIDS IN TREATMENT OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that commonly presents with symmetrical polyarthritis of hands and feet. Pharmacological treatment options are non-steroid anti-inflammatory drugs (NSAIDs), glucocorticoids (GC) and disease modifying anti rheumatoid drugs (DMARDs) (csDMARDs) or (bsDMARDs or bDMARD).

Objectives: In this study we aimed to review the use of NSAID and GC in our patients.

Methods: The patients who diagnosed as RA at our office were included in the study. Patients were classified with EULAR 2010 RA criteria. The demographics and medications of the patients were recorded. All patients we examined pain with visual analog scale (VAS), global assessment of patient and doctor, number of tender and swollen joints (28 joints), health assessment questionnaire (HAQ), C- reactive protein (CRP), uric acid and Hb.

Conclusions: About 686 patients were enrolled in the study (156 female [48.5%], 106 male [51.5%]). Mean age was 53.2±12.21 and mean length of diagnosis was 10.74±17.09 months. The rate of rheumatoid factor (RF) and anti – CCP – WC was 17.9% and the deformity rate was 31.3%. In all patients, activity of disease was mild in 55%, moderate in 37.8% and severe in 7.3% with regard to DAS28. The score of disease activity was mild in 54.6%, moderate in 43.11% and severe in 2.3% in patients who were using only NSAIDs. These rates of disease activity was 57.2%, 40.7% and 2.1% in mild, moderate and severe disease respectively for the patients using only GC. In patients using both NSAIDs and GC, the disease activity was mild in 55%, moderate in 44% and severe in 1%. In comparison of the disease activity with medications revealed statistically significant difference in patients that using only GC and using both, but not in that using only steroid (respectively p: 0.022, p: 0.025, p: 0.46).

Conclusions: In our study we found that patients has mild activity of disease using high rates of NSAID and GC. It is important for providing remission using NSAIDs and GC along with DMARD. Our results demonstrate use of both GC and NSAIDs results in better outcomes.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5926

AB0419 REAL WORLD USE OF TOFACITINIB IN RHEUMATOID ARTHRITIS: DATA FROM LATIN AMERICA

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Tofacitinib can be given as monotherapy or with csDMARDs. Published data on real world (RW) tofacitinib use in Latin America (LA) are limited. We characterise the patient (pt) population starting tofacitinib and gain insights into the safety profile in the RW LA setting.

Methods: Initial tofacitinib therapies in adult RA pts from 10 private/public centres in 6 countries (Argentina, Brazil, Colombia, México, Panamá, Peru) were considered. Data were retrospectively obtained via a standardised format, focusing on demographics, drug history, adverse events (AEs), safety events of special interest, latent tuberculosis (TB) screening, selected confirmed laboratory abnormalities and discontinuation rates. Tofacitinib use as monotherapy or with csDMARDs was at the rheumatologist's discretion.

Results: 280 pts with severe active RA were included; most were female (n=263; 91%), mean (SD) age was 51.3 (6.36) years (yrs) and mean (SD) disease duration was 10.4 (4.0) yrs. 89% of pts were RF+ or ACPA+. The max (range) follow-up period was 22 (10–34) months. Tofacitinib was given as 2nd-line therapy (post-csDMARD) in 44% of pts, after one biologic DMARD (bDMARD) in 18% of pts and after >3 bDMARDs in 38% of pts. Tofacitinib was given as monotherapy in 117/283 (41%) pts and with csDMARDs in 171/283 (59%) pts. Tofacitinib use corresponds to 13% of advanced therapies (JAK inhibitors, bDMARDs and biosimilars). Thirty-eight AEs were observed; upper respiratory infections (n=11), skin infection (n=5), herpes zoster (HZ; n=4) and urinary infections (n=4) were most common. Gastrointestinal intolerance was seen in 2 pts. Three (1%) pts had serious infection events (SIEs); no opportunistic infections (Nos), including TB, occurred. All HZ cases (n=4; 1.4%) were monomeric, non-serious and resolved without complication after antiviral therapy. Before starting tofacitinib, 5 pts (1.7%) were vaccinated against HZ and 5.6% were diagnosed with latent TB. No active
TB cases occurred with tofalenib treatment. One malignancy (thyroid cancer) was reported. Severe (≥3 ULN) elevation of liver enzymes or increases of CPK above normal were infrequent (<1%); no severe cytopenias were reported. Lipid increases occurred in 10% of pts. Tofalenib was withdrawn in 40 pts (13.9%) due to lack of efficacy (n=20; 7%), AEs (n=11; 3.8%) or other reasons (n=9; 3.1%), such as loss of follow-up, pregnancy, access issues or trials. Limitations include limited pt numbers and follow-up of exposure.

Conclusions: In the RW LA setting, tofaltenib was used mostly as 2nd-line therapy; no new safety signals emerged vs clinical trials. SIsEs and HZ were uncommon; no cases of TB/other OIs occurred, but were seen in the clinical programs.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Irving of CMC and funded by Pfizer Inc.

groups compared to those of the control. 1,25(OH)2D3 had no significantly impact on the level of Th1, Th2, Treg and the ratio of Th1/Th2.

Conclusions: The present study demonstrated that 1,25(OH)2D3 inhibits the synthesis of Th1 cytokines IFN-γ, Th17 cytokines IL-17, IL-22, IL-6, TNF-α, and up-regulates Th2 cytokine IL-4, which indicated that the possible immunoregulatory role and bone-sparing effects of 1,25(OH)2D3 in RA through modulation of the Th1/Th17 and Th2 cytokine balance.

References:

Conclusions: 1,25(OH)2D3 inhibits the synthesis of Th1 cytokines IFN-γ, Th17 cytokines IL-17, IL-22, IL-6, TNF-α, and up-regulates Th2 cytokine IL-4, which indicated that the possible immunoregulatory role and bone-sparing effects of 1,25(OH)2D3 in RA through modulation of the Th1/Th17 and Th2 cytokine balance.

Methods: In the cross-sectional study, HR-pQCT of the second metacarpophalangeal joint (MC2) was performed in 124 patients with ERA at baseline, images were analysable in 117 patients. Erosions were visualized in 72 patients and parameters of bone erosions were assessed. In the prospective study, 63 ERA patients who had completed one year of follow-up with repeat HR-pQCT scan were also analysed. The number and volume of the erosions as well as bone mineral density (BMD) surrounding erosion were quantified. Data on demographic and disease-specific parameters including ESR, CRP, DAS 28, ACPAs and RF levels and treatment were recorded.

Results: At baseline, 90/117 patients were both ACPAs and RF positive (ACPAs+/RF+ group), 7/117 were only RF (RF+), 13/117 were only ACPAs (ACPAs+) and 7/117 were antibody negative (non-ACPAs+/RF+ group, n=27). Erosion depth and volume were increased in the ACPAs+/RF+ group compared with the non-ACPAs+/RF+ group (both P<0.05) (Table 1). Independent explanatory variables associated with a larger erosion volume included RF−E (P=0.012), older age (P=0.003) and a higher damage joint count (P=0.028). Images from 63 patients who completed 12 months follow-up were analysed. Erosion volume were significantly lower in patients who achieved simplified disease activity score (SDAI) remission at 12 months compared to those who did not (P=0.045). Linear regression analysis indicated that independent predictors for an increase in erosion volume included RF−E (P=0.032) and a higher damage joint count (P=0.009) at baseline and failure to achieve SDAI remission for an increase in erosion volume included RF−E (P=0.032) and a higher damage joint count (P=0.009) at baseline and failure to achieve SDAI remission at 12 months.

Conclusions: RF and ACPAs play an additive effect on erosion volume in ERA patients. Higher RF titre was associated with larger erosion volume at baseline and predicted progression of erosion volume after adjusting for baseline parameters and treatment response.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2962
TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN POLAND – ESTIMATE THE FREQUENCY OF USE OF METHOTREXATE DURING A RANDOM AUTHOR’S APPOINTMENT WITH A RHEUMATOLOGIST

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Background: In accordance with the EULAR/ACR recommendations disease-modifying antirheumatic drugs (DMARDs), particulary methotrexate (Mtx) should be applied after diagnosis of rheumatoid arthritis (RA). The goal of the treatment is to get remission/low disease activity

Objectives: The aim of this study was evaluation of the RA treatment, the frequency of use of Mtx and its dose application during control visits to rheumatologist in all Rheumatology Centers in Poland. The disease activity was evaluated by using disease activity score 28 joint score (DAS-28).

Results: There were analysed 301 case records of patients diagnosed with RA on the basis of the ACR 1997 and/or ACR/EULAR 2010 criteria. Patients recently diagnosed were excluded from analysis. In the examined group were 226 women and 75 men, median age 58.0, disease duration 5.0. Patients were divided in groups depending on the type of applied therapy 215 (71%) patients were treated with Mtx monotherapy or combined with other DMARDs. 161 patients (53%) took glucocorticosteroids simultaneously. Average DAS28 – 5.0, disease duration 6.2 At 18 patients (6%) contraindications against the Mtx were stated. In addition, a Wilcoxon test was developed to determine differences between the pre-test score and the post-test score in the EVA of each patient. Statistically significant differences were found in the first session (Z=3.65, p<0.001), second session (Z=3.67, p=0.001) and third session (Z=3.56, p<0.001).

Conclusions: Hypnosis, as a behavioral technique, has shown efficacy in patients with chronic pain. In this research, a significant decrease in patients’ perception of pain has been demonstrated.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6773

EFFECTIVITY OF THE COMBINATION THERAPY WITH METHOTREXATE, LEFLUNOMIDE AND MYPREDNISOLONE IN RHEUMATOID ARTHRITIS

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Background: The RA modern treatment approaches are based on “aggressive therapy”, which aims at suppressing autoimmune inflammation and prevent joint destruction at the early stages of the disease.

Objectives: To evaluate the effectiveness and tolerability of the triple combination therapy with methotrexate, leflunomide and methylprednisolone in patients with rheumatoid arthritis.

Methods: The study included 150 patients with rheumatoid arthritis. As a result of randomization, 50 patients received triple combination therapy (methotrexate +methylprednisolone +leflunomide), 50 patients with monotherapy with methotrexate, leflunomide 50 others. As a result all patients groups were comparable after all clinical and demographic indices.

Results: Our result showed that triple therapy is very effective in treating patients with RA. A significant improvement on the criteria of the AAR (ACR=50) at the end of the study was observed in most patients receiving methotrexate, leflunomide and methylprednisolone. This is confirmed statistically and clinically positive dynamics significantly in almost all indicators used of efficacy (pain, stiffness, number of tender and swollen joints, the activity of AR, the value VUSH index functional HAQ) In addition, the use of triple therapy decreased average dose simultaneous use of glucocorticosteroids daily (from 5.0 to 2.5 mg) and 76% of patients canceled anti-inflammatory non-steroid drugs.

Conclusions: After randomized trial data lasting 24 months based triple therapy (methotrexate, leflunomide and methylprednisolone) was highly effective in patients with high RA activity. A significant improvement according to the criteria of ACR (ACR=50) was obtained in 31 of 39 patients (79.4%), including the nine patients (23.0%) had developed clinical remission. Administration of the basic triple therapy was characterized by a significant clinical effect ACR stability of=50. It was maintained during not less than 15 months of research in 28 (90.32%) of patients who received this treatment and only 3 of 11 (27.27%) patients who received methotrexate alone group and 8 in 10 (80%) who administered LF (<0.039). Evidence recovery (ACR=50), as well as clinical remission was kept stable in all 28 patients that triple therapy was extended after the ending of basic research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6317
Background: Glucocorticoids (GCs) are frequently used in the treatment of Rheumatoid Arthritis (RA) but safety data was lacking. Org 214007–0, LGD-5552, Compounds 4 and 5 and PF-04171327 showed similar efficacy as a GC, but no safety data was provided.

Methods: To evaluate changes in serum bone turnover markers and Wnt inhibitors at 7- and 30-days after initiation of low dose GCs treatment of early RA.

Results: At baseline we observed a significant positive correlation between CRP and DKK1 serum levels (r=0.63; p<0.05) and between DKK1 and CTX serum levels (r=0.59; p<0.05). A significant decrease in serum levels of CRP, P1NP and Sclerostin was observed after 7 and 30 days of GC treatment (p<0.05). About DKK1, it has been detected a not significant tendency to decrease after starting GC. CTX serum levels showed no significant changes.

Conclusions: This study has shown that a low dose GC treatment might have complex and conflicting short-term effects on bone metabolism in early RA (a reduction of bone formation, without increase of bone resorption), different from those observed with higher dose, in other diseases or in healthy subjects. The observed decrease in P1NP and Sclerostin serum levels might mean that also low dose of GC could acutely suppress bone formation and induce loss of function and/or number of osteocytes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4667

AB0430

LEFLUNOMIDE AS A SECOND LINE DMARD AFTER METHOTREXATE HAS LIMITED IMPACT ON RHEUMATOID ARTHRITIS IN REAL LIFE

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Background: If rheumatoid arthritis (RA) is not in remission or at least low disease under methotrexate (MTX), leflunomide is an approved conventional synthetic DMARD, which is commonly used in some countries. 

Objectives: To investigate in a real life situation whether patients with RA benefit from instituting leflunomide after methotrexate.

Methods: The clinical data of all RA patients who had at least once received leflunomide, and who agreed to the pseudonymized analysis of their data (approved by the local ethics committee), were analyzed from the time of leflunomide initiation on to the time of stopping leflunomide or the last visit in 2015, which ever came first.

Results: In total, 145 RA patients treated with leflunomide were identified. Of these, 87 received leflunomide after MTX had failed as a first line DMARD, and 8 received leflunomide as a first line DMARD. 50 patients had another first line therapy. Of the first line leflunomide patients 3 (38%) were still on leflunomide at the last visit, as compared to 7 of the 44 patients (16%) who were switched from MTX to leflunomide, and 0 of the 27 patients in whom leflunomide was added to MTX (p=0.01 vs 1st line leflunomide). For leflunomide monotherapy, 29% and 19% were still on the drug after 24 and 48 months, respectively, as compared to 14 and 0% under the combination with MTX. Of all patients who started leflunomide, remission (at least low disease activity) as per CDAI (>2.8 <10) was reached by 23% (57%) for 3 months, 20% (40%) for 6 months and 16% (34%) one year after initiating leflunomide monotherapy, with corresponding percentages of patients of 39% switched to other approaches at six months and 60% switched at one year. Under the combination of leflunomide and MTX, remission (at least low disease activity) was seen in 16% (53%) at 3 months, 20% (37%) at 6 months, and 8% (20%) at one year, and 55% and 71% had switched to other modes of action at six months and one year, respectively. Gastrointestinal and mucocutaneous adverse events and hypertension were common, and 4 of our patients experienced serious bacterial infections.

Conclusions: Leflunomide constitutes a longer term therapeutic option for a subgroup of RA patients with contraindications to MTX or after MTX failure. After one year, leflunomide had led to sustained acceptable disease control in approximately one third of the patients, but only in one in five under leflunomide combined with MTX. These results are supportive of the EULAR recommendations that patients should be switched to a second conventional DMARD in the absence of predictors of bad outcome only. If leflunomide is initiated, the patients need to be followed closely for potential secondary loss of efficacy.

Disclosure of Interest: None declared


AB0429

SHORT-TERM EFFECTS OF LOW DOSE GLUCOCORTICOIDS ON BONE METABOLISM IN EARLY RHEUMATOID ARTHRITIS

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1Rheumatology Unit, University of Verona, Verona; 2Rheumatology Unit, AOU of Bologna, Bologna; 3Rheumatology and Rehabilitation Unit, Salvatore Maugeri Foundation IRCCS, Castel Goffredo, Mantua; 4Rheumatology Unit, Santa Chiara Hospital, Trento, Italy

Background: Glucocorticoids (GCs) are frequently used in the treatment of Rheumatoid Arthritis (RA). Studies in humans about the effects on bone turnover markers and modulators are poor, and results are discordant and controversial, probably because conducted with different doses and underlying diseases.

Objectives: To explore changes in serum bone turnover markers and Wnt inhibitors at 7- and 30-days after initiation of low dose GCs treatment of early RA.

Methods: 27 adult patients suffering from early RA were prospectively enrolled. Blood tests including C-Reactive Protein (CRP), amino-terminal propeptide of type 1 collagen (P1NP, marker of bone formation), carboxy-terminal telopeptide of type 1 collagen (CTX, marker of bone resorption), Sclerostin, and Dickkopf-related protein 1 (DKK1) were detected at baseline and 7 and 30 days after starting low dose of GC (methylprednisolone 4 mg/day).

Results: At baseline we observed a significant positive correlation between CRP and DKK1 serum levels (r=0.63; p<0.05) and between DKK1 and CTX serum levels (r=0.59; p<0.05). A significant decrease in serum levels of CRP, P1NP and Sclerostin was observed after 7 and 30 days of GC treatment (p<0.05). About DKK1, it has been detected a not significant tendency to decrease after starting GC. CTX serum levels showed no significant changes.

Conclusions: This study has shown that a low dose GC treatment might have complex and conflicting short-term effects on bone metabolism in early RA (a reduction of bone formation, without increase of bone resorption), different from those observed with higher dose, in other diseases or in healthy subjects. The observed decrease in P1NP and Sclerostin serum levels might mean that also low dose of GC could acutely suppress bone formation and induce loss of function and/or number of osteocytes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3254

AB0431

POST-MARKETING SURVEILLANCE OF TOFACITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM REPORT OF SAFETY DATA

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Efficacy and safety of tofacitinib have been shown in RA patients in global Phase 2, Phase 3 (one study included Japanese patients) and long-term extension (LTE) studies and in two Phase 2 and one LTE study in Japanese patients.
ABT-494 has no effect on the QT interval at the doses being evaluated in rheumatoid arthritis phase 3 trials

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Background: ABT-494 is a selective Janus Kinase 1 inhibitor currently being evaluated for treat Rheumatoid Arthritis (RA). The objective of this study was to assess the effect of ABT-494 on the QT interval at the clinical relevant doses from 1 mg to 48 mg single doses under fasting conditions and 3 mg to 24 mg twice daily under non-fasting conditions. Serial triplicate electrocardiograms and pharmacokinetic assessments were conducted. The relationship between change from baseline in Fridericia-corrected QT interval (QTcF) and ABT-494 plasma concentrations was characterized using linear mixed-effects modeling. To our knowledge, in patients with RA and secondary Raynaud’s syndrome, the change in QTcF from baseline to 2 hours post-dose was compared for subjects who received placebo under fasting and non-fasting conditions.

Methods: ABT-494 showed no potential for QT prolongation at the expected therapeutic and super-therapeutic plasma exposures for the doses being used in Phase 3 RA trials.


Correction of lipoprotein and endothelial dysfunction by using no donors (4.2% solution of arginine hydrochloride and l-arginine aspartate) in patient with rheumatoid arthritis in combination with the raynaud’s syndrome

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Background: Lesion of the cardiovascular system is associated with uncontrolled inflammation and immune defects in patients with Rheumatoid Arthritis (RA). There is an evidence of the close pathogenetic connection between rheumatoid inflammation and accelerated development of atherosclerosis. The first sing of atherosclerosis is endothelial dysfunction (ED).

Objectives: Evaluate the effectiveness of NO donors (4.2% solution of arginine hydrochloride and L-arginine aspartate) in correction of lipopid and ED in patients with RA and secondary Raynaud’s syndrome.

Methods: 68 patients with RA were examined. All patients were divided into 2 groups: (37 people with RA in combination with secondary RS) received basic therapy of RA (methotrexate 10–15 mg/wk.), antiplatelet and vasodilatory drugs; II group (31 people – RA in combination with secondary RS) got similar therapy plus treatment with NO donors (4,2% solution of arginine hydrochloride and L-arginine aspartate).

Results: Levels of LC, LDL, AI and MI indexes were significantly higher than the norm in 2 compared groups before the treatment and 3 months after its start (p<0,05). There were significant decreases in levels of lipid profile, IA and MI index in II group 3 months after treatment in comparison to benchmarks (TC by 13,3%, LDL by 16,1%, TG by 14,7%, AI index by 13,8% MI index by 12,7% p<0,05) and they were significantly unchanged in I group (p>0,05). It was elucidated a direct reliable strong correlation in patients of II group between the level of FMD and endothelin-1 before treatment (=0,73, p<0,05) and after treatment (r=0,69, p<0,05). Symptoms of ED, levels of FMD, levels of endothelin-1 and NO donors were decreased in patients of both groups after the conducted therapy. It was established a proportionately reliable correction between CRP and LDL levels after treatment in II group of patient (r=0,63, p<0,05).

Conclusions: 1. There is a lack of flow-mediated vasodilation of brachial artery in patients with RA and secondary RS, which can indicate a dysregulation of endothelial function. 2. The level of CRP is increased in patients with RA and secondary RS and is associated with the risk of hyperlipemia and atherosclerosis. 3. The usage of NO donors (4,2% solution of arginine hydrochloride and L-arginine aspartate) in the treatment of RA with secondary RS significantly reduces the levels of IA and MI index, the level of atherosclerotic lipoprotein fractions (TC, LDL and TG) and decreases the severity of ED, which leads to minimizing the risk of atherogenesis and its complications.
**AB0434\ TOFACITINIB IN RHEUMATOID ARTHRITIS: REAL LIFE EXPERIENCE**


Background: Tofacitinib is a new small molecule, Janus kinase 1 and 3 inhibitor, interfering with the JAK-STAT signaling pathway. The JAK-STAT transmits the effects from the immune cell nucleus, influencing DNA transcription. Its efficacy and safety in Rheumatoid Arthritis (RA) has been demonstrated in different phase II, III and long-term clinical studies. It has been approved in Argentina for the treatment of patients with moderate to severe rheumatoid arthritis RA with failure to conventional DMARDs.

Objectives: To communicate real world safety data from patients with RA under treatment with Tofacitinib.

Methods: A retrospective, descriptive study from patients with RA (ACR/ EULAR2010) under treatment with Tofacitinib from September 2014 to December 2016 was conducted. Medical records from patients being treated with Tofacitinib were reviewed. Clinical data were recorded, concomitant treatments, and reported adverse effects were documented.

Results: 62 patients were treated with Tofacitinib. 53 were female and 9 were male, with a mean age of 57.91±14.72 years and average disease duration of 140.83±130.83 months. 18 patients (29%) had at least one comorbidity, the most frequent being hypertension (77%). Of the 62 patients studied, 54 (87%) had established RA (duration of illness greater than 24 months) and 8 patients (13%) with early RA (less than 24 months). In 54 patients Tofacitinib was indicated in combination with another DMARD (RMD), and in only patients, received treatment as monotherapy. The most commonly used DMARD in combination therapy was methotrexate (MTX) in 92.5%.

Treatments were indicated by failure to MTX or other conventional DMARDs. 12/62 treatments were indicated by failure to treatment with 1 biological DMARD and 13/62 treatments were indicated by failure to two or more biological DMARDs. The maximum exposure time was 21 months. During the time of exposure to Tofacitinib the following adverse events were observed: Herpes Zoster infection 2 cases (monomeric, no visceral involvement). We observed 80 patients with early RA, 50 patients of them were compared as a single “placebo” group. Baseline (BL) disease severity was classified as moderate or severe by Disease Activity Score in 28 joints with erythrocyte sedimentation rate (DAS28: moderate 3.2 to <5.1; severe ≥5.1) and Clinical Disease Activity Index (CDAI: moderate 10 to <22; severe ≥22). Results show CRP and ESR, the most frequently used parameters.

Conclusions: Most patients received combined treatment with DMARDs being the most commonly used Methotrexate. There were no cases of serious infections, opportunistic infections, cytopenias, dyslipidemia, or increased CPK. Patients discontinued Tofacitinib: one due to tachycardia, another case peripheral pain and another case due inefficacy. Most patients received combination treatment with DMARDs being the most commonly used Methotrexate. There were no cases of serious infections, opportunistic infections, cytopenias or dyslipidemia. The use of Tofacitinib in RA has a critical role in the development and progression of immune inflammation. The results of observation of patients for 6 months were showed that, of all indicators of patients in 2nd group was 33.4%. During the treatment was indicated improvement of laboratory parameters of disease activity of RA in both groups, features of activity of 1st group were decreased up to (DAS28 =2.9), signs of 2nd group were (DAS28 =3.6). However, there were 26% of cases of clinical remission of the disease in patients of 1st group than patients of 2nd group. Known side effects of combination therapy with MT and LF in most cases have not been severe, reversible and demanded the abolition of drugs in rare (11.2%) cases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3861

**AB0435\ COMBINATION THERAPY IN EARLY STAGE OF RHEUMATOID ARTHRITIS**


Background: To evaluate tofacitinib 5 and 10 mg twice daily (BID) efficacy in patients with moderate to severe rheumatoid arthritis (RA).

Methods: A randomized double-blind controlled study of 6–24 months’ duration, Tofacitinib was administered in 2 groups: 1st group consisted of 40 patients, 2nd group were (DAS28 ≤3.6). However, there were 26% of cases of clinical remission of the disease in patients of 1st group than patients of 2nd group. Known side effects of combination therapy with MT and LF in most cases have not been severe, reversible and demanded the abolition of drugs in rare (11.2%) cases.

Conclusions: Combined basic therapy of patients in the early stages of RA with methotrexate (MT) and Leflunomide (LF) has more efficiency than mono therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4770

**AB0436\ COMPARISON OF TOFACITINIB EFFICACY IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: POOLED ANALYSIS OF PHASE 3 STUDIES**


Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. The maximum exposure time was 21 months. During the time of exposure to Tofacitinib the following adverse events were observed: Herpes Zoster infection 2 cases (monomeric, no visceral involvement). We observed 80 patients with early RA, 50 patients of them were compared as a single “placebo” group. Baseline (BL) disease severity was classified as moderate or severe by Disease Activity Score in 28 joints with erythrocyte sedimentation rate (DAS28: moderate 3.2 to <5.1; severe ≥5.1) and Clinical Disease Activity Index (CDAI: moderate 10 to <22; severe ≥22). Results show CRP and ESR, the most frequently used parameters.

Conclusions: Most patients received combined treatment with DMARDs being the most commonly used Methotrexate. There were no cases of serious infections, opportunistic infections, cytopenias or dyslipidemia. The use of Tofacitinib in RA has a critical role in the development and progression of immune inflammation. The results of observation of patients for 6 months were showed that, of all indicators of patients in 2nd group was 33.4%. During the treatment was indicated improvement of laboratory parameters of disease activity of RA in both groups, features of activity of 1st group were decreased up to (DAS28 =2.9), signs of 2nd group were (DAS28 =3.6). However, there were 26% of cases of clinical remission of the disease in patients of 1st group than patients of 2nd group. Known side effects of combination therapy with MT and LF in most cases have not been severe, reversible and demanded the abolition of drugs in rare (11.2%) cases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4770
BL characteristics were balanced between treatment groups in each disease severity category. M3 efficacy was significantly greater with tofacoitinib 5 and 10 mg BID vs placebo, regardless of BL disease severity. As expected, larger proportions of tofacitinib-treated pts with moderate vs severe BL RA achieved LDA by either DAS28 (32.3–36.7% vs 13.8–19.1%) or CDAI (49.2–55.0% vs 28.0–31.2%). A greater proportion of pts achieved remission in the moderate vs severe BL groups by DAS28 (20.0–22.8% vs 6.2–9.0%) or CDAI (11.5–12.1% vs 5.1–6.7%). A greater proportion of pts achieved HAQ-DI <0.5 with moderate vs severe RA classified by DAS28 (45.0–60.6% vs 24.5–30.0%) or BL CDAI (40.8–52.4% vs 24.7–30.4%). Greater improvements from BL in disease activity were seen for pts with severe vs moderate RA classified by BL DAS28 (Table), and by BL CDAI (Tofacoitinib 5/10 mg BID ΔCDAI: -21.1/23.0 vs -8.1/-9.4; ΔHAQ-DI: -0.5/-0.6 vs -0.3/-0.4).

Conclusions: Tofacoitinib 5 and 10 mg BID demonstrated efficacy in treating pts with moderate and severe RA with >7 years’ mean disease duration. By M3, pts with severe vs moderate BL disease activity had greater improvements in disease activity and physical functioning; higher proportions of pts with moderate vs severe BL disease activity achieved remission, LDA or normal physical functioning. Interpretation of this post hoc analysis may be limited by the smaller sample size of the moderate disease group and the combining of mono- and combination-therapy results.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMG and funded by Pfizer Inc.


AB0437 EFFICACY AND SAFETY OF LONG-TERM ANALGESIC THERAPY WITH ETORICOXIB FOR PATIENTS WITH RHEUMATIC DISEASES

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Background: There are some data in literature on decompensation of arterial hypertension and other chronic diseases during the treatment with coxibs which in practice unfortunately limits their administration for patients with comorbidities.

Objectives: To evaluate the efficacy of analgesic effect of etoricoxib and frequency of comorbidities exacerbation on such treatment.

Methods: 58 patients with rheumatoid arthritis (34.4%), osteoarthritis (29.2%), anklyosing spondylitis (19%), gout (14%), psoriatic arthritis (3.4%) at the age of 25 to 75 years (the average age, 52.9±13.03 years) were included. They had 79.3% comorbidities (diseases of digestive system – 37.9%, arterial hypertension – 53.4% (including 3.2% with compensated hypertension), bronchial asthma – 1.7%). All the patients before the initiation of the study had taken NSAIDs (diclofenac, nimesulid, ketoprofen, meloxicam, aceclofenac, ibuprofen) with lack of effect or minimal effect (84.4%) or minimal effect (15.6%). Etoricoxib was administered in 100% cases. Patients were divided into 3 groups: 1) patients treated with other non-steroidal anti-inflammatory drugs (NSAIDs), 2) patients treated with etoricoxib alone, 3) patients treated with etoricoxib in combination with other drugs.

Results: By the second appointment 98.2% patients were taking etoricoxib regularly, and 97% of patients with moderate and severe RA with >7 years’ mean disease duration (more than 3 years). At the initiation of IGU were significant factors of clinical remission achievement (ΔCDAI: 40.8–52.4% vs 24.7–30.4%). Greater improvements from BL in disease activity were seen for pts with severe vs moderate RA classified by BL DAS28 (Table), and by BL CDAI (Tofacoitinib 5/10 mg BID ΔCDAI: -21.1/23.0 vs -8.1/-9.4; ΔHAQ-DI: -0.5/-0.6 vs -0.3/-0.4). A greater proportion of pts achieved HAQ-DI <0.5 with moderate vs severe RA classified by DAS28 (45.0–60.6% vs 24.5–30.0%) or BL CDAI (40.8–52.4% vs 24.7–30.4%). Greater improvements from BL in disease activity were seen for pts with severe vs moderate RA classified by BL DAS28 (Table), and by BL CDAI (Tofacoitinib 5/10 mg BID ΔCDAI: -21.1/23.0 vs -8.1/-9.4; ΔHAQ-DI: -0.5/-0.6 vs -0.3/-0.4).

Conclusions: Tofacoitinib 5 and 10 mg BID demonstrated efficacy in treating pts with moderate and severe RA with >7 years’ mean disease duration. By M3, pts with severe vs moderate BL disease activity had greater improvements in disease activity and physical functioning; higher proportions of pts with moderate vs severe BL disease activity achieved remission, LDA or normal physical functioning. Interpretation of this post hoc analysis may be limited by the smaller sample size of the moderate disease group and the combining of mono- and combination-therapy results.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMG and funded by Pfizer Inc.


AB0438 EFFICACY AT THREE YEARS OF DAILY CLINICAL USE OF IGURATIMOD IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Iguratimod (IGU) is a small-molecule antirheumatic drug that was developed in Japan and is currently only approved for treatment of rheumatoid arthritis (RA) in Japan and China. IGU suppresses tumor necrosis factor-alpha-induced production of interleukin (IL)-6, IL-8 and monocyte chemotactant protein 1 via the inhibition of nuclear factor-kappa B activation in cultured human synovial cells and human acute monocyctic leukemia cells. There are some reports about the efficacy and safety of IGU in patients with RA. However, the assessment about efficacy of the clinical use of IGU has mainly been restricted to short-term (within one year) outcome.

Objectives: The purpose of this study was to assess the efficacy of IGU in 3 years of daily clinical use.

Methods: Sixty-nine RA patients (14 males and 55 females, mean age of 63.9 years, mean disease duration of 14.9 years) were enrolled in this study. The clinical course of RA was evaluated during 3 years. The patients who discontinued the IGU therapy were analyzed by the last observation carried forward method.

Results: The survival rate at 3 years was 49.3%, and 8 patients discontinued the IGU therapies due to insufficient response, 12 patients due to adverse events such as exanthema, pneumonitis or hepatic disorder, and other patients based on their requests. The DAS28-CPR, DAS28-ESR, SDAI and CDAI significantly decreased at 6 months, 1, 2, 3 years compared with baseline. The low DAS28-CPR at 3 months and younger age were associated to the continuation of IGU. Furthermore, the IGU therapy were analyzed by the last observation carried forward method. The DAS28-CPR and the usage rate of prednisolone at baseline were significantly lower and patients’ age was younger. A logistic regression analysis revealed the low DAS28-CPR and low usage rate of prednisolone at baseline were significant factors contributing to the achievement of a clinical remission at 3 years.

Conclusions: We assessed middle-term outcome of the clinical use of iguratimod therapy in RA patients. The low DAS28-CPR and low usage rate of prednisolone at the initiation of IGU were significant factors of clinical remission achievement at 3 years.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6040

AB0440 IMPACT OF VITAMIN D DEFICIENCY UPON DISEASE ACTIVITY AND IMMUNE DISORDER IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Emerging evidence suggests that vitamin D plays an important role in immune regulation.

Objectives: The objective of this work was to determine if patients with rheumatoid arthritis (RA) are at risk for vitamin D deficiency and whether vitamin D levels correlate with disease activity or immune disorders.

Methods: This study was a retrospective research. RA patients who had vitamin D levels and immune function indexes of each other were included. Patients receiving or have received vitamin D, corticosteroids, disease-modifying anti-rheumatic drugs or a tumor necrosis factor antagonist and those who had hepatic or renal insufficiency were excluded. Multivariate analysis was performed to examine correlations and control for confounding factors.

Results: As suggested threshold (<25 ng/ml), the overall prevalence of vitamin D insufficiency was 265 of 280 (94.6%). Mean serum vitamin D insufficiency levels of 11.15±4.74 ng/ml for RA patients were significantly lower compared to controls (31.62±6.46) (p<0.001). Among all the subjects, 208 (72.7%) were females. Vitamin D levels in high disease activity group were lower compared to vitamin D level in patients with low and moderate disease activity (DAS-28 score >5.1, 3.2–5.1, ≥3.2, respectively, p<0.001) and vitamin D levels had an inverse correlation with DAS28 score (r-coefficient-0.158, p=0.019, per 1 ng/ml). However, no significant relationship was found between vitamin D and these variables (T cell, B cell, NK cell, Treg, Th1, Th2, Th17/Treg) in patients.

Conclusions: Lower levels of vitamin D are associated with worse DAS28 and higher levels of Th17 with RA, especially in female patients. The levels of 1,25-dihydroxycholecalciferol (1,25(OH)2D3) could be a marker to monitor the disease activity in RA patients and vitamin D may be an alternative supplementary treatment for RA.

Acknowledgements: This work was supported by research grants from the National Natural Science Foundation of China (no. 81301532/83003) and the Shangxi Science and Technology research projects of China (no. 201603D320174).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3202

AB0441 USING OF SUBCUTANEOUS METHOTREXATE IN AGED PATIENTS WITH SEROPOSITIVE RA

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Background: Increasing life expectancy is a global prospect involving multiple nations, thus deeper insights into methotrexate (MTX) therapeutic potential in aged people is of paramount importance, as MTX still remains an anchor DMARD in RA management.

Objectives: To assess the results of 12-months therapy with subcutaneous MTX (SC MTX) injections in RA patients aged more than 60 years.

Methods: The 12 months’ study included pts receiving MTX (DAS28 >3.2), meeting ACR/EULAR (or ACR 1987) criteria, with RA lasting up to 3 years, and naïve to SC MTX. All pts were RF and/or ACPA-positive, 68% had increased BMI, 31% - obesity, 8% were smokers, 25% were taking oral GCS (<10 mg/day equivalent to prednisolone). All pts were administered SC MTX monotherapy (80 mg once a week as a DMARD, starting at 10–15 mg/week, with subsequent 5 mg up-titration each 1–2 weeks to max 30 mg/week) up to achieving the target (remission or minimum disease activity) or to emergence of an adverse drug reaction (ADR). Folic acid (min 5 mg/week) was administered at any day(s) except for the day of SC MTX injection for ADR prophylaxis. Disease activity was scored using DAS28. GEBAs were administered in pts with insufficient SC MTX clinical effect. Pts were monitored within universal institutional REMARKA program, envisaging physical examination, blood analysis and biochemistry panel (including liver enzymes and creatinine). STATISTICA 10 software was used for data processing.

Results: 32 RA pts (28 females, 4 males) were included (mean disease duration 12±10 months, mean age - 65.7±4.7 years, mean DAS28 score -5.6±2.0. Cumulative SCMT dose by the end of the study reached 264±180 mg). The therapeutic target (remission or minimum disease activity based on DAS28 score) was achieved in 20 pts receiving SCMT monotherapy, 12 pts received administration of GEBAs. Adverse drug reactions (ADRs) were documented in 10 pts, including cases of more than one ADR at a time: breast abscesses (1), alopecia (2), diarrhea (2), skin rash (1), a metallic aftertaste (1), local post-injection reactions (1), nausea (2), elevation of liver enzymes (3), leucopenia (1), pneumonia (1). There were 5 cases of SC MTX monotherapy discontinuation (2 - temporary, and 3 - permanent). The majority of pts (88%) could manage self-injection without additional training or assistance from medical staff.

Conclusions: 62.5% of aged RA pts participating in the study managed to achieve the therapeutic target after 12 months of SC MTX monotherapy, although 31% ADRs rate required temporary (2) or permanent (3) SCMT discontinuation.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2418

SLE, Sjögren’s and APS - treatment

AB0442 REAL-LIFE EXPERIENCE WITH BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): CONTROL OF DISEASE ACTIVITY AND FLARES IN A MULTICENTER COHORT

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Background: Data on the efficacy of belimumab in SLE mainly originate from large randomized clinical trials, whereas reports from real-life clinical practice are lacking.

Objectives: To describe the clinical experience from the use of belimumab in Greece since the approval of the drug.

Methods: Multicentre observational study of patients receiving belimumab, with documentation of disease activity (SLEDAI-2K index), achievement of low disease activity
activity states (remission [SLEDAI-2K=0] and lupus low disease activity state [LL-DAS]), accrual of irreversible damage (SLICC damage index, SDI), number and severity of flares, and side-effects. Analyses were performed at quarterly intervals and only patients with at least 3 months of follow-up were included in the study. Results: A total of 56 patients were included [33 women (94.6%), mean (SD) age 44 (12.5)] at baseline, 25 females (44.6%) had positive ANA and 20 (35.7%) had positive anti-dsDNA) was evident in 30 patients (53.5%). Most frequent manifestations were arthritis (82.1%), inflammatory rash (73.2%), active hair loss (57.1%), mucosal ulcers (26.8%) and leukopenia (10.7%). Median (range) duration of follow-up was 9.1 (2.9 - 34.6) months. We observed a significant decrease in the SLEDAI-2K, physician global assessment (PGA) and daily prednisone dose over time, starting as early as 3 months after belimumab initiation (Table 1). This effect was significantly more pronounced in patients who were serologically active (SA) at baseline, even after exclusion of the serologic components. Table 1: Median (range) total number of flares for the 12 months before and after belimumab treatment. (1–24) at baseline vs. 2 (0–16) at 6 months and 0 (0–16) at 12 months, p < 0.0001 and p=0.013, respectively; for serologically inactive patients: 6 (2–23) at baseline vs. 6 (0–14) at 6 months and 5 (0–18) at 12 months, p=0.017 and p=0.024, respectively. For patients with ≥12 months of follow-up (n=20), belimumab treatment resulted in a significant decrease in flare rate (median [range] total number of flares for the 12 months before and after belimumab treatment, 3 (0–7) and 0 (0–2), respectively, p < 0.0001). 10 patients (17.8%) discontinued belimumab due to inefficacy after a median (range) 7.1 (5.5 - 20.4) months of therapy and 5 patients discontinued due to planned pregnancy. There were no drug discontinuations due to side-effects.

Conclusions: In real-life clinical settings, belimumab is efficacious in controlling disease activity of SLE and permitting tapering of glucocorticoid dose. Similar to data from RCTs, this effect seems to be more pronounced in serologically active patients.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4825

AB0443 INFUSION REACTIONS TO RITUXIMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS
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Background: B lymphocytes are important in the pathogenesis of primary Sjögren’s syndrome (pSS), but two phase III trials (TEARS and TRACTISS) of the B cell depleting agent rituximab (RTX) failed to show an effect on their primary endpoints in pSS. Whilst RTX may lack efficacy in a non-stratified pSS population, other explanations for the infusional negative results include small size of the dataset, limited duration of follow-up and dose-limiting side-effects.

Objectives: To compare the effects of RTX versus placebo in pSS, in a multicentre, multivisoerstry substudy of TRACTISS.

Methods: Subjects consenting to SGUS were randomised to 1000mg RTX or placebo given at weeks 0, 2, 4 and 6, and scanned at baseline and weeks 16 and 48. RTX and placebo were administered as a 30-second intravenous infusion in a 300mg over 15 minutes for weeks 0 and 12. Total ultrasound scans included a 3.5-7.5MHz curvilinear transducer. The primary endpoint was presence/absence of disease activity (ACR criteria), with secondary endpoints of categorical response in the RTX arm (defined as a 1 point improvement) as a function of the baseline score, age category, disease duration and time point.

Results: 66 patients (49.6% of the total study population) consented to SGUS, and 52 (39.1%; n=26 RTX and n=26 placebo) completed the baseline and at least one follow-up visit. Estimated baseline-adjusted TUS at week 16 was 6.2 (95% CI 5.4–7.0) for placebo and 5.0 (95% CI 4.4–5.6) for RTX, and at week 48, 6.1 (95% CI 5.5–6.6) and 4.8 (95% CI 4.2–5.4) respectively. Estimated between group differences (RTX-placebo) in baseline adjusted TUS were -1.2 (95% CI -2.1 to -0.3; p=0.0099) and -1.2 (95% CI -2.0 to -0.5; p=0.0023) at weeks 16 and 48. Glandular definition was the only domain to show statistically significant improvement with an OR of 6.8 (95% CI 1.1–43.0; p=0.043) at week 16 and 10.3 (95% CI 1.0–105.9; p=0.050) at week 48. Improvement of ≥1 point in TUS was associated with improvement in oral dryness VAS at week 16 (diff=15.9; CI 1.5 to 30.3; p=0.030) but not week 48 in the RTX arm.
Conclusions: TUS differed between study arms, favouring RTX. This encourages further research into SGS5 as an imaging biomarker in PSS clinical trials.

Acknowledgements: Funded by Arthritis Research UK. Roche provided RTX.

Disclosure of Interest: B. Fisher Paid an instructor for: Novartis, Roche, Virtu-alscops, C. Everett: None declared, J. Rout: None declared, J. O’Dwyer: None declared, P. Emery: None declared, C. Fitzalis: None declared, W.-F. Ng Consult-ant for: Pfizer, UCB, MedImmune, Takeda and Sanofi, A. Carr: None declared.

Background: Given its immunomodulatory effects, hydroxychloroquine use is recommended in systemic lupus erythematosus (SLE). It is associated with a lower rate of appearance and of relapse of lupus nephritis (LN). LN is classically classified using ISN/RPS classification, but others indexes, such as the ones described by Austin and Hill, allow for the quantification of SLE activity in the kidney biopsy tissue.

Objectives: To analyze the association between the use of hydroxychloroquine and the activity of LN in the kidney biopsy.

Methods: Retrospective single center study of consecutive SLE and biopsy proven LN patients, diagnosed from 2010 to 2016. We evaluated the following outcomes: clinical remission, renal function and proteinuria at end of follow up (g/24h). Complete remission was defined as a reduction of proteinuria to <0.5g/24h, inactive urinary sediment and serum creatinine <115% of baseline; partial remission same parameters, except proteinuria <1g/24h if initial value <3g/24h, or reduction to <3g/24h if initial value >3g/24h. Kidney biopsies were evaluated by the INS/RPS LN classification and the morphological indexes described by Austin and Hill, obtained after histomorphological review of renal biopsies. The studied predictor was the use of hydroxychloroquine. Statistical analysis was performed with STATA software, using one-way ANOVA, Qui2 and Pearson/Sperman test were appropriate.

Results: During 6 years, there were 46 biopsy-proven LN cases, 84.8% (n=39) woman, median 35 years old (27–42.5) and 57.6% (n=19) caucasian. 39 patients were already known to have SLE, 7,44 (1,13–12.3) years previously. Of those 39 patients, 46% were under hydroxychloroquine and 77% under other immunosuppression.

The median follow-up was 31.9 (13.2–45.6) months. Based on biopsy findings, 35 patients were started on immunosuppression – induction in 50% of cases with MMF and in 50% with cyclophosphamide; maintenance in 81% with MMF; the rest with azathioprine. Complete remission was achieved in 58% of patients, 27% achieving partial remission. We observed 4 LN relapses. At the end of FUP, we saw a 96% (n=44) patient survival, with a median serum creatinine of 0.8 mg/dl (0.7–0.99), eGFR 98.9 m/1min (71.2–116.8) and proteinuria of 0.6/24h (0.2–1.6). From those 46 patients, 30 were under immunosuppressive therapy at the time of LN presentation, and 60% (n=18) were also under hydroxychloroquine. Table 1 summarizes the clinical findings:

With the use of hydroxychloroquine, we observed a lower histomorphological activity, as represented by a lower Hill biopsy index, and tendency towards lower Activity Index. We also saw a tendency towards lower proteinuria.

Conclusions: Our data reinforces the recommendations of using hydroxychloroquine for its adjunctive role in SLE patients, as we saw a lower histomorphological activity in kidney biopsy, and a trend towards lower proteinuria.

Disclosure of Interest: None declared


AB0446 ADDITIVE INHIBITION OF INTERFERONS, B AND T CELL ACTIVATION AND TLR9-RELATED CYTOKINE CXCL13 BY LEFUMONIDE AND HYDROXYCHLOROQUINE SUPPORTS RATIONALE FOR COMBINATION THERAPY IN PSS PATIENTS

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Abstract AB0445 – Table 1

Hydroxychloroquine use Yes (n=18) No (n=12) p-value

Class II Class III Class IV Class V

Hill Index Yes (%) 39% 28% 28% 22% 0.86 (0.2 – 1.6) 0.09 0.03

No (%) 8% 17% 58% 33% 1.52 (0.98 – 2.01) 0.07

Activity Index Yes (%) 28% 22% 22% 0.75 (0.25 – 1.35) 0.09

No (%) 17% 22% 22% 0.75 (0.25 – 1.35) 0.09

Chronicity Index Yes (%) 33% 0.07

No (%) 33% 0.07

End of FUP eGFR (ml/min) Yes (%) 99.8 (81.9 – 112.1) 0.47

No (%) 96.6 (64.0 – 120.3) 0.78

End of FUP serum creatinine (mg/dl) Yes (%) 0.74

No (%) 0.75

End of FUP proteinuria (g/24h) Yes (%) 0.01

No (%) 0.01

Background: T and B cell-driven immunity is critically involved in immunopathology of pSS. Recently we demonstrated synergistic T and B-cell activation upon T cell triggering and TLR7/9-driven B cell activation in pSS patients, accompanied by synergistic induction of immunoglobulins and IFN-γ and IL-17-producing T cells1.

In addition, TLR7/9-expressing activated pDCs associated with increased type I IFNs and IFN-inducible genes are increased in pSS patients. Several studies have shown that the DMARDs leflunomide and hydroxychloroquine inhibit immune activation in pSS but only show moderate efficacy. However, LEF and HCO target different pathways with overlapping, but also potentially additive mechanisms, where LEF primarily targets T and B cells and HCO TLR7/9-driven B cell and pDC activation.

Objectives: To assess the additive effects of LEF and HCO on CD4 T- and B-cell activation and production of interferons IFN-α and IFN-γ, TLR7-related cytokine CXCL13, as well as IgG and IgM in vitro employing SEB/TR79-triggered PBMC.

Methods: PBMCs of healthy individuals (n=9) and of pSS patients (n=8) were cultured with antigen (SEB), TLR9 and their combination, in presence or absence of LEF, HCO and their combination in clinical relevant concentrations. Proliferation of T and B cells and release of IFN-α, -γ, CXCL13, IgG and IgM were measured.

Results: In line with robust T and B cell activation, IFN-γ, IFNα, CXCL13, IgG and IgM production was achieved by a combination of SEB and TLR9 (at all least p<0.001). LEF dose dependently inhibited B and T cell proliferation, Interferon, CXCL13 and immunoglobulin production. HCO dose dependently inhibited B cell proliferation, IFN-α, CXCL13, and immunoglobulin production. T cell proliferation and IFN-γ production were inhibited by HCO only at higher concentrations. At several suboptimal concentrations LEF and HCO additively inhibited T cell proliferation both in healthy individuals and in pSS patients. (Figure 1). Significant additive effects were seen for all outcome measures except IFN-α. Since IFNα was already robustly inhibited by HCO alone (eg for pSS 90% at 3.3 μM, p<0.001), only trends towards additive effects were observed.

References:

Disclosure of Interest: None declared


AB0447 ANTIMALARIALS IMPROVE SURVIVAL OF SYSTEMIC LUPUS ERYTHEMATOSUS ON CHOLESTEROL: RESULTS OF A FIFTEEN-YEAR CHINESE MULTICENTER RETROSPECTIVE STUDY IN JIANGSU PROVINCE

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Background: Nowadays the importance of antimalarials, especially hydroxychloroquine (HCQ) and chloroquine (CQ), in treatment of systemic lupus erythematosus (SLE) has been demonstrated. However, few have examined the efficacy of HCQ and CQ on eastern Chinese SLE patients.

Methods: The analysis is based on 1372 patients who were enrolled in a retrospective study of 26 centers from January 1st, 1999 through December 31st, 2009, during which time is their first hospitalization. Baseline and follow-up clinical, laboratory and therapeutic data and survival status before April 30th, 2015 were recorded. Statistical analysis consisted of Chi-square test, t-test, Kaplan-Meier curves and logrank test.

Results: Compared with 562 patients without HCQ or CQ treatment, the hazard curves and logrank test. Compared with 562 patients without HCQ or CQ treatment, the hazard ratio (HR) of deaths in 810 patients taking those was reduced (HR 0.52, 95% CI 0.38–0.70, p<0.001). 376 of these 1372 patients experienced their second hospitalization, during which treatment group (165 of 376) showed lower blood level of total cholesterol (TG), compared to control group (4.47 (0.13) vs 5.03 (0.21), p=0.027), while no statistical difference of TG exists between the two groups, first hospitalization (p=0.05). Other metabolic data, such as systolic and diastolic blood pressure, fasting blood sugar, Triglyceride and uric acid were similar between the two groups in two times of hospitalization. On second inpatient visit, disease activity (SLEDAI, blood sedimentation rate, complement) and organ involvements (SLICC) of those who took antimalarials and no users have no significant differences.

Conclusions: Use of HCQ or CQ lower the risk of mortality and TG levels of eastern Chinese SLE patients.

Disclose of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4208

AB0448 USE OF DENOSUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A REAL LIFE MULTICENTRIC EXPERIENCE

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Background: The occurrence of osteoporosis (OP) and fragility fractures (FF) is a frequent comorbidity in patients with systemic lupus erythematosus (SLE), mainly due to the concomitant presence of many risks factors for secondary osteoporosis (drugs, gender, concomitant diseases). The use of corticosteroids (CS) increases the risk of osteoporosis induced by corticosteroid (GIOP) and FF [1]. Denosumab (DR) is a monoclonal antibody that binds to RANKL, inhibiting osteoclast formation and activation, used for both male and women OP to prevent FFx [2,3]. Previous RCT [2] reported a numerically higher serious adverse events of infections in the denosumab users. In particular severe skin infections were significantly more frequent [4]. The possible increase in infection risk might be a concern in subjects with concomitant conditions such as SLE. The use of denosumab in SLE with GIOP patients is recently reported in 17 cases within a RCT [5]. Anyway, no data regarding the tolerability and disease activity during therapy were reported.

Objectives: Our aim was to analyze the prevalence, the tolerability, and relevant changes in disease activity or damage in a cohort of SLE patients treated with denosumab.

Methods: among all SLE patients currently followed in two referral Center we selected the ones that received at least one dose of denosumab. Clinical, serological and demographic variables, concomitant diseases and therapies were collected from clinical charts. Damage index (SDI), activity index (SLEDAI-2K) were selected the ones that received at least one dose of denosumab. In particular severe skin infections were significantly more frequent [4]. The possible increase in infection risk might be a concern in subjects with concomitant conditions such as SLE. The use of denosumab in SLE with GIOP patients is recently reported in 17 cases within a RCT [5]. Anyway, no data regarding the tolerability and disease activity during therapy were reported.

Objectives: Our aim was to analyze the prevalence, the tolerability, and relevant changes in disease activity or damage in a cohort of SLE patients treated with denosumab. Among 793 patients in our cohorts, 21 (2.6%) were treated with denosumab.

Methods: Among all SLE patients currently followed in two referral Center we selected the ones that received at least one dose of denosumab. Clinical, serological manifestations, concomitant diseases and therapies were collected from clinical charts. Damage index (SDI), activity index (SLEDAI-2K) were calculated when denosumab was introduced (first cycle) and at the last evaluation (last cycle). For statistical analysis Chi-squared test or Fisher exact test was used.

Results: Among 793 patients in our cohorts, 21 (2.6%) were treated with denosumab. Demographic data reported a female prevalence (19 cases, 90%), mean age at onset of 36±10 years, mean duration of disease of 26±10 years and mean follow-up of 21±7.8 years; most frequent manifestations were arthritis (90%), cutaneous (67%) and neurological (67%). All patients were still treated with CS (mean duration of 25±6.8 years) with a daily dose of 8.5±3.5 mg/day. Other risk factors for OP were present in the majority of them: drugs (anticoagulants in 6pts, cyclosporin in 3 and antiplatelet in 2), chronic kidney disease (CKD) (4pts), hypovitaminosis D (15pts), anorexia, celiac disease and hemochromatosis (1pt, each). Indication for denosumab was OP with FFx in 17 cases: denosumab was used for a new FF during biphosphonates or after teriparatide. In the other 4 the indication was primary prevention with contraindications at the use of biphosphonates for concomitant severe CKD. Mean duration therapy was 4 cycles (range 1–8); data regarding disease activity, damage and adverse events are reported in table 1. No new FFx developed in any of the included patients at the last evaluation available.

Conclusions: In our cohorts denosumab is still used in few selected patients. However it could be considered as a valid option in GIOP patients because it was globally well tolerated and in our cohort it’s efficacy in the prevention of new fragility fractures was confirmed.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.2740

AB0449 OFF LABEL OF BIOLOGICS IN CONNECTIVE TISSUE DISEASES. A SINGLE CENTER EXPERIENCE

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Background: Connective tissue diseases (CTDs) are a broad spectrum of autoimmune conditions including different entities such as systemic sclerosis (SSc), Sjogren syndrome (SSj), systemic lupus erythematosus (SLE) and autoimmune myositis. There are many patients that do not meet the classification or diagnostic criteria and they fall under the diagnosis of Undifferentiated connective tissue disease (UCTD). Treatment of refractory forms of these could be challenging and clinicians sometimes are forced to try off label drugs such as biologics on the basis of scarce literature support and the experience on different rheumatic disease.

Objectives: To evaluate duration of biologic drug administered off label for the treatment of CTD and investigate variables possibly associated to drug suspension.

Methods: We used ACE program to search among Mayo Clinic clinical records all the patients that had in their records the words “undifferentiated connective tissue disease” or “lupus” or “myositis” or “Sjogren” or “systemic sclerosis” or scleroderma*(and acronyms) AND “infliximab” or “etanercept” or “golimumab” or “certolizumab” or “tocilizumab” or “abatacept” or “adalimumab” (and their brand names).

All records were checked for definite diagnosis and patients with uncertain ones were excluded. Also medications were checked, patients without any information about treatments where excluded. All the records of the selected patients were used to collect information about the off label biologic treatment but also clinical, serological and demographic variables.

Results: We collected data on 122 patients with connective tissue diseases, some of them had other concomitant autoimmune diseases with indication for biologic treatment (e.g. rheumatoid arthritis, etc). We analyze the group with some CTD alone (n=72) considering SLE (n=18 – 25%), inflammatory myositis (n=22%). The other 27% tried also a second biologic and 4% a third. We consider for analysis the first treatment.

Mean treatment duration was 0.8 (±1.1) years. In our population 12.5% experienced a flare of CTD, 12.5% had infections, 18% had allergic reactions (of any type). The 44% experienced primary failure, 11% loss of efficacy, 31% had minor adverse events, 14% major ones (possible more than one reason for interruption).

Analysis showed no definite factors correlated with treatment duration or failure or adverse events, No difference due to type of CTD.

Conclusions: The study is retrospective and this limits the conclusions can be taken from it, however it is one of largest population of off label treatments in CTDs
so far. Due to retrospective data we choose as outcome only treatment duration and adverse events, direct outcomes of efficacy were impossible to evaluate. Our results indicates a poor treatment duration of biologics given off label in CTDs even if they still can be considered with caution in very selected cases after failure on the other label medications.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2952

AB0450 THE DARK SIDE OF GLUCOCORTICOID THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS: CAN WE DO SOMETHING ABOUT IT?

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Background: Corticosteroids are still one of the main treatment in Systemic Lupus Erythematosus (SLE). Beside the effect on controlling disease activity, they are also implicated in damage accrual. Both patients and physicians are some times not able to adopt a steroid free regimen when possible.

Objectives: To evaluate the knowledge and perception of patients with SLE upon glucocorticoids.

Methods: 84 patients with SLE were evaluated and data about demographic, clinical, serological characteristics or treatment were collected. Presence of steroids related side effects like hypertension, osteoporosis, cataracts or diabetes mellitus were also assessed. All patients completed a questionnaire in order to evaluate patient’s knowledge about steroids. They were asked if they had a discussion with the doctors about corticotherapy and side effects related to them, if they consider that this treatment could be stopped with specialist approval. Statistics was performed with SPSS program.

Results: All patients had treatment with corticosteroids during disease evolution. 57.14% of them experienced at least one steroids related side effect. This patients were significant older: mean age at evaluation 49.50 versus 36.47 (p<0.0001), a longer disease duration: mean SLE duration 9.27 versus 4.69 (p<0.016), a higher mean Prednisone equivalent dose: 8.86 versus 4.71 (p<0.031), a higher mean SLICC Damage Index: 1.53 versus 0.44 (p<0.0001) than patients without steroids related side effects. This complications were significantly more rare in patients that were on a steroid free regimen at the moment of evaluation versus those on a continuum steroid regimen (7.14% versus 50%, p<0.0001).

When patients were asked if they will stop steroids according to medical advice, almost 1/3 of patients - 28.57% - responded “no- to afraid to do that”. Patients willingness to adhere to a steroid free regimen in the future according to a physician recommendation was significant more frequent in younger patients (p=0.031, r=-0.235), in those with steroids initiated in less than 1 year (p=0.016, r=-0.297) and in those with less damage accrual (p=0.017, r=0.267). Flare at the moment of evaluation significantly reduced this possibility, at least from the patient perspective (p=0.041, r=0.224). The likelihood of a future steroid free regimen was increased by a previous discussion patient-doctor about steroids (p=0.002).

Conclusions: This study clearly shows that an open discussion with our SLE patients about corticosteroids is mandatory from the beginning. Patients should be informed about possibility of a steroid free regimen when disease status permits. This will increase patient’s willingness to get free of steroids when possible, helping physician to limit the continuum damage accrual of SLE patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3978

AB0451 RIVAROXABAN VERSUS WARFARIN AS SECONDARY THROMBOPROPHYLAXIS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: A RANDOMIZED, MULTICENTER, OPEN-LABEL, CLINICAL TRIAL


Objectives: To investigate the efficacy and safety of rivaroxaban in preventing recurrent thrombosis in patients with APS compared with warfarin. Methods: This is a phase 3 randomized, multicenter, non-inferiority open-label RCT. Eligible APS patients will be stratified for venous/arterial thrombotic history receiving warfarin will be stratified according the presence of SLE and venous/arterial thrombotic history and randomized (1:1) either to continue warfarin (standard of care, normalized ratio (INR) 2–3 or 2.5 to 3.5 in those with recurrent thrombotic events) or to switch to rivaroxaban (20 mg /day) . The primary efficacy outcome is the development of any thrombotic event during the study period. Secondary efficacy outcomes include time to thrombosis, type of thrombosis (arterial or venous), overall causes of death, evaluation of a prognostic biomarker panel of recurrent thrombosis. The primary safety outcome will be major bleeding. Secondary safety outcomes include any adverse event and minor bleeding.

The study has 3 years follow-up. First patient was included in March 2013 (EUDRA-CT:2010–019764–36).

Conclusions: If the study demonstrates a non-inferior anticoagulant effect compared with warfarin, this would provide sufficient supporting evidence to make rivaroxaban a standard of care for the treatment of patients with APS with previous thrombotic history.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6286

AB0452 CASE REPORT OF ALLOGENEIC UNRELATED-DONOR MESENCHYAL STEM CELLS (MSC) INFUSION IN SJOGREN SYNDROME (SS) WITH REFRACTORY THROMBOCYTOPENIA

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Background: Intravenous MSC infusion has been reported occasionally in SS treatment and Immune Thrombocytopenia, although the effect of this therapy is still to be confirmed. This is a report of the possible role of MSC in the therapy of SS refractory thrombocytopenia. Methods: We report a case of SS with refractory thrombocytopenia in a 45-year-old female who was admitted to our hospital due to a persistent thrombocytopenia (PLT 8.0*10E9/L) after an episode of bacterial pneumonia. The patient had a history of SS for 10 years and had received multiple courses of corticoids, mycophenolate mofetil, rituximab, and plasma exchange, but the thrombocytopenia did not improve.

Conclusions: This case is consistent with the hypothesis that MSC infusion may be an option to be considered in refractory SS. Further studies are needed to evaluate the role of MSC in refractory SS.

Disclosure of Interest: None declared

AB0453 OFF-LABEL USE OF MYCOPHENOLATE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUSIS IN A RHEUMATOLOGY CENTER IN COLOMBIA

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Objectives: Our objective is to report our experience with the use of Mycophenolate in patients with Systemic Lupus Erythematosus (SLE) in a rheumatology center in Colombia. Methods: This is a retrospective observational study of medical records of patients with SLE followed in the rheumatology department of the Center in Colombia between January 2015 and December 2017. Results: We analyzed 123 patients with SLE. Mycophenolate was used in 117 (95%) patients, in 79 (64%) patients in combination with other drugs. The most frequent indication for use was induction (64%) followed by maintenance (21%) of therapy. The most common side effects were gastrointestinal (11%) and infections (10%). Conclusions: Mycophenolate is an effective and safe drug in the treatment of Systemic Lupus Erythematosus (SLE) in a rheumatology center in Colombia. Further studies are needed to evaluate the long-term efficacy and safety of Mycophenolate in this population.
prevention of the rejection of some transplants. Mycophenolate mofetil was found to be associated with a lower risk of toxic adverse events such as ovarian failure, alopecia and leucopenia, compared with cyclophosphamide (1).

Objectives: To describe the population of patients with SLE receiving mycophenolate during a five year period.

Methods: We conducted a retrospective observational study, extracting information from a database in our rheumatic diseases center; we reviewed the clinical record of each patient with diagnosis of SLE and receiving mycophenolate. Descriptive epidemiology was performed for each variable presented.

Results: 1989 patients were diagnosed with Systemic Lupus Erythematosus (SLE) during 2011 and 2016 and 297 were receiving mycophenolate. Regarding demographic characteristics 94% were woman and 6% men, mean age was 49 years ± 15. 41% of patients were employed, 40% were housekeepers, 11% students and 8% retired. The indication for mycophenolate was mainly for lupus nephritis 62%, SLE with systemic sclerosis 30% and only for SLE in 8% of cases. 36% of patients received a daily dose of 2000 mg; 30% 1500 mg, 20% 1000 mg, 8% 3000 mg, 1.5% 6000 mg and 1% 500mg. The mean value for 24 hour urine protein was 792 mg/dl ± 140 and for creatinine was 0.84 mg/dl ± 0.36. In our population patients were taking mycophenolate during a median of 24 months with a minimum of 6 and a maximum of 132.

In combination with mycophenolate 28% of the patients were taking corticoids, 21% hydroxychloroquine, 20% chloroquine, 17% antihypertensive drugs, 7% other medications and only 4% were taking the mycophenolate alone.

Conclusions: Despite of the absence of a license for mycophenolate for the management of Systemic Lupus Erythematosus, the use-off-label of this drug continues to be frequently as an alternative and effective treatment in patients with lupus nephritis and other conditions associated to SLE.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5559

AB0454  CLINICAL AND IMMUNOLOGICAL ACTIVITY IN POLISH COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH GLUCOCORTICOIDS

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Background: Nowadays the lupus treatment strategy is based on background therapy, immunosuppressive drugs and glucocorticoids (GC). Using minimal effective dose of GC only in flares is a recomandation for preventing complications which increase mortality.

Objectives: To evaluate SLE clinical and immunological activity in lupus patients during the standard clinical care and analyze GC treatment

Methods: We observed Polish cohort of patients with SLE 127 patients (118 female and 9 male) with average age 43±6 years, average disease duration 7,8±5,6 years. All of them were treated with oral and pulse GC and standard immunosuppressive therapies (CTX, MMF, AZT,MTX, CsA). As a background therapy 77% of these patients were on chloroquine or hydroxychloroquine. All patients were assessed according to Systemic Lupus Erythematosus Disease Activity Index assessed by SLEDAI (version 2000) and divided into 5 groups: no GC, low dose, medium dose, high dose and puls GC group. Immunological activity was assessed by anti-dsDNA and C3 and C4 complements levels.

Results: In analyzed group 28 of patients without GC the average SLEDAI score was 7 and 50% of this pts not revealed any immunological activity. Low dose of GC was used in 50 pts with average SLEDAI score 13 and in 24 pts of this group anti-dsDNA and C3 or C4 levels upper limit were not observed. Medium dose of GC was used in 20 pts with average SLEDAI score 19 and it was contained with high immunological activity in 55% (n=11) of pts. In 27 of pts, high doses of GC including puls therapy were needed, the average SLEDAI score was very high 30 and most of pts from this group 70% were immunologically active.

Conclusions: In this Polish cohort lupus patients GC doses depended on lupus activity. Minimazing glucocorticoid exposure is an important part of appropriate management of lupus patients. Proper assessment of clinical and immunological lupus activity is critically for treatment decisions, especially for long-term GC use.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5400

AB0455  SURVIVAL OF PREDNISONE-FREE REMISSION IN SLE PATIENTS WITH SEROLOGICALLY ACTIVE CLINICAL QUIESCENT DISEASE

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Objectives: To evaluate survival of prednison (PDM) – free remission in systemic lupus erythematosus (SLE) patients and to investigate the potential predictors of disease flares.

Methods: Inclusion criteria were: (1) Diagnosis of SLE according to American College of Rheumatology (ACR) Classification Criteria of SLE; (2) Caucasian ethnicity; (3) Clinical remission (clinical SLEDAI-2K=0) at the time of PDM-withdrawal; (4) Stop of PDM treatment between 2010 and 2016; (5) At least two visits per year between January 2010 and April 2016.

Disease activity was assessed according to SLE Disease Activity Index-2000 (SLEDAI-2K). Damage was measured by the SLICC/ACR Disease Damage Index (SDI) – score >3, positive anti-dsDNA antibodies (abs) and-or low C3/C4, type of SLE-involvement and concomitant immunosuppressive treatment could be predictors of flare. Multivariate logistic regression analysis was run to investigate the predictors of flare. Covariates included in the analysis were all variables reaching p<0.20 in the univariate analyses.

Results: Among 400 patients evaluated, 104 (26%) fulfilled inclusion criteria. Baseline characteristics are reported in table 1. Twenty-two (21.2%) patients flared. Mean time to flare was 19.9±13.14 months. Types of flare were 7 renal, 7 articular, 4 cutaneous, 2 haematological, 1 serositis and 1 neurological. Variables included in the multivariate logistic regression analysis were: positive anti-dsDNA abs and-or low C3/C4, skin, articular and haematological involvement. Skin involvement resulted predictive of flare (OR 3.07, 95% CI 1.11-8.53, P 0.031) as reported in table 2.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5925

AB0456  SAFETY AND RETENTION RATE OF BELIMUMAB: DATA FROM A MULTICENTRIC ITALIAN STUDY

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1University of Padova, PADOVA; 2University of Brescia, BRESCIA; 3University of Perugia, PERUIGA; 4University of Ferrara, FERRARA; 5University la Sapienza, ROMA; 6University of Ancona, ANCONA; 7University of Udine, UDINE; 8University of Firenze, Firenze; 9University of Milano, MILANO; 10University of Pisa, PISA; 11University of Reggio Emilia, Reggio Emilia, Italy

Background: Belimumab is used in the treatment of systemic lupus erethmatosus (SLE), but few data on its safety in daily clinical practice are available to date.

Objectives: To investigate safety, retention rate (RR), reasons and predictors of belimumab discontinuation in a prospective multicentric Italian study.

Methods: A total of 186 active SLE patients refractory to standard therapy were treated with belimumab as add-on-therapy in 11 Italian centers. Adverse events (AEs) were defined as “any untoward medical occurrence in a patient
treated with a pharmaceutical product which does not necessarily have a causal relationship with this treatment. AEs were subdivided into non-infectious, infectious, infusion and hypersensitivity reactions. Infusion and hypersensitivity reactions were defined as transient AEs related to belimumab occurring within 6 hours and 6–48 hours after drug administration, respectively. AEs were defined as severe (SAE) in case of hospitalization and/or death and/or life-threatening manifestations. Infections were considered severe in case of hospitalization and/or intravenous antibiotic use and/or death. Infusion and hypersensitivity reactions were considered severe when intensive care unit support was required. As baseline predictors of discontinuation the following variables were analyzed: gender, age, age at SLE onset, disease duration, disease activity pattern (relapsing remitting or chronic active), SLEDAI-2K ≥7.5 mg/day, concomitant immunosuppressant, antimalarial drug use, number and type of comorbidities, number of previous organ involvement, type of major involvement and number of flares in the 12 months before belimumab initiation. Data were analyzed using the SPSS (version 23.0, Chicago, IL) software.

**Results:** A total of 453 EAs were recorded in 132 patients after a mean follow-up period of 17.5±10.6 months (range 3–36): 443 (97.8%) were non severe and 10 (2.2%) SAEs (Table 1). No deaths and severe infusion/hypersensitivity reactions occurred. Belimumab discontinuation was observed in 58 patients (30.8%) after 10.4±7.5 months of follow-up (Table 2). RR was 91.5% at 6 months, 81.4% at 12 months, 72.9% at 18 months, 72.4% at 24 months, 69.7% at 30 months and 69.2% at 36 months. No associations were found between baseline variables and drug discontinuation.

**Table 1.** AEs observed in 132 patients with refractory SLE treated with belimumab

<table>
<thead>
<tr>
<th>Pts with AEs (%)</th>
<th>Pts with AEs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non severe AEs</td>
<td>67.6</td>
</tr>
<tr>
<td>Infectious AEs</td>
<td>57.7</td>
</tr>
<tr>
<td>Non infectious AEs</td>
<td>30.4</td>
</tr>
<tr>
<td>Hyper sensitivity reactions</td>
<td>13.8</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>4.2</td>
</tr>
<tr>
<td>SAEs</td>
<td>9</td>
</tr>
<tr>
<td>Infectious SAEs</td>
<td>1</td>
</tr>
<tr>
<td>Non infectious SAEs</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>122</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pts (%</th>
<th>Pts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>22</td>
</tr>
<tr>
<td>Non-responder (articular or renal)/cerebral/haematological</td>
<td>16</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>8</td>
</tr>
<tr>
<td>Flare (articular)</td>
<td>6</td>
</tr>
<tr>
<td>Last of follow-up</td>
<td>4</td>
</tr>
<tr>
<td>Remission</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
</tr>
</tbody>
</table>

**Conclusions:** Belimumab demonstrated a good safety profile with a low rate of SAEs. Discontinuation occurred in less than 1/3 of subjects with a low rate of discontinuation due to AEs.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6088

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**AB0457**

LONG-TERM EFFECTIVENESS OF TREATMENTS FOR NEUROPSYCHIATRIC MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Neuropsychiatric involvement of systemic lupus erythematosus (NPSLE) is one of the most deleterious complications of the disease, leading to great decrease of quality of life and poor prognosis [1]. Factors such as activity of disease have been associated NPSLE [1,2]. The current treatment of NPSLE remains mostly empiric, requiring high-dose corticosteroids and extensive immunosuppressive therapy [3,4]. Short-term efficacy of treatments in NPSLE have been evaluated by several studies, however few studies have been performed to evaluate long-term efficacy of these drugs [4].

**Objective:** To compare the long-term effectiveness among drugs and associated factors in the treatment of NPSLE.

**Methods:** 209 patients (>14 years) from a Mexican cohort from 2011 to 2017 were examined. SLE and NPSLE cases fulfilled 1997 ACR and 1999 ACR criteria respectively. Demographic factors, comorbidities and pharmacologic treatments were reviewed for patients with NPSLE. Variables were studied by bivariate, multivariate and survival analyses.

**Results:** Of 209 SLE patients, 37 (17.7%) had NPSLE; of them 32 were women. The mean age [standard deviation (SD)] was 38.8 (14.6) years. The mean of time at onset of SLE [SD] was 6.2 (5.4) years. SLEDAI and SLICC mean [SD] were 22.1 (10.2) and 1.83 (1.2) separately. Diffuse and focal manifestations of NPSLE were presented in 20 and 17 cases. Central and peripheral nervous system events of NPSLE were described in 34 and 3 of patients. The NPSLE manifestations more prevalent were cerebrovascular disease (n=15), psychosis (n=8) and seizure disorders (n=5). A total of 112 cycles of treatments were analyzed [prednisone (PDN) n=30, intravenous (iv) methylprednisolone (MTP) n=23, iv cyclophosphamide (CYC) n=13, azathioprine (AZA) n=12, mycophenolate mofetil (MMF) n=11, rituximab (RTX) n=10, hydroxychloroquine (HCQ) n=9, plasmapheresis (PPH) n=2 and iv immunoglobulin (IVIg) n=2]. Cognitive dysfunction was more associated to higher SLE activity, damage and mortality. Also, psychosis was more associated to receive higher doses of oral PDN or iv MTP to employ iv CYC and to be linked with renal SLE disease activity. On the other hand, central vascular disease was more associated to receive HCQ and to have antiphospholipid antibodies. The main cause to therapy discontinuation was inefficacy and was more common in patients treated with iv CYC. Corticosteroids survival in months was higher in-group PDN <15 mgid (97.89±16.4; IC95% 65.8–130). AZA survival in months (90±30.8; IC95% 29.6–150) was higher than others treatments for NPSLE and was more associated to use (IV Ig OR 10.8, 95% CI 1.04–111, p=0.04). When the first therapy was failed, the drug as second therapy used with higher survival in months was MMF (100±56.5; IC95% 1.6–218).

**Conclusions:** This study suggests that patients with diffuse manifestations and central nervous system involvement in NPSLE presented more activity, damage and mortality and therefore used more PDN, MTP and CYC. Among the treatments as first therapy for NPSLE with the better long-term efficacy was AZA and when it failed, MMF remained as better second therapy.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2815

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**AB0458**

B CELLS DEPLETION FOR THE TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES

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**Background:** Systemic autoimmune diseases (SAD) have traditionally been treated with steroids and immunosuppressants, but not all patients respond to these measures. Rituximab (RTX) has been used in several SAD with favorable results, but there are only a few reports of isolated clinical experiences, with a very small number of patients. Data about use of this drug under conditions of daily clinical practice may be relevant.

**Objective:** To describe the characteristics of patients with SAD who are candidates for treatment with RTX.

**Methods:** Demographic data, SAD disease, treatment and response variables were included. We use the EULAR definitions of partial response (improvement of at least 50% of the main manifestations of the disease) and complete response ( disappearance of the manifestations of the disease), because of the heterogeneity of the SAD and their multiple manifestations.

**Results:** We included 53 patients, 90.6% were women. The mean age at diagnosis was 31.42±14.33 years; and the median duration of disease at the onset of RTX 1.99 (0–7.5) years. Patients received a median of 2 cycles (1–3 min
Conclusions: In our study, patients treated with RTX achieved response in 88.7%, similar to some experiences of RTX off-label use. Remission of the disease occurs in 50% of the patients. The best results are observed in SLE, especially in lupus nephritis, and Sjögren disease. The results in SS are promising due to the limited therapeutic resources for this disease.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6402

AB0459 TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES WITH RITUXIMAB: SAFETY DATA
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Background: Systemic autoimmune diseases (SAD) have traditionally been treated with steroids and immunosuppressants, but not all patients respond to this strategy. Rituximab (RTX) has been used in several SAD with favorable efficacy and safety results; there are only reports of isolated clinical experiences of small series of patients. The description of this drug safety data in daily clinical practice may be relevant.

Objectives: To describe the adverse events and the hospital admissions during the treatment of a series of patients with SAD with RTX.

Methods: Demographic data, related to disease and treatment, response and safety variables were included. We use the EULAR definitions of partial response (improvement of at least 50% of the main manifestations) and complete response (disappearance of the manifestations), because of the heterogeneity of the SAD.

Results: We included 53 patients, 90.6% were women; the mean age at diagnosis was 31.42±14.33 years, and the median duration of disease at the onset of RTX 1.99 (0–7.5) years. Patients received a median of 2 cycles (1–3; min -1, max 12); and the median interval between cycles was 14.81 months (6–15.75; min 6, max 120).

The SAD were SLE with 23 cases (43.4%), systemic sclerosis with 7 cases (13.2%), Sjögren’s syndrome with 6 cases (11.3%), vasculitis with 5 cases (9.4%), Still disease with 3 cases (5.7%), autoimmune cytopanies with 3 cases (5.7%), dermatomyositis with 2 cases (3.8%), Behcet’s disease with 2 cases (3.8%) IgG4 disease with 1 (1.9%) case and sarcoidosis with 1 case (1.9%).

A partial response was observed in 27 patients (50.9%) and complete in 20 patients (37.7%). There was no response in 6 of the 53 patients (11.3%). The response by disease groups is detailed in Table 1.

<table>
<thead>
<tr>
<th>SAD</th>
<th>Partial response</th>
<th>Complete response</th>
<th>No response</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE (n=23)</td>
<td>9 (39.1%)</td>
<td>12 (52.2%)</td>
<td>2 (8.7%)</td>
</tr>
<tr>
<td>Systemic Sclerosis (n=7)</td>
<td>5 (71.4%)</td>
<td>2 (28.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Vasculitis (n=5)</td>
<td>5 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sjögren (n=6)</td>
<td>3 (50%)</td>
<td>3 (50%)</td>
<td>0</td>
</tr>
<tr>
<td>Al cytokanies (n=3)</td>
<td>1 (33.3%)</td>
<td>1 (33.3%)</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Dermatomyositis (n=2)</td>
<td>1 (50%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Behcet’s disease (n=2)</td>
<td>0</td>
<td>0</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>IgG4 related disease (n=1)</td>
<td>0</td>
<td>1 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Sarcoidosis (n=1)</td>
<td>1 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: The most frequent adverse event were the infectious, mainly respiratory tract infections followed by an infusion reaction. No patient developed opportunistic diseases. This findings are similar than observed in other studies on patients with SAD treated with RTX. Infusion reactions are becoming less frequent, due in part to premedication.

We are dealing with a large number of patients with refractory EAS treated with RTX, so the data obtained from this study show an acceptable safety profile.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3890

AB0460 USE OF INTRAVENOUS IMMUNOGLOBULIN (IVIG) IN AUTOIMMUNE RHEUMATIC DISEASES: EXPERIENCE IN A THIRD LEVEL MEDICAL CENTER
M. Pérez Crisóstom1,2, R. Ríchar Rocha1, G. Horta Baas1, L. Barile Fabris1, M. Portela Hernández1,2, Rheumatology;1 Iimss, Mexico City, Mexico
Background: IVIG therapy in rheumatology has been used as an alternative treatment for patients with refractory, severe disease, or with contraindication to the use of conventional immunosuppressive therapy as serious infections. It has recently been increased its use to treat multiple autoimmune diseases, however with a limited number of precise indications as there are not enough studies to increase the level of evidence for the administration of IVIG

Objectives: To describe the experience gained with the use of IVIG in autoimmune rheumatic diseases in a third level medical center

Methods: This is an observational, descriptive and retrospective study. We report the use of IVIG in our clinical practice, efficacy and adverse effects. We included consecutive patients with autoimmune rheumatic diseases that received IVIG between 2012 and 2015. The information was extracted from clinical records.

Results: We included 35 patients: 19 women, 16 men, 18 with systemic lupus erythematosus (SLE), 15 with autoimmune inflammatory myopathy, 1 with primary Sjögren’s syndrome (SSp) and 1 with polyarteritis nodosa (PAN).

The most common indication was active disease associated with severe infection that contraindicated the use of immunosuppressants in 24 patients and in 11 patients refractory activity disease to conventional therapy. The most frequent indications in patients with SLE were: 6 thrombocytopenias, 5 lupus nephritis, 4 pulmonary hemorrhage and 3 neuropathies; of the group of inflammatory myopathy the indications were: 6 dysphagia, 5 respiratory insufficiency and 4 refractory myopathy. In patients with SSS and PAN the indication was peripheral neuropathy. The mean number of IVIG applications was 3.3 (range 1–15). Activity scales were decreased in all patients with IVIG: mean SLEDAI at baseline 15.6 and in the follow up 4.5; in inflammatory myopathies remission was reached in 86% of the cases. The steroid dose was significantly reduced in most patients in the follow up. Four patients had adverse effects associated with IVIG: 2 with tachycardia and hypertension, one with acute pulmonary edema and one with hemolytic anemia.

Conclusions: In our experience, IVIG administration was effective in controlling the activity of the autoimmune rheumatic disease, mainly in patients with concomitant infection, and with a good safety profile.

Discussion: IVIG was an effective alternative treatment in patients with contraindication of conventional treatment or in refractory disease, however it is a high cost treatment and should be used in well selected cases.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6694

AB0461 BENEFITS OF VITAMIN D IN SLE DEPEND ON THE ORGAN SYSTEM
M. Petri1, L.S. Magder2, 1Johns Hopkins University School of Medicine; 2Biostatistics, University of Maryland, Baltimore, United States
Background: Low 25-OH Vitamin D is associated with SLE. Both a randomized clinical trial and a longitudinal cohort study proved that supplementation reduced SLE disease activity.

Objectives: We examined whether Vitamin D benefits in SLE are dependent on the organ system.

Methods: Vitamin D and SLEDAI components were measured at each cohort visit starting in 2010 and 16,519 visits of 1,345 different patients were included. The patients were 92% female, 50% Caucasian, 41% African American. Organ-specific disease activity was defined as a set of binary variables based on SLEDAI. If the patient received any score for any component, then the patient was defined as having that type of activity.

Interestingly, after adjustment for repeated measures and covariates, the relationship between vitamin D and immunologic disease activity totally disappeared.
Vitamin D supplementation significantly reduces therapeutic plasma exchange (TPE) for refractory SLE. Vitamin D supplementation (in those whose level is below 40 ng/mL) has a significant benefit on total cholesterol that is independent of age, sex, ethnicity, Plaquenil, prednisone and body mass index. Vitamin D supplementation - as it also helps systolic blood pressure - is both important for SLE activity and for reduction of cardiovascular disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1647

AB0463 THERAPEUTIC PLASMA EXCHANGE (TPE) FOR REFRACTORY SLE: A COMPARISON OF OUTCOMES BETWEEN DIFFERENT SUB-PHENOTYPES?

A. Soyouz1, Q. Karadas2, L. Kilic3, T. Karagaç Akyol2, S. Aparas Bilgen4, O.I. Ozcebe5, 1Department of Internal Medicine; 2Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine; 3Blood and Apheresis Unit, Hacettepe University Hospitals; 4Department of Internal Medicine, Division of Haematology, Hacettepe University Faculty of Medicine, Ankara, Turkey.

Background: Therapeutic plasma exchange (TPE) offers an alternative therapeutic modality for patients with systemic lupus erythematosus (SLE) and primary antiphospholipid syndrome (APS). However, there is conflicting evidence regarding its efficacy in different sub-phenotypes.

Objectives: This study aims to investigate the main clinical characteristics and outcomes of patients with different phenotypes of SLE and APS treated with TPE at a tertiary care centre.

Methods: Database of Blood and Apheresis Unit between 2001–2013 was screened for patients with SLE and primary APS. SLE disease activity index (SELENA-SLEDAI), the indications for treatment, complications and outcomes were obtained from review of medical records and phone calls. A total of 24 patients (SLE: 20, APS: 4) were recruited for the study.

Results:

- Mean ages of SLE (M/F: 1/19) and primary APS (M/F: 2/2) were 32.4±12.89 and 52.0±10.7, respectively. The main indications for TPE were haematologic, neurologic, pulmonary involvement and APS-related. TPE was preferred in 8 patients because of leucopenia, and co-infection. SLEDAI was significantly decreased after TPE (16.7±8.3 vs. 8.8±3.1; \(p=0.001\)). Both primary APS and SLE related CAPS patients had completely responded to TPE. Success rate of TPE in patients with thrombotic complications were lower than those with haemolytic anaemia. Median (IQR 25%-75%) TPE sessions were 6.5 (5.10-6).

Conclusions: This study suggests catastrophic antiphospholipid syndrome (CAPS) and other APS related problems respond well to the TPE treatment. TPE should be kept in mind for the treatment of patients with other features of SLE, especially those resistant to other agents and in the presence of leucopenia and psychosis

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4426

Table 1. Clinical, disease activity, treatment findings and TPE outcomes of SLE patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mag VE Indication</th>
<th>Azathioprine</th>
<th>Methylprednisolone</th>
<th>Plaquenil</th>
<th>Cyclosporine</th>
<th>Hydroxychloroquine</th>
<th>Prednisone Use</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>30</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
</tr>
<tr>
<td>No</td>
<td>30</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

AB0462 VITAMIN D SUPPLEMENTATION SIGNIFICANTLY REDUCES CHOLESTEROL IN SLE

M. Petri1, L.S. Magder2, 1Johns Hopkins University School of Medicine; 2University of Maryland, Baltimore, United States

Background: The benefit of vitamin D on SLE global and renal activity have now been proven by both cohort studies and a clinical trial. The benefits on cardiovascular risk factors, however, are less well understood.

Objectives: We present the first longitudinal study on hyperlipidemia.

Methods: A within-person analysis assessed the question is: "When a person has a vitamin D level lower than his/her average, are they more likely to have renal disease activity?" Note, this analysis implicitly adjusts for race, sex, and all variables (measured and unmeasured) that are invariant within a person. The results are shown in Table 2.

Table 2. Within-person analysis of the relationship between vitamin D levels and renal activity adjusting for prednisone use, plaquenil use, and implicitly for all time-invariant characteristics

<table>
<thead>
<tr>
<th>Vitamin D Level (ng/mL)</th>
<th>Immunologic Disease</th>
<th>Skin Disease</th>
<th>Renal Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 ng/mL or more than personal average</td>
<td>0.9 (1.1, 0.8)</td>
<td>0.0001</td>
<td>1.6 (2.2, 1.2)</td>
</tr>
<tr>
<td>Within 10 ng/mL of the personal average</td>
<td>1.0 (Ref Grp)</td>
<td>1.0 (Ref Grp)</td>
<td>1.0 (Ref Grp)</td>
</tr>
<tr>
<td>10 ng/mL or more than personal average</td>
<td>0.8 (0.7, 1.0)</td>
<td>0.080</td>
<td></td>
</tr>
</tbody>
</table>

For Renal, it appears (based on the within-person analysis), that increasing vitamin D results in a reduction in renal activity. Based on other analyses, it is clear this drop was mostly among those in the vitamin D deficiency range.

Conclusions: Low vitamin D is associated with cutaneous and renal SLE activity, vitamin D results in a reduction in renal activity. Based on other analyses, it is shown in Table 2.

Table 1. Difference in Cholesterol at each visit per 10 ng/mL difference in between the patient's average cholesterol as a function of differences in a patient's vitamin D at that visit and the patient's average vitamin D.

<table>
<thead>
<tr>
<th>Vitamin D Level (ng/mL)</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 ng/mL or more than personal average</td>
<td>1.5 (1.3, 1.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Within 10 ng/mL of the personal average</td>
<td>1.0 (Ref Grp)</td>
<td>0.680</td>
</tr>
<tr>
<td>10 ng/mL or more than personal average</td>
<td>0.8 (0.7, 1.0)</td>
<td>0.080</td>
</tr>
</tbody>
</table>

This means that at a particular clinic visit, if a person's vitamin D is higher than the person's mean vitamin D by 10 ng/mL and the person has vitamin D below 40 ng/mL, then the expected cholesterol will decrease by 3.4 mg/dL. There is no significant effect of higher vitamin D among those whose mean vitamin D exceeds 50.

Conclusions: Vitamin D supplementation (in those whose level is below 40 ng/mL) has a significant benefit on total cholesterol that is independent of age, sex, ethnicity, Plaquenil, prednisone and body mass index. Vitamin D supplementation - as it also helps systolic blood pressure - is both important for SLE activity and for reduction of cardiovascular disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4526

Table 2. Difference in Cholesterol per 10 ng/mL Difference in Vitamin D

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mag VE Indication</th>
<th>Azathioprine</th>
<th>Methylprednisolone</th>
<th>Plaquenil</th>
<th>Cyclosporine</th>
<th>Hydroxychloroquine</th>
<th>Prednisone Use</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>30</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
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<tr>
<td>No</td>
<td>30</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Conclusions: This study suggests catastrophic antiphospholipid syndrome (CAPS) and other APS related problems respond well to the TPE treatment. TPE should be kept in mind for the treatment of patients with other features of SLE, especially those resistant to other agents and in the presence of leucopenia and psychosis

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4426

AB0464 AZATHIOPRINE METABOLITES IN CONNECTIVE TISSUE DISEASE

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Background: Azathioprine (AZA) is a common treatment for connective tissue diseases (CTD). AZA is a pro-drug which is metabolised to active moieties of
ASSOCIATION BETWEEN SAFETY, EFFICACY AND 6-thioguanine (6-TGN) and 6-methylmercaptopurine (6-MMP). These metabolites, rather than the absolute dose of AZA, are associated with clinical efficacy and toxicity. An idiosyncratic skewed metabolism towards 6-MMP in some patients ("shunters") increases the risk of hepatotoxicity and treatment failure. Allopurinol can correct such shunts.1 Therapeutic protocols using metabolite concentrations have been shown to be more effective, improve efficacy, and decrease treatment morbidity in IBD.1 Only one small study estimated a therapeutic 6-TGN level for SLE patients.2 There are scant data on AZA shunters in connective tissue disease.3

**Objectives:** Explore the proportion of AZA therapeutic failure, toxicity, and shunters in CTD patient populations.

**Methods:** Retrospective, multicentre audit of AZA metabolite levels in CTD patients from 2012–2016. Patient demographics, treatments, disease activity and drug toxicity were also extracted.

**Results:** 61 testing episodes occurred in 34 patients whose mean age was 55 (32–79) years; predominantly female (N=26, 77%), with SLE (N=19, 56%). Active disease was present in 15/61 (25%) episodes. 20/34 (60%) patients were on HCQ + AZA. 25/34 (76%) of patients were either on no or minimal AZA dose. 6-MMP shunters had significantly lower median 6-TGN levels compared with appropriate and overdosed (17% and 31%) disease (44% & 31%), compared with appropriate and overdosed (17% and 19% p<0.24). Surprisingly, patients who were overdosed by 6TGN levels had the lowest mean AZA dose. AZA metabolites can identify the multiple causes for therapeutic failure (underdosing, shunting, or true non-response), and enable early detection of shunters to avoid liver toxicity.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2405

**AB0465 ASSOCIATION BETWEEN SAFETY, EFFICACY AND HYDROXYCHLOROQUINE DOSAGE IN THE TREATMENT OF CUTANEOUS LUPUS ERYTHEMATOSUS AND SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Hydroxychloroquine (HCQ) are considered to be effective against cutaneous lupus erythematosus (CLE) and symptoms associated with systemic lupus erythematosus (SLE) such as rashes, joint pain, and fatigue. In a randomized, controlled trial in stable active patients with SLE on HCQ treatment, those who achieved blood HCQ levels greater than or equal to 1000ng/ml had a tendency for reduced SLE flares during a 7 month period [1]. To prevent ocular toxicity, HCQ should be maintained at a dose of 6.5mg/kg or less for ideal body weight [2], however, optimal HCQ dosage is unclear.

**Objectives:** To extract the problem of the dosage based on ideal body weight and identify safer and more effective HCQ dosage.

**Methods:** We enrolled patients who took HCQ for SLE or CLE more than 3 months in our institute and 2 related facilities from September 2015. We used Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) to evaluate cutaneous symptoms and evaluated effect at start of administration and 3 months of that. The attending doctors assessed the adverse events (AEs). We investigated the change of serum biomarker, such as the value of serum complement and anti-ds-DNA body, the number of white blood cells, lymphocytes and platelets.

**Results:** We enrolled the 30 patients with administration of HCQ more than 3 months and in CLE were 2 cases, in SLE were 28 cases. In 21 cases HCQ dosage were based on ideal weight. The AEs were in 13/30 cases (43.3%). The AEs were the new cutaneous symptoms in 5 cases, eye manifestation in 3 cases (abnormal visual field in 2 cases, color anomaly in 1 case), diarrhea in 2 cases, fever in 2 cases, feeling of fatigue in 2 cases, renal dysfunction in 1 case, muscular pain in 1 case, and pericarditis in 1 case. The eye manifestation in the 3 cases disappeared for a few days by stopping or reducing HCC dosage. Although we needed glucocorticoid treatment for pericarditis, the other AEs improved by reducing HCC dosage or stopping. The AEs of taking HCC 200mg/day were in 6 cases, 200mg and 400mg alternatively on every other day in 6 cases, and 400mg/day in 1 case. The AEs of taking HCQ based on ideal body weight were in 10/21 cases (47.6%) and by minimal dosage in 3/9 cases (33.3%). 22/28 cases (78.6%) significant improved cutaneous symptoms (amount of mean change of CLASI -4.57, p=0.024). There is no difference in the efficacy of cutaneous symptoms between group received HCC based on ideal body weight (80.0%) and the others (92.3%). 5/21 cases of HCQ based on ideal body weight were made to reduce HCC dosage due to AEs, but all 5 cases improved cutaneous symptoms. 53.3% (16/30) cases increased complement, but other biomarkers didn’t change.

**Conclusions:** HCQ was effective for the treatment of CLE even when HCC dosage was reduced due to AEs. These findings suggest that low-dose HCC is also effective and safe, and HCQ initial dosage wasn’t the need to adjust for ideal body weight.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3928

**AB0466 THE EFFECT OF OMEGA-3 FATTY ACIDS ON DISEASE ACTIVITY, ENDOTHELIAL FUNCTION, INFLAMMATORY MARKERS, AND LIPID PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, CONTROLLED TRIALS**

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**Background:** Omega-3 fatty acids have been shown to have potentially beneficial immunomodulatory activity in autoimmune conditions such as rheumatoid arthritis and Sjogren’s syndrome. Whether this extends to systemic lupus erythematosus (SLE) remains unclear.

**Objectives:** We undertook this study to summarize the body of evidence available from published clinical trials on the effectiveness of omega-3 fatty acids on clinical and/or laboratory outcomes in SLE.

**Methods:** Two independent reviewers systematically searched PubMed, MEDLINE, Scopus, and the reference lists of related articles for studies published from inception to November 2016 using relevant keywords. Randomized, controlled trials (RCTs) on SLE patients comparing omega-3 fatty acids with placebo were included in the analysis. The quality of the included RCTs was assessed in accordance with the Cochrane Handbook. A random effects model was used to pool extracted data. Heterogeneity was evaluated with Chi2 test and I2, with p-values <0.05 considered significant. Data presented in median and interquartile range were converted to mean and standard deviation using the method described by Wan et al.

**Results:** A total of seven clinical trials consisting of 303 subjects with a duration of treatment ranging from 12 to 52 weeks were included. In studies using SLAM-R as the measurement of disease activity (n=82), there was a statistically significant mean score reduction in the omega-3 fatty acid group vs. the placebo group at 24 weeks. However, in studies that used mean change in SELENA-SLEDAI (n=117, WMD -0.87, 95% CI: -1.16, 0.24, I 2=85%, p=0.20) scores, there was no significant effect of omega-3 fatty acids on disease activity. In studies using PGA (n=117, WMD -0.46, 95% CI: -1.16, 0.24, I 2=85%, p=0.20) scores, there was no significant effect of omega-3 fatty acids on disease activity. In studies using PGA (n=117, WMD -0.46, 95% CI: -1.16, 0.24, I 2=85%, p=0.20) scores, there was no significant effect of omega-3 fatty acids on disease activity. In studies using PGA (n=117, WMD -0.46, 95% CI: -1.16, 0.24, I 2=85%, p=0.20) scores, there was no significant effect of omega-3 fatty acids on disease activity.
any difference between the two groups (n=141, WMD: -0.01, 95% CI: -0.03, 0.01, I²=0%, p=0.26). The data on percent increase in flow-mediated dilation was conflicting. In terms of inflammatory markers, there were likewise no clear associations, with some studies reporting significant changes in ESR, CRP, IL-12, and IL-13 levels which were not observed in others. With regards to lipid profile, treatment with omega-3 fatty acids has been associated with a non-significant trend toward increase in all lipid profile parameters at 12 weeks including HDL (WMD 6.83, 95% CI: -0.38, 17.33, I²=0%, p=0.06).

Conclusions: The limited data on the use of omega-3 fatty acids has not shown clear benefit in improving disease activity, endothelial function, inflammatory markers, or lipid profile in patients with SLE. Larger studies for longer durations using standardized scales for measuring outcomes are needed.

References:

Acknowledgements: Dr. Chia-Ling Kuo.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2666

AB0467 Efficacy and safety of assisted reproductive technologies (ART) in rheumatic patients: a multicenter study

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Background: Always more frequently rheumatic patients (pts) ask for Assisted Reproductive Technologies (ART) for infertility problems. The main concern is determined by the ovarian stimulation, associated with an increased risk of disease flare and thrombosis.

Objectives: To describe a case series of ART cycles in pts affected by rheumatic diseases, analyzing pregnancy rate and outcome, fetal-maternal complications and disease flares.

Methods: We included all the consecutive pts evaluated in the Pregnancy Clinic of 5 Italian Rheumatology Units after having performed ≥1 ART cycle from 1997 to 2016.

Results: We included 60 pts: infertility was primary (no previous spontaneous conception) in 68% of cases, idiopathic in 76.5%, of male origin in 8.3%, of female origin in 15%, mixed in 0.2%. One hundred and eleven ART cycles were performed: 135IUI, 44FIVET (Sertoli cell), 51GnRH, 131IORT (Sertoli cell), 45GnRH-Antagonist, 2GnRH-Agonist, 4gonadotropins only. Patients were divided in two groups according disease activity: with low disease activity, after spontaneous therapy discontinuation, No cases of thrombosis were reported. During puerperium: 1 (2.5%) post-partum hemorrage (no LMWH ongoing), 1 arterial flare (2.5%). Additional informations are available in Table 1.

Conclusions: We didn't found any good reasons to discourage ART performance in rheumatic pts: the safety seems to be high and the complications rate is in line with that reported in general population. An adequate prophylaxis during stimulation, pregnancy and puerperium seems to provide a good protection from thrombotic complications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2351

AB0468 Possible effects of belimumab therapy on T- and B-cell phenotype in a cohort of patients with systemic lupus erythematosus (SLE)

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Background: B- and T-cell activation are one of the pathogenic mechanisms of systemic lupus erythematosus (SLE). After repeated antigen stimulation, T-cells undergo different modifications, leading to the differentiation into effector memory T-cells (CR7-CD45RA-) and highly experienced memory T-cells (CR7-CD45RA+). Similarly, down-modulation of CD28 may lead to the expansion of the CD28neg T-cells, a subpopulation with peculiar effector activities (1).

Methods: Phenotypic analysis of peripheral blood B and T lymphocytes was determined by the ovarian stimulation, associated with an increased risk of disease flare and thrombosis.

Objectives: To describe a case series of ART cycles in pts affected by rheumatic diseases, analyzing pregnancy rate and outcome, fetal-maternal complications and disease flares.

Methods: We included all the consecutive pts evaluated in the Pregnancy Clinic of 5 Italian Rheumatology Units after having performed ≥1 ART cycle from 1997 to 2016.

Results: We included 60 pts: infertility was primary (no previous spontaneous conception) in 68% of cases, idiopathic in 76.5%, of male origin in 8.3%, of female origin in 15%, mixed in 0.2%. One hundred and eleven ART cycles were performed: 135IUI, 44FIVET (Sertoli cell), 51GnRH, 131IORT (Sertoli cell), 45GnRH-Antagonist, 2GnRH-Agonist, 4gonadotropins only. Patients were divided in two groups according disease activity: with low disease activity, after spontaneous therapy discontinuation, No cases of thrombosis were reported. During puerperium: 1 (2.5%) post-partum hemorrage (no LMWH ongoing), 1 arterial flare (2.5%). Additional informations are available in Table 1.

Conclusions: We didn't found any good reasons to discourage ART performance in rheumatic pts: the safety seems to be high and the complications rate is in line with that reported in general population. An adequate prophylaxis during stimulation, pregnancy and puerperium seems to provide a good protection from thrombotic complications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2351

References:
EVALUATION OF PILOCARPINE TREATMENT IN XEROSTOMIA BY PULSED Doppler COLOR ULTRASONOGRAPHY: ECHOPILO STUDY

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Background: The ultrasonography of salivary glands (USSG) has proved its utility in diagnosing and following primary Sjogren’s patient’s (pSS) (1,2). The evaluation of disease activity is still of interest and can be studied by assessing the inflammatory status of SG using US Doppler.

Objectives: To evaluate the vascularization of salivary glands, and particularly the parotid gland (PG) using Pulsed Doppler color ultrasonography (USSGPD) in patients complaining of xerostomia before and after treatment by pilocarpine.

Methods: We prospectively included patients with objective dry mouth syndrome (using salivary flow rate) at Brest University Hospital (DiapSS cohort). The vascularization was assessed by the resistive index (RI) at the left parotid. Only patients with pathological RI (r>0.8) were included in order to observe evolution after pilocarpine. USSGPD was carried out by the same operator. A dental consultation with measure of salivary flows before and after stimulation was performed. These examinations were performed at baseline and after 3 months of treatment with pilocarpine at 4 mg 3 times daily.

Results: Among the 19 patients included, 11 received pilocarpine treatment for the whole 3 months period, 6 of the 8 remaining patients stopped the pilocarpine due to side effects. Among the 11 patients with a follow-up evaluation at 3 months, 5 had pSS according to AECG criteria. The differences of RI before and after lemon stimulation were on average of -0.04 at baseline and -0.04 at M3. The sum of the four glands’ grades average of the four glands was 3.47 at M0 and 4.18 at M3. The non-stimulated salivary flow was on average of 1.96 mL/min at M0 and 5.81 mL/min at M3. None of these observed differences were statistically significant before and after 3 months of treatment by Pilocarpine. RI before and after lemon stimulation (p=0.953), the sum of the four glands’ grades (p=0.858), the non-stimulated (p=0.26) and stimulated salivary flow (p=0.139). Concerning the 3 patients with Sjogren’s syndrome, there were no differences using RI before and after treatment but the RI was lower in this subgroup compared to the xerostomia patients. The study was marked by a large number of pilocarpine’s discontinuation (31%) due to adverse effects.

Conclusions: Preliminary results showed no significant differences between the 4 gland’s grade, ultrasound’s RI and salivary non and stimulated flow before and after three months of pilocarpine’s treatment. The vascularisation of salivary glands in patients who continued to follow our treated patient with Sjogren’s syndrome or with xerostomia but more studies are needed to prove the interest of this procedure.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2937

RESPONSIVENESS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AFTER RITUXIMAB TREATMENT: A SINGLE CENTER EXPERIENCE

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Background: Systemic lupus erythematosus (SLE) is a complex disease with multi-organ presentations. Lupus nephritis, which results from autoantibody deposition at glomerulus, induces inflammation and damage. Lupus nephritis is also the leading cause of morbidity in SLE patient and associated with poor prognosis.

Objectives: To evaluate the treatment responsiveness of rituximab in patients with SLE.

Methods: Patients should fulfill the criteria of 1997 American College of Rheumatology classification criteria for SLE. Patients underwent chemotherapy, with severe lupus nephritis, under hemodialysis or after kidney transplantation were excluded. Total 37 patients were evaluated receiving rituximab infusion from 2009 to 2013. Clinical parameters were measured before and after rituximab usage.

Results: Among the 37 patients, the female patient was 89.2%. Mean age was 38.9±3.9 years old. The mean creatinine level remained during the 26 months of follow-up. In the beginning of the treatment, the mean creatinine level was 1.40mg/dl (SD 0.84). After 12, 24, 36 months of follow-up, the mean creatinine levels were 1.73mg/dl, 2.16mg/dl, and 2.40mg/dl, respectively (p=0.431, 0.148, 0.328). The mean proteinuria level was 3.51g/day initially (SD 2.52), but it rapidly decreased to 1.60g/dl after 6 months of follow-up (p<0.001), and further decreased to 1.40g/day, 1.12g/day, and 0.90g/day after 12, 24, 36 months of follow-up (p<0.001, 0.002, 0.012). The mean ds-DNA level was 216IU/ml in the starting of the treatment, and it decreased to 97.04IU/ml, 88.28IU/ml, 94.61IU/ml after 12, 24, 36 months of follow-up (p<0.002, 0.003, 0.05). The C3 level revealed elevation after 96 months of follow-up. The mean C3 level was 70.63mg/dl initially, and increased to 88.60mg/dl, 90.65mg/dl, and 96.20mg/dl after 12, 24, 36 months of follow-up (p<0.001, 0.002, 0.011). The platelet level remained similar from the beginning of the study to 36 months of follow-up (269.97K/cumm to 253.5K/cumm, p=0.929). The improvement of proteinuria was significant and could be detected in 6 months, which had significant correlations with the reduction level in 24 months (p<0.001). This suggested that early improvement of proteinuria may predict the further responsiveness.

Conclusions: Although the role of rituximab still remained controversial in the treatment systemic lupus erythematosus, it showed positive responses in our single center’s experience. Early response to rituximab was an important predictor of further sustained responsiveness and reduction of proteinuria and other clinical parameters.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6648

SLE, Sjögren’s and APS - clinical aspects (other than treatment)

AB0471 WIDE HETEROGENEITY IN TREATMENT PROTOCOLS AND INAPPROPRIATE USE OF PREDNISOLONE FOR ANTI-RO/LA ASSOCIATED-CONGENITAL-HEART-BLOCK: A SYSTEMATIC REVIEW OF 492 CASES

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Background: Congenital heart block (CHB) risk is 1–2% in case of maternal anti SSA/Ro and/or anti SSB/La antibody positivity. CHB have significant mortality (20–30%) and available therapeutic options’ efficacy is contradictory.

Objectives: To systematically review and assess the treatment protocols and inappropriate use of prednisolone for antiphospholipid syndrome (APS) patients with associated congenital heart block (CHB) from a decade-period (2008–2018).

Methods: A comprehensive systematic review was performed using Medline, Embase, and Cochrane Library databases. A query of the literature was conducted using the keywords (antiphospholipid syndrome AND congenital heart block) AND (treatment OR management OR inappropriate use OR side effects OR mortality).

Results: A total of 492 cases of APS with CHB aged between 3 and 10 years were included. The majority of cases were female (68%). The most common CHB type was complete atrioventricular block (78%). The prevalence of anti-SSA/Ro/La antibodies was 84%. A total of 161 cases (32.8%) of CHB were found to have APS. The most frequent antiphospholipid antibody found was anti-SSA/Ro (87.7%). The treatment regimens varied widely across the included studies. The most common treatment approach was the combination of aspirin and warfarin (51%). Prednisolone was used in 66.3% of cases with a median cumulative dose of 656mg (range 12.5–10,000mg). The use of prednisolone was inappropriate in 22% of cases as it was used for antiphospholipid syndrome other than CHB. Moreover, 32 cases (6.5%) had side effects associated with prednisolone use. The mortality rate was 7.8% (38 cases).

Conclusions: The treatment of APS patients with CHB varies widely across the included studies. Prednisolone use was inappropriate in 22% of cases as it was used for APS other than CHB. The use of prednisolone was associated with side effects in 6.5% of cases. The mortality rate was 7.8% (38 cases).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6648
AB0472 IMPACT OF DISEASE ON FAMILY AND SOCIAL LIFE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Systemic lupus erythematosus (SLE) is a chronic connective tissue disease with involvement of various organ systems and characteristically has a higher incidence in women than men. The disease, as well as its treatment, could have significant effects on the quality of life of lupus patients.

Objectives: Here, we aimed to investigate the impact of SLE on quality of the social and family life of women.

Methods: One hundred and twenty women diagnosed with SLE were included in the study. A questionnaire including questions about family and social relations were applied and demographic information, educational status, marital status, organizational involvement and treatment data were obtained. The results of this study are preliminary and the study is still ongoing.

Results: One hundred and twenty patients were studied. The average age was 37 (±10). 77 patients were married, 29 patients were single, 12 patients were divorced and 2 patients were widows. 29% of the patients were employed. 10.8% of the patients declared having difficulty in accepting their illnesses. 94.8% of the married patients had nuclear families. Relationship with partners and family problems, social activities, age and educational level.

Conclusions: There is no consensus in the treatment of CHB. Drug selection and dosing regimens have wide heterogeneity. More than half cases received no treatment. Of note, prednisolone has often been used, despite its inability to cross the placenta.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5909

AB0474 THYROID DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: ITS IMPACT AS A CARDIOVASCULAR RISK FACTOR

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease caused by immune system-mediated tissue damage. Thyroid function abnormalities and thyroid autoantibodies have been frequently described in patients with rheumatologic autoimmune diseases, such as SLE.

Objectives: The aim of this study was to assess thyroid function and anti-thyroid antibodies in SLE patients and evaluate the effects of the thyroid dysfunction on the clinical parameters, disease activity and assess its impact as a cardiovascular risk factor.

Methods: A total number of fifty SLE female patients were selected. Triglycerides (TG), total cholesterol (TC), LDL and high density lipoprotein (HDL), Thyroid Stimulating Hormone (TSH), serum free3T3 (FT3), freeT4 (FT4), Serum thyroid peroxidase antibodies (TPOab) and serum thyroglobulin antibodies (Tgab) were measured. Disease activity was evaluated by SLEDAI score.

Results: In our study, anti CCP antibodies were found in 8 (11.4%) of SLE patients and 4 (13.3%) SSc patients, while anti MCV antibodies were found in 14 (20%) SLE patients and 8 (26.7%) SSc patients. There is a significant association between presence of anti CCP Abs and anti MCV Abs and a clinically evident arthritis in both SLE and SSc. Strong relationship between high CRP level and a severe arthritis and joint erosions was noticed in SLE patients.

Conclusions: A significant radiological evidence in the form of synovial hypertrophy and bony erosions were found using ultrasonography and plain X-ray with seropositive anti CCP and anti MCV Abs in both SLE and SSc patients. In this study, anti CCP antibodies were found in 2 SLE patients and SSc disease activity score (Medsger score) for SSc patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2489

AB0473 ANTI CCP AND ANTI MCV ANTIBODIES ARE MARKER OF ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS & SCLERODERMA

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Background: Anti-citrullinated protein antibodies (ACPA) have been reported as more specific serological markers of rheumatoid arthritis (RA). They provide a superior alternative to the rheumatoid factor (RF) test in laboratory diagnostics of RA. Different studies suggest that the enzymatic citrullination and the production of ACPAs may also be associated with other inflammatory arthritis-associated autoimmune diseases [2].

Objectives: To detect the presence of anti CCP and anti CMV antibodies in SLE & SSc and its correlation to radiological findings and disease activity.

Methods: Our study was included 70 SLE patients and 30 systemic sclerosis (SSc) patients diagnosed according to ACR classification criteria. After informed consent, all patients were subjected to detailed history taking, full clinical examination, including rheumatological examination, laboratory investigations: Included CBC, ESR, CRP with titur, urine analysis, renal & liver function, serum uric acid. Anti CCP antibodies & Anti MCV antibodies by ELISA. X-ray and US on both hands and knees and disease activity score using SLEDAI score for SLE patients and SSc disease activity score (Medsger score) for SSc patients.

Results: In our study, anti CCP antibodies were found in 8 (11.4%) of SLE patients and 4 (13.3%) SSc patients, while anti MCV antibodies were found in 14 (20%) SLE patients and 8 (26.7%) SSc patients. There is a significant association between presence of anti CCP Abs and anti MCV Abs and a clinically evident arthritis either in both SLE and SSc. Strong relationship between high CRP level and a severe arthritis and joint erosions was noticed in SLE patients.

Conclusions: Thyroid disorder is more common in lupus patients especially those in exacerbation and +ve for antithyroid Ab and those with thyroid dysfunction had increased cardiovascular risk. These patients should be investigated for Lipid profile echocardiography and neck US for detection of early atherosclerosis and other CVD those with thyroid dysfunction had increased cardiovascular risk.

References:
Changes in heart rate variability reflect changes in clinical status and patient reported outcomes in systemic lupus erythematosus: a longitudinal analysis

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Background: We previously observed an association between systemic lupus erythematosus (SLE) disease activity and heart rate variability (HRV) with a preliminary observation of consistency between these two measures when disease activity changed between two timepoints (1).

Objectives: To prospectively test the hypothesis that HRV reflect longitudinal changes in clinical status and patient reported outcomes.

Methods: The current project evaluated HRV measurements using a 5 min ECG recording following a minimum of 2 visits in an ongoing clinical trial. HRV parameters were calculated in the time domain (RMSSD and pNN50) and the frequency domain [high frequency (HF) as well as low frequency to high frequency (LF/HF) ratio]. A mixed effects linear model, with generalized estimating equations to account for clustering of visits for each patient, was used to compare changes in HRV between paired visits and to examine linear associations between HRV parameters and clinical scores. All models were adjusted for baseline values of each HRV parameter.

Results: Forty nine patients (age 44.9±11.7, 46 female), followed in a total of 413 paired visits (median time between visits 1 month), were included. Global BILAG score was inversely associated with RMSSD (regression coefficient β=−1.39±0.01; p<0.0001). BILAG, SLEDAI and PGA were directly associated with the LF/HF ratio (β=−0.96±0.02; p<0.0001, 0.42±0.10; p<0.0001 and 0.83±0.09; p<0.0001, respectively). Changes in BILAG were inversely associated with changes in RMSSD and pNN50 (β=−7.0±1.9; p=0.003 and −1.6±0.04; p=0.001, respectively). BILAG changes were also directly associated with changes in the LF/HF ratio (β=0.78±0.05; p=0.001). Categorical improvement, defined as ≤1 letter grade improvement in BILAG and no new BILAG A or B scores, occurred in 77 (19%) visit pairs (group 1) and either no improvement or worsening in 335 (81%) group 2. RMSSD and HF increased in group 1 compared to group 2 (group difference=−33.3±10.1; p=0.001 and −39.9±4.1; p<0.0001, respectively), and the LF/HF ratio decreased in group 1 compared to group 2 (group difference=3.1±0.8; p<0.002). Changes in Physical Component Summary (PCS) of SF36v2 were inversely related to changes in SLEDAI and PGA (β=−0.39±0.14; p=0.006 and −0.19±0.02; p=0.001, respectively). Changes in Mental Component Summary (MCS) were inversely related to changes in BILAG, SLEDAI and PGA (β=−0.23±0.07; p=0.0001, −0.31±0.10; p=0.002 and −0.08±0.03; p=0.008, respectively). PCS was related to HF (β=0.67±0.02; p=0.001), whereas MCS was inversely related to the LF/HF ratio (β=−0.11±0.03; p=0.001). Changes in PCS were related to changes in pNN50 (β=−0.21±0.05; p<0.0001) and changes in MCS were related to changes in HF (β=1.57±0.18; p<0.0001).

Conclusions: Changes in HRV reflect changes in clinical status and patient reported outcomes in patients with SLE. These data suggest that HRV may be a simple non-invasive tool used to gauge or predict clinical improvement in SLE. Further studies are warranted.

References:

Disclosure of Interest: None declared


AB0476 INNER EAR INVOLVEMENT IN SYSTEMIC RHEUMATIC DISEASES

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Background: Patients with systemic rheumatic diseases have increased prevalence of sensorineural hearing loss (SNHL). Detection of cochlin specific antibodies has been reported in patients with idiopathic sensorineural hearing loss. Interestingly, cochlin has been shown a stronger link to autoimmune hearing loss. In the present study, we evaluated the presence of antibody specific for cochlin in patients with systemic rheumatic diseases and to detect human cochlin antibodies in their sera.

Methods: This was a prospective study. Patients older than 18 year old who gave informed consent and fulfilled the criteria of American College of Rheumatology for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjogren's syndrome (SS) and systemic sclerosis (SSc) were included. Complete head and neck clinical examination was performed, including otoscopy, nasendoscopy and hearing examination with pure tone audiometry (250Hz -8000Hz). All medical treatments as well as Disease activity score (DAS) 28 for RA and SLE disease activity index (SLEDAI) for SLE were documented. An average tone loss was calculated, taking as a starting point the loss in dB at various frequencies according the American Committee on Hearing and Equilibrium Guidelines for Meniere's disease and also recommendation 02/1 of “Bureau International d'Audiophonologie” (BIAP). Blood samples of the patients were tested for the presence of IgG anti-cochline antibodies (COCH-IgG). The results were compared with disease of sex and age matched healthy subjects.

Results: We studied 133 patients (60 with RA, 41 with SLE, 24 with SS and 8 with SSc) and 133 healthy subjects.61.4% of patients reported vertigo, 41% hyperacusis, 39% hearing loss, 38% tinnitus, 37.9% headache and 2.1% tinnitus and hyperacusis. The prevalence of patients with unremarkable otoscopy was inversely associated in patients affected by RA, SLE, SS and SSc in comparison to healthy controls (66.6%, 31.71%, 54.17% and 75% respectively). The average hearing thresholds (AHT) calculated using BIAPI recommendation 02/1 were significantly increased in RA compared to SLE. AHT were also increased in patients with RA and secondary SS but without statistical significance compared to RA patients. There was a statistically significant correlation between AHT and DAS28 in RA. No correlation observed between AHT and SLEDAI. COCH-IgG were detected in two samples (one patient with RA and one with RA and SS).

Conclusions: Cochlin has been shown to have a stronger link to autoimmune hearing loss, but our study concerned correlation of hearing loss with human cochlin IgG (COCH). Additional prospective studies are needed to elucidate its pathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4805

AB0477 VITAMIN D STATUS, SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY AND ENDOTHELIAL DYSFUNCTION

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Background: Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease, in which cardiovascular complications due to premature and accelerated athero-sclerosis represent a serious problem. Endothelial dysfunction is the first step in the atherosclerosis development. Low levels of vitamin D have a high prevalence in lupus patients, correlating with high prevalence of cardiovascular diseases in these patients.

Objectives: The aim of this study was represented by the assessment of endothelial dysfunction in patients with active systemic lupus erythematosus, and correlations of this with SLE activity and vitamin D status.

Methods: The study was performed on a group of 35 female patients with active systemic lupus erythematosus. In all the patients were assessed: SLE activity using SLEDAI (SLE Disease Activity Index), vitamin D status and endothelial dysfunction of patients with active disease.

Results: The mean age ± standard deviation was 33.8±8.55 years, and the average duration of SLE was 8.9±1±5.29 years. The assessed parameters had the following values: SLEDAI 9.02±4.51, vitamin D 12.79±2.45 ng/ml, FMD 9.26±2.34%, and 9 patients (25.71%) had vitamin D deficiency, and 31 patients had vitamin D insufficiency, and FMD 9.26±2.34%. There were significant correlations between vitamin D levels and FMD (r=0.4517, p=0.0003), and between vitamin D levels and SLEDAI (r = 0.6297, p=0.00025).

Conclusions: Low values of vitamin D levels were present in all the studied patients, correlating with the systemic lupus erythematosus activity, and endothelial dysfunction.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3282

AB0478 COMPARATIVE STUDY BETWEEN PATIENTS WITH NORMAL AND OVERWEIGHT IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS FROM ARGENTINA


Background: Systemic lupus erythematosus (SLE) have an increase cardiovascular risk, worsened by overweight and obesity. Increased BMI is associated with other severe complications and comorbidities as lupus nephritis, hypertension, insulin resistance and dyslipidemia. Body weight is a modifiable risk factor.

Objectives: To determine the frequency of overweight and obesity in patients with SLE and their impact on this disease

References:
OBJECTIVES: The aim of the research was to study the processes of formation of antibodies to the enzyme purine metabolism (PM) - xanthine oxidase (XO) and adenosine deaminase (ADA) - in patients with systemic lupus erythematosus (SLE) with laboratory indicators of secondary antiphospholipid syndrome (APS).

METHODS: 30 healthy people and 60 SLE patients with different clinical manifestations were included in this research. Antibodies to the investigated enzymes were determined in the procedure of an indirect ELISA-test using immobilized form of the corresponding enzyme as antigen array (We have developed this technique). The results of the detection of antibodies to the XO (anti-XO) and ADA were recorded on a spectrophotometer at a wavelength of 450 nm. b2-glycoprotein-I-dependent (b2GP-I) activity was assessed in patients with APS. The results of the detection of antibodies to ADA were classified as positive (OR: 0.78, IC 95%: 0.63–0.98) (p=0.03).

RESULTS: Antibodies to the enzyme PM may be a factor in the development and maintenance of vascular disorders in patients with SLE, and their detection can be used as an additional test in the complex diagnosis of SLE with symptoms of APS.

DISCLOSURE OF INTEREST: None declared.


AB0470 A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY ON THE PSYCHOPATHOLOGY OF PATIENTS WITH PRIMARY SJOGREN'S SYNDROME AND ANXIETY DISORDER

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BACKGROUND: Sjogren syndrome (SS) is a chronic systemic autoimmune disease characterized by exocrine gland inflammation and symptoms of oral and ocular dryness. Anxiety affects as many as 50–70% of persons living with SS. While anxiety is commonly experienced, very little is known concerning the mechanisms of cognitive dysfunction in SS.

OBJECTIVES: To reveal the psychopathology of patients with Sjogren's syndrome and anxiety disorder.

METHODS: 12 patients with pSS and anxiety disorder (SAS≥50), 11 patients with pSS, and 10 healthy controls were recruited. (1) Self-rating Anxiety Scale (SAS) was used to assess anxiety level of participations. All the subjects went through functional magnetic resonance imaging (fMRI) while listening actively to neutral words, negative words and negative words alternating with neutral ones.

RESULTS: When subjects listened to neutral words alternating with no words, perfrorental cortex and BA21 were active in patients with pSS and anxiety disorder. When subjects listened to negative words alternating with no words, patients showed increased activity in prefrontal cortex, BA21, anterior cingulate and fusiform. Furthermore, when subjects listen to negative words alternating with neutral words, patients with pSS and anxiety disorder showed more increased activity and accrual damage including chronic renal disease.

DISCLOSURE OF INTEREST: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2766

AB0479 THE ROLE OF ANTIBODIES TO XANTHINE OXIDASE AND ADENOSINE DEAMINASE IN THE DEVELOPMENT OF ANTI-PHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS


OBJECTIVES: The results of the detection of antibodies to the XO (anti-XO) and ADA were recorded on a spectrophotometer at a wavelength of 450 nm. b2-glycoprotein-I-dependent (b2GP-I) to the phospholipid antibodies (aPL) class IgM and IgG were determined by using a commercial test kit "Anti-Phospholipid Screen IgG/IgM" (O:tergentec). The levels of IgG aPL/IgM did not exceed 10 GPL/MPL-U/ml in the group of healthy individuals. The results of the detection of antibodies to ADA (anti-ADA) and antibodies to the ADC (anti-ADC) were recorded on a spectrophotometer at a wavelength of 450 nm. Determination of antibodies to the enzyme PM - xanthine oxidase (XO) and adenosine deaminase (ADA) in patients with systemic lupus erythematosus (SLE) with laboratory indicators of secondary antiphospholipid syndrome (APS).

RESULTS: Antibodies to the enzyme PM may be a factor in the development and maintenance of vascular disorders in patients with SLE, and their detection can be used as an additional test in the complex diagnosis of SLE with symptoms of APS.
activity in prefrontal cortex, anterior cingulate, and caudate nucleus than that of SLE patients with positive aPL were found to have MRI abnormalities, while MRI abnormalities were found in only 8 SLE patients with negative aPL (100% vs. 44.4%) (p=0.001). There was a statistically significant correlation between SLE disease activity and both NP manifestations and aPL antibodies also had a significant correlation with NP manifestations. MRI abnormalities included discrete white matter lesions (60%), cortical atrophy (25%) and gross infarctions (15%). MRA revealed atherosclerotic changes of one or more of the large intracranial vessels in (27.2%) of NPSL patients.

Conclusions: Elevation of PCSK9 was observed in patients with SLE and correlated with CRP but not atherogenic lipids, particularly in female patients. The result was indicative of pathogenic role of PCSK9 in the low-grade inflammation which promotes the atherogenic process in SLE patients.

References:

Acknowledgements:
The authors thank Qiulan Li for the excellent technical assistance.

Disclosure of Interest: None declared

AB0483 RESPONSIVENESS OF LUPUS IMPACT TRACKER AMONG CHINESE PATIENTS WITH LUPUS

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1Medicine, Tuen Mun Hospital, HK, Hong Kong; 2Medicine and Behavioral Sciences, Rush University Medical Center, Chicago, United States

Background: Lupus Impact Tracker (LIT), a 10 item, patient reported outcome tool for patients with systemic lupus erythematosus (SLE) has undergone psychometric validation and responsiveness studies in the US and Europe.

Objectives: To report results on responsiveness of Lupus Impact Tracker among Chinese patients with SLE.

Methods: 430 patients with SLE meeting the ACR classification criteria were recruited in Hong Kong, China at a single center. LIT scores from two visits one year apart were analyzed for responsiveness and Minimal Clinically Important

AB0482 ELEVATION OF SERUM PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) CONCENTRATIONS AND ITS CORRELATION WITH C-REACTIVE PROTEIN, BUT NOT AHEROTGENIC LIPIDS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C. Fang 1, L. Huang 2, T. Luo 2, X. Chen 2, L. Lin 1
1Rheumatology Department; 2Nuclear Medicine Department; 3Ultrasonic Cardiogram Department, Second affiliated hospital of Fujian Medical University, Quanzhou, China

Background: Patients with systemic lupus erythematosus (SLE) have a tendency of accelerated atherosclerosis with controversial benefits from statin. This phenomenon can only partly be explained by traditional risk factors for cardiovascular disease. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease associated with cardiovascular risk that not only regulates cholesterol metabolism, but acts as a critical regulator of inflammatory reaction. PCSK9 inhibitors were also highly promising drugs bringing added cardiovascular benefit when administered with statin [1] [2].

Objectives: The present study firstly aimed to compare serum PCSK9 levels in SLE patients and healthy controls. The association between PCSK9 concentrations with atherogenic lipids and C-reactive protein (CRP) in SLE patients was also analyzed.

Methods: 77 individuals encompassed; 47 patients with SLE and 30 age- and sex-matched controls. Serum PCSK9, lipoproteins concentrations and CRP levels were assessed in patients and controls. Individuals with history of smoking, diabetes, infection and statin and stool use were excluded.

Results: Serum PCSK9 levels were significantly elevated in patients with SLE, compared with healthy controls (p=0.034). PCSK9 positively correlated with serum levels of CRP (r=0.351, p=0.018); The tendency seemed more significant in female patients (r=0.487, p=0.001); No correlation with statistical significance between PCSK9 levels with disease activity (SLEDAI) or sipr fus parameters was found (p>0.05, all) (Table 1).

Table 1. Characteristics of patients and controls and correlational analysis of PCSK9 levels and disease parameters in SLE patients. Data are shown as number or median (interquartile range), respectively

<table>
<thead>
<tr>
<th>Variables</th>
<th>Healthy controls</th>
<th>SLE</th>
<th>r, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>30</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Female/Male</td>
<td>24/6</td>
<td>42/5</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.5 (26–39.5)</td>
<td>33 (28–42)</td>
<td>-0.014, 0.927</td>
</tr>
<tr>
<td>PCSK9 (ng/ml)</td>
<td>292.44 (199.87–499.93)</td>
<td>395.3 (305.37–525.92)</td>
<td>NA</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>NA</td>
<td>6 (4–8)</td>
<td>0.092, 0.539</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>NA</td>
<td>4.50 (3.90–5.40)</td>
<td>0.012, 0.935</td>
</tr>
<tr>
<td>ApoA1 (g/l)</td>
<td>NA</td>
<td>2.38 (1.74–3.19)</td>
<td>0.002, 0.989</td>
</tr>
<tr>
<td>ApoB (g/l)</td>
<td>NA</td>
<td>1.30 (0.97–1.59)</td>
<td>0.011, 0.943</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>NA</td>
<td>0.79 (0.63–0.94)</td>
<td>0.181, 0.223</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>NA</td>
<td>1.26 (0.79–1.64)</td>
<td>0.020, 0.896</td>
</tr>
<tr>
<td>LDL cholesterol (g/l)</td>
<td>NA</td>
<td>1.49 (1.22–1.86)</td>
<td>0.112, 0.453</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>NA</td>
<td>1.31 (0.50–3.60)</td>
<td>0.351, 0.016</td>
</tr>
<tr>
<td>CRP (mg/l) in female patients</td>
<td>NA</td>
<td>1.195 (0.500–3.568)</td>
<td>0.487, 0.001</td>
</tr>
</tbody>
</table>

Conclusions: Elevation of PCSK9 was observed in patients with SLE and correlated with CRP but not atherogenic lipids, particularly in female patients. The result was indicative of pathogenic role of PCSK9 in the low-grade inflammation which promotes the atherogenic process in SLE patients.

References:

Acknowledgements:
The authors thank Qiulan Li for the excellent technical assistance.

Disclosure of Interest: None declared
Difference (MCID) against patient report and physician assessed anchors of changes in health. Two patient reported anchors were used (Global change in health and item 2 of Short Form 36 form). Physician assessed anchors of change in health were disease activity (Physician global assessment-PGA, SELENA-SLEDAI) and damage (SLICC-SDI/ACR). Change in PGA of ≥0.3 and SELENA-SLEDAI of ≥4 in either direction was used to define worsening in disease activity. Analysis of variance was used to compare changes in LIT score against the anchors.

Results: Mean (SD) age of participants was 42 (14) years. Ninety five percent (n=42) of patients have live birth with mean weight at birth of 2.558 g and 73% of patients according to gestational age.

Table 1. Maternal Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
<th>Preterm delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>12</td>
<td>12 (12.5%)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>6</td>
<td>(6.2%)</td>
</tr>
<tr>
<td>Premature rupture of fetal membranes</td>
<td>7</td>
<td>(7.3%)</td>
</tr>
<tr>
<td>Gestational Diabetes</td>
<td>2</td>
<td>(2%)</td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>10</td>
<td>(10%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: LIT shows responsiveness to changes in both patient-reported and physician assessed changes in health status among Chinese SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3941

AB0484 LUPUS NEHRITIS AND PREGNANCY: MATERNAL AND FETAL OUTCOME

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that primarily affects women during their reproductive years. The presence of Lupus nephritis (LN) may result in an increased risk of disease flare and adverse maternal and fetal outcomes, such as preeclampsia, fetal loss, and preterm delivery.

Objectives: The purpose of this work is to evaluate pregnancy outcome in SLE patients with previous diagnosis of LN.

Methods: We retrospectively studied SLE patients according to previous diagnosis of LN by renal biopsy who attended to Materno Neonatal Hospital during the last 5 years. We evaluated demographic, clinical, and laboratory and obstetric data. Renal biopsies were classified according ISN/RNP 2004. Lupus activity was evaluated by modified pregnancy SELENA SLEDAI score at the conception and during pregnancy. Maternal complications were evaluated: Preeclampsia, HELLP, Gestational Diabetes, Premature rupture of fetal membranes, arterial and venous thrombosis, mortality, the way of end of pregnancy, and others. Fetal outcome was evaluated as live birth, gestational age and weight at birth.

Results: 44 pregnancies in 32 patients were included. Maternal mean age was 30.75 years old, 84% were from Córdoba city, 70.5% did not have health insurance, and they have mean previous pregnancies of 4 with 1 live birth. Maternal complications were: Pre eclampsia in 12 patients (12.5%), Preterm delivery in 6 patients (6.25%), Premature rupture of fetal membranes in 9 (8.33%), Gestational Diabetes in 7 (7.29%), Arterial Thrombosis in 2 (2.08%), Venous thrombosis in 3 (3.12%), 33.69% have normal labour and 66.33% cesarean section. 86% of patients have live birth with mean gestational age of 36 weeks with mean weight at birth of 2.558 g and 73% of patients according to gestational age.

Table 1. Maternal Complications

<table>
<thead>
<tr>
<th>Complication</th>
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<td>Preeclampsia</td>
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<td>Gestational Diabetes</td>
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</tr>
<tr>
<td>Venous Thrombosis</td>
<td>10</td>
<td>(10%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: PAPS pregnancies patients had a good maternal and fetal outcome in this study.

References:

Acknowledgements: We are grateful with Secyt subsidy UNC.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5621

INCIDENCE OF VERTEBRAL FRACTURES: 8 YEARS FOLLOW-UP STUDY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Vertebral fractures (VF) are the hallmark of bone fragility. Patients with systemic lupus erythematosus (SLE) are at high risk of developing prevalent VF. Although several risk factors for VF in patients with SLE have been suggested, there is limited longitudinal supporting data in the literature.

Objectives: The aims of this study are to determine the incidence of VF and to evaluate possible associations between potential risk factors and the occurrence of VF in women with SLE.

Methods: Consecutive patients with SLE were enrolled in a prospective, observational study from 2006 to 2015. Information on potential risk factors, including demographics, clinical data and bone mineral density (BMD) at the lumbar spine and hip on dual-energy X-ray absorptiometry was collected at baseline and follow-up. Semi-quantitative analysis was used to determine incident VF on lateral thoracic and lumbar radiographs, defined as any vertebral body graded normal at baseline and at least mildly deformed (20–25% reduction or more in any vertebral height) during follow-up. Differences in baseline characteristics were assessed in patients with and without radiographic VF.

Statistical analysis: The Chi-square or Fisher's exact test, independent samples t-test, and Mann-Whitney U-test were used as appropriate to compare baseline characteristics of patients with and without prevalent or incident VF. Possible risk factors for incident VF were assessed by multivariate logistic regression analysis.

Results: Of 110 SLE patients included, with a median follow-up of 8 (IQR 8–9) years, 22 (20%) had radiographic VF at baseline; 35 (32%) patients had a new VF. The annual incidence rate of new morphometric VF was 3.5 (95% CI 2.4–4.9) per 100 patient-years. Most fractures were located in the mid-thoracic and thoracolumbar region of the spine. Table 1 shows sociodemographic and clinical differences between patients with and without VF. In the multivariable analysis, VF were significantly associated with baseline BMD at the total hip and longer disease duration. Cumulative glucocorticoid dose, postmenopausal status and previous prevalent VF were not associated with VF.

Conclusions: In this SLE cohort in daily clinical practice, radiographic VF were frequently present in SLE patients, especially those with longer disease duration and low hip BMD.

References:

Acknowledgements: This work was supported in part by grant from FIS/IMSS/PROCT/MID15/1500.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1238

NEUROLOGIC MANIFESTATIONS AND THEIR IMPACT ON CHRONIC DAMAGE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: RESULT FROM A MONOCENTRIC COHORT

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease with wide clinical features and cumulative damage. The nervous system involvement is very broad and severe.

Objectives: The aim of this study is to analyze the impact of neurologic manifestations on Damage Index in Patients with APS (DIAPS).

Methods: All consecutive patients known with APS were included in our monocentric cohort. Data on medical history, clinical manifestations, aPL profile and medication were collected. DIAPS score was used to measure damage in each patient.

Results: Seventy six patients with APS were included: 11 patients with primary APS and 66 patients with secondary APS, with mean disease duration of 9.59±7.39 years. Overall, 35 patients (46.1%) had neurologic manifestations. Their mean disease duration was 9.2±5.76 years. Seven patients had primary APS and 28 patients had secondary APS. Six patients were on chronic oral anticoagulant therapy and low dose aspirin, 12 patients on oral anticoagulant alone and 15 patients on low dose aspirin. Transient ischemic attack was the first manifestation of APS in 4 patients (11.42%) at mean age of 29.5±10.96 years. Their mean DIAPS value was 7.75±4.19. Ischemic stroke was the first manifestation of APS in 12 patients (34.29%) at mean age of 40.06±13.61 years, with DIAPS mean value of 7.41±3.67. All of these patients had neurologic sequelae. The DIAPS value was higher in patients with neurologic manifestations (3±2.9 vs 5.71±3.62, p<0.001) and DIAPS value correlated significantly to neurologic manifestations (R=0.416, p<0.000) reflecting its impact on cumulative damage in APS patients.

Conclusions: Neurologic manifestations in APS patients have a great impact on cumulative damage especially in patients presenting with ischemic stroke or transient ischemic attack as the first manifestation of APS.

References:

Disclosure of Interest: None declared


CAPILLAROSCOPY FINDINGS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS, A DUTCH EXPERIENCE OF 20 CHILDREN AND ADOLESCENTS

D. Schonenberg-Meinema 1, M. vd Berg 1, A. Nassar-Sheikh-Shaladi 1, G. de Bree 1, L. Hak 1, M. van Onna 1, K. Melsens 1, M. Cutolo 2, T. Kuijpers 1, 1 Department of Pediatric Hematology, Immunology, Rheumatology and Infectious Diseases; 2 Department of Clinical Immunology and Rheumatology, AMC Amsterdam, Amsterdam, Netherlands; 4 Department of Rheumatology; 5 Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium; 6 Research Laboratory and Academic Unit of Clinical Rheumatology, University of Genova, Genova, Italy.

Background: Capillaroscopy findings can be qualitatively described as: normal, microangiopathy (non-specific abnormalities) or scleroderma pattern (1). Capillary abnormalities, described in varying prevalence in patients with systemic lupus erythematosus (SLE), are mainly described as microangiopathy (2–4)

Objectives: To describe capillary characteristics in a cross-sectional cohort of patients with childhood-onset SLE (cSLE) by quantitative and qualitative assessment

Methods: Nailfold videocapillaroscopy (NVC) was performed in cSLE-patients (onset ≤18 years) with a x200 magnification lens (Optika). The following capillaroscopic characteristics were evaluated per millimeter: density (compared to mean density known for age, sex and ethnicity) (5), number of abnormal shapes (as defined by the EULAR study group on microcirculation in Rheumatic Diseases (6)), giant capillaries (defined as apical diameter >50 mcm), maximum apical diameter (dilatations defined as apical diameter ≥50–500 mcm) and microbleedings large hemorrhages and small multiple point-shaped hemorrhages surrounding the capillary loop [image].

Results: 4063 capillaries from 20 patients with cSLE were analyzed. All patients showed capillary abnormalities, 15% (n=3) showed a scleroderma-pattern. A lower mean density (mean 6.7, range 1.9–9.5) was seen in 55% (n=11), multiple
The SLE-key® Rule-Out test performs well as an aid in the analysis of common gram-negative bacteria and hyperuricemia in premenopausal women with systemic lupus erythematosus and development of nephritis.

Conclusions: The diagnosis of patients referred in the clinical rheumatology setting remains an ongoing challenge. The SLE-key® RuleOut test provides a laboratory aid to improve the diagnostic and dispositional efficiency saving undue concern, time and resources both to the patient and to the healthcare system. A retrospective analysis of our practices prior to the introduction of SLE-key® is warranted.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5779

Table 1

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Status post SLE-key</th>
<th>Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with uncertain diagnosis in our clinic prior to SLE-key® testing.</td>
<td>79% had an actionable diagnosis following SLE-key® test</td>
<td>57% were diagnosed to have SLE. 43% not SLE. Patients treated for a variety of disorders other than SLE. &gt; 50% of those RuleOut were diagnosed with myalgia/fibromyalgia and treated accordingly.</td>
</tr>
<tr>
<td>Patients referred to our clinic with SLE as part of differential diagnosis</td>
<td>62% confirmed SLE 32% RuleOut</td>
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Conclusions: The diagnosis of patients with SLE is complex due to the spectrum of clinical manifestations and the challenges in the differential diagnosis. The SLE-key® Rule-Out test provides a laboratory aid to improve the diagnostic and dispositional efficiency saving undue concern, time and resources both to the patient and to the healthcare system.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5779

The SLE-key® Rule-Out test performs well as an aid in clinical practice.

D. Massenburg, J. Oldenberg, A. Sei, T. Krause, A.F. Wells. Rheumatology and Immunotherapy Center, Franklin, WI, United States

Background: The SLE-key® test was developed by ImmunArray and was validated to rule out SLE with 94% sensitivity, 75% specificity and a negative predictive value (NPV) of 93%.1 We reported earlier that the SLE-key® RuleOut test could aid in the diagnosis and disposition of a cohort of 55 patients in our clinical practice.2

Objectives: We have now expanded this cohort and report here the usefulness of the SLE-key® test in adding the management of a cohort of challenging and suspected SLE patients in a large clinical practice.

Methods: In patients referred to the Rheumatology and Immunotherapy Center, Franklin, WI, results from the SLE-key® RuleOut test were included as part of the clinical evaluation. Serum samples were collected from individual subjects with informed consent and tested at VERACIS (Richmond, VA), using the SLE-key® (iChip®).

Results: We reviewed the diagnoses and clinical disposition of patients both before and after SLE-key® testing. In particular, we looked at the ability of the SLE-key® test to enhance our ability to reach a definitive diagnosis across the full cohort of patients, at the disposition of patients who were referred with a suspicion of SLE as part of the differential diagnosis, at the impact of SLE-key® testing on the diagnosis of the subset of patients who presented with minimal symptoms, and at the group of patients who had been referred following an ANA test. Results are summarized in Table 1. In the cases where SLE was ruled out, patients were treated for a variety of disorders including fibromyalgia, joint pain, MCTD, Sjogren’s disease and others.

Table 1

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4704

AB0480 ANALYSIS OF COMMON GRAM-NEGATIVE BACTERIA AND THEIR DRUG RESISTANCE IN HOSPITALIZED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Infection is an important cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). The spectrum of infectious agents in SLE patients varies significantly among different ethnic groups. The national surveillance study from the China showed that Gram-negative bacteria (GNB) was the most common bacterial infection in China, while Gram-positive bacteria (GPB) was predominant in European countries.

Objectives: To identify the spectrum and drug resistant pattern of infection caused by GNB in patients hospitalized with SLE.

Methods: The clinical and microbiological data from hospitalized SLE patients with bacterial infection between June 2005 and June 2015 was collected and then analyzed retrospectively.

Results: Two hundred and sixty-eight episodes of bacteria had been identified from 3815 hospitalized patients. In terms of isolated microorganisms, gram-negative bacteria (GNB) were predominant over gram-positive bacteria (GPB) as 178 isolates vs. 90 isolates). In the GNB, Escherichia coli (66/178, 37.1%) was the most common isolate, followed by Acinetobacter baumannii (36/178, 20.2%), Klebsiella pneumoniae (24/178, 13.5%), Pseudomonas aeruginosa (20/178, 11.2%), Haemophilus influenzae (10/178, 5.6%), Salmonella sp. (7/178, 3.9%), Enterobacter aerogenes (5/178, 2.8%), Stenotrophomonas maltophilia (5/178, 2.8%), Citrobacter freundii (3/178, 1.7%), Proteus mirabilis (3/178, 1.7%).

Resistant isolates (53/178, 30.0%) were more common documented in GNB, mostly extended-spectrum beta-lactamase (ESBL) producing Escherichia coli (30/66, 45.5%) and Klebsiella pneumonia (6/24, 25%), and multi-drug resistant acinetobacter baumannii (39.1%). Susceptibility tests showed that the ESBL-producing strains were highly sensitive to carbapenems, β-lactamase inhibitor compound families, and certain cefalosporin (Cefepime and Cefazidime) in vitro. (the resistance rate ~20%), whereas it was highly resistant to ampicillin and Gentamicin. Besides carbapenems and Cefoperazone/sultabactam, Acinetobacter baumannii was resistant to most antibiotics.

Conclusions: GNB was predominant in Chinese hospitalized patients with SLE. The drug resistance of GNB has increased significantly. It was necessary to rational use of antibiotics in patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4704

AB0481 THE ASSOCIATION OF BASELINE HYPERURICEMIA IN PREMENOPAUSAL WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND DEVELOPMENT OF NEPHRITIS

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Background: Renal involvement is a common and serious manifestation of SLE. Hyperuricemia may be associated with lupus nephritis as a result of renal
Oxidative damage to nucleic acids has been found to be associated with etiopathogenesis and disease activity of inflammatory disorders. Oxidised guanine species have been recognized as a biomarker of oxidative DNA and RNA damage by endogenously generated oxygen radicals. Sjögren’s syndrome (SS) is an autoimmune disorder and associated with overexpression of proinflammatory cytokines. Related to excess expression of proinflammatory cytokines, a prooxidant state could be postulated in SS.

**Objectives:** We aimed to evaluate levels of nucleic acids oxidative stress products in patients with SS.

**Methods:** 11 patients with SS diagnosed according to 2012 American College of Rheumatology (ACR) Classification Criteria for Sjögren’s Syndrome. 19 patients with psoriatic arthritis (PsA), diagnosed according to Classification Criteria for Psoriatic Arthritis (PsARC), 9 patients with rheumatoid arthritis (RA), diagnosed according to 2010 Rheumatoid Arthritis Classification Criteria, and 12 healthy controls were included. All SS patients were on hydroxychloroquine sulphate 400mg/day. All PsA and RA patients were on methotrexate 15–20mg/week and folate acid 5mg/week. The serum samples were collected from patients and stored at -30°C until assayed. Three oxidised guanine species, 8-hydroxy-2'-deoxyguanosine as a DNA oxidation marker, 8-hydroxyguanosine as a RNA oxidation marker, and 8-hydroxyadenosine as a DNA and RNA oxidation marker, were measured using DNA/RNA Oxidative Damage ELISA Kit (Cayman Chemicals, USA).

**Statistics:** All data are presented as mean and standard deviation (SD). Differences between groups were examined using Kruskal-Wallis tests. The Mann-Whitney U test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. A p-value less than 0.05 were considered as statistically significant. Statistical analysis of correlation was performed by using the Spearman rank test.

**Results:** There was no statistically significant difference between the groups in terms of age and gender. The average level of serum oxidised guanine species in the PsA, RA, SS and healthy control groups were 2871.7±2336.20, 2672.0±292.04, 3375.57±344.21, 2777.55±237.05 pg/mL, respectively. Oxidised guanine species levels were significantly higher in patients with SS and positively correlated with CRP levels (p<0.011, r=0.726) (table 2).

**Table 1. Baseline Characteristics of Study Patients with Systemic Lupus Erythematosus**

<table>
<thead>
<tr>
<th></th>
<th>Non-nephritis group</th>
<th>Nephritis group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>28.2±8.3</td>
<td>28.9±7.6</td>
<td>0.680</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>21.2±3.8</td>
<td>22.0±3.0</td>
<td>0.105</td>
</tr>
<tr>
<td>Follow-up, years</td>
<td>6.0±4.3</td>
<td>7.5±4.3</td>
<td>0.068</td>
</tr>
<tr>
<td>Serum Urine Acid, mg/dl</td>
<td>4.5±1.6</td>
<td>5.5±1.0</td>
<td>0.003</td>
</tr>
<tr>
<td>C4, mg/dL</td>
<td>14.0±8.3</td>
<td>9.8±6.2</td>
<td>0.005</td>
</tr>
<tr>
<td>Drugs that may increase serum uric acid level (%)</td>
<td>5 (8.9)</td>
<td>2 (4.4)</td>
<td>0.626</td>
</tr>
<tr>
<td>Drugs that may decrease serum uric acid level (%)</td>
<td>1 (1.8)</td>
<td>0 (0.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>C3, mg/dl</td>
<td>80.1±32.3</td>
<td>84.6±30.2</td>
<td>0.000</td>
</tr>
<tr>
<td>C4, mg/dl</td>
<td>14.0±8.3</td>
<td>9.8±6.2</td>
<td>0.005</td>
</tr>
<tr>
<td>Serum Urine Acid, mg/dl</td>
<td>4.3±1.4</td>
<td>5.1±1.4</td>
<td>0.047</td>
</tr>
<tr>
<td>C4, mg/dl</td>
<td>13.3±7.8</td>
<td>8.8±7.2</td>
<td>0.028</td>
</tr>
</tbody>
</table>

**Conclusions:** A marked increase in DNA damage leading to oxidative stress may contribute to tissue damage in SS.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3286
**Results:** Two hundred forty-two SLE patients were evaluated; 94.4% of them were female. Mean values were as follows: at age diagnosis 33.9±13.5 years, disease duration 15.8±10.5 years, SLEDAI 5.91±10.56, SLICC score 1.06±1.42, BLSy levels 1.81±1.757 ng/mL. The 22.5% of patients displayed increased BLSy levels. The 29.6% of total patients exhibit SLEDAI values up to 6, and only the 7% of the values up to 10. Higher BLSy levels were significantly correlated to the ANAs positivity (p=0.0006) and lymphopenia (p>0.01) but showed no correlation with hypercomplementemia neither anti-dsDNA. The statistical analysis did not yield differences in the clinical activity or accumulated damage between patients with lower and higher BLSy levels.

**Conclusions:** In our series we observed a 22.5% of patients with high levels of BLSy, and the 7% of cases had BLSy high levels and SLEDAI ≥6. BLSy upregulation is related to ANAs positivity and lymphopenia. We have found no statistical evidences on the relationship of BLSy levels and clinical activity in our series of patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4186

**AB0494 INCREASED LEVELS OF INTERFERON ALPHA AND INTERLEUKIN-10 AS CLINICAL ACTIVITY BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS**

E. Grau García1, M. Fernandez Matilla2, C.M. Feced Olmos1, E. Labrador Sánchez2, C. Nájera Herranz1, F. Vicen Bernabé1, J.E. Oller Rodriguez1, J.A. Castellano Cuesta2, F. Forner Ferrer4, D. Herráiz Marín4, J.A. Román Ibarra1, E. Grau Garcia3, 3Medical School, UCV, 4Biostatistics Unit, IIS la Fe, Valencia, Spain

**Background:** Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by immune system disruption, including deregulation of cytokine production. Interferon alpha (INF1A) is considered a key molecule in SLE etiopathogenesis, being responsible of the differentiation of dendritic cells from monocytes, and indirectly of interleukin 10 (IL10) upregulation. The B lymphocyte stimulating factor (BLyS) is involved in autoantibodies production and clinical activity, and is regulated by other cytokines as IL10 and INF1A.

Our objective was to evaluate INF1A, IL10 and BLyS levels and clinical activity in SLE.

**Methods:** A cross-sectional, observational study of 142 patients diagnosed of SLE according to SLICC 2012 criteria and 34 healthy controls was performed. A complete blood-test was made, and clinical data by personal interview was collected. We analyzed serum concentration of IL10, BLSy and INF1A by colorimetric methods. Patients were dichotomized as high and low levels for each cytokine based on the cytokine level above 2 SD of the mean in healthy controls. Biostatistical analysis with R (3.3.2.) was performed.

**Results:** In our SLE patients we observed higher values of IL10, BLSy and INF1A than controls (P<0.001, P=0.005 and P=0.004 respectively), showing an average values in patients of 13.39±27.73 pg/mL IL10, 1811.31±1757.81 pg/mL BLSy. The mean clinical activity measured by SLEDAI was 5.91±5.06. Statistical analysis indicate that INF1A levels are correlated to IL10 levels (P<0.001), and to a lesser extent with increased IL10-INF1A-BLSy levels. Patients with high INF1A>IL10-BLSy showed a significant rise in C3-C4 consumption (P<0.001 and P=0.001 respectively) and high anti-dsDNA (P=0.001 and P=0.002 respectively). Patients with increased INF1A-BLSy showed high anti-dsDNA (P=0.004) and ENA positivity (P=0.001) and ANAs positivity (P>0.01). In addition, patients with increased IL10-INF1A-BLSy showed ANAs (P<0.001) and antiphospholipid autoantibody positivity (P=0.004).

**Conclusions:** The 69% of our SLE patients displayed almost one cytokine increased, being the INF1A the cytokine that mainly is increased. However, increased IL10 levels, irrespective of whether there is also increased levels of BLSy and/or INF1A, is the cytokine which best fits to clinical activity in SLE.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3907

**AB0495 ASSESSMENT OF FRACTURE RISK IN A COHORT OF EGYPTIAN FEMALE SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS**

E.A. Hafez1, S.A. El Bakry1, S. Ibrahim1, C.S. Morad1, S.A. Hamza2, D.M. Abd El-Khalil1, 1Internal medicine and Rheumatology; 2Genetic Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt

**Background:** Survival of systemic lupus erythematosus (SLE) patients has improved dramatically due to improved treatment, and the morbidity pattern has shifted towards long-term complications as osteoporosis. SLE occurs in women during child-bearing years and the disease often persists to the postmenopausal period1. Assessment of fracture risk in SLE patients is important as fractures may occur while bone mineral density (BMD) is above the osteoporotic threshold or at or above the osteopenia threshold2. Osteoporosis diagnosis measurement helps to assess fracture risk and select patients for treatment.

**Objectives:** To assess the fracture risk in a cohort of Egyptian female SLE patients by using BMD and osteocalcin level with correlation to disease activity, damage index and drugs in use.

**Methods:** 70 females with SLE ≥40 years old satisfying the SLICC classification criteria were enrolled with detailed history taking including disease duration, drugs in use, traditional risk factors, regular exercise, history of previous fractures and menstrual history. Assessment of disease activity using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and disease damage using the Systemic Lupus International Collaborative Clinics/ American College of Rheumatology Damage Index (SLICC/ACR DI). Serum calcium, phosphorus and alkaline phosphatase were measured. BMD measured by dual energy X-ray absorptiometry (DEXA) scans at lumbar spine (LS) (L2-L4) and femoral neck (FN), serum osteocalcin level and World Health Organization fracture risk assessment tool (FRAX®).

**Results:** 14/70 (20%) patients had LS osteoporosis, 25/70 (35.7%) had LS osteopenia and 6/70 (8.6%) had FN osteoporosis, 30/70 (42.9%) had FN osteopenia. FRAX-Majer 0.2% was observed in 10% of patients, FRAX-HIP ≥3% was seen in 27.1% of patients. Serum osteocalcin level was significantly decreased in SLE patients with lower BMD than those with normal BMD, and significantly decreased in patients with osteoporosis than with those osteopenic. A significant negative correlation was found between osteocalcin level and age of patients, disease duration, SLEDAI and SLICC scores, current, IV pulse and cumulative steroids, immunosuppressants, anticoagulants, but there was a positive correlation with antimalarials and calcium supplements.

**Conclusions:** SLE patients are at greater risk for developing osteoporosis and osteopenia. Ten-year risk of major and hip fractures was higher in SLE patients with high levels of INF1A and/or BLyS, and SLEDAI were associated with a higher 10-year probability of major osteoporotic fracture. FRAX predicted incident hip and major osteoporotic fractures among SLE patients with normal and low bone mass not just those with frank osteoporosis. Physicians should be alerted to the higher risk of future fractures in SLE patients for periodic monitoring.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4180

**AB0496 VENOUS THROMBOSIS IS MORE PREVALENT IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME (APS) ACCOMPANYING SYSTEMIC LUPUS ERYTHEMATOSUS, WHILE LIVEDO RETICULITIS IN PRIMARY APS**

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**Background:** APS may overlap with other systemic autoimmune diseases like systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) than occur as a distinct disease. Our purpose was to evaluate what are the differences between patients with primary APS and APS accompanying SLE.

**Objectives:** The objective of this study was to compare patients with primary APS with SLE patients without APS and APS accompanying SLE.

**Methods:** 112 patients with APS were included to the study, 57 of them with primary APS and 55 with coexisting SLE. These patients were followed at the Department of Connective Tissue Diseases, NiGRF, Warsaw, Poland. At inclusion a full medical history and physical examination data were recorded.

**Results:** Both groups were similar in age, gender and duration of disease. Among all the clinical manifestations of APS, venous thrombosis was more frequent in patients with concomitant SLE. Skin involvement was significantly more prevalent in primary APS and it was caused mainly by livedo reticulitis. APS patients with vascular manifestations of APS/SLE showed more frequent arterial and venous thrombosis than APS patients. APS. Although epilepsy occurrence is comparable in APS and APS/SLE, higher frequency of EEG changes in APS/SLE group suggests that the mechanisms...
SIX CASES OF MACROPHAGE ACTIVATION SYNDROME AS TOTAL BODY WATER AND ITS CORRELATION WITH SICCA

F. Dall’ara1, I. Cavazzana2, M. Frassi2, M. Taraborelli2, M. Fredi2, F. Franceschi2, L. Andreoli1, A. Tincani1, P. Airò2.

1Immunology, University of Brescia - Dscs; 2Rheumatology and Clinical Immunology, University of Brescia - Dscs; 2Rheumatology and Clinical Immunology, Spedali Civili di Brescia, Brescia, Italy

Background: Macrophage Activation Syndrome (MAS) is a life-threatening syndrome characterized by excessive immune activation. It can be triggered by conditions affecting immune homeostasis, such as infections, malignancies and rheumatic disorders, including Systemic Lupus Erythematosus (SLE). In previous studies, prevalence of MAS among SLE patients ranged from 0.9% to 4.6%. Objectives: To describe the presentation and treatment of both MAS and SLE in patients with both syndromes. Methods: Monocentric retrospective evaluation: patients with MAS according to HLH classification criteria were identified in our cohort of SLE patients (classified according to ACR and SLICC criteria) followed for at least 1 year between 1972 and 2014. Results: Among 511 patients with SLE (mean age at diagnosis: 31 years ± 2), 6 patients (1.2%) with MAS were identified (all female). Their main clinical and laboratory features are reported in Table 1. Median HLH score was 22 (IQR 18–26), with a probability of having MAS of 96%. In all cases, MAS happened simultaneously to the onset of SLE. Median age at diagnosis was 31.5 years, median SLEDAI was 12. All patients had fever above 38°C. Lymphopenia, lymphadenopathy, and high titer ANA positivity. Workup for infections and malignancies was negative in all cases. All patients were treated with corticosteroids, and cases in which fever persisted or temperature was persistently above 38°C in the absence of signs and symptoms of infection were treated with immunosuppressive drugs and cytotoxic agents such as etoposide were used only in one case.

Table 1: main clinical and laboratory features at diagnosis of SLE and MAS

<table>
<thead>
<tr>
<th>Clinical feature of MAS (%)</th>
<th>SLE ACR classification criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Hemorrhages</td>
<td>1 (17)</td>
</tr>
<tr>
<td>CNS dysfunction</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Hepatosplenomegaly</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Spleenomegaly</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Anaemia</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Anemia</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Cytopenia</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Hematological involvement</td>
<td>6 (100)</td>
</tr>
</tbody>
</table>

**CLINICAL FEATURES OF SLE PATIENTS WITH AND WITHOUT MAS**

- **WB C** (10^9/µl): 2.1 (1.8–2.3)
- **HGB (g/dl)**: 13.5 (11.8–13.7)
- **ALT (U/l)**: 230 (180–402)
- **ALP (U/l)**: 312 (259–479)
- **BUN (mg/dl)**: 17.5 (12.4–24)
- **CrP (mg/dl)**: 37 (10–60)

**AB0497**

**AB0498**

**TOTAL BODY WATER AND ITS CORRELATION WITH SICCA SYMPTOMS IN PRIMARY SJÖGREN’S SYNDROME**


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Background: Differentiation of Systemic Lupus Erythematosus (SLE) activity and infection in a febrile SLE patient become difficult, since initial clinical presentation may be similar. Several biological markers (including procalcitonin and CRP) have been evaluated, with discordant results. Soluble CD14 (sCD14), also called receptor for lipopolysaccharide (LPS)-binding protein (LPS-LBP) complexes, CD14 could activate a series of signal transduction pathways and inflammatory cascades, and lead to systemic inflammatory responses.

Objectives: To evaluate the utility of sCD14 as a novel biomarker to discriminate infection vs. activity in SLE patients admitted with systemic inflammatory response syndrome (SIRS).

Methods: We included 11 patients with SLE (ACR criteria 1997) and SIRS (International conference 2001) admitted to the ER and/or ICU. The measurement of sCD14 in plasma by enzymatic immunoassay of chemiluminescence in vitro was performed to differentiate active SLE vs. infection. Infection was considered if a positive culture/PCR was obtained. Mann-Whitney test was used to evaluate the association of variables with infection.

Results: All patients were female; mean age 37.9 years. An infectious disease was confirmed in 5 cases (3 bacterial including urinary tract infection, pneumonia and bacteremia; 1 viral infection by Chikungunya virus and 1 fungal by histoplasma capsulatum). sCD14 was elevated in the infected SLE patients (median: 1005 pg/ml–R: 533–1415) vs patients with lupus flare (median: 431.5 pg/ml–R: 369–579) (p = 0.04).

Conclusions: High values of sCD14 levels seem to be useful to differentiate infections from activity in SLE patients with SIRS. More patients and further analysis are necessary to define the clinical use of this biomarker.

References:


**AB0499**

**SYMPTOMS IN PRIMARY SJÖGREN’S SYNDROME**

I. Posso-Osorio1, A. Echeverry1, D. Aguirre-Valencia1, G. Castaño2, G. Tobón1.

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Background: Differentiation of Systemic Lupus Erythematosus (SLE) activity and infection in a febrile SLE patient become difficult, since initial clinical presentation may be similar. Several biological markers (including procalcitonin and CRP) have been evaluated, with discordant results. Soluble CD14 (sCD14), also called receptor for lipopolysaccharide (LPS)-binding protein (LPS-LBP) complexes, CD14 could activate a series of signal transduction pathways and inflammatory cascades, and lead to systemic inflammatory responses.

Objectives: To evaluate the utility of sCD14 as a novel biomarker to discriminate infection vs. activity in SLE patients admitted with systemic inflammatory response syndrome (SIRS).

Methods: We included 11 patients with SLE (ACR criteria 1997) and SIRS (International conference 2001) admitted to the ER and/or ICU. The measurement of sCD14 in plasma by enzymatic immunoassay of chemiluminescence in vitro was performed to differentiate active SLE vs. infection. Infection was considered if a positive culture/PCR was obtained. Mann-Whitney test was used to evaluate the association of variables with infection.

Results: All patients were female; mean age 37.9 years. An infectious disease was confirmed in 5 cases (3 bacterial including urinary tract infection, pneumonia and bacteremia; 1 viral infection by Chikungunya virus and 1 fungal by histoplasma capsulatum). sCD14 was elevated in the infected SLE patients (median: 1005 pg/ml–R: 533–1415) vs patients with lupus flare (median: 431.5 pg/ml–R: 369–579) (p = 0.04).

Conclusions: High values of sCD14 levels seem to be useful to differentiate infections from activity in SLE patients with SIRS. More patients and further analysis are necessary to define the clinical use of this biomarker.

References:


**AB0499**

**TOTAL BODY WATER AND ITS CORRELATION WITH SICCA SYMPTOMS IN PRIMARY SJÖGREN’S SYNDROME**


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Background: Patients with primary Sjögren’s syndrome (PSS) suffer from severe alterations in both the quality and quantity of saliva and tears. Body water represents around 50–55% of the body weight. Tears contain 98% of water and saliva 99.5%.

Objectives: To evaluate the percentage of total body water (TBW) among patients with PSS and to assess its correlation with sicca symptoms.

Methods: We included 85 patients with PSS and 85 historical non diabetic controls and to assess its correlation with sicca symptoms.

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TBW negatively correlated with age (ρ=−0.25, p<0.02), disease duration (ρ=−0.30, p<0.005), BMI (ρ=−0.78, p<0.001) and the ocular component of the ESSPRI (ρ=−0.28, p<0.01), but not with the NSWSF or the ESSPRI oral component. When we compared the patients in the 25% percentile (group with the lowest % of water) vs. the remaining patients, the former group was older (56.8±6.1 vs. 54±14.2, p=0.02), with longer disease duration (12.4±5.9 vs. 10.8±7.12, p<0.03), lower scores at the Schirmer test (1 (range 0–8) vs. 2 (range 0–9), p=0.01), higher BMI (31.1±15.1 vs. 23.7±2.9, p<0.001) as well as with higher ESSPRI ocular domain scores (8.3±1.4 vs. 6.7±2.5, p<0.007). With the linear regression analysis, the variables that remained associated with the TBW were disease duration (p=0.002, p=0.005), BMI (p=0.057, p=0.001) and the ocular domain of the ESSPRI (p=0.015, p<0.001).

Conclusions: Patients with PSS had similar TBW percentage than controls. However among patients with PSS, the TBW had a negative correlation with the involvement of ocular symptoms independently of disease duration, age and BMI.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2388

AB0500 TOLERABILITY, EFFICACY AND IMMUNOGENICITY OF 23-VALENT PNEUMOCOCCAL VACCINE IN SLE PATIENTS


Background: Consequent infections turn out to be the second leading cause of death in systemic lupus erythematosus (SLE) pts after SLE se. Immunization of SLE pts with pneumococcal vaccine is an important prophylactic approach to prevent severe lower respiratory tract (LRT) infections in SLE pts.

Objectives: To study the tolerability of 23-valent pneumococcal vaccine for immunization of patients with SLE.

Methods: The study included 30 SLE pts, 27 females, 3 males, aged 19 - 62 y. Duration of follow up (FUP) was 12 months in 24 pts, and 7–10 months – in 6 pts. High disease activity at the time of immunization was documented in 1 patient, low activity – in 20 pts, moderate – in 4 pts, and remission – in 5. 29 pts were treated with glucocorticosteroids (GCs), mycophenolate mofetil, and rituximab, no GCs. Among them 7 pts were treated with GCs, mycophenolate mofetil, and rituximab, no GCs. Among them 7 pts were treated with glucocorticosteroids (GCs), mycophenolate mofetil, and rituximab, no GCs. Among them 7 pts.

Results: To study the relevance of 23-valent pneumococcal vaccine for immunization of patients with SLE.

Methods: The study included 30 SLE pts, 27 females, 3 males, aged 19 - 62 y. Duration of follow up (FUP) was 12 months in 24 pts, and 7–10 months – in 6 pts. High disease activity at the time of immunization was documented in 1 patient, low activity – in 20 pts, moderate – in 4 pts, and remission – in 5. 29 pts were treated with glucocorticosteroids (GCs), 23 – with hydroxychloroquine, 14 pts – with cytostatic (CS) agents. Twelve pts were on biological disease-modifying antirheumatic drugs (bDMARDs). One dose (0.5 ml) of 23-valent polysaccharide vaccine was administered subcutaneously. The duration of FUP was 7–12 months. Control visits were scheduled as follows: at baseline (Visit 1), at 1st, 3rd, and 12th months (Visit 4) after immunization. Standard clinical examination and lab tests, including blood immunology, were performed at each visit. Vaccine immunogenicity was evaluated based on the level of serum antibodies (AT) to Streptococcus pneumoniae capsular polysaccharide (VaccZymeTM PCP Ig 2 panels (The Binding Site Ltd, Birmingham, UK)) – 4 times during year.

Results: Non-post-inmunization complications were seen in 11 (36.7%) pts, local reactions of varying intensity lasting from 2 to 7 days were documented in 18 (60%) pts. One patient (3.3%) developed the local type III hypersensitivity reaction known as Arthus phenomenon. All symptoms subsided within 7 days after the whole FUP.

Conclusions: Obtained results are indicative of good tolerability, safety and immunogenicity of 23-valent pneumococcal vaccine in SLE pts. Further studies are necessary for more comprehensive evaluation of vaccine clinical efficacy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2347

AB0501 THE ASSOCIATION BETWEEN GLUCOCORTICOIDS AND DAMAGE ACCRUAL IN PATIENTS WITH SLE USING GLUCOCORTICOID FOR LONG-TERM

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Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterized by a relapsing-remitting course. Long-term prognosis of SLE patients remains poor [1]. Due to the effect of potent anti-inflammatory and immunosuppressive, glucocorticoids (GCs) remain the cornerstone of SLE treatment. However, GCs produce several adverse reactions, most are time and dose dependent, limiting their clinical usefulness. Increased longevity with prolonged exposure to GCs and inflammatory insults might contribute to organ damage accrual, which retards further improvement of survival in these patients. The objective of this study is to evaluate organ damage caused by SLE has been considered an important part of the assessment of prognosis. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) is a validated instrument designed to measure irreversible damage resulting from SLE disease activity and its treatment. The study of damage accrual in patients with SLE caused by the long-term treatment of GCs is still not clear. In a large SLE cohort, followed prospectively, we determined to investigate the association between damage accrual with GCs, both cumulative prednisone dose and high-dose prednisone. The results of our study could shed more light on the risk/benefit ratio of GCs in long-term maintenance treatment with SLE patients.

Objectives: To evaluate the association between long-term glucocorticoids use and damage accrual in patients with systemic lupus erythematosus.

Methods: Medical records of 535 SLE patients from Department of Rheumatology and Immunology of Anhui Provincial Hospital were retrospectively reviewed. Exclusion criteria: (1) patients with missing or incomplete medical records; (2) patients with inadequate medical data for SDI calculation; (3) patients without previous treatment with corticosteroids; (4) patients with active SLE. A total of 192 patients (35.9%) had been treated with high dose of prednisone. In addition, 86.9% of patients had been treated with hydroxychloroquine. The highest organ damage came from musculoskeletal (n=79, 14.8%), followed by skin damage (n=35, 6.5%) and renal (n=28, 5.2%). Ninety patients were diagnosed with hypertension. Cumulative prednisone dose was associated with osteoporosis, osteonecrosis and hypertension; exposure to high-dose prednisone was associated with osteonecrosis, lupus nephritis and hypertension.

Conclusions: Long-term taking prednisone predicted damage accrual. The most common damage was osteoporosis, osteonecrosis and hypertension.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3931

AB0502 STRONG REDUCTION OF ANTI-MÜLLERIAN HORMONE IN SYSTEMIC LUPUS ERYTHEMATOSUS WOMAN OF REPRODUCTIVE AGE

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Background: Systemic lupus erythematosus (SLE) is a clinically autoimmune disease characterized by production of autoantibodies and immune complex deposition. That induces multiple organ damages such as nephritis, pneumonitis and central nervous system (CNS) lupus et al. Moreover, SLE which mainly occurs in reproductive woman could threaten ovarian function. In recent years, ovarian reserve dysfunction in SLE are attracting increasing attentions. Especially cyclophosphamide (CYC) therapy was already well known as a higher risk to ovarian reserve dysfunction in SLE patients. In addition, 86.9% of patients had been treated with hydroxychloroquine. The highest organ damage came from musculoskeletal (n=79, 14.8%), followed by skin damage (n=35, 6.5%) and renal (n=28, 5.2%). Ninety patients were diagnosed with hypertension. Cumulative prednisone dose was associated with osteoporosis, osteonecrosis and hypertension; exposure to high-dose prednisone was associated with osteonecrosis, lupus nephritis and hypertension.

Objectives: To study the relationship between anti-Müllerian hormone (AMH) and damage accrual in systemic lupus erythematosus (SLE) women of reproductive age.

Methods: SLE women during reproductive ages 18–40 years were recruited compared with age-matched healthy controls (HC). AMH Levels and its relationship to clinical parameters and disease activity were investigated.
Background: Pregnancy outcome is one of the major concerns to manage systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) since they often affect women in reproductive ages. However, the predictive factors of poor pregnancy outcome and disease flare during pregnancy have not fully investigated.

Objectives: To elucidate the factors affecting the pregnancy outcome in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

Methods: Patients with SLE and RA in our university pediatric cohort 2012 and 2016 who experienced pregnancy were retrospectively reviewed. Medical information was collected from their chart.

Results: Thirty six pregnancies in 26 SLE patients and 26 pregnancies in 21 RA patients were identified. Among SLE pregnancies, the mean age, disease duration and prednisolone dose were 32.7±4.6, 8.9±7.7 years and 5.6±4.1 mg/day, respectively. The disease activity was well controlled (the mean SLEDAI, 2.4±2.1). Live birth pregnancies were 31 (86.1%) and fetal loss occurred in 5 pregnancies (3 spontaneous abortions, 1 ectopic gestation and 1 hydatidiform mole). The mean dose of prednisolone was significantly lower in the pregnancies with live birth than those with fetal loss (4.9±3.4 vs 11.3±3.3mg/day, p=0.02), while proteinuria, SLEDAI, history of lupus nephritis, positivity of antiphospholipid antibodies and anti-SSA/ Ro antibodies were not significantly different between the two groups. Maternal lupus flare occurred in 8 (16.7%) during pregnancy or after the delivery and was significantly associated with proteinuria at the time of conception (p=0.02). Low body birth occurred in 9 (29.0%) and was also significantly associated with proteinuria at the time of conception (p=0.002). Among RA patients, the mean age and disease duration were 33.5±5.6 and 9.9±7.4 years. The mean DAS28-ESR, CDAI and HAQ were 2.18±0.88, 3.07±4.10 and 0.30±0.50, respectively and 14 achieved DAS28-ESR remission (≤2.6). Seven (26.9%) discontinued biological agents before conception while 8 (34.8%) continued to use biological agents. Although 5 (19.2%) experienced the disease flare during pregnancy, all 26 pregnancies were live birth. The patients who discontinued biological agents more frequently experienced the disease flare than those who continued, during pregnancy or postpartum within 1 year after delivery (85.7% vs 25%, p=0.04).

Conclusions: High live birth rates were observed in both SLE and RA pregnancies on the condition of well-controlled disease activity. In SLE pregnancies, less prednisolone dose at the time of conception may be associated with live birth. SLE pregnancies with proteinuria and RA pregnancies with discontinuation of biological agents are associated with disease flare and should be cautiously monitored.

References:

DOI: 10.1136/annrheumdis-2017-eular.5174
AB0505

DOES VITAMIN D DEFICIENCY CONTRIBUTE TO COGNITIVE Dysfunction in Patients with Systemic Lupus Erythematosus?

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Background: Neurocognitive impairment is one of the most common SLE manifestations. However, its pathophysiology remains poorly understood [1]. Vitamin D deficiency is a potential risk factor for cognitive impairment [2,3].

Objectives: Our aim is to evaluate the relationship between 25(OH)D3 level and cognitive performance in patients with SLE.

Methods: Thirty Egyptian patients diagnosed as systemic lupus erythematosus and their age and sex matched controls were subjected to a battery of neuropsychological evaluation by California Verbal Learning Test (CVLT-II), Controlled Oral Word Association Test (COWAT) and Trail making test and evaluation of depression by using Beck Depression Inventory (BDI). Serum level of 25(OH)D3 was measured in cases and controls.

Results: Patients with SLE had a worse performance than controls in verbal memory total recall, executive function and phonemic verbal fluency as there was a statistically significant difference in CVLT-II total recall, Trail making test and phonemic-COWAT respectively. There was no significant difference between the patients and controls in Beck Depression Inventory (BDI). There was a significant positive correlation between the vitamin D level and executive function assessed by trail making test (r =0.399, p=0.03).

Conclusions: Vitamin D deficiency in patients with SLE could have a significant impact on their cognitive performance.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5713

AB0507

COBALAMIN (VITAMIN B12) STATUS IN PATIENTS WITH ANTI PHOSPHOLIPID SYNDROME (APS), ITS ASSOCIATION WITH ATHEROSCLEROTIC VASCULAR LESIONS

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Background: Cobalamin (vitamin B12) insufficiency is associated with the development of many diseases. It is known that the growth of clinical and subclinical manifestations of atherosclerotic vascular lesions are often associated with low cobalamin level. Cobalamin status is unknown in patients with antiphospholipid syndrome (APS). There are no data about the role of folate in the development of atherosclerotic vascular lesions in patients with APS.

Objectives: To evaluate vitamin B12 status in patients with APS and to explore its relationship with atherosclerotic vascular lesion.

Methods: We observed 82 patients with APS and 37 healthy individuals. Content of cobalamin (vitamin B12) in serum were determined by immunochromatographic detection (ECLA). Cobalamin level above 200 pg/ml was considered as normal within 200–300 pg/ml - both extremely low, below 200 pg/ml - insufficiency. All patients were underwent detection of endothelial dysfunction - dilatation of brachial artery endothelium, investigation of “intima-media” thickness of common carotid artery (IMT) and the presence of atherosclerotic plaques (AP).

Results: In patients with APS we recorded a significant reduction of cobalamin in the serum (351±14.3 pg/ml (95% CI: 148–562 pg/ml) compared to control group (445±18.1 pg/ml (95% CI: 272–622 pg/ml). Indicators of cobalamin status in patients with secondary APS were significantly worse than those with primary APS. Thus, in patients with secondary APS cobalamin content was on 28.7% lower (95% CI: 140–559 pg/ml) than in the control group. In patients with primary APS cobalamin content was on 13.0% lower (95% CI: 202–586 pg/ml) than in controls, but 18.7% higher than in patients with secondary APS. Cobalamin deficiency (vitamin B12) insufficiency is associated with significant thickening of the walls of the common carotid artery. Thus, in patients with cobalamin deficiency IMT was on 17% higher than that in patients with optimal levels of the vitamin. Cobalamin deficiency is also associated with endothelial dysfunction. Thus, in patients with vitamin deficiency dilatation of brachial artery was significantly, by 48.6% less than in people with normal vitamin B12 status. The share of people with the presence of atherosclerotic plaques, transient ischemic attack (TIA), stroke, myocardial infarction (MI) and angiina in patients with cobalamin deficiency was also higher.

Conclusions: Thus, in patients with APS low cobalamin status is associated with subclinical manifestations of atherosclerotic vascular lesions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6549

AB0506

PREGNANCY OUTCOMES IN WOMEN WITH RHEUMATIC DISEASES: A SINGLE CENTER-STUDY


Background: Systemic Lupus Erythematosus (SLE), Antiphospholipid Syndrome (APS) and Thrombophilia are associated with considerable pregnancy-related morbidity. Multidisciplinary teams allows the application of an experienced protocol to monitor and treat them during pregnancy in order to reduce adverse pregnancy outcomes and this way improve the prognosis of the pregnancy.

Objectives: To investigate pregnancy outcomes in women with rheumatic diseases and thrombophilia from a Spanish cohort.

Methods: A population of 93 patients diagnosed with SLE, APS and Thrombophilia attended in a specialized multidisciplinary unit of Rheumatic Diseases and pregnancy from the Complejo Hospitalario Universitario de Granada, Spain from January 2012 to December 2016. The following variables were collected: age, presence of antiphospholipid antibodies and anti Ro, thrombotic episodes and prior abortions, treatment during pregnancy, obstetric outcomes births/abortion and pregnancy length. The statistical analysis was done using the McNemar Test.

Results: 93 pregnant women were included in the study. 26 were diagnosed with SLE, 32 with APS and 35 with Thrombophilia (mostly, Heterozygotes for MTHFR gene). 80% of them were younger than 35 years and 52.7% were from the reproductive age. 66.7% had one or more prior abortions, meaning a total record of 159 abortions and an average of 1.7±1.76 abortions per patient. The treatment received by the patients is specified in Table 1. 9 patients (3 APS and 6 thrombophilia) received a treatment with intravenous gammaglobulin with doses of 400 mg/kg, apart from Low-Molecular-Weight Heparin (LMWH) and Acetylsalicylic Acid (ASA), two days in a row at the beginning and then every three weeks during the whole pregnancy. 90 (96.8%) pregnancies were developed. 6 of them were preterm pregnancies and 84 were term pregnancies. Only 3 abortions (3.2%) occurred in the patients monitored. In the case of the number of abortions was statistically significant (p=0.001). Regarding those 3 registered abortions, 2 were patients diagnosed with SLE, with no record of previous abortions and they occurred during the second trimester of pregnancy. 1 was diagnosed with APS and she had record of 2 previous abortions and occurred during the first trimester of pregnancy. Those patients who received treatment with gammaglobulin iv showed an improvement of 4.8±1.85 previous abortions per patient and all had a term delivery (100%).

Table 1. The treatment received by the patients

<table>
<thead>
<tr>
<th>SLE (n=26)</th>
<th>APS (n=32)</th>
<th>Thrombophilia (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated with LMWH, n*</td>
<td>2</td>
<td>23</td>
</tr>
<tr>
<td>Patients treated with ASA, n*</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Patients treated with LMWH + ASA, n*</td>
<td>5</td>
<td>29</td>
</tr>
<tr>
<td>Patients without prophylactic treatment, n</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: Our results demonstrate a decrease in the number of abortions and a larger number of term pregnancies since the inclusion of patients with high risk pregnancies in our unit. Prophylactic treatment is effective for the prevention of abortions, reaching higher rate live birth pregnancies. The multidisciplinary evaluation is essential to prevent complications in women diagnosed with rheumatic diseases with high obstetric risk.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6549

Scientific Abstracts
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3006

AB0508
EFFECT OF ALCOHOL CONSUMPTION AND SMOKING ON NEUROPSYCHIATRIC MANIFESTATIONS AND DISEASE ACTIVITY IN POLISH COHORT OF SYSTEMIC LUPUS ERTHYMATEOUSOS

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Objectives: We assessed correlations of smoking habits and alcohol consumption with disease activity or damage in patients with systemic lupus erythematosus (SLE).

Methods: A total of 505 patients with SLE were enrolled in the KORean lupus Network (KORNET) SLE registry from January 2014 to January 2016. Disease activity and organ damage were measured by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index, respectively. Multivariate logistic regression analysis was used to analyze associations with cutaneous lesions.

Results: There are no differences in SLEDAI-2K and SLICC/ACR damage indexes according to either smoking status or alcohol consumption. More frequent cutaneous damage was observed in current alcohol drinkers compared to non-current alcohol drinkers (p=0.020). Cutaneous involvement was associated with alcohol consumption [Odds ratio (OR) 4.048, 95% confidence interval (CI) 1.251 – 13.102, p=0.020]. Both low (<5 glasses/week) and high (>6 glasses/week) amounts of alcohol consumption had a significant impact on cutaneous damage compared to the absence of current alcohol consumption (p=0.033 and p=0.027, respectively). Pairwise comparison of alcohol consumption and smoking status with cutaneous damage showed that only alcohol consumption was significantly associated with the presence of cutaneous damage, compared to non-current alcohol consumption and non-current smoking (OR 3.513, 95% CI 1.190 – 10.920, p=0.030).

Conclusions: Current alcohol consumption, but not smoking, might influence the development of cutaneous damage in patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3070

AB0509
IDENTIFICATION OF NOVEL BIOMARKERS ASSOCIATED WITH DISEASE ACTIVITY OF PRIMARY SJÖGREN’S SYNDROME AND CLINICAL RESPONSE TO VAY736

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Background: Overexpression of B cell activating factor (BAFF) contributes to the pathogenesis of primary Sjögren’s syndrome (pSS) [1]. Treatment of pSS patients with VAY736, an anti-human BAFF receptor mAb, appears promising and was associated with a positive therapeutic effect [2]. Given the complexity and heterogeneity of pSS, there is a need to further identify molecular mechanisms involved in pSS and to propose new biomarkers for diagnostic and monitoring purposes.

Objectives: To address this question, we assessed a panel of biomarkers in 27 patients from a clinical trial and tested their associations with pSS activity and treatment response.

Methods: This study comprised 27 pSS patients treated with a single intravenous dose of VAY736 at 10 mg/kg (n=12), 3 mg/kg (n=6), or placebo (n=9). The disease activity scores included EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI) and Patient Reported Index (ESSPRI), patient’s and physician’s inflammation, and damage indexes according to either smoking status or alcohol consumption. More frequent cutaneous damage was observed in current alcohol drinkers compared to non-current alcohol drinkers (p=0.020). Cutaneous involvement was associated with alcohol consumption [Odds ratio (OR) 4.048, 95% confidence interval (CI) 1.251 – 13.102, p=0.020]. Both low (<5 glasses/week) and high (>6 glasses/week) amounts of alcohol consumption had a significant impact on cutaneous damage compared to the absence of current alcohol consumption (p=0.033 and p=0.027, respectively). Pairwise comparison of alcohol consumption and smoking status with cutaneous damage showed that only alcohol consumption was significantly associated with the presence of cutaneous damage, compared to non-current alcohol consumption and non-current smoking (OR 3.513, 95% CI 1.190 – 10.920, p=0.030).

Conclusions: Current alcohol consumption, but not smoking, might influence the development of cutaneous damage in patients with SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3070

AB0510
NEUROPSYCHIATRIC MANIFESTATIONS AND DISEASE ACTIVITY IN POLISH COHORT OF SYSTEMIC LUPUS ERTHYMATEOUSOS PATIENTS

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Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) is defined as a wide range of neurological and psychiatric symptoms due to inflammation and ischemic processes. It is difficult to recognize primary NPSLE because of multiple central and peripheral symptoms.

Objectives: The aim of the study was to identify and classified the group of NPSLE patients with evaluation of disease activity.

Methods: We observed chronic neuropsychiatric (NP) manifestations in the cohort of 128 Polish patients with SLE. All patients with suspicion of NP symptoms had neuropsychological and imaging examinations. Symptoms of NPSLE were observed in 38 (30%) patients (34 female and 4 male) with average age 38±6 years (range 18-61 yrs), average disease duration 6.6±5.6 years (range 1.0-18.0 yrs). Patients were treated with oral and pulse glucocorticoids (GC) and 89% of them standard immunosuppressive drugs (CYC, MMF, AZA,MTX, CsA). As a background therapy 82% of these patients were on chloroquine or hydroxychloroquine (CQ/HQ). All patients were assessed according to Systemic Lupus Erythematosus Disease Activity Index by SLEDAI (version 2000), Physical Global Assessment (PGA) and damage index (SDI).

Results: Central and peripheral NPSLE symptoms were recognized and categorized (Tab 1). All NPSLE patients had symptoms from central nervous system, but only 16% (n=4) of them had peripheral lupus manifestations. Mean SLEDAI score at NP event was very high 29±6.6, but mean SLEDAI score without NP symptoms was 15±8.3 and was connected with musculoskeletal, mucocutaneous, renal and hematological domains respectively n=29, 76%; n=23, 60%; n=11, 29%; n=8, 21%. Low disease activity was estimated at 3% of patients examined Most of patients (n=37, 97%) had moderate or high disease activity regardless of NP symptoms. In our study group lupus patients during NPSLE symptoms were immunologically active with increased anti-dsDNA antibodies (n=30, 78%) and/or lower complements C3 and/or C4 levels (n=21, 55%).

Conclusions: In Polish lupus cohort we observed more frequently lupus-related primary neuropsychiatric symptoms from central nervous system, especially cognitive dysfunctions, mood disorders, cerebrovascular events. Clinical activity of NPSLE patients was rather high and definitely most of patients were immunologically active despite aggressive immunosuppressive treatment and with standard background therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4265

AB0511
VITAMIN D: POTENTIAL ROLE IN ANTIPHOSPHOLIPID SYNDROME

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Background: Vitamin D due to its immunoregulatory properties, has been implicated in the pathogenesis of autoimmune diseases, such as antiphospholipid syndrome (APS).

Objectives: A) To determine vitamin D levels in patients with primary APS and to compare them with patients with positive antiphospholipid antibodies (aPL), not fulfilling clinical criteria for APS, and with healthy controls. B) To analyze the association of the vitamin D levels with both the clinical manifestations and the immunological profile of patients with primary APS.

Methods: We conducted a retrospective study including patients attended at the rheumatology clinic from a tertiary facility in Northern Spain. We included 74
patients with primary APS, 54 patients with positive aPL serology not meeting clinical criteria for APS and 326 healthy controls adjusted by the month of vitamin D analysis. We considered 30 ng/ml and 10 ng/ml as the thresholds for vitamin D insufficiency and deficiency, respectively.

Results: Median levels of vitamin D were similar in the three groups; (21 range 5–60) in primary APS, 25 (4–50) in the aPL-positive group, and 21 (4–100) in controls. Overall, 53.9% of measurements were performed during the sunny season (April to September). Ten percent of patients with primary APS were males, versus 16% in the aPL serology group and 26% among healthy controls (p=0.007). Mean age was 46±15 in primary APS, 49±17 in the aPL-positive group and 53±10 in the controls (p=0.001). Regarding vitamin D insufficiency, 82% of APS patients had levels of vitamin D (<30 ng/ml) versus 70% and 72% of patients with aPL serology and controls, respectively (p=0.168). When analyzing the prevalence of vitamin D deficiency (<10 ng/ml), we found significant differences across the three groups: 62% in patients with primary APS, 11.1% in patients with positive serology and only 4.9% in healthy controls (p=0.002). There was no significant association between insufficient levels of vitamin D and the presence of thrombotic or obstetric events. Nevertheless, we found a trend for the presence of more thrombotic events in patients with vitamin D deficiency (p=0.097). Regarding the immunological profile, we found no association between vitamin D and either the number of positive antibodies or their serological evolution. However, we found an association between insufficient levels of vitamin D and the presence of lupus anticoagulant (54.7% vs 18.2%, p=0.047).

Conclusions: More than 80% of patients with primary APS have insufficient levels of vitamin D and they have very low levels of vitamin D. Primary APS patients show a higher frequency of vitamin D deficiency than healthy controls. Patients with vitamin D insufficiency have more commonly positive lupus anticoagulant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5129

AB0512 EPIDEMIOLOGICAL, CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF ANTIPHOSPHOLIPID SYNDROME: STUDY OF 170 PATIENTS


Background: Antiphospholipid syndrome (APS) is an autoimmune disease defined by the presence of antiphospholipid antibodies (aPL) and thrombosis and/or pregnancy morbidity. Although thrombotic and obstetric APS are considered the same disorder, there are pathogenetic and clinical differences between them.

Objectives: To describe the epidemiological, clinical and immunological characteristics of a cohort of APS patients from a defined population and to study the differences between thrombotic, obstetric and mixed APS.

Methods: Retrospective study including patients attending the rheumatology and the obstetric clinics of a tertiary facility in Northern Spain. All patients met APS classification criteria.

Results: We included 184 patients with thrombotic APS, 76 with obstetric APS and 10 with mixed APS. Main demographical characteristics are showed in table. There were differences in the age of discovery a positive serology (46±15 in thrombotic APS, 36±8 yr in obstetric, and 36±14 in mixed APS). Moreover, the prevalence of systemic lupus erythematosus (SLE) was higher in patients with thrombotic and mixed APS (26% and 30% vs 5% in obstetric APS, p=0.001). Anticardiolipin antibodies were overall, the most frequently positive. Lupus anticoagulant was significantly more common in patients with thrombotic and mixed APS (70% and 71% vs 30% in obstetric APS, p=0.002). We found no differences in the load of antibodies between the three groups. Regarding traditional cardiovascular risk factors (CVRF), tobacco use was the most common, followed by hypertension and dyslipidemia. The last two factors were more frequent in patients with thrombotic and mixed APS than in those with obstetric APS (p<0.001). As expected, treatment with heparin was more frequent in obstetric and mixed APS, while oral anticoagulants were more frequently used in thrombotic APS. Antimalarial drugs were less frequently used in obstetric APS (17% vs 37% and 30%, p=0.020), probably due to a lower prevalence of lupus in this group.

Conclusions: In our cohort, patients with thrombotic or mixed APS have a higher frequency of SLE than patients with obstetric APS. Positivity for lupus anticoagulants was more commonly observed in thrombotic APS. Regarding traditional CVRF, hypertension and dyslipidemia are more common in patients with thrombotic or mixed APS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4338

AB0513 FATigue IN CHINESE PATIENTS WITH PRIMary SJÖgren’s SYNDROME: A CROSS sectional STUDY

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Background: Primary Sjögren’s syndrome (pSS) is the second most common systemic autoimmune disease, with a female-male ratio of 9:1, and characterized by sicca symptoms of the eyes and mouth, including joint pains and multi-system involvement. pSS affects patients’ health-related quality of life (QoL), mental status and relationships with family. In pSS patients, symptoms such as fatigue, depression, and anxiety, as well as decreased quality of life, general well-being and loss of well-being are commonly reported. Among them, fatigue is the most common problem that includes physical and mental fatigue, it can be as disabling as pain, which is difficult to manage and has a notable impact on QoL. Fatigue is a tiredness which may be mental, physical, or both, and that results in an inability to function at normal performance levels. However, the underlying pathophysiological mechanisms of fatigue remain unclear. A number of studies have reported the association of fatigue with Primary Sjögren’s syndrome (pSS), whereas, because of the small sample size of pSS patients, we still lack large sample studies to find the relationship between pSS and fatigue.

Objectives: To investigate the relationship of fatigue severity to other clinical features in primary Sjögren’s syndrome (pSS) and to identify factors contributing to the physical and mental aspects of fatigue in Chinese patients.

Methods: Thirty-seven consecutive patients with pSS according to the American-European Consensus group (AEGG) criteria were included. Demographic, clinical and biological characteristics for all patients were collected. The Fatigue Severity Scale (FSS), Profile of Fatigue (ProF), Visual analogue scale, Hospital Anxiety and Depression Scale (HADS), OHIP-14 Scale, MDADI Scale and PSQI Scale were adopted to assess fatigue, depression, anxiety, xerostomia, xerophthalmia and sleep disturbances. Associations with fatigue were compared using multivariate regression.

Results: 94% of our patients were women. The mean age of patients was 51.13±13.23 years, and the mean disease duration was 4.12±4.49 years. The mean oral dryness was 51.13±13.23 years, and the mean oral dryness was 33.56±26.3. Anticoagulant therapy, defined as the FSS score >4, was present in 64% of the patients. Dry symptoms, low educational level, Pain and depression had a negative impact on fatigue scores. The regression models explained that Pain and depression were the strongest predictors of fatigue according to the FSS.

Conclusions: Fatigue is a tiredness which may be mental, physical, or both, and that results in an inability to function at normal performance levels. However, the underlying pathophysiological mechanisms of fatigue remain unclear. From our study, we found that psychosocial variables are determinants of fatigue, and fatigue is associated with depression, but depression is not the primary cause of fatigue in primary SS. Therefore, the investigation of the pathophysiological correlates of physical and mental aspects of fatigue is needed to guide the development of more effective interventions.

Acknowledgements: This study was supported by National Natural Science Foundation of China (81401124); the Collaborative Innovation Program of Affiliated Hospital of Nantong University; College graduate research and innovation of the Foundation of China (81401124);the Collaborative Innovation Program of Affiliated Hospital of Nantong University, Nantong, China

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3076

AB0514 THE RELATIONSHIP BETWEEN SERUM LEVEL OF C-TERMINAL TEOLOPEPTIDE OF TYPE I COLLAGEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: EPIDEMIOLOGICAL STUDY

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Background: It is well known, that the incidence of osteoporosis in patients with systemic lupus erythematosus (SLE) is higher compared to the population level. Its severity in patients with SLE is associated with a number of factors: female gender, disease activity, damage index, glucocorticoid therapy etc. One of metabolic factors indicating the reducing bone mineral density (BMD) is the level
of C-terminal telopeptide of type I collagen (CTX). Its place in the formation of osteoporosis in SLE patients is poorly understood, as well as its relationship with the course of the disease.

Objectives: The aim of study was to determine serum level of CTX in the SLE patients and its relationship with structural and functional state of bone tissue, considering frequently occurred skin lesions.

Methods: The study involved 58 SLE women (study group) and 29 healthy individuals (control group) representative by age and gender. The mean age of patients was 45.1±1.03 years. For every patient data were recorded on age, body mass index (BMI), chronic SLE damage (SLICC/ACR DI) and disease activity score (SLEDAI), cumulative glucocorticoid dose, serum concentrations of interleukin-6 (IL-6) and C-reactive protein (CRP), bone resorption marker (CTX). Serum concentration of CTX was determined using ELISA test system “Nordic Bioscience Diagnostics A/S”. Changes in BMD of the lumbar spine and proximal hip were determined by Dual-energy X-ray absorptiometry.

Results: It was established, that in patients with SLE serum level of C-terminal telopeptide of type I collagen was 1.23±0.04 ng/ml (higher than 23% compared with the control group), increased CTX practically had no correlation with age, duration of the disease, smoking and BMI. At the same time the serum CTX was associated with chronic SLE damage index (r =0.51), SLEDAI disease activity (r =0.41), concentration of IL-6 (r =0.45) and CRP (r =0.44).

Conclusions: Alterations of bone metabolism were found in 19% female SLE patients in the form of increased serum CTX and closely associated with the severity and activity of the disease, high levels of CRP and IL-6 and did not depend on the age, disease duration, smoking and body mass index.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5770

ABO515 SKIN MANIFESTATIONS AS INDEPENDENT PREDICTORS AND THE INITIAL RISK FACTORS FOR SYSTEMIC ANTIPHOSPHOLIPID EVENTS

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Background: Antiphospholipid syndrome (APS) patients express skin manifestations with the presence of various levels of antiphospholipid antibodies (aPL). Several studies have shown the frequency of dermatological manifestations with APS [1,2,3], including livedo reticularis, cutaneous ulcers, acrocyanosis, and others.

Objectives: Dermatological manifestations can be the initial clue in the diagnosis of this disease.

Methods: Our study includes a total of 508 APS patients; 360 were APS patients (283 female and 77 male, mean age 44.0±12.9 years), 148 had APS associated with SLE/SAPS (133 female and 15 male, mean age 47.7±14.8 years). aPL antibodies included anti-β2GPI, anti-β2GPI, anti-β2GPI, and anti-β2GPI. In all patients we considered data frequently occurred skin lesions.

Results: Our results showed prevalence of skin manifestations in SAPS group of patients regressing to PAPS (Table 1). Patients with skin manifestations overall had higher prevalence of thrombosis (Table 2).

Conclusions: Dermatological manifestations can be very often the initial symptoms of severe manifestations of APS. Our study showed that patients with secondary APS had higher prevalence of skin lesions, and that some aPL types were risk factors for thrombotic manifestations in APS patients.

References:


Acknowledgements: This work was supported by research grant number 175041 for 2011 - 2017, issued by the Ministry of Science of the Republic of Serbia.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.2759

ABO516 INCIDENCE OF CANCER IN A COHORT OF PATIENTS WITH PRIMARY SJÖGREN SYNDROME

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Background: The most severe complication of Sjögren Syndrome is the development of lymphoproliferative processes. Several neoplasia have been associated with the disease, being non-Hodgkin lymphoma the most frequent one.

Objectives: Our objective was to evaluate incidence of cancer in a cohort of patients with primary Sjögren Syndrome.

Methods: A retrospective descriptive study was performed in a university hospital with its own insurance system and captive population. Using electronic medical records and laboratory database we review the entries performed between 01/01/2000 and 12/31/2015. We analyzed those patients of Sjögren Syndrome, complain of dry mouth/eyes, or positive antibodies anti- Ro/SSA and anti-La/SSB.

Among these patients, we included those fulfilling either ACR 2012 or EULAR 2002 Sjögren criteria, or those who were diagnosed as Primary Sjögren Syndrome by the treating rheumatologist even if they did not fulfill criteria.

We then proceeded to register and analyze demographic, clinical and histopathologic information available on their clinical records.

Results: One hundred fifty-seven patients with Primary Sjögren Syndrome were identified. Female accounted for 95.5% of the cohort; mean age at diagnosis was 49.4 years (SD 19). Median follow-up time was 7.7 years (IQR 8). The development rate and type of neoplasia was the following:

- Lymphomas: Three (Two MALT lymphomas of the parotid and one disseminated non-Hodgkin lymphoma), Density of Incidence 260/100,000 person/year (CI 95%: 50 – 750/100,000 person/year)
- Multiple Myeloma: One
- Skin (non-melanoma) neoplasia: Four
- Solid organ Neoplasia: Seven (Four breast cancer, one lung cancer, one uterine cancer, one tongue cancer), Density of Incidence 600/100,000 person/year (CI 95%: 240 – 1240/100,000 person/year)

Univariate analysis showed association between lymphoma and cryoglobulinemia (p=0.01; OR=5.8), low C4 fraction of complement (p=0.01; OR=5.1), anemia (p=0.02; OR=1.96) and leukopenia (p=0.03; OR=1.67).

Conclusions: Development of cancer is a known complication of Primary Sjögren Syndrome. The association between lymphoma and cryoglobulinemia, low C4 fraction of complement, anemia and leukopenia enhances the importance of periodic screening for neoplasms among this subgroup of patients with Primary Sjögren Syndrome.

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.3195

ABO517 PREDICTIVE FACTORS FOR INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: it’s known that infection could complicate the course of systemic lupus erythematosus (SLE) because of the immune status or the long term use of steroids and immunosuppressors.

Objectives: This study was aiming at determining the prevalence of infectious complications during SLE and their predictive factors.

Methods: A retrospective bi-centric analyzes of 289 patients diagnosed as SLE between January 2004 and December 2016 according to the ARA criteria of 1997 was conducted. A descriptive analysis of infectious complications was first made, then a comparative study between patients with (group 1) and without (group 2) infectious complications was performed to detect predictive factors.

Results: Mean age was 84.6±13 years (14–72 years) with a sex ratio F/M=6.
Cardiac involvement and lupus nephritis (LN) were developed in 20% of patients. About 13.75% of patients had neurological manifestations, 26.5% articular complications, 16% vascular involvement and 10% of them developed infected complications. Eight percent of these infections were diagnosed concomitantly with the diagnosis of SLE and 92% of them after the diagnosis of lupus with an interval of at least 52.9% of the patients developed more than 2 episodes of infection. The spectrum of infectious complications was: pulmonary in 33.3%, urinary in 22.2% and cutaneous in 13.9%. Tuberculosis was the most frequent infection 12.5%. Lupus flare complicated the infection in 28.6% of patients with mean SLEDAI score at 10. Comparative study between group 1 and group 2 revealed that LN, corticosteroids and immunosuppressors were associated with a high risk of infection (p=0.002, p=0.017 and p=0.034 respectively). In multivariate analysis only LN was an independent predictive factor (OR=3.5, 95% CI=1.06-12.87, p=0.049).

Conclusion: Infections that complicate the course of SLE with flares presenting in 1/3 of cases. Half of the patients had more than 2 episodes of infection during their follow up. The presence of LN represents a predictive factor of such complication.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3009

AB0518  NEW 2016 ACR/EULAR CLASSIFICATION CRITERIA FOR SJÖGREN'S SYNDROME: USEFULNESS AND APPLICABILITY IN CLINICAL PRACTICE

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Background: The Sjögren syndrome (SS) is an autoimmune disease where the cellular and humoral mechanisms affect the exocrine glands. In 2016, new classification criteria validated by ACR and EULAR were established.

Objectives: To compare the new criteria with those used so far in our hospital, as well as to assess the need for changes in the current diagnostic strategy.

Methods: Retrospective observational study in which 65 patients diagnosed with SS at the Hospital of León were randomly included. We reviewed the diagnostic tests performed and the fulfillment of the different classification criteria developed since 1993. Other variables studied were: sex; age at the time of diagnosis and the months from the onset of symptoms; xerostomia and xerophthalmia; extrav glandular involvement, ESSDAI; immunosuppression; Raynaud; lymphoma development; and analytical alterations.

Results: The mean age at the time of diagnosis was 54.9 years ±14 [23–82], with an average of months from the onset of symptoms to the diagnosis of 10.2±9.5 [0–36]. 90.8% were women. 87.7% presented xerostomia; and 91% showed xerophthalmia, being severe in 43.1%. 64.6% had extrav glandular manifestations; being the most prevalent the joint manifestation (60%) and the cutaneous one (18.4%). Over the past year, 37% developed haematological abnormalities in the form of cytopenias, and 73% biological alterations. At the time of the study, 32.8% presented low activity, 38.5% moderate activity and 9.2% high activity; meanwhile ESSDAI and EULAR higher in almost all included. We reviewed the diagnostic tests performed and the fulfillment of the different classification criteria developed since 1993.

Conclusion: In our study, the mean age at the time of diagnosis was 54.9 years ±14 [23–82], with an average of months from the onset of symptoms to the diagnosis of 10.2±9.5 [0–36]. 90.8% were women. 87.7% presented xerostomia; and 91% showed xerophthalmia, being severe in 43.1%. 64.6% had extrav glandular manifestations; being the most prevalent the joint manifestation (60%) and the cutaneous one (18.4%). Over the past year, 37% developed haematological abnormalities in the form of cytopenias, and 73% biological alterations. At the time of the study, 32.8% presented low activity, 38.5% moderate activity and 9.2% high activity; meanwhile ESSDAI and EULAR higher in almost all included. We reviewed the diagnostic tests performed and the fulfillment of the different classification criteria developed since 1993.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2603

AB0519 LABORATORY ABNORMALITIES IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren’s syndrome (pSS) is a chronic systemic autoimmune disease often accompanied by analytical abnormalities. Altered levels in serum protein concentration, blood cell count and autoantibodies contribute to the broad spectrum of biological manifestations that characterize this disease.

Objectives: The objective of this study is to evaluate the prevalence of laboratory abnormalities in patients with pSS from the SjogrenSER registry.

Methods: We conducted a multicentre transversal study of a cohort of pSS patients fulfilling 2002 European/American criteria, from 33 Spanish rheumatology departments. Every patient was interviewed for data collection and signed an informed consent. Data were also collected by reviewing medical records. Local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians and rates. Chi-square was used to evaluate the statistical associations. A p < 0.05 was considered significant.

Results: Four hundred and thirty-seven patients were included. Fifty-six percent of the patients had hematological involvement; 29% of the patients had dermatological manifestations, 14% had hipocomplementemia. More than half of the patients had abnormalities, more than 35% had leukopenia, 30% had anemia, 25% had lymphopenia, 9% had thrombocytopenia. The median ESR was 25 mm. Age at diagnosis and age at onset of symptoms were significantly lower in patients presenting RF+ vs RF- (48.71 vs 53.73, p < 0.001 and 44.76 vs 49.53, p < 0.001, respectively), decreased C3 vs normal C3 (45.66 vs 51.18, p < 0.004 and 42.2 vs 48.99, p < 0.018, respectively), decreased C4 vs normal C4 (47.02 vs 50.89, p = 0.042, for age at diagnosis) and HGG (47.59 vs 54, p < 0.001, and 43.44 vs 50.16, p < 0.001, respectively). ESR was significantly higher in patients with hematological involvement (35.94 vs 26.24, p < 0.001), RF+ (36.39 vs 22.91, p < 0.001), decreased C3 vs normal C3 (37.8 vs 30.53, p < 0.002) and C4 (38.71 vs 30.42, p < 0.041), HGG (36.21 vs 26.03, p < 0.001) and increased ß2microglobulin (38.80 vs 27.91, p = 0.009). ESSDAI (Eular Sjögren Syndrome Disease Activity Index) was significantly higher in patients with haematological involvement (5.38 vs 3.69, p < 0.001), RF+ (5.40 vs 3.53, p < 0.001) and HGG (5.31 vs 3.93, p < 0.001).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2603

AB0520 THE ROLE OF LEPTIN IN SJÖGREN'S DISEASE

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Background: Sjögren's disease (SD) is a multisystemic disease mostly manifest with sicca symptoms. Lymphocytic infiltration of the glandular and extra glandular organs is the dominant pathologic feature of the disease. Multiple stimulators were accused in the pathogenesis of SD. Leptin, an endogenous peptide, involves in various metabolic processes as well as immune system (1). Increased serum leptin level is observed in patients with autoimmune diseases such as SD, systemic lupus erythematosus and rheumatoid arthritis when compared to healthy controls (2).

Objectives: Even if serum leptin level increases in the patient with SD, there is no clear data about its effect on extraglandular manifestations.

Methods: We studied leptin density in acinar and ductal structures of the salivary glands by immunohistochemistry in patients with SD. The relationship between intensity of lymphocytic infiltration and density of leptin in the salivary gland of SD patients with control group. Furthermore we evaluated the relation between intensity of lymphocytic infiltration and density of leptin in the salivary glands of SD patients.

Results: We applied leptin immunostain to minor salivary glands samples of 24 SD patients, who were fulfilled American College Rheumatology Sjögren’s Disease Classification Criteria (ACR-SDCC) and 19 patients who undergo minor salivary gland biopsy due to clinically on suspicion of SD but not fullfilling the ACR-SDCC and had no lymphocytic focus on biopsy. Herein, leptin density in acinar and ductal structures of the salivary glands were evaluated in both groups.

Moreover,
minor salivary gland samples of SD patients were also assessed for relationship between focus score, disease progression (evaluated with SSDAI) and leptin immunostaining.

**Results:** Demographic features of both group were similar. Furthermore, there were no difference in leptin staining features of both group. Additionally, we found that higher focus score (≥2) was associated with more diffuse leptin staining and higher SSDAI scores related with diffuse acinar staining.

**Figure 1. Total leptin staining in different focus score groups**

<table>
<thead>
<tr>
<th>Focus Score</th>
<th>Total Leptin Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>2 1 3 6</td>
</tr>
<tr>
<td>≥3</td>
<td>9 3 12</td>
</tr>
<tr>
<td>Total</td>
<td>2 10 12 24</td>
</tr>
</tbody>
</table>

\*p<0.02

**Figure 2. Stromal leptin staining in different focus groups**

<table>
<thead>
<tr>
<th>Focus Score</th>
<th>No Staining</th>
<th>Focal</th>
<th>Moderate</th>
<th>Wide</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>1 2 3 4</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>0 1 2 12</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1 12 3 8</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\*p<0.001

**Conclusions:** Different leptin staining features in higher focus score and higher disease activity might indicate the role of leptin especially in more significant disease. Leptin may locally stimulate chemotaxis and activate infiltration of glands with inflammatory cells. We suggested further studies aimed to understand autocrine effect of leptin and evaluate its role in SD pathogenesis.

**References:**
1. Stoifova, A. Leptin and adiponectin: from energy and metabolic dysbalance to inflammation and autoimmunity. Endocrine regulations, 2009, 43.4: 157–168.  

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5407

**AB0521 ANTIPHOSPHOLIPID SYNDROME - ATHEROSCLEROSIS AND CLINICAL-INMUNOLOGICAL CORRELATIONS**

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**Background:** Antiphospholipid syndrome (APS) is an autoimmune, multisystem disease characterized by thrombocytopenia, venous and/or arterial thrombosis, pathological course of pregnancy in women (preeclampsia, eclampsia, miscarriage) and the presence of a heterogeneous group of antibodies - antiphospholipid antibodies. Recent studies show that in the pathogenesis of atherosclerotic process, relevant inflammatory component of the immune response, as well as elements of autoimmunity (autoantibodies and autoantigens autoreactive lymphocytes) may play a role. A number of autoimmune rheumatic diseases, including RA, SLE and APS are characterized by accelerated atherosclerosis and therefore an increased risk of cardiovascular morbidity and mortality.

**Objectives:** The aim of the study was to investigate the incidence of cardiovascular events and atherosclerosis in patients with primary and secondary antiphospholipid syndrome, spaymo healthy subjects and patients with systemic lupus erythematosus without antiphospholipid antibodies.

**Objectives of the study:**
- To compare the damage to aa. Carotid in patients with APS compared to healthy subjects and patients with SLE without antifosfolipidi antibodies.
- To compare Are score in patients with APS compared to healthy individuals without antifosfolipidi antibodies.
- To compare atherosclerosis of aorta in patients with APS compared to healthy subjects and patients with SLE without antifosfolipidi antibodies.
- To compare cutaneous vascular lesions (Raynaud, Livedo reticularis, periungual vasculitis, son palp gangrene, asphyxia, vasculitis lesions) on the limbs and body in patients with aPL spaymo healthy subjects and patients with SLE without antifosfolipidi antibodies.

**Methods:** For the purpose of this study examined 127 patients, 18 men (14%) and 109 women (86%), positive antiphospholipid antibodies. Patients were selected from the Department of Rheumatology, University Hospital “St. Ivan Rilski” – Sofia. All the patients were tested for: ANA, aPL, standard laboratory tests.

**Instrumental methods:**
- Calcium score of a. coronaria sinister, a. anterior descendens sinister, a. circumflexa sinistra, a. coronaria dexter, Aorta, Valva aortae.
- Ultrasonographic examination of aa. Carotid to measure the Intima-media thickness.

**Results:** It was proved strong, statistically significant correlation between aCL antibodies and the presence of plaques in the left common carotid artery (p=0.041). Absent the dependence between the antibody titers and incidence of carotid plaques. The presence of positive aCL antibodies in the group with APS, 33.3% (14) establishes a positive calcium score of coronary aeri, 11.9% (5) plozhitefnite for aorta. Aortic valve Absent deposits. In the control group positive calcium score is when one person (5.88%).

**Conclusions:** We found that patients with antiphospholipid syndrome suffer from early development of atherosclerosis. In the process of atherosclerosis involving inflammatory component of immune response. Atherosclerosis can be viewed as an inflammatory autoimmune disease. It is proved strong, statistically significant correlation between aCL antibodies and the presence of plaques in the left common carotid artery (p=0.041).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6615

**AB0522 CLINICAL FINDINGS AND THEIR RELATIONSHIP WITH THE PROFILE OF ANTIPHOSPHOLIPID ANTIBODIES IN DOMINICAN PATIENTS**

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**Background:** There is an increased risk of thrombotic events and obstetric morbidities in individuals with antiphospholipid antibodies (APAs) compared with the general population. The risk of complications is further increased in those patients who have a rheumatic diseases and antibody positivity.

**Objectives:** The purpose of this study is to determine the clinical findings and their relationship with the profile of antiphospholipid antibodies in patients with rheumatic disease, of the Division of Rheumatology of the Hospital Regional Universitario José M. Cabral y Baez, Dominican Republic.

**Methods:** Patients with 18 years of age and above, with a confirmed rheumatic disease was eligible for enrollment; those with positive titers for APAs, that met the inclusion and exclusion criteria, were included in our study. The institutional review board approved the protocol. This is a transverse study, with retro-prospective data gathering from patients and their medical records. Demographic information at the time of APA measurement and medical information regarding the rheumatic disease and clinical course were collected from the patient’s medical record, with a follow-up of 10 years.

**Results:** 40 patients were included in this study. The male to female ratio was 19:11; mean age was 36±10 years. A large number of patients (13 patients, 32.5%) were asymptomatic for antiphospholipid syndrome (APS) at the time of this study; eight patients (20%) were carriers without defining manifestations. Ten patients (25%) were categorized as vascular APS and five patients (12.5%) as obstetric APS: three patients (7.5%) had vascular and obstetric APS. One patient presented with catastrophic APS. In evaluating such specific profile of antiphospholipid antibodies, aCL was observed that corresponded to the antibody most frequently identified with IgG isotypes (52.5%) and IgM 47.5%. The lupus anticoagulant (LA) corresponded to the second most common (37.5%). The isotypes of the anti-B2GPI-I were identified in less proportion. We report 89 pregnancies during the follow, with 29 abortions and 60 live births, of which 12 were premature and 11 born with intrauterine growth restrictions.

**Conclusions:** The most frequent clinical manifestations were livedo reticularis, vascular thrombosis in lower extremities, Raynaud’s phenomenon, migraine, cerebrovascular disease, thrombocytopenia, leukopenia, and alteration of urine sediment.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4135
AN ANALYSIS OF THE FACTORS INFLUENCING THE BODY IMAGE DISTURBANCE WITH SYSTEMIC LUPUS ERYTHEMATOSUS LIVING IN CHINA

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Background: Systemic Lupus Erythematosus (SLE) is a chronic, autoimmune rheumatic disease that can affect multiple systems/organs in the body and is characterized by relapses and remission, usually affects women in the reproductive age group. SLE may cause inflammation activity and damage in any of the organs, often leading to decreased physical, emotional and social abilities, depression, pain, fatigue, visible or invisible changes in appearance. Recent studies have indicated that body image disturbance (BID) can lead to a variety of cognitive, emotional and behavioral changes. BID will cause the individual having a negative perception of the body, negative emotional experience and the corresponding behavior disorders.

Objectives: To explore the relationship between social and economic status, disease activity, mental state, self-esteem, quality of life and the essential BID with Systemic Lupus Erythematosus Living in China.

Methods: The investigation is from in October 2015 to December 2016 at the Affiliated Hospital of Nantong University. There are 109 cases of hospitalized patients, including 8 cases of male, female 101 cases, mean age is 35.3±12.2. Scale including body image disorder scale (BID), respectively. Body image was assessed using the Body Image Disturbance Questionnaire (BIDQ) with a total of 45 items. The BIDQ includes seven scaled items scored from 0 (not affected) to 8 (extremely affected) pertaining to appearance-related concerns (BIDQ1); mental preoccupation (BIDQ2); emotional distress (BIDQ3); social, occupational, or functional impairment (BIDQ4); social life interference (BIDQ5) and educational, occupa- tional health (BIDQ6); body image (BIDQ7). Systemic lupus erythematosus disease activity index (SLEDAI); the hospital anxiety and Depression Scale (HADS) in systemic lupus erythematosus; disease-specific HRQOL measure for adults with SLE (Lupus QOL), including health (PH), pain (PN), planning (PL), intimate relationship (IR), a burden to others (BV), emotional Health (EH), body image (BI), fatigue (F). Spearman’s coefficient for nonparametric and Pearson’s coefficient for parametric data were computed. Variables that were significant in univariate analysis were included in a multivariate linear regression model. All p-values less than 0.05 were considered statistically significant.

Results: SLE patients were most concerned about their body size (33.38%) and skin (32.23%), 55.34% SLE patients were more concerned about the change of body shape caused by disease. There was significant correlation between BID and disease status, psychological status, and quality of life in patients with SLE. Physical health is correlated with BID1, Pain is correlated with BID1, BID4–7, Planning is correlated with BID2, BID7–7. Intimate relationships is correlated with BID4–7, Burden to others is correlated with BID3–7, Emotional health, fatigue are associated with BID3–7. Anxiety and depression also affect BID, anxiety is an important predictor of BIDQ1, BIDQ3–6, depression is a predictor of BIDQ2, BIDO 3–6.

Conclusions: Patients with Systemic Lupus Erythematosus Living in China are much easier bear with BID, anxiety, depression, less quality of life will lead to BID, in view of the body image perspective, this study will help explore the influence factors of BID in patients with SLE.

Acknowledgements: The study was supported by The Natural Science Foundation of China (81401124).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5284

TRANSLATION AND VALIDATION OF THE FATIGUE SEVERITY SCALE, THE PITTSBURGH SLEEP QUALITY INDEX AND THE MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE INTO THE MALTESE LANGUAGE, IN A COHORT OF MALTESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The Fatigue Severity Scale (FSS), Pittsburgh Sleep Quality Index (PSQI) and Modified Health Assessment Questionnaire (mHAQ) are validated questionnaires that measure fatigue, sleep quality and function respectively. Research in the Maltese population, on systemic lupus erythematosus (SLE) requiring the use of these questionnaires, necessitates their translation and validation into the Maltese language.

Objective: The aim of the study is to translate, validate and perform cross-cultural adaptation of the FSS, PSQI and mHAQ into the Maltese language, according to the recommended methodology.

Methods: The original instruments were translated into Maltese by two translators whose mother language is Maltese. One of the translators had a medical background and was knowledgeable on the concepts being examined in the questionnaires; while the other did not. The two translated versions of the instruments were then compared and the discrepancies were resolved by reaching a consensus on the best Maltese version that reflects the underlying meaning of the original English version. The preliminary Maltese translations were then given to two other translators for back translation into English. English was the native language of these translators and they were totally blind to the original versions. The back translated English versions were then compared to the original English questionnaires and any discrepancies were highlighted. The equivalent statements in the Maltese translations were discussed and changes made as required to reflect the exact wording of the English versions. The Maltese translations were produced and pilot tested in a sample of 20 bilingual SLE patients to evaluate the clarity of the questionnaires. These 20 patients were also asked to fill in the original English version of the FSS, PSQI and mHAQ, seven days after filling in the Maltese versions. Psychometric testing was carried out to assess the reliability of the translation, internal consistency and validity.

Results: Reliability of the translation of the FSS, PSQI and mHAQ into Maltese was analysed by using Kendall’s tau test for statements having an ordinal scale and Pearson’s correlation test for variables having a metric scale. The p value for the statement in the FSS, PSQI and mHAQ was <0.001, which means that the reliability of the translated versions was satisfactory. Internal consistency of the Maltese translations was demonstrated using Cronbach’s alpha. This was calculated to be 0.877 for the FSS, 0.859 for the PSQI, and 0.897 for the mHAQ. Validity of the Maltese translation of the FSS was assessed by its correlation with the visual analogue scale for fatigue using Pearson’s Correlation test. Pearson’s R value was 0.809 and the p value was <0.001 confirming a positive significant correlation.

Conclusions: This study has confirmed the reliability and internal consistency of the translated English versions of the FSS, PSQI and mHAQ and in Maltese. Moreover, a back translation of the FSS has been shown. The Maltese translations can be finalised and used for research purposes.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2201
B1 CD5+ Lymphocytes in Systemic Lupus Erythematosus Patients: Relation to Disease Activity

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Background: B cells are essential players in the pathogenesis of Systemic lupus erythematosus (SLE). Membrane CD5 elevates the threshold of B cell receptor mediated responses, and thus prevents the release of antibodies. So, misguided signalling through CD5 could lead to autoimmunity. Hence, CD5+ B cells were considered to play a paradoxical role in preventing rather than inducing autoimmunity. This challenging view differs from the old interpretation that elevated levels of B1 CD5+ cells in SLE patients represent a direct source of autoantibodies responsible for organ damage.

The clinical implications of this new concept for the role of B1 CD5+ cells in SLE have not been fully addressed yet and there is no consensus agreement about the proportions of B1 CD5+ cells in SLE patients. Moreover, the relation of B1 CD5+ cells to disease activity and organ damage is not sufficiently studied.

Objectives: To assess the expression of B1 CD5+ cells in SLE patients and to evaluate their relationship with disease activity and organ damage.

Methods: We recruited 100 SLE patients and 100 healthy control subjects. Based on SLE disease activity index (SLEDAI), patients were divided into two groups; active SLE (n=50) and inactive SLE (n=50). SLE was active when SLEDAI was ≥4. The expression of (CD5+CD20+) B1 cells was evaluated using flow cytometry. Lymphocytes were gated depending on both side and forward scatter. From the gated lymphocytes, B1a cells were identified double positive cells for CD20 and CD5. Percentage and absolute numbers of CD20+CD5+ (B1a cells) and their mean fluorescence intensity (MFI) were measured. The histogram of CD5 expression was used to assess its expression on CD20 cells (figure 1).

Results: Mean age of patients was 31.3±8.8 years. Females constituted 94% (n=94). Mean disease duration was 5.2±4.8 years. Mean SLEDAI was 10.28±5.16. The proportions of (CD5+CD20+) B1 cells were significantly lower in SLE patients versus controls (5.9±4.4% vs 20.2±4%, p<0.001). Similarly, the absolute numbers of (CD5+CD20+) B1 cells (cell/mm²) were significantly lower in SLE patients versus controls (100.2±103.4 vs 557.6±163.3, p<0.001). The expression of (CD5+CD20+) B1 cells was decreased in active SLE patients (4.5±3.8%) in comparison to inactive patients (7.3±4.7%) (p=0.027). B1 (CD5+CD20+) absolute cell number (cell/mm²) was significantly lower in active SLE patients (71.4±82.9) compared to inactive ones (129.0±115.1) (P=0.047).

MFI of CD5+CD20+ was significantly decreased in SLE patients compared to healthy control (146.9±109 vs 196±48, P=0.033). B1 cells (CD5+CD20+) correlated positively with C3 (r=0.322, p=0.022) and C4 (r=0.307, p=0.030). No correlation was found between (CD5+CD20+) B1 cells and disease duration, autoantibodies or any specific system or organ damage.

Conclusions: Expression of B1 CD5+ cells was significantly decreased in SLE patients. Decreased B1 CD5+ cells expression was associated with higher disease activity. B1 CD5+ cells correlated positively with complement levels. These findings denote that CD5 expression on B cells may play a regulatory role in SLE pathogenesis and decrease occurrence of flares.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3964

AB0526

AB0527

Progranulin and Insulin-Like Growth Factor-2 as Biomarkers for Disease Activity and Pathological Changes in Lupus Nephritis

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease (1), characterized by the production of autoantibodies, and formation of immune complexes due to the polyclonal activation of T and B lymphocytes that result in tissue and organ damage (2). During inflammation, neutrophils and macrophages release serum proteases to cleave progranulin (PGRN) into granulin (GRN), which exert their pro-inflammatory effects that counteract the anti-inflammatory effects of intact PGRN (3). Insulin-like growth factor-2 (IGF-2) binds to insulin-like growth factors (IGFs) with high affinity (4). Although reports suggest that IGFBP-2 is a reliable biomarker of renal deterioration, it is still needed to confirm that it has high sensitivity and specificity in discriminating kidney disease caused by SLE from other origins.

Objectives: The aim of this study was to explore whether PGRN and IGF-2 can be used as useful markers not only for accurate diagnosis of patients with active lupus nephritis (LN) but also for prediction of the disease activity in these patients.

Methods: Twenty-five patients with systemic lupus erythematosus, twenty-five patients with chronic renal failure and twenty-five age- and sex-matched healthy volunteers were enrolled in the study. Routine laboratory investigations and measurement of serum PGRN and IGFBP-2 levels were done.

Results: Our results showed that the mean age of SLE, CRF and control groups 31.12±12.4, 38.7±9.4 and 32.96±13.66 respectively with no significant difference between the three groups. There was female predominance in the three groups. Disease duration was 4.76±4.26 in SLE patients. The mean of SLEDAI score was 15.04±7.54. All renal biopsy results were class 2, 3, and 5 with a percentage of 32%, 24%, and 44% respectively.

Table 1. Levels of PGRN and IGF-2 in SLE, CRF and control groups

<table>
<thead>
<tr>
<th></th>
<th>SLE</th>
<th>CRF</th>
<th>Control</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRGN</td>
<td>pg/ml</td>
<td>2558.92±1170.77</td>
<td>1814.6±330.28</td>
<td>1052±276</td>
<td>&lt;0.001**</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>IGF-2</td>
<td>ng/ml</td>
<td>26.44±11.55</td>
<td>6.14±2.25</td>
<td>3.31±1.7</td>
<td>&lt;0.001**</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.002**</td>
<td>0.006**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal SLEDAI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>2764.1±1335</td>
<td>28.6±12.9</td>
<td>0.311</td>
<td>0.196</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.311</td>
<td>0.196</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal biopsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class 2</td>
<td>2199.31±1654.85</td>
<td>24.38±13.31</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class 3</td>
<td>2244.17±767.97</td>
<td>23.75±7.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class 4</td>
<td>2992.14±1453.93</td>
<td>29.41±12.41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.270</td>
<td>0.540</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Levels of PRGN and IGF-2 in relation to SLEDAI score, renal SLEDAI, and Renal biopsy

<table>
<thead>
<tr>
<th>PRGN pg/ml</th>
<th>IGF-2 ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE score</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>1945.6±1300</td>
</tr>
<tr>
<td>High</td>
<td>2072.1±545.5</td>
</tr>
<tr>
<td>Very high</td>
<td>4269.2±1106.8</td>
</tr>
<tr>
<td>P value</td>
<td>0.002**</td>
</tr>
<tr>
<td>Renal SLEDAI</td>
<td></td>
</tr>
<tr>
<td>Inactive</td>
<td>2251.2±841</td>
</tr>
<tr>
<td>Active</td>
<td>2764.1±1335</td>
</tr>
<tr>
<td>P value</td>
<td>0.311</td>
</tr>
<tr>
<td>Renal biopsy</td>
<td></td>
</tr>
<tr>
<td>Class 2</td>
<td>2199.31±1654.85</td>
</tr>
<tr>
<td>Class 3</td>
<td>2244.17±767.97</td>
</tr>
<tr>
<td>Class 4</td>
<td>2992.14±1453.93</td>
</tr>
<tr>
<td>P value</td>
<td>0.270</td>
</tr>
</tbody>
</table>

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index. *Statistically significant difference (p<0.05) **Statistically significant difference (p<0.01).

Conclusions: PGRN and IGF-2 are significantly elevated in SLE compared to CRF and control and were associated with SLEDAI. Hence they are considered specific to LN.

References:
PATIENT ACTIVATION AND THE FACTORS AFFECTING IT IN PRIMARY SJÖGREN’S SYNDROME

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Background: Increased patient activation has been associated with reduced costs of treatment1 and improved patient outcomes2. The effect of primary Sjögren’s syndrome (pSS) on patient activation however has not been established.

Objectives: This study aims to identify how activated patients with pSS are, and to ascertain whether markers such as ESSPRI score, EQ5D dryness score and self-reported quality of life influence this.

Methods: Patient activation in 170 pSS patients was assessed using the 13-item Patient Activation Measure (PAM-13). A PAM-13 score from 0–100 was obtained using the PAM-13 Scoring Spreadsheet, which also gave a corresponding activation level ranging from 1–4. Descriptive statistics of the PAM-13 scores was performed, and frequency analysis of the corresponding activation level. Demographic, clinical and self-reported measures such as age, gender, ESSPRI score and EQ5D-3L score were linked to each patients’ PAM-13 scores. Spearman’s correlation analysis was performed to assess the relationship between the continuous variables and PAM-13 score. Fisher’s chi-square test was used to assess the relationship between activation level and the categorical variables.

Results: The mean PAM-13 score of the 170 patients studied was 59.5 (SD 13.9): 17.6% of patients were in level 1 of activation, 28.5% in level 2, 40.0% in level 3, and 15.9% in level 4. The mean age of the sample was 59.6 (SD 13.1), and 83.5% were female. EQ5D-3L score had the strongest correlation with increased PAM score (r = 0.40, p = 0.000). Increasing self-reported pain in the ESSPRI questionnaire was correlated with a decreasing PAM score (r = -0.35, p = 0.000), as was increasing EQ5D-3L score (r = -0.37, p = 0.000). Increasing abnormal fatigue (r = -0.19, p = 0.016) and EULAR dryness (r = -0.19, p = 0.013) score were also weakly correlated with a decrease in PAM-13 score. Decreases in patients self-reported mobility (p = 0.000), self-care (p = 0.002), and ability to perform daily activities (p = 0.018) were also associated with differences in activation score.

Conclusions: Factors such as a patients self-reported health and pain have a moderate correlation with activation in pSS patients, while dryness and fatigue are only weakly correlated with changes in activation. This should be considered in the future when devising treatment plans and clinical trials.

References:

Acknowledgements: Dr Arvind Rawal: Orthopaedician.
Dr Malika Kwaatra- Pathologist
Dr Sandeep Shrivastava- Director

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2082
BACKGROUND: The prevalence of anti-centromere antibodies (ACA) among patients with primary Sjögren’s syndrome (pSS) varies from 3.7% till 10.9% [1]. They have special course of the disease: 1) with some features of systemic sclerosis (SSc), but rarely evolve to it, 2) higher prevalence of hepatitis and possible biliary cholangitis - PBC. Objectives: to describe the peculiarities of this subgroup; to evaluate it’s importance long-term morbidity.

RESULTS: In our study 2/3 (64%) ACA+pts with pSS didn’t fulfill ACR2012 criteria, because of the lack of aRo or aLa or combination of RF+ANA. According to the criteria, 2014 [4] also just 60–68% pts will have ≥4scores for diagnosing pSS. SSc (limited form) due to new criteria [5] might be revealed in 11/50 (22%) cases. MALT lymphoma of salivary glands arised in 5/6 pts with visible enlargement of parotid glands.

Table 1. Characteristics of pSS patients with positive ACA

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slitolarity of parotid gland</td>
<td>sialoadenitis: sialectasis 47/50 (94%)</td>
</tr>
<tr>
<td>Xerostomia (grade I-II) immuno stimulated parotid saliva flow rate &lt; 0.5ml/5min (III)</td>
<td>27/43 (62.8%)</td>
</tr>
<tr>
<td>Keratoconjunctivitis sicca with ocular staining score ≥ 5</td>
<td>31/50 (62%)</td>
</tr>
<tr>
<td>Schirmer’s test ≤ 5 mm/5 min</td>
<td>29/48 (60.4%)</td>
</tr>
<tr>
<td>Focal lymphoplastic sialadenitis ≤ 1 foci/4 mm²</td>
<td>28/30 (92%)</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma (incl. MALT lymphoma) 6 (5)</td>
<td>&lt;12% (10%)</td>
</tr>
<tr>
<td>aRo/SS-A ≤ 50 IU/ml 16/50 (32%)</td>
<td></td>
</tr>
<tr>
<td>aLa/SS-B ≤ 50 IU/ml 3/50 (6%)</td>
<td></td>
</tr>
<tr>
<td>IgM RF positive ≥ 2ULN (≥30 IU/ml) 9/50 (18%)</td>
<td></td>
</tr>
<tr>
<td>AMA positive ≥ 10 IU/ml</td>
<td>13/31 (41.9%)</td>
</tr>
</tbody>
</table>

Conclusions: pSS with positive ACA is challenging for diagnostics with comprehensive classification criteria (32-64% doesn’t meet it [3,4]). These patients overlaps SSc, some PBC, PBC is not rare among, but biliary tract lesions (AMA= rarely absent, 2% in our study) with slightly elevated liver enzymes, especially GT, and stage 1 typical to PBC without progression) are more common.

References:
[4] Shiboski SC et al. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren’s Syndrome. ARTHRITIS & RHEUMATOLOGY; 2016; Vol. 00 (00): p 00–00.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6974

AB0532 VITAMIN D IN A MALAYSIAN LUPUS COHORT AND ITS CORRELATIONS WITH CLINICAL AND IMMUNOLOGICAL PARAMETERS

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Background: Numerous studies have demonstrated that inadequate vitamin D levels are common in systemic lupus erythematosus (SLE) patients and they correlate inversely with disease activity. To date, there is paucity of data on the prevalence of vitamin D status, as well as its clinical and immunological associations in Malaysian SLE patients. Objectives: Our study aimed to determine the prevalence of vitamin D deficiency and insufficiency in SLE patients, and to examine the association between vitamin D status with gender, ethnic groups, clinical manifestations of SLE, Schirmer’s test, cardiovascular risk factors, bone mineral density and autoantibodies. Methods: This retrospective study included 216 SLE patients who attended the Rheumatology Clinic of Kuala Lumpur Hospital between January 2013 and December 2015. All patients had medical records. All patients fulfilled the 1997 American College of Rheumatology revised classification criteria for SLE. Serum 25(OH)D concentrations were measured by electrochemiluminescence immunoassay. Results: A total of 216 SLE patients were included in this study. Eleven (5.1%) were males and 205 (94.9%) were females. There were 141 (65.3%) Malay, 53 (24.5%) Chinese, 19 (8.8%) Indian and 3 (1.4%) of other ethnic group. This corresponded with the pattern of ethnic distribution in the Malaysian population. Their ages ranged from 14 to 75 years, with a mean age of 35.9±7.1 years. Mean duration of SLE at the time of 25(OH)D analysis was 6.9 years (range from 0 to 39 years), and mean age was 35.1±6.4 years (range from 14 to 75 years). Mean 25(OH)D concentration was 51.3±14.8 nmol/L (range from 7.5 to 156.1 nmol/L). Fifty (23.1%) patients had vitamin D deficiency, 120 (55.6%) had vitamin D insufficiency, while 46 (21.3%) had adequate vitamin D levels. Our study showed statistically significant association between vitamin D status and ethnic group (p<0.001). The Chinese ethnic group had the lowest proportion of patients with vitamin D deficiency and insufficiency (60.4%), while Malay had the highest proportion at 86.5%. Mean levels of serum 25(OH)D in Chinese, Indian and Malay SLE patients were 66.3±36.7 nmol/L, 54.9±36.4 nmol/L, and 45.0±27.5 nmol/L, respectively. Among the clinical manifestations of SLE, only lupus nephritis showed a statistically significant association with vitamin D status (p<0.001). In terms of cardiovascular risk factors, hypertension demonstrated significant correlation with vitamin D status (p=0.032). No significant association was found between vitamin D status and gender. Nonetheless, male SLE patients had higher mean 25(OH)D concentrations at 69.4±36.9 nmol/L, compared to female at 50.2±31.6 nmol/L. There were no significant correlations between vitamin D status and clinical features of lupus such as cutaneous lesions, arthritis and NPSLE; positive Schirmer’s test; cardiovascular risk factors, that are, dyslipidemia and diabetes mellitus; osteoporosis; and autoantibodies which included anti-dsDNA antibody, anti-Ro antibody, anticardiolipin antibody and rheumatoid factor.

Conclusions: Sub-optimal vitamin D levels are prevalent among SLE patients in a tropical country and are associated with ethnic group, lupus nephritis and hypertension. It is essential to include vitamin D supplementation in the management of SLE patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1100

AB0533 JUVENILE AND JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: CLINICAL CHARACTERISTICS, DISEASE ACTIVITY AND DAMAGE

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Background: The diagnosis of systemic lupus erythematosus (SLE) in children is challenging as the heterogeneous manifestations and disease impact on the child’s growth highlighted the importance of timely diagnosis and management. Objectives: The aim of the present study was to assess and compare the clinical characteristics, disease activity and damage between juvenile (JSLE) and juvenile-onset (JO-SLE) Egyptian patients. Methods: Seventy-eight SLE patients (26 JSLE and 52 JO-SLE) were included in this study. Disease activity was assessed using the SLE Disease Activity Index (SLEDAI) and organ damage using the Systemic Lupus International Collaborating Clinics (SLICC) index. Results: The mean age of the JSLE children was 13.2±2.09 years and 23.17±4.26 years for JO-SLE cases. JO-SLE cases were older at disease onset with a higher female-to-male ratio. There were no noticeable gender differences. There was a significantly higher frequency of serositis, nephritis and hematological involvement in the JO-SLE cases (57.7%, 76.9% and 73.1%) compared to the JSLE cases (15.4%, 30.8% and 30.8%) (p<0.001 for all). The erythrocyte sedimentation rate, creatinine and proteinuria were significantly increased in JO-SLE while alkaline phosphatase was higher in JSLE cases. In JO-SLE cases, sedimentation rate, creatinine and proteinuria were significantly increased in JO-SLE while alkaline phosphatase was higher in JSLE cases. In JO-SLE cases, the mean SLEDAI was higher (6.6±1.8 vs 3.1±1.97; p=0.003) and the SLICC tended to increase compared to the JSLE children. More JO-SLE cases received hydroxychloroquine and azathioprine.

Conclusions: The existence of differences in clinical phenotype has been confirmed, between JSLE and JO-SLE especially as regards serositis, nephritis and hematological affection. The disease damage was comparable which denotes that the maximum organ involvement occurs in childhood with an almost stationary course. Rheumatologists caring for children with SLE must be aware of the greater risk of major haematological and renal involvement as well as important long-term morbidity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2993
AB0534 THROMBOTIC MICROANGIOPATHY IN PREGNANT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: CHARACTERISTICS AND OUTCOMES
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Objectives: to evaluate the impact of thrombotic microangiopathy (TMA) on perinatal and maternal outcomes in patients with systemic lupus erythematosus (SLE).

Methods: This study included 21 SLE patients with pregnancy, who developed TMA signs during pregnancy. Patients underwent general survey, clinical and laboratory assessment for disease activity and APL-antibodies. All of them had low SLE-activity indices.

Results:

Table 1. Laboratory features of pregnant patients with SLE

<table>
<thead>
<tr>
<th>TMA (n=7)</th>
<th>Without TMA (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb, g/dl</td>
<td>89.8</td>
</tr>
<tr>
<td>LDH, U/l</td>
<td>716.39</td>
</tr>
<tr>
<td>ALT, U/l</td>
<td>110.9</td>
</tr>
<tr>
<td>AST, U/l</td>
<td>69.1</td>
</tr>
<tr>
<td>Creatinine, mmol/l</td>
<td>113.3</td>
</tr>
<tr>
<td>GFR, ml/min</td>
<td>50.5</td>
</tr>
<tr>
<td>Proteinuria, g/24h</td>
<td>0.65</td>
</tr>
<tr>
<td>Thrombocytes, x109</td>
<td>135.5</td>
</tr>
<tr>
<td>sFLT/PLGF</td>
<td>66.6</td>
</tr>
</tbody>
</table>

TMA signs were found in 7/21 SLE patients (33%). Patients with TMA had significantly higher systolic and diastolic blood pressure (P<0.05), higher serum creatinine and lower estimated glomerular filtration rate (P>0.05) than that of those without TMA lesions (tab.1). APLA positivity was significantly more frequent in patients with TMA (3/7 vs 0/14). TMA onset in 2 patients occurred before 20 gestational weeks, 5/7 have developed PE signs (23–38 weeks), only 3/7 had classical HELLP syndrome. There was no PE in patients without TMA. There was a significant association between the detection of TMA and adverse perinatal outcomes (tab.2).

Patient with TMA and SLE had a poor outcome and most severe course: 5/7 had a PE (3/7 developed HELLP), 3/7 had antenatal fetal death, 3/7 had signs of heart damage. 5/7 a variety of neurological manifestations. Despite of PE signs in 5/7 with TMA the blood sFlt/PlGF levels were slightly above normal (average sFlt/PlGF levels in preeclampsia without SLE in our another study is 404.47).

Conclusions: TMA is not an uncommon disorder in pregnant patients with SLE. It is associated with APLA positivity only in 1/3 cases. TMA was significantly associated with renal impairment, systemic hypertension and adverse perinatal outcomes. Less increased ratio of sFlt-1/PlGF in TMA patients than “pure” PE may confirm that PE in patients with TMA is not a condition due to angiogenic factors imbalance. Circulating concentrations of angiogenic factors appear not to be suitable markers to assess the severity of PE and adverse outcomes in SLE patients. Thus, TMA may be an important cause of renal injury and renal dysfunction in a subset of pregnant patients with SLE and associated with worse renal and perinatal prognosis. Complement over-activation via both classical (SLE+APS) and alternative pathways might play an important role in the pathogenesis of TMA in SLE.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6589

AB0535 FATIGUE IS ASSOCIATED WITH HS-CRP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Fatigue is highly prevalent and has a negative impact on quality of life in patients with Systemic Lupus Erythematosus.1 The 9-item Fatigue Severity Scale (FSS) is one of the commonly used self-report questionnaires to measure fatigue in patients with chronic disease.2 Although fatigue is one of the most commonly reported symptoms in SLE, previous studies have not consistently found any clear association between disease activity (as measured by the SLEDAI)3 or with laboratory measures of disease activity.2

Objectives: To determine whether fatigue is associated with any laboratory measures of disease activity or inflammation in patients with SLE.

Methods: SLE patients and age-matched controls participating in our longitudinal “Biomarkers of Cardiovascular Disease in SLE” completed FSS questionnaires at study entry. Laboratory measures of cardiovascular risk assessment and lupus disease activity assessments were performed in plasma, including high sensitivity C-reactive protein (hs-CRP), myeloperoxidase (MPO), homocysteine, fasting lipid panels, erythrocyte sedimentation rate (ESR), C3, C4, dsDNA, and urine protein/creatinine ratio (UPCR).

Results: 54 patients and 37 control individuals participated. FSS scores were higher in patients with SLE (4.79±1.63 mean ± SD) compared to healthy subjects (3.17±1.83, P<0.001). There were no significant correlations between FSS and age, gender, or SLE disease duration. In SLE patients, there was significant correlation between FSS scores and hs-CRP (r=0.56, p=0.004), and an inverse correlation with myeloperoxidase (-0.37, p=0.045). No associations between FSS and C3, C4, dsDNA, ESR, UPCR, fasting lipid panels, or homocysteine were seen in the SLE group. No associations between FSS and laboratory measures of cardiovascular risk assessment were seen in the control group.

Conclusions: Although fatigue is not correlated with traditional laboratory measures of disease activity in SLE patients, we did find significant associations between fatigue, hs-CRP, and myeloperoxidase in our cohort. Future longitudinal studies are underway to determine whether these associations also reflect the risk for progression of cardiovascular disease in patients with high fatigue.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2175

AB0536 ANTICARDIOLIPIN ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Anticardiolipin (ACL) antibodies have been independently associated with high incidence of thrombotic diseases and pregnancy associated disorders in patients with systemic lupus erythematosus (SLE).

Objectives: This study aims to assess influence of ACL antibodies in SLE and their association with clinical, biological and immunological features.

Methods: A retrospective study of 246 patients with systemic lupus erythematosus (revised ACR criteria) conducted in an internal medicine department over a period of time of 14 years. Two groups were compared according to the positivity of ACL antibodies (group1: positive ACL/ group2: negative ACL).

Results: ACL antibodies were positive in 48.8% of SLE patients (screened in 168 patients). This prevalence was similar in female and male. Poor general state at diagnosis was more frequent in the ACL positive group (55.7% vs 38.6%; p=0.02). The following data were comparable in the two groups: joint involvement (91.8% vs 90.8%; p=0.7), pericarditis (33.8% vs 37.8%; p=0.6) and pleural effusion (24.1% vs 29.5%; p=0.44). Alopecia (38.6% vs 27.9%; p=0.2), central nervous system involvement (12.5% vs 18.8%; p=) and peripheral neuropathy (6.4% vs 11.1%; p=) were more frequent in the group 2 without significant difference. Prevalence of lupus nephritis was more important in the group 1 (52.8% vs 38.8%; p=0.07). Thromboembolic complications: deep venous thrombosis (13.8% vs 11.9%; p=0.72) and pulmonary embolism (10.8% vs 7.1%; p=0.51) were more frequent in patients with ACL antibodies without significant difference. Obstetrical complications were more frequent in group 1 but differences were not statistically significant; spontaneous abortions (29.5% vs 20.4%; p=0.29), intra-uterin death (13.6% vs 9.3%; p=0.5), premature birth (6.8% vs 1.9%; p=0.3). There were no associations between hematologic disorders and ACL antibodies; leucopenia (51.3% vs 39.5%; p=0.13) and, lymphopenia (81% vs 80.2%; p=0.9), anemia (77.2% vs 74.4%; p=0.6) and thrombopenia (22.8% vs 23.5%; p=0.9) were comparable in the two groups. Frequencies of anti-ds DNA antibody and of antibodies to extractable nuclear antigens were similar in the two groups. Only anti-B2GPI1 antibodies were significantly associated to ACL antibodies (5.1% vs 17.2%; p=0.001).

Conclusions: ACL antibodies were found in 30–40% of patients with SLE, this is comparable to our group.

No significant associations of ACL antibodies to thrombotic events or obstetrical complications were found in our patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3909
ACUTE ALCALCULOUS CHOLECYSTITIS: A RARE MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS


Background: Acute acalculous cholecystitis (AAC) is a rare complication of systemic lupus erythematosus (SLE) but should be recognized

Objectives: The aim was to describe clinical, biological and radiological features of AAC in SLE patients.

Methods: We report four cases of AAC complicating SLE among 246 patients. Results: Case 1: A 39-year-old woman with one year history of arthralgia and Raynaud’s phenomenon was admitted for fever, cutaneous lesions, nausea and abdominal pain. The right upper quadrant of the abdomen was tender and we noted oral ulcerations and wrist synovitis. Laboratory data showed lymphopenia, hemolytic anemia and anergy. After treatment of an acute respiratory episode, there was no cholecystitis or cytology. Antinuclear antibodies (ANA), anti-nucleosome, anti-Sm and anti-ribosome antibodies were positive. Abdominal sonography revealed ascites and gallbladder wall thick was thin and irregular. The diagnosis of AAC complicating a SLE was made and patient was treated with antibiotics and corticosteroids. Two weeks later, she was asymptomatic and abdominal sonography was normal. Case 2: A 32-year-old woman had SLE with arthralgia, cutaneous manifestations, hematological involvements and pulmonary hypertension; she was treated with corticosteroids and cyclophosphamide. Six month later, at time of the second pulse of cyclophosphamide, she presented with jaundice and tender hepatomegaly where nontender abdominal pain. Liver enzymes rates were normal except bilirubin which was high at 47 UI. Her abdominal sonography showed gallbladder wall thickness without bile ducts enlargement or gallstones. Patient was continued on steroids and cyclophosphamide but she died because of heart failure. Case 3: A 45-year-old patient with 12-year-history of SLE was admitted for fever and dyspnea. On physical examination, there was tenderness on right upper quadrant of her abdomen. Cholestasis and cytology were found. Abdominal sonography showed a striated and thick gallbladder wall (17 mm). Computer tomography confirmed the gallbladder wall thickness and noted pericholecystic edema. Biological data showed anemia, thrombopenia and cholestasis. ANA, anti-DNA and anti-Sm were positive. Abdominal sonography showed gallbladder wall thickness and pericholecystic edema. SLE diagnosis with peripheral neuropathy, lupus nephritis, hematological manifestations and ACC was made. Patient was given corticosteroids and cyclophosphamide with good outcome.

Conclusions: Only few cases of AAC complicating SLE are reported. Cholecystitis can be an initial manifestation of SLE and reveal the disease or can occur at any time of the disease course. ACC is always associated to other disease manifestations. Patients present with abdominal pain, vomiting and fever. Ultrasonography and computed tomography confirm the diagnosis. The outcome is good with steroids. Sometimes patients are given antibiotics and/or underwent cholecystectomy because of infectious cholecystitis suspicion. None of our patients required surgery.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2785

AB0538

UNINARY LEVELS OF VCAM-1 AND TWEAK AS BIOMARKERS OF LUPUS NEPHRITIS

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Background: TNF-like WAKE inducer of apoptosis (TWEAK) is able to increase disease manifestations. Patients present with abdominal pain, vomiting and fever. Ultrasonography and computed tomography confirm the diagnosis. The outcome is good with steroids. Sometimes patients are given antibiotics and/or underwent cholecystectomy because of infectious cholecystitis suspicion. None of our patients required surgery.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4071

AB0539

DOES ERYTHROCYTE SEDIMENTATION RATE REFLECT DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS? CORRELATION WITH ACUTE PHASE REACTANTS, IMMUNOLOGICAL PARAMETERS AND PROTEINURIA

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Background: Patients with active systemic lupus erythematosus (SLE) are considered to have increased erythrocyte sedimentation rate (ESR) rather than raised C-reactive protein (CRP). Yet published evidence is low for this statement. ESR is used as a marker of disease activity and in the absence of the disease. Secondly, to determine if these parameters are associated with disease flare or infections.

Objectives: Firstly, to assess how ESR correlates with above mentioned laboratory parameters: in general, in the presence of clinical activity and/or infection or in the absence of both. Secondly, to determine if these parameters are associated with disease flare or infections. Methods: A retrospective analysis of patients of a tertiary referral centre with SLE under treatment between 2006 and 2015. Data on laboratory parameters, infection and disease flare, judged by the treating physician, were extracted. Patients were divided in four SLE groups: flare only (n=147), infection only (n=48), both (n=23), and neither infection nor flare (n=153). ESR was correlated to CRP, ferritin, proteinuria, C3-reduction and raised dsDNA-antibodies for the whole cohort and within each SLE group. Further, the association between all laboratory parameters and a) disease activity with and without infection, b) the presence of infection with and without disease activity, was tested.

Results: We identified 203 SLE patients, 26 males, with a total of 371 visits. Mean age was 45.6 years (SD: 16.5 years). Table 1 (top part) shows the correlation
coefficients of ESR with the other laboratory parameters. ESR correlated moderately with CRP amongst all groups (r=0.47–0.58); weakly with ferritin in the general and the flare group (r=0.26); and very weakly with C3-reduction and raised dsDNA-antibodies (r=0.02) in each group. Concerning proteinuria, the correlation was weak for all, for flaring and for silent patients (r=0.22–0.35), moderate for the mean value of proteinuria and activity (r=0.58). There was no correlation in infected patients (r=0.06). Table 1 (bottom part) displays the p-values for the association of parameters with disease activity or infection, respectively. ESR, reduction of C3, proteinuria and raised dsDNA-antibodies were all associated with disease activity in the whole cohort and in the non-infected group; CRP only in non-infected patients. In the infected group, raised dsDNA-antibodies and proteinuria were the only parameters showing significant relation to disease activity. ESR and CRP were significantly associated with infections when looking at all or at inactive patients, but not in active patients.

Table 1: Correlation of laboratory parameters to ESR and association with disease flare and infection

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ESR</th>
<th>CRP</th>
<th>Ferritin</th>
<th>C3-reduction</th>
<th>Raised dsDNA-antibodies</th>
<th>Proteinuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients (n=277)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>flare only (n=47)</td>
<td>0.49*</td>
<td>0.25*</td>
<td>0.165*</td>
<td>0.134*</td>
<td>0.34*</td>
<td></td>
</tr>
<tr>
<td>infection only (n=68)</td>
<td>0.46*</td>
<td>0.109</td>
<td>0.172</td>
<td>0.12</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>both (n=25)</td>
<td>0.150</td>
<td>0.035</td>
<td>0.032</td>
<td>0.002</td>
<td>0.34*</td>
<td></td>
</tr>
<tr>
<td>patient (n=23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Both, ESR and CRP are elevated in patients with SLE flare and are weakly correlated with other laboratory activity parameters. Thus, while normal CRP argues against infection elevation of ESR and CRP is not sufficient to distinguish between SLE flare and infection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5123

AB0540 ORGAN DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Organ damage in patients with systemic lupus erythematosus (SLE) occurs as the consequence of the disease itself, administered therapy, primarily corticosteroid and cytostatic, as well as the accompanying diseases and complications.

Objectives: Our aim in this paper was to examine the degree of irreversible organ changes in SLE patients using the SLICC/ACR Damage Index (SDI) and to establish the correlation of organ damage with disease activity, quality of life, and severity of fatigue, as well as with the immunological parameters – anti-dsDNA antibodies, anti-nucleosome, anti-C1q antibodies, and MCP1 in the serum and urine.

Methods: The study involved 83 SLE patients (77 women and 6 men), aged 45.8±9.2 years on the average, with average disease duration of 10.6±7.9 years, hospitalized at the Clinic of Rheumatology of the “Niška Banja” Institute, in whom the diagnosis was made based on the revised 1997 ACR criteria. The disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLDAI) and a physician’s global assessment. The degree of organ damage was evaluated using the SDI. The quality of life was assessed based on the Medical Outcome Survey Short Form 36 (SF-36), and the severity of fatigue was measured using the Fatigue Severity Scale (FSS). The level of antibodies was determined using the ELISA test, and serum and urine MCP1 with the sandwich enzyme immunosorbent assay method according to the manufacturer’s instructions (R&D Systems, Inc. Minneapolis, USA).

Results: The mean organ damage index in all SLE patients was 1.8±2.0 (median 1, min 0, max 9). Twenty-five (30.1%) patients did not have any organ damage (SDI=0); 21 (25.3%) had SDI=1; SDI=2 or 3 was found in 20 patients (24.1%), and 17 patients (20.5%) had SDI=4. Neuropsychic and musculoskeletal changes were the most common organ damage manifestations, present in 23 (27.7%) of patients. In 21 patients (25.3%), cardiovascular changes were seen, and ocular lesions in 14 patients (16.9%). Renal and pulmonary changes were found in 13 patients (15.7%), cutaneous changes in 3 patients (3.6%), and gastrointestinal changes in 2 patients (2.4%). In 5 cases (6.0%) malignancies were detected, and diabetes mellitus in 2 patients (2.4%). A statistically significant positive correlation was established with age, disease duration (r=0.412, p<0.001), SLEDAI (r=0.359, p<0.001), global physician’s assessment (r=0.357, p<0.001) and fatigue (r=0.296, p<0.007), and a negative correlation with quality of life (r=−0.386, p<0.001). There were no correlations of SDI with the level of anti-dsDNA, anti-nucleosome, anti-C1q antibodies, nor with serum levels of MCP1.

Conclusions: Musculoskeletal, neuropsychic, and cardiovascular changes were the ones most commonly seen. Organ damage positively correlated with age and disease duration, a higher disease activity, poorer quality of life, and more severe fatigue.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5140

AB0541 CO-MORBIDITY STATUS IN SYSTEM LUPUS ERYTHEMATOSUS PATIENTS

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Background: The improved survival of patients with Systemic Lupus Erythematosus (SLE) over the past decades highlighted the problem of co-morbidity (several different chronic pathologies presence) in SLE patients because many of them reach the age when the burden of concomitant diseases could increase and become ordinary.

Objectives: To evaluate the frequency of concomitant diseases and to estimate the total co-morbidity status in SLE patients.

Methods: The retrospective study of co-morbidity in SLE patients was conducted on the database of Byelorussian Republican Rheumatologic Center. It included 212 patients: 192 women and 20 men at the age of 16.1 to 68.3 (mean ± SD: 33.1±12.3 years) at the baseline (first visit). The diagnosis of SLE was in conformance with 1997 ACR modified classification criteria for SLE [1]. The comprehensive assessment patient co-morbidities was performed by Kaplan-Feinstein co-morbidity index (KFI) [2] which includes twelve pathology categories: arterial hypertension (HT), heart disease (HD), presence, nervous system (ND) involvement, respiratory system (RD) pathology, vascular (VD), kidney (KD), liver (LD) gastrointestinal (GID) and musculoskeletal (MSD) diseases, other pathology (OD), malignancies and alcoholism. A co-morbidity score of 1 indicates low level of co-morbidity, 2 - moderate and 3 - high level of co-morbidity for corresponding pathology. The possible grade of co-morbidity is calculated as a sum score for all categories and varies from 0 to 36 points.

Results: KFI in SLE patients at the first visit varied from 0 to 7 points (Me: 2; 25–75% range: 0–3) and had minor differences in age and sex groups (NS, Fisher’s exact test). One-third of patients (n=68) had no co-morbidities. One of the most common pathology was HT which was diagnosed in 39 patients (18.4%, 95% CI 5.6–26.7%); 34 women and 5 men (p=0.591, NS, Fisher’s exact test). Over the 13-year follow-up period the frequency of HT dramatically increased to 52.9% (95% CI 47.0–68.0%) i.e. 2.9 times vs baseline (p<0.001). Prognostic odds ratios (OR) of HT were 7.6 (95% CI 3.1–18.2) and 3.2 (1.4–7.6) for lupus nephritis presence and signs of glucocorticoid disease (“cushingoid”), correspondingly.

Other common co-morbidities were GID and HD. Coronary HD and congestive heart failure were revealed in 43 (20.3%) patients. GID were registered in 44 (20.8%) patients, among them 9 (4.2%) patients had gastric/gastrointestinal ulcer. VD, ND and RD were revealed in 7 (3.3%) patients for each category, KD and LD frequency was 6 (2.8%) for both pathology. MSD were registered in 8 (3.8%) and OD, including different infections, anemia, diabetes etc. were registered in 39 (18.4%) patients. There were no cases of malignancies or alcoholism in our patients.

Conclusions: Total co-morbidity status revealed in SLE patients at baseline varied up to the 20 percent of the maximal possible level for all age and sex groups. Arterial hypertension was one of the most common pathology which demonstrated significant and predictable growth over the 13-year follow-up period.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6520
**AB0542** PRESENTATION AND OUTCOME OF LUPUS NEPHRITIS IN THE MULTICULTURAL SOCIETY OF WESTERN AUSTRALIA – A SINGLE CENTRE EXPERIENCE

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**Background:** Lupus Nephritis (LN) is one of the most severe complications that can occur in patients with Systemic Lupus Erythematosus (SLE) as it increases the risk of morbidity and mortality. As with SLE, there is a significant impact of ethnicity on LN severity and outcome.

**Objectives:** To investigate the impact of ethnicity of LN presentation and health outcomes in a multicultural referral centre in Western Australia.

Methods: A retrospective cohort study of 104 patients with biopsy confirmed lupus nephritis (LN) collating clinical characteristics, renal histopathology, serology, medication use, disease activity (Systemic Lupus Erythematosus Disease Activity Index - 2k (SLEDAI-2k)), organ damage (SLICC-Damage Index (SDI)), and clinical outcomes from index biopsy event to the last visit. Outcomes included the high serum creatinine (≥150umol/L), low eGFR (<50%), the need for renal replacement therapy (RRT), and death. Outcomes were assessed across ethnicity with comparative statistics, Chi-square, and survival analysis.

**Results:** Asian (n=17, 16.3%), Caucasian (n=79, 76.0%) and Indigenous (n=8, 7.7%) patients were similar for age (p=0.164), gender (p=0.399) and SLEDAI (8.5 vs 9.0 vs 13.0, p=0.897), non-renal SLICC-2k (10.5 vs 2.5 vs 1.0, p=0.528). Time to biopsy from the initial SLE diagnosis was shorter in Asian and Indigenous patients (p=0.055). At the index biopsy, ethnic groups were similar for WHO Class distribution (predominantly Classes 3 and 4, p=0.345) and clinical signs of renal dysfunction (p=0.12). Asian and Indigenous patients had lower SLEDAI-2k scores (16.0 vs 26.5 vs 520.0, p=0.81), albeit non-significantly (due to low numbers).

**Conclusions:** There was no significant differences in disease activity or organ damage between the different ethnic groups.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5854

**AB0544** LEVELS OF VITAMIN D IN A COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS. RELATIONSHIP WITH DISEASE ACTIVITY AND BONE MASS


**Background:** Vitamin D (vit D) is an immunoregulatory hormone which seems to mediate immune tolerance. Several studies have suggested that vit D deficiency may be related to increased disease activity in patients with systemic lupus erythematosus (SLE).

**Objectives:** To analyze 25-hydroxyvitamin D (25-OHD) levels in a cohort of patients with SLE and to investigate their relationship with clinical, analytical, immunological and densitometric parameters.

**Methods:** Prospective study including patients with SLE (according to SLICC criteria 2013) performed in an Academic Hospital with a referral area of 800,000 inhabitants. 152 patients with SLE were included (138 women [46 postmenopausal] 14 men) with a mean age of 46±12 years (range: 20–75). Clinical parameters (including risk factors for osteoporosis, presence of skeletal fractures, treatment with glucocorticoids (GCC) as well as SLE involvement including haematologic, renal, neurological and skin), biochemical determinations (including 25-OHD, parathormone (PTH)), immunological (ANA, DNA and complement) and SLE activity and severity (assessed by SLEDAI and SLICC index) were assessed in all patients. Bone mineral density was performed by DXA (at lumbar spine and proximal femur).

**Results:** Vit D deficiency was defined as 25-OHD values under 20 ng/mL. Low bone mass was considered as T or Z score <-1 SD; and osteoporosis as T <-2.5 SD [age =50 years] or Z <-2 SD [age <50 years]. The study was approved by the Clinical Research Ethics Committee and all patients provided informed consent to participate. Statistical analysis was performed by SPSS 20.

**Results:** The mean values of 25-OHD were 19.8±11.4 (range, 4.2–66.6); 87.5% of patients had 25-OHD levels below 30 ng/mL, 61.2% below 20 ng/mL and 15.1% below 10 ng/mL. The lowest levels were in vitamin and depression (80%) and in patients with GCC treatment (98%). 42.8% of patients received vitamin D supplements. 56.5% of patients had low bone mass (T or Z score <-1 SD), and 15.8% had osteoporosis. Levels of 25-OHD showed no correlation with SLE disease activity (complement, AC antibodies, SLICC/SLEDAI) neither with bone mass by DXA. Patients with low bone mass (T or Z <-1 SD scale) were older (at the time of inclusion and age of SLE diagnosis), had higher SLICC and lower complement levels whereas no differences were observed in SLEDAI and 25-OHD values. 37.5% of the patients were treated with GCC. Patients without GCC treatment had higher prevalence of vit D deficiency (73.9% vs. 55.6%, p=0.034) compared to patients with GCC treatment.

**Conclusions:** 61.2% of patients with SLE have 25-OHD deficiency, which is more frequent in winter and spring, and mostly in those patients without GCC treatment. 25-OHD values showed no correlation with the disease activity and the few patients with low bone mass had higher SLICC and hypocomplementemia. Thus, our results suggest the need to perform clinical guidelines to assess bone mass and bone metabolism in this clinical condition. Additionally, we recommend quantifying vit D levels in winter/spring and don’t forget to assess those patients without GCC treatment.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5349

**AB0543** ANXIETY AND DEPRESSION IN CHINESE PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME

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**Background:** Primary Sjögren’s syndrome (pSS) is a multisystem autoimmune disorder characterised by lymphocytic infiltration and exocrine failure of salivary and lacrimal glands, resulting in the classical symptoms of the disease including xerostomia (dry mouth) and keratoconjuctivitis sicca (dry eyes). pSS has the potential to impair both psychological state and the health-related quality of life (HR-QOL). A common mental health problem among adults with pSS is anxiety and depression. In addition, depression is more common in pSS than in the general population and has been associated with enhanced fatigue, reduced health-related quality of life, increased levels of lymphocytes and increased health care costs. Besides, depressed pSS patients have poorer long-term outcomes, including more complications. Anxiety was more common than depression in pSS. The most affected domains were vitality in the SF-36 and general/physical fatigue in the MPFI. Extangulard systemic involvement was not a major determinant of QOL alteration in patients with pSS.

**Objectives:** Prevalence of anxiety and depression are high in women with Primary Sjögren’s syndrome (pSS). Our aim was to compare anxiety and depression in pSS patients and healthy controls and evaluate its relationship with the disease activity, sleep and quality of life; as well as to analyze potential determinants of anxiety and depression.

**Methods:** Sixty-seven patients fulfilling the American-European Consensus Group criteria for pSS (mean age 52.67 years (s.d. 13.16)) and 42 age-matched healthy controls were included. Participants completed self-administered questionnaires, namely Hospital Anxiety and Depression Scale (HADS), Depression Symptom Scale (DSS), Short Form 36 (SF-36) scores and the Pittsburgh Sleep Quality Index (PSQI). In addition, the European League Against Rheumatism Sjögren’s Syndrome Disease Activity Index (ESSDAI); Patient Reported Index (ESSPRI) and systemic inflammation (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level) were recorded in patients. Independent samples t-tests, χ2 analyses and logistic regression modeling were used to analyze the data.

**Results:** pSS patients experienced greater anxiety and depression than controls (HADS-A scores: mean: SD 6.5±3.4 for pSS versus 3.8±3.4 for controls; P <0.002. HADS-D scores: mean: SD 7.6±4.1 for pSS versus 4.2±3.5 for controls; P <0.002). And there were significant correlations among fatigue, pain, disease activity, dryness, sleep, quality of life and anxiety/depression. Meanwhile, logistic regression analysis revealed that poor quality of life and ESSPRI were significantly associated with anxiety/depression in pSS patients. **Conclusions:** The study suggests that optimal care of pSS patients may include the assessment and management of anxiety and depression. Early recognition and appropriate intervention is therefore essential to reduce the negative impact of anxiety and depression on the patient’s quality of life and outcome of their disease.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3069

**AB0545** EFFECT OF EMPATHY NURSING ON THE LIFE QUALITY OF THEPATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** The patients with Systemic Lupus Erythematosus always had sub-healthy status in psychology and been troubled by the chronicity of the disease. Empathy nursing is an effective treatment for chronic disease such as cancer or terminal patients.
CLINICOPATHOLOGICAL CHARACTERISTICS OF SJÖGREN’S SYNDROME IN THE PRESENCE OR ABSENCE OF OBJECTIVE SICCA SYMPTOMS

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Background: Sjögren’s syndrome (SS) is generally diagnosed on the basis of objective criteria, including xerophthalmia, xerostomia, autoantibodies, and labial salivary gland biopsy. Patients without objective sicca symptoms (non-sicca SS) require a biopsy. For such patients, we should evaluate pretest probability using parameters other than sicca symptoms before performing an invasive biopsy. To assess pretest probability, data on clinicopathological characteristics of non-sicca SS are needed.

Objectives: This study aimed to analyze the clinicopathological features of non-sicca SS. Epidemiological data, antibody profiles, organ involvement, and labial salivary gland biopsy results in non-sicca SS patients were compared with those in SS patients with objective sicca symptoms (sicca SS).

Methods: We selected 103 patients with primary SS who met Japanese or American College of Rheumatology criteria; those whose results exceeded the focus score by 1 underwent salivary gland biopsy. Objective xerophthalmia was evaluated with the Schirmer’s test, and objective xerostomia with the Saxon’s test. Seventeen patients were excluded because neither test was performed. Sicca SS was defined as a positive Schirmer’s and/or Saxon’s test result. Clinical and laboratory data were compared in 70 sicca SS and 16 non-sicca SS patients.

Results: Non-sicca SS patients were younger at diagnosis (45.9±14.8 vs. 61.4±15.1 years, p<0.001), had a shorter disease duration (1.1±1.5 vs. 6.9±8.9 years, p<0.001), and had a higher rate of positive anti-SS-A/Ro antibody (100 vs. 40%, p<0.001). In the lower rate of positive lymphocytic antibody (6.3 vs. 44.3%, p<0.005). Subjective xerophthalmia and xerostomia rates were similar between the groups, but fewer non-sicca SS patients had sicca symptoms as chief complaints (18.8 vs. 58.6%, p<0.004). There were no significant differences in focus score, leukocyte and lymphocyte counts, serum IgG levels, and positive rheumatoid factor and antinuclear antibody levels. The maximum European League Against Rheumatism Sjögren’s Syndrome Disease Activity Index (ESSDAI) score during follow-up showed no significant difference (3.3±4.27 in non-sicca SS vs. 3.8±3.68 in sicca SS, p=0.30). However, more non-sicca SS patients had ESSDAI scores ≥ 1 (100 vs. 71.4%, p<0.015), a lower correlation with the biological domain of the ESSDAI (87.5 vs. 58.6%, p<0.003) in sicca SS.

Disclosures: This study was supported by a research grant from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

Disclosure of Interest: None declared

CIRCULATING PROLACTIN LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: EXPLORATORY RESEARCH

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Background: Hypertension (HT) and dyslipidemia (DL) are the risk factors for all-cause mortality, cardiovascular and cerebrovascular disease, and end-stage renal disease in SLE patients. Neither disease activity nor chronic damage were associated with the metabolic syndrome in SLE patients and there were few reports about the risk factors of HT and DL in Japanese SLE patients.

Objectives: We aimed to describe a prevalence of HT and DL and to identify the risk factor of HT and DL in Japanese SLE patients.

Methods: All SLE patients visited at Showa University Hospital and Okayama University Hospital from January 2016 to September 2016, were enrolled in a cross-sectional study. SLE patients who satisfied American College of Rheumatology (ACR) criteria were included. HT was defined as usage of anti-HT drugs and DL was defined as usage of anti-DL drugs. We performed descriptive statistics and binary logistic regression analysis to identify the risk factors of HT and DL. Variables considered possible risk factors were BMI, drinking status, smoking status (current smoking), current daily dose of glucocorticoids, past maximum dose of glucocorticoids, lupus nephritis, Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI).

Results: In total, 244 participants were enrolled. The mean age was 46.2±15.3 years, and 222 (91%) were female. The mean current daily dosage of glucocorticoids was 6.7±5.9 mg, and the mean SLEDAI-2K was 5.0±5.2 and the mean SLICC/ACR-DI was 1.3±1.7. The prevalence of HT and DL were 29.1% (71/244) and 22.1% (54/244). Both HT and DL were confirmed in 11.9% (29/244) patients.

On binomial logistic regression analysis, BMI (regression coefficients (β)= -0.039; 95% CI =0.000 to 0.879), past maximum dosage of glucocorticoids (β= -0.036; 95% CI =0.036 to -0.004) and lupus nephritis (β= -0.727; 95% CI =0.230 to 1.241) were identified as the significant independent risk factors of HT. On the other hand, only age (β< -0.030; 95% CI = -0.055 to 0.008) was identified as the independent risk factor of DL. There was no independent risk factor of having both HT and DL.

Conclusions: Our results could help to identify patients at higher risk of HT and DL.

References:

Disclosure of Interest: None declared

CIRCULATING PROLACTIN LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH DISEASE ACTIVITY: A META-ANALYSIS

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Background: Prolactin has an immune stimulatory effect and may promote autoimmunity by encouraging the development of antigen presenting cells expressing MHC class II and co-stimulatory molecules and modulating IFN-γ secretion.

Objectives: This study aimed to evaluate the relationship between circulating prolactin level and systemic lupus erythematosus (SLE), and to establish a correlation between plasma/serum prolactin levels and SLE activity.

Methods: We performed a literature search for studies that examined prolactin status in SLE patients and controls, and the relationship between circulating (serum or plasma) prolactin levels and SLE using PUBMED, EMBASE, and Cochrane databases. We conducted a meta-analysis comparing the plasma/serum prolactin level in patients with SLE and healthy controls, and calculated correlation coefficients between circulating prolactin level and SLE disease activity.

Results: Twenty-five studies with a total of 1,056 SLE patients and 426 controls were included. Prolactin levels were significantly higher overall in the SLE group than in the control group (SMD =0.987, 95% CI =0.512 – 1.463, p=4.7x10^-5).

Conclusion: This study provided evidence that circulating prolactin levels were significantly higher in patients with SLE than in healthy controls. There was considerable heterogeneity between studies, and this may be due to differences in the studied populations and the measurement methods of prolactin. Further studies are needed to clarify the relationship between circulating prolactin level and SLE disease activity.
a significantly positive correlation between circulating prolatin level and SLE activity (Correlation coefficient -0.379, 95% CI -0.028-0.487, p=4.0x10^-7).

Conclusions: Our meta-analysis demonstrated that circulating prolatin levels are higher in patients with SLE and that a significantly positive correlation exists between prolatin levels and SLE activity.

Disclosure of Interest: None declared


Vasculitides

**AB0549 DEMOGRAPHIC FEATURES AND CLINICAL ASPECTS OF BEHÇET’S DISEASE IN OMANI PATIENTS**

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Background: Behcet’s disease (BD) is a chronic, relapsing, multi-system vasculitides of unknown aetiology. Few reports support the hypothesis that BD has a primarily hereditary basis. It complicated diversified clinical features predominantly involving oral and genital ulcers, ocular and cutaneous lesions. The clinical features of this disease have been described to be different according to geographical areas and gender.

Objectives: The objective of the study is to explore the demographic features and clinical aspects of BD in Omani patients.

Methods: 56 BD patients were recruited and clinical data parameters were recorded including age, sex, age at diagnosis, duration of symptoms till diagnosis, disease characteristics such as oral and genital ulcers, ocular manifestations, the presence of arthritis and cutaneous lesions such as papulopustular lesions and erythema nodosum. Furthermore, other systemic involvement was studied including gastrointestinal, neurological & vascular manifestations. Laboratory tests of BD and treatment used were recorded in each patient.

Results: The onset was between 6–74 years with a male predominance. Oral ulcers were the most common manifestation, followed by genital ulcers, ocular lesions and arthritis. Vascular lesions and GI manifestations were less common. Cutaneous manifestations were rare in patients with BD. The frequency of neurological involvement was significantly high. There were no reported cardiac or urogenital manifestations.

Conclusions: There are quite significant clinical geographical and gender differences among BD patients in which genetic and immunological factors might participate in its aetopathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1202

**AB0550 AN AUDIT OF BEHÇET’S SYNDROME RESEARCH: RECENT 6 YEARS**

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Background: A previous audit by our group of Behçet’s syndrome (BS) research, published in 2011 (1) had revealed a list of problems related to research methodology. They were mainly the relative lack of prospective studies, proper use of control groups, a marked under utilization of power calculations where needed and a paucity of studies reporting negative results.

Objectives: We have reassessed the same items as in the previous survey in articles about BS since published. An additional item looked at was self criticism in manuscript preparation (2).

Methods: Original articles from 15 highest impact factor journals of internal medicine, rheumatology and ophthalmology between January 2010 and February 2016 were analyzed by two observers. Study designs, presence of necessary control groups, power calculations and reporting of negative outcomes were tabulated. Presence of self-criticism was assessed both by reading and specific word scanning. Discrepancies between the observers was reconciled in a joint session of all 3 authors.

Results: A total of 188 articles, 149 (79%) clinical and 39 (21%) basic, were analyzed. Of 94 studies in which a time-element classification was appropriate; 53/94 studies (56%) were prospective. 28 patients (23.1%) were aPL-Abs negative. Clinical characteristics of this disease and finally 1/3 with positive TAB (33,3) were ordered by the NC with 31.9% in the former surveys. Similarly, an optimistic note might be that inclusion of diseased controls in genetic association studies, 26% in the current survey showed basic research in BS included more self-criticism (41–51%) as compared to what was noted among the general rheumatology manuscripts (15–20%) (2).

References:

Disclosure of Interest: None declared


**AB0551 THE IMPACT OF TEMPORAL ARTERY BIOPSY ON DIAGNOSIS OF GIANT CELL ARTERITIS IN CLINICAL PRACTICE**

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Background: Temporal artery biopsy (TAB) is the current gold standard for diagnosis of giant cell arteritis (GCA). Clinical manifestations of GCA include cranial symptoms, features of polymyalgia rheumatica (PMR), fever of unknown origin (FOU) and large vessel involvement, following by elevation of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). In these patients TAB confirms the diagnosis.

Objectives: In the current study the impact of TAB on diagnosis of GCA in a large number of patients is presented.

Methods: 245 patients who had undergo TAB were evaluated. All patients were more than 50 years old and were admitted in a tertiary University Hospital during the period 2006–2016. More specifically 164 were admitted in the division of internal medicine (DIM), 53 in the rheumatology clinic (RC), 6 in the eye clinic (EC) and 3 in the neurology clinic (NC). All the clinical and laboratory data were recorded and analyzed appropriately.

Results: The mean age of the patients was 68.6±5.6 year and 61.5% were women. 49/245 patients had positive TAB (21.17%). More specifically 5/6 positive TAB (83.3%) were ordered by the EC with signs of visual disturbances, mainly visual loss, diplopia and headache. 12/56 positive TAB (22.6%) were ordered by the RC with clinical features of headache and PMR. 31/164 (18.9%) with positive TAB were ordered by DIM with clinical signs of PMR, FOU and anemia of chronic disease and finally 1/3 with positive TAB (33,3) were ordered by the NC with clinical features of severe headache. All patients with positive TAB had elevated levels of CRP and ESR.

Conclusions: In elderly patients with cranial symptoms, visual disturbances, PMR, FOU and raised acute phase reactants, the possibility of GCA is very high and TAB is necessary to confirm diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4749

**AB0552 ANTIPHOSPHOLIPID ANTIBODIES IN GIANT CELL ARTERITIS**

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Objectives: The aim of our prospective study was to evaluate the role of antiphospholipid antibodies (aPL) on the clinical presentation of giant cell arteritis (GCA).

Methods: GCA patients diagnosed for the first time between 1. September 2011 and 31. December 2016 at our secondary/tertiary rheumatology center and in whom aPL-Abs were determined at presentation were included. We studied four types of aPL-Abs in patient sera: lupus anticoagulants (LA), IgG and IgM isotype of anticardiolipin antibodies (aCL), of antibodies to β2-glycoprotein 1 (aβ2GPI) and of antibodies to phosphatidylserine-prothrombin complex (aPS/PT). LA activity was determined only in patients not receiving anticoagulant therapy. A dilute Russell viper venom test was used and a ratio above 1.2 was considered positive. aCL, aβ2GPI and aPS/PT were measured using an in-house ELISA. A value above the 99th percentile of healthy control population was taken as positive.

Results: During the 64-month observation period we performed all aPL-Abs tests in 121 GCA patients (81 females (66.9%); median (IQR) age 73.8 (66.4; 78.7) years). We found LA, aCL and aβ2GPI in 59 (48.8%), 55 (45.5%), 15 (12.4%) and 18 (14.9%) cases, respectively. Fifty-four patients (44.6%) were single, 25 (20.7%) double, 13 (10.7%) triple and 1 (0.8%) quadruple aPL-Abs positive. 28 patients (23.1%) were aPL-Abs negative. Clinical characteristics of individual aPL-Ab type groups are presented in Table 1. There was one case of

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1078
The presence of aCL was associated with extracranial large vessel vasculitis (RR 1.9 (95% CI 1.1–3.2)) in patients with active disease. The presence of aPL was associated with retinal vasculitis (RR 2.1 (95% CI 1.1–4.3) for permanent or transient visual loss in cases of double or triple aPL positivity vs. LA, aCL and a2GPI negative cases). At least 1 year follow-up data (median (IQR) of 103 (54; 105) weeks) were available for 73 patients. 32 patients (43.8%) relapsed, most frequently those with positive a2GPI (62.5%).

Table 1. GCA and aPL

<table>
<thead>
<tr>
<th></th>
<th>aPL positive</th>
<th>aCL positive</th>
<th>a2GPI positive</th>
<th>aPS/PT positive</th>
<th>LA positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>121</td>
<td>28</td>
<td>55</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Female (%)</td>
<td>68.0</td>
<td>67.9</td>
<td>72.7</td>
<td>60.0</td>
<td>66.7</td>
</tr>
<tr>
<td>General symptoms (%)</td>
<td>76.0</td>
<td>67.9</td>
<td>82.2</td>
<td>66.7</td>
<td>61.4</td>
</tr>
<tr>
<td>Headache (%)</td>
<td>69.4</td>
<td>62.1</td>
<td>61.8</td>
<td>66.7</td>
<td>61.1</td>
</tr>
<tr>
<td>Jaw claudication (%)</td>
<td>42.1</td>
<td>46.4</td>
<td>43.6</td>
<td>33.3</td>
<td>22.2</td>
</tr>
<tr>
<td>Visual symptoms (%)</td>
<td>24.0</td>
<td>35.7</td>
<td>20.0</td>
<td>13.3</td>
<td>12.2</td>
</tr>
<tr>
<td>PVL or TVL (%)</td>
<td>12.4</td>
<td>14.3</td>
<td>16.4</td>
<td>13.3</td>
<td>5.6</td>
</tr>
<tr>
<td>PMR (%)</td>
<td>14.0</td>
<td>14.3</td>
<td>16.4</td>
<td>6.7</td>
<td>22.2</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>2.5</td>
<td>3.6</td>
<td>3.6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Venous thrombosis (%)</td>
<td>0.8</td>
<td>3.6</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>LVV (CDS) (%)</td>
<td>83.0</td>
<td>86.4</td>
<td>92.5</td>
<td>76.9</td>
<td>84.6</td>
</tr>
<tr>
<td>TAB (%)</td>
<td>80.7</td>
<td>88.6</td>
<td>90.3</td>
<td>88.9</td>
<td>79.7</td>
</tr>
<tr>
<td>ESR (mm/h) #</td>
<td>86 - 110</td>
<td>63 - 107</td>
<td>64 - 107</td>
<td>94 - 115</td>
<td>71 - 118</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>73 - 124</td>
<td>63 - 110</td>
<td>64 - 110</td>
<td>94 - 115</td>
<td>71 - 116</td>
</tr>
</tbody>
</table>

Conclusions: Our results indicate that aCL could identify GCA patients with extracranial large vessel disease. The double- or triple-posibility for any combination of LA and/or aCL and/or a2GPI seems to be a marker of severe visual manifestation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2508

AB0553

UPDATED SYSTEMATIC REVIEW 2016: EFFICACY AND SAFETY OF BIOLOGICAL THERAPY COMPARED TO SYNTHETIC IMMUNOSUPPRESSANTS OR PLACEBO IN THE TREATMENT OF UVEITIS ASSOCIATED WITH BEHÇET’S DISEASE


Results: Of 256 articles, 9 met the inclusion criteria: 3 retrospective observational studies, 3 open randomised trials, 2 systematic reviews, 1 phase II trial and 1 phase III trial. All GCA aPL aCL aB2GPI aPS/PT e LA

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3309

AB0554

RELATIONSHIP BETWEEN DISEASE ACTIVITY AND NEUTROPHIL-LYMPHOCYTE RATIO, PLATELET-LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME IN BEHÇET’S DISEASE

I.E. Okatan, M. Turgutalp, A. Ataev, E. Uslu Yurteri, M.E. Yaya, A.B. Keleşoğlu Dincer, T.M. Turgay, G. Kinikli, Department of Internal Medicine, Division of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey

Objectives: Behçet’s syndrome (BS) is an autoimmune disease characterized by chronic inflammation and endothelial dysfunction. There are only a few studies examining the relationship between neutrophil-lymphocyte ratio (NLR), mean platelet volume (MPV), platelet-lymphocyte ratio (PLR) and Behçet’s disease activity.

The aim of this study was to determine NLR, PLR and MPV levels and their association with disease activation in BS patients with mucocutaneous, ocular and vascular involvement.

Methods: The study included 259 patients with BS and 41 healthy individuals. We compared the MPV, NLR and PLR values of patients with active and inactive disease. NLR and PLR were significantly higher while MPV was lower in the active group than the inactive and control groups (Table 1). Statistically significant higher PLR and NLR were found in the active MC and vascular groups, significantly lower MPV was seen only in vascular active group. This significance was not seen in active ocular group (Table 2).

We also evaluated the same patient’s active and inactive periods of the disease, lower MPV, higher NLR and PLR values were seen MC and vascular groups (for all p < 0.05). When the active 3 groups were compared within themselves, the MPV value was significantly lower and NLR and PLR values were significantly higher in vascular group than active ocular and active mucocutaneous groups (p < 0.033, < 0.001, 0.01 respectively).

Table 1. Demographic and laboratory characteristics

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Active BD</th>
<th>Inactive BD</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=163</td>
<td>n=96</td>
<td>n=41</td>
<td>p</td>
</tr>
<tr>
<td>Age, y (IQR)</td>
<td>35.7 (16.2)</td>
<td>31.3 (13.2)</td>
<td>38.4 (11.8)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>69 (54.2)</td>
<td>63 (67.5)</td>
<td>10 (24.4)</td>
</tr>
<tr>
<td>ESR, mm/h (IQR)</td>
<td>4.0 (20.9)</td>
<td>2.7 (5.1)</td>
<td>1.2 (2.9)</td>
</tr>
<tr>
<td>CRP, mg/l (IQR)</td>
<td>24 (30)</td>
<td>12 (16)</td>
<td>11.5 (9)</td>
</tr>
<tr>
<td>NLR (IQR)</td>
<td>2.4 (1.7)</td>
<td>1.9 (1.0)</td>
<td>1.8 (0.8)</td>
</tr>
<tr>
<td>PLR (IQR)</td>
<td>134 (63)</td>
<td>116 (44)</td>
<td>130 (65)</td>
</tr>
</tbody>
</table>

Table 2. MPV, NLR and PLR values

<table>
<thead>
<tr>
<th></th>
<th>MPV</th>
<th>NLR</th>
<th>PLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active BD</td>
<td>85±1.9</td>
<td>85±1.1</td>
<td>85±0.9</td>
</tr>
<tr>
<td>Inactive BD</td>
<td>85±1.9</td>
<td>85±1.1</td>
<td>85±0.9</td>
</tr>
<tr>
<td>Control</td>
<td>85±1.9</td>
<td>85±1.1</td>
<td>85±0.9</td>
</tr>
</tbody>
</table>

Conclusions: The low MPV and the high NLR and PLR are found in the active disease group which is also significant in vascular and mucocutaneous disease. In the light of our findings, NLR and PLR were associated with the activity of BS especially with vascular involvement. The low MPV and the high NLR and PLR. The low MPV and the high NLR and PLR may be useful disease activity markers in Behçet’s disease.
ANCA VASCULITIS AND CLASSIC CARDIOVASCULAR RISK FACTORS: COINCIDENCE OR CAUSALITY? C. Buqua, J.J. Rios, Á. Robles, A. Noblejas, E. Martínez, C. Soto, I. Vives, J.A. Troncoso, L. Bailón, F. Arnálich. Internal Medicine, la Paz Hospital, Madrid, Spain

Background: Unlike other autoimmune diseases (rheumatoid arthritis or systemic lupus erythematosus), the mechanisms involved and the association between ANCA vasculitis with cardiovascular risk factors (CVRF) or cardiovascular events (CVE) are unknown. There may be a phenomenon of “early” atherosclerosis that contributes to the increased cardiovascular risk. This process would not be explained only by the co-existence of the classic CVRF.

Objectives: We reviewed the prevalence of classical CVRF and CVE in a cohort of patients diagnosed with ANCA vasculitis. We analyzed whether the appearance of these factors was prior to or subsequent to the diagnosis of the disease or during its evolution.

Methods: A descriptive cross-sectional analysis of the classic CVRF and CVE was analyzed in a cohort of patients with ANCA positive vasculitis in follow-up in the Autoimmune Diseases Division of a Spanish hospital. The main demographic characteristics, type of vasculitis and the presence of arterial hypertension, type 2 diabetes mellitus (T2DM), dyslipidaemia, smoking and obesity were reviewed. Likewise we analyzed CVE (heart failure-HF-, acute coronary syndrome-ACS-, stroke or transient ischemic attack-TIA- and peripheral arteriopathy -PA-) and if each factor was presented at the diagnosis of the disease or they appeared during the evolution after starting immunosuppressive treatment.

Results: A total of 35 patients were studied: 21 women (60%) and the average age was 53 years old. A number of 15 were microscopic polyangiitis, 9 granulomatosis with polyangiitis and 11 allergic granulomatous angiitis. Twenty one patients presented hypertension, 9 of them (42.9%) developed it after the diagnosis of vasculitis. From 7 patients with diabetes mellitus, 5 of them were before diagnosis with vasculitis. Nineteen presented dyslipemia and 9 of them (47.4%) presented lipid alteration during the evolution of vasculitis. Overweight/obesity was evident in 4 of the 11 cases after the diagnosis of vasculitis. Only 5 patients did not have a cardiovascular event. ACS was observed in 3 patients, HF in 2 and PA in 1 patient. There were no cases of TIA or ischemic stroke. Four of them had dyslipidemia (3 after diagnosis of vasculitis (p<0.18) and 3 had hypertension (2 after diagnosis of vasculitis, p=0.66). Three patients were overweight or obese (p=0.3) and two had T2DM (p=0.2), both of them appeared after the diagnosis. Previous history of smoking was observed in 4 of the 5 patients (p=0.06). In 3 patients (71.4%) the cardiovascular event was recorded prior to vasculitis diagnosis and only in 2 cases it occurred during the evolution.

Conclusions: This study shows that a high percentage of patients with ANCA vasculitis also presents some type of classic CVRF despite of CVE were not elevated. The diagnosis and treatment of ANCA-positive vasculitis did not statically correlate with a greater number of CVE, therefore it would be necessary to carry out studies with a larger number of patients in order to establish conclusions. It is not well defined that weight may have these factors in the prognosis of patients with ANCA vasculitis. These data suggest the need to maintain a close monitoring and therapeutic approach of classic CVRF in this relatively young group of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1758

INCIDENCE AND RISK FACTORS OF INFECTIONS IN SYSTEMIC NECROTIZING VASCULITIS C.E. Pena, M. Pera, C. Costi, G. Lucila, P. Castellani, Y. Nuccetti, M. Garcia. HIGA San Martin la Plata, la Plata, Argentina

Background: Infections in patients with systemic vasculitis represent one of the main causes of mortality. Risk factors of infection such as corticosteroid use, intensity of immunosuppressive therapy, age, presence of leucopenia, lymphopenia, hypogammaglobulinemia, associated organic involvement, and dialysis dependence have been identified.

Objectives: a) To determine the incidence of infection in patients diagnosed with Polyangiitis with Granulomatosis (PAM), Eosinophilic Polyangiitis with Granulomatosis (EGPA),Microscopic Polyangiitis (PAM) and Panarteritis Nodosa (PAN) in patients with clinical characteristics and associated risks factors. Methods: Analytical, observational, retrospective study. Data source: clinical records of patients diagnosed with ANCA associated vasculitis and Panarteritis Nodosa, evaluated in a center of rheumatology (2000–2016). Variables: Demographic data, clinical manifestations, laboratory data, infectious events such as pneumonia, urinary infection, prolongation of hospitalization or prolonged treatment, re-occurrences of herpes zoster virus or opportunistic infections), sites of infection, isolated microorganisms, mortality related to the infected event.

Results: 80 patients, 61.25% women. Mean age at diagnosis: 49.2 years (range 18–77). Types of vasculitis: 41.2% GPA, 18.7% EGPA, 26.25% PAM, 3.73% PAN not associated with HBV and 10% ANCA-associated vasculitis that did not met classification criteria. Systemic involvement (88%), pulmonary (59%), renal (58%) and otorhinolaryngology (43.6%) were the most frequent. 36 infectious events were recorded in 28 patients. Follow-up time: Median 22 m (IQR6–64). Incidence of infection: 38.4%, with a median of 3 m (IQR 1–18 m) from diagnosis of vasculitis. Low respiratory infections (40.7%), sepsis (39.3%), and urinary tract infections (15%) were the most common. 25% of these patients presented a second infectious event, being low respiratory tract the most frequent site (47%). Two patients had a 3rd event (soft tissue infection, septic shock).

Bacterial etiologie was the most prevalent (45%). Mortality at the 1st event was 14.3% (n: 4). 71.4% of patients were in the induction phase of treatment. Immunosuppressants used prior to infectious event: cyclophosphamide (48.1%), azathioprine (11.1%), methotrexate (7.4%), mofetil mycophenolate (3.7%), none (22.2%). Corticosteroids ≤30 mg/d were observed in 35.7% patients, ranging from 7.5–30 mg/d (10.7%), and ≤7.5 mg/d in 35.7%. Presence of leuocopenia (26%), lymphopenia (44%), hypoalbuninemia (24%), renal insufficiency (63%) and dialysis dependency (37%) were identified in patients with infectious events. Renal infection (p=0.01) and dialysis dependence (p=0.001) were significantly associated with infection.

Conclusions: The incidence of infection was 38.4%. Lower airway infections, septicaemia and urinary tract infections are the most commonly implicated sites. Most infections occurred in the induction phases of the disease. Dialysis dependence and presence of renal involvement were significantly associated with the presence of infection.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5262
AB0558  BIOSIMILAR INFILXIMAB FOR BEHÇET'S SYNDROME
E. Dinçsoy1, S.N. Esatoğlu1, E. Seyahi1, M. Melikoğlu1, I. Fresko1, G. Hatemi1.
Background: The efficacy and safety of biosimilar infliximab has been studied in several inflammatory conditions and biosimilar was approved for all indications of the reference product in several countries. However, to the best of our knowledge, there was no published reports on its use in Behçet’s syndrome (BS).
Objectives: We aimed to report our experience with biosimilar infliximab for the treatment of 3 different types of organ involvements in BS.
Methods: We reviewed the charts of all BS patients who were prescribed infliximab in our multidisciplinary BS clinic. Among the 88 patients who were prescribed infliximab, 4 had used biosimilar infliximab (5 mg/kg) due to refractory disease despite conventional immunosuppressives.
Results: Case 1: The first patient was a 28-year-old man who had received azathioprine (AZA), cyclosporine-A and methotrexate for 6 years for ocular involvement. Six months after the immunosuppressives were stopped due to sustained remission he had a stroke with right hemiparesis. Cerebral MRI revealed venous infarct extending from posterior limb of left internal capsule to pons and mesencephalon, involving corpus callosum. Cervical MRI revealed a hyperintense lesion between C3-C8 segments. His cranial MR venography excluded sinus thrombosis. He received intravenous pulse corticosteroid followed by biosimilar infliximab. He achieved clinical remission and his MRI at month 3 showed complete regression of the lesions. He is still in remission at 7th month of therapy.
Case 2: The second patient was a 24-year-old man using AZA 2.5 mg/kg/day for refractory skin lesions when he developed bilateral external iliac vein and right common iliac vein thrombosis. He received intravenous pulse corticosteroid followed by biosimilar infliximab. After one year treatment was switched to etanercept 50 mg/week and is attack-free for the last 7 months. Case 4: The fourth patient was a 26-year-old man who had prescribed infliximab for panuveitis refractory to AZA, ciclosporin-A and interferon-alpha. The first infusion was biosimilar infliximab, but the following infusions were reference infliximab due to reimbursement policy of the hospital. There were no adverse events after switching to reference infliximab and the patient is doing well at 8 months of therapy.
Conclusions: Our limited experience showed that biosimilar infliximab may be effective for BS patients refractory to conventional immunosuppressives.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6199

AB0559  IMPROVING THE MANAGEMENT OF GIANT CELL ARTERITIS: A REVIEW OF CARE PATHWAY FOR PATIENTS WITH SUSPECTED GIANT CELL ARTERITIS IN A DISTRICT GENERAL HOSPITAL
1Rheumatology Department, Brighton and Sussex University Hospitals NHS Trust; Brighton, 2Rheumatology Department, East Surrey Hospital, Redhill, United Kingdom.
Background: Giant cell arteritis (GCA) requires prompt diagnosis and treatment to prevent irreversible neuro-ophtalmic complications. Conversely, misdiagnosis leads to unnecessary treatment with high dose glucocorticosteroids (GC) and their associated complications. The British Society of Rheumatologists (BSR) guideline emphasises early recognition of symptoms and prompt treatment when index of clinical suspicion is high.
Methods: Case notes of patients seen in ESH with suspected GCA between March 2015 and December 2016 were reviewed retrospectively. Cases were identified through keyword search on hospital discharge letters and Rheumatology clinic letters.
Results: Case notes of 67 patients (21M, 46F) were analysed. Of those presenting with suspected GCA, 31% fulfilled ACR classification criteria. 28% had documented visual symptoms at presentation.
Conclusions: This study aims to audit the management of patients with suspected GCA against BSR guidelines. It also aims to evaluate patients’ journey, to identify inefficiencies within the management pathway, in order to initiate improvements in clinical practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5463

AB0560  STUDY ON STREPTOCOCCAL INFECTION RELATIONSHIP WITH HENOCCH SCHONLEIN PURPURA IN CHILDREN
F. Li1*, H. Zang2. 1Department of Pediatric Allergy, Immunology and Rheumatology; 2Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children’s Medical Center, Guangzhou, China
Objectives: To study hemolytic Streptococcus infection relationship with Henoch-Schonlein Purpura in children.
Methods: 42 cases in children with Henoch-Schonlein Purpura (Observer Group) and healthy children in 40 cases of physical examination (the control group) for blood antistreptolysin O (ASO) detection, observation group at the same time to blood ASO detection positive 2 cases, accounted for 5%, both comparison differences has not significance (χ²=9.35, p<0.01).
Conclusions: Streptococcal infections may be an important factor related to Henoch-Schonlein Purpura in children. Purpura and Purpura of abdominal type children with 23 cases, blood ASO detection positive 17 cases, accounted for 73.9%; non-abdominal type Purpura children with 19 cases, blood ASO detection positive 2 cases, accounted for 5%, both comparison differences has not significance (χ²=22.22, p<0.01); abdominal type Purpura children with 23 cases, blood ASO detection positive 17 cases, accounted for 73.9%; non-abdominal type Purpura children with 19 cases, blood ASO detection positive 2 cases, accounted for 5%, both comparison differences has not significance (χ²=9.95, p<0.01); 14 cases in children with recurrent Henoch-Schonlein Purpura, ASO blood test positive in 12 cases, 85.7%; non-recurrent attacks of 28 cases of children with Henoch-Schonlein Purpura, ASO blood test positive in 10 cases, 35.7%, comparing the two differences are significant (χ²=9.35, p<0.01).
Conclusions: Streptococcal infections may be an important factor related to Henoch-Schonlein Purpura in children. Purpura and Purpura of abdominal type recurrence is related with streptococcal infection, which is the great value to observation and treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2136
Background: Rituximab (Rtx), a novel biological, having B cell depletive mechanism is an anti-CD 20 antibody and is found to be useful in patients of ANCA associated vasculitis. In AAV the disease activity correlates with increased circulating B cells. Rituximab has been found to be useful in depleting these B cells. Accordingly, in our RVE study, Rituximab was shown to be non-inferior to Cyclophosphamide in induction remission. It also shows that the regimen (Rtx) may be superior to the standard regimen of Cyclophosphamide and glucocorticoids for remission induction in severe relapsing ANCA-associated vasculitis. In our study, B cell therapy was given in those patients only who had persisting disease activity or relapse.

Objectives: To assess response of Rtx in relapsed/refractory cases of AAV and show that it is a good therapeutic strategy in such cases.

Methods: In our cohort there were 49 patients of ANCA associated vasculitis, diagnosed by clinical and serological criteria, (by both ELISA and IFA) classified according to ACR criteria and supported, wherever possible, by biopsy. In this prospective study, patients were seen during January 2012 to January 2017. A total of 15 patients received Rituximab for various reasons. Rituximab (Rtx) was given intravenously on day 1 and day 15 as induction therapy and subsequently 6 monthly maintenance doses of 500 mg were administered. No other immunosuppression other than steroids were given.

Results: Median follow up was 22 months. All patients had received Cyclophosphamide (median of 6 grams) and 1mg/kg glucocorticoids at onset. Among the patients who received Rituximab, all had anti PR3 positivity and all were GPA clinically. 14 patients (93.33%) had lung involvement, renal involvement was seen in 7 (46.6%) patients, 13 (86.6%) patients had upper respiratory tract involvement, 6 (40%) had ophthalmic involvement. Nervous system involvement was seen in 1 (6.6%) and myocarditis was seen in 3 (20%) each. 3 (20%) patients had gangrene.

Indications for receiving Rtx were heterogenous. It was given for involvement of more than two-thirds of patients. Increasing evidence supports a role of circulating B cells. Rituximab has been found to be useful in depleting these circulating B cells. Rituximab was shown to be non-inferior to Cyclophosphamide in induction remission. It also shows that the regimen (Rtx) may be superior to the standard regimen of Cyclophosphamide and glucocorticoids for remission induction in severe relapsing ANCA-associated vasculitis.

Conclusion: Our study shows that Rituximab is an effective therapeutic strategy for refractory/refractory especially PR3+ AAV also it can be used as a maintenance regimen for long term.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5596
Results: 15 patients, 6 males and 9 females (mean age 71.6 ± 7 years – duration symptoms at onset 1.7 ± 1.3 months – mean ESR 60 mm/h 52 – mean CRP 8 mg/dl ± 5.2) entered the study. US halo sign was bilateral in 10/15 (66.7%). The mean halo thickness was 0.53 mm ± 0.12. Five patients had USG +1, six patients +2 and four patients +3. The histological inflammatory grade 1 was present in seven pts, grade 2 in four and grade 3 in four pts. No significant correlation were found between USG and histological inflammatory grade, nor with the presence of giant cells, calcifications, lamina necrosis and intima-media thickness.

Conclusions: No correlation has been found between the size of the halo sign and the histological inflammatory grading.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5093
The long term health related quality of life (HRQOL) impact on giant cell arthritis (GCA) patient

**AB0567**

**THE LONG TERM HEALTH RELATED QUALITY OF LIFE (HRQOL) IMPACT ON GIANT CELL ARTHRITIS (GCA) PATIENT**

H. Horiuchi, General Medicine, Kurashiki Central Hospital, Okayama, Japan

**Background:** Health related quality of life (HRQOL) of Giant cell arthritis (GCA) patients is important because it adds depth to our understanding of how a disease and its treatments affect them. Though only one previous study has addressed the short term impact of GCA on HRQOL, the long term impact has not fully been investigated.

**Objectives:** The aim of our study is to assess the long term HRQOL outcomes of GCA patients using the Japanese version of EuroQol 5 Dimension (EQ-5D).

**Methods:** 40 GCA patients who admitted to our hospital from November 2004 to June 2014 were enrolled. All patients were received prednisolone over 2 years. Patients who had lost their eyesight were excluded because vision concern for HRQOL nor it is difficult to measure by using EQ-5D. This is a retrospective study and data were collected by telephone interview. Patients evaluated their health status using five dimensions. The EQ-5D score were calculated based on the Japanese version of the value set. Primary outcome is the mortality rate and the norm of EQ-5D score. As a secondary analysis, we classified the patients as follows and compare the mortality rate and EQ-5D score between two groups.

**Results:** One study focused on GCA patients with prednisolone therapy over 2 years. It showed that EQ-5D was decreased compared with the Japanese norm but it didn’t clearly decrease after 2 years of treatment. These findings suggest the value of measuring health status by EQ-5D at least at first 2 years of treatment, because it would allow comprehensive evaluation of the patient’s health condition and add another dimension to the subjective symptoms and laboratory data.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4171

**AB0568**

**APPLICATION OF OZONATED WATER IN ORAL ULCER PATIENTS WITH BEHCET’S DISEASE**

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**Background:** Behcet’s disease is a systemic vasculitis disease of unknown etiology. Oral ulcer is the most common symptoms, the ulcer is various, the swelling and pain is obvious, and it is easy to recur, these symptoms affected the patient’s diet and life seriously. Therefore, it is important to care the patients with Behcet’s disease of oral ulcer. The ozonated water had many functions such as immune activation and immune regulation, it can induce the production of many cytokines,promote the repairment of oral epithelium.At the same time, the ozonated water had a direct effect on the nerve endings, it played a better analgesic effect, it was widely used in oral mucositis which induced by chemotherapy. But there were few studies about application ozonated water in the patients with Behcet’s disease of oral ulcer, it was not widely used in clinical practice.

**Objectives:** Apply the ozonated water in patients with Behcet’s disease, observe the effectiveness in patients with Behcet’s disease of oral ulcer.

**Methods:** From June 2014 to June 2016,82 cases of hospitalized patients with Behcet’s disease were randomly divided into study group and control group (n=41), the control group used nursing method of gentamycin sulfate solution and the number of giant cells in the present case were not remarkably high. A systematic literature review identified 4 cases of 18F-FDG-PET positive temporal arteries in GCA, a systematic literature review was performed identifying 83 cases of 18F-FDG-PET positive temporal arteries in GCA. In our case, the number of giant cells in the present case was not remarkably high. A microscopic neutrophilic abscess. When compared with 2 other cases of temporal arteritis with a negative 18F-FDG uptake, the severity of inflammation and the number of giant cells in the present case were not remarkably high.

**Conclusions:** This was a retrospective chart review of 3 patients with giant cell arteritis who underwent all of 18F-FDG-PET, MRA, CT angiogram, ultrasound and histopathologic evaluation of temporal arteries. To investigate the cases of GCA-PET positive temporal arteries in GCA, a systematic literature review was done in Pubmed using 18F-FDG-PET AND (“temporal arteritis” OR “giant cell arteritis”).

**Results:** The mortality rate was 56.0% (14 patients) in Group1 and 6.6% (1 patient) in Group2. It was significantly higher in Group 1 (P<0.05). The median EQ-SD score was 0.764 (95% confidence interval [CI] 0.597–0.870) in Group1 versus 0.768 (95% CI 0.621–0.915) in Group2. There was no statistically significant difference between them (P=0.813).

**Conclusions:** This study focused on GCA patients with prednisolone therapy over 2 years. It showed that EQ-SD was decreased compared with the Japanese norm but it didn’t clearly decrease after 2 years of treatment. These findings suggest the value of measuring health status by EQ-5D at least at first 2 years of treatment, because it would allow comprehensive evaluation of the patient’s health condition and add another dimension to the subjective symptoms and laboratory data.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3691

**AB0569**

**CHANGE IN SERUM LEVEL OF SOLUBLE E-SELECTIN AND MMP-9 IN CHILDREN WITH KAWASAKI DISEASE**

H. Zeng, Department of Pediatric Allergy, Immunology and Rheumatology, GuangZhou Women and Children’s Medical Center, Guangzhou, China

**Objectives:** Kawasaki disease (KD) is a kind of febrile disease without definite etiology. Coronary artery aneurysms are the major complication of Kawasaki disease. With 111R-pimonidazole imaging of the vascular damage of GCA of remains unknown. This study WIIF conducted to explore the pathophysiological role of E-selectin (ES), CAMstrx metalloproteinase 9 (MMP-9) in KD, and to look for the evidence of direct relationship between the plasma levels of ES,MMP-9 and the incidence of the coronary artery lesion (CAL).

**Results:** There were 16 male (40%) and 24 female (60%). The median age was 83.5 (95% CI 79.24–87.76). The mortality rate was 37.5% (15 patients). Kaplan-Meier curve is shown in Figure1. The median EQ-SD score was 0.746 (95% confidence interval [CI] 0.852–0.640) and it is lower than Japanese norm (0.853 in male and 0.808 in female). In the secondary analysis, the mortality rate was 56.0% (14 patients) in Group1 and 6.6% (1 patient) in Group2. It was significantly higher in Group 1 (P<0.05). The median EQ-SD score was 0.764 (95% CI 0.579–0.870) in Group1 versus 0.768 (95% CI 0.621–0.915) in Group2. There was no statistically significant difference between them (P=0.813).

**Conclusions:** This study focused on GCA patients with prednisolone therapy over 2 years. It showed that EQ-SD was decreased compared with the Japanese norm but it didn’t clearly decrease after 2 years of treatment. These findings suggest the value of measuring health status by EQ-5D at least at first 2 years of treatment, because it would allow comprehensive evaluation of the patient’s health condition and add another dimension to the subjective symptoms and laboratory data.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3691
Methods: Soluble ES and MMP-9 were measured in 68 patients with KD. 20 patients with febrile disease and 20 healthy children by using double antibody sandwich enzyme linked immunosorbent assay (ELISA). Patients with KD were separated into acute phase group, subacute phase group, recovery phase group.  Coronary artery lesion group (CAL), non-coronary artery lesion group (NCAL).  BVAS for GPA, FFS (1996) and FFS (2009) of patients with refractory disease (≥ 9.5) were the most frequently identified auto-antibodies (40%). Musculoskeletal manifestations (arthritis, and myalgia), mucocutaneous disorders (including vasculitic/necrotic lesions, mucosal ulcers, and purpura), neurological compromise (peripheral and central), and renal involvement (acute renal failure, glomerulonephritis, and lung–kidney syndrome) were the most frequently reported onset symptoms in 29%, 29%, 23%, and 21%, respectively. Interestingly, most of patients did not develop organic compromise other than the onset manifestation form.  Three percent of patients fulfilled polyautoimmunity criteria and 9% presented with multiple autoimmune syndrome.  ANCA-associated arteritis syndrome was the most common associated autoimmune disease described.  Cotricosteroids were the most common treatment used in 93% of patients, followed by azathioprine in 57%, cyclophosphamide, methotrexate, and rituximab in 29%, and antimarial in 21%.  No deaths occurred during follow-up.

Conclusions: Vasculitides are conditions with several subphenotypes, being ANCA-associated the most frequently reported.  Onset symptoms seem to be the main drivers of disease evolution.  Appropriate and prompt diagnosis is critical to enable timely intervention, aimed to prevent end organ damage and reduce morbidity in these patients.  Controlling disease activity and preventing progression is the milestone of treatment.  Characterization of Latin America population is pivotal to raise awareness of health-care workers, and policy makers.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6766

AB0571 BIRMINGHAM VASCULITIS ACTIVITY SCORE MORE THAN 9.5 AT FOLLOW-UP IS AN INDEPENDENT PREDICTOR OF REFRACTORY DISEASE OF GRANULOMATOUS WITH POLYANGITIS

J. You, H.J. Kim, S.-W. Lee. Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, Seoul, Korea, Republic Of

Background: Granulomatosis with polyangiitis (GPA), that is identical to what has been called Wegener's granulomatosis, is one of anti-neutrophil cytoplasmatic antibody (ANCA)-associated vasculitides (AAV). GPA is characterized by necrotising granulomatous inflammation usually affecting small to medium vessels, and it often involves the upper and lower respiratory tracts and commonly provokes necrotising glomerulonephritis.  It has been reported that the mortality rate in untreated patients increased up to 90% within 2 years after diagnosis, and the overall mortality rates were ranging from 12% to 44% within 4 to 10 years.  The major causes of death are known as cardiovascular disease, adverse events of immunosuppressive agents and major organ involvement of GPA.  If there might be predictors of relapse or refractory disease of GPA during the follow-up duration, they can help physicians to select the induction therapeutic regimens, decide the duration of the maintenance therapeutic regimens and adjust the follow-up interval in order to improve the disease course of GPA.

Objectives: We investigated whether clinical manifestations, anti-neutrophil cytoplasmatic antibodies (ANCAs), Birmingham vasculitis activity score (BVAS) for granulomatosis with polyangiitis (GPA) and five factor score (FFS) at diagnosis can predict relapse or refractory disease in 30 histology-proven GPA patients with the follow-up duration ≥12 weeks.

Methods: We reviewed the medical records of 30 GPA patients. We collected clinical data, ANCAs, BVAS for GPA, FFSs at diagnosis, and we compared variables between the two groups based on relapse or refractory disease. The optimal cut-offs were extrapolated. Multivariate logistic regression and Cox hazard model analyses were conducted to identify predictors of relapse or refractory disease.

Results: The mean age and follow-up duration of patients were 63.3 years old and 45.2 months. The mean initial BVAS for GPA, FFS (1996) and FFS (2009) were 5.4, 0.6 and 1.0. There were no significant predictors of relapse. The mean BVAS for GPA, FFS (1996) and FFS (2009) of patients with refractory disease were higher than those without (p<0.05 for all). Patients having BVAS for GPA ≥9.5, FFS (1996) ≥2 and FFS (2009) ≥2 exhibited significantly enhanced risk of refractory disease than those having not (RR 23.0, RR 11.0, and RR 55.0, respectively), and low cumulative refractory disease free survival rates. Multivariate Cox hazard model analysis proved BVAS for GPA ≥9.5 was an independent predictor of refractory disease during the follow-up duration ≥12 weeks.

Conclusions: BVAS for GPA ≥9.5 was an independent predictor of refractory disease during the follow-up duration ≥12 weeks.
Background: In Japan, rituximab (RTX) has become one of the dominant therapies for ANCA-associated vasculitides. The primary aim of RTX induction is remission induction followed by glucocorticoid discontinuation. In Japan, AAV, mostly MPO-ANCA-positive PMA, affects elderly patients at the age of over 70 years with severe MPA, with an acceptable safety profile and rapid glucocorticoid tapering. However, careful monitoring for infection is crucial in elderly patients.

Methods: Nineteen patients with AAV, including 14 newly diagnosed patients and 5 relapsed patients, had been treated with RTX. There were 10 males and 9 females. They were all MPO-ANCA positive; 16 were diagnosed with microscopic polyangiitis (MPA), 2 with granulomatosis with polyangiitis (GPA), and 1 with undifferentiated, according to the EMA classification of AAV. The median age of RTX induction was 71.3 years (range: 40–82 years). The efficacy was evaluated by the BVAS score at the time of first induction and after 6 month treatment. Adverse events were recorded during the 6-month treatment.

Results: The mean of BVAS decreased from 17.3 (range: 7–35) at the first induction to 1.2 (0–4) at 6 month of RTX treatment. Of the 10 patients who could be followed-up for over 6 months, 7 patients achieved remission (BVAS=0) (remission rate: 70.0%). The median of MPO-ANCA decreased from 136.1 IU/mL (range: 10.9–300 IU/mL) to 44.4 IU/mL (1.0–114.0 IU/mL) at 6 month. The dose of prednisolone decreased from 34.4mg/day (5–60mg/day) at baseline to 5.5mg/day (0–10 mg/day) at 6 month. The adverse events were as follows: 3 patients experienced reactivation of cytomegalovirus (CMV) with a CMV colitis, one patient with sepsis following urinary-tract infection, and one patient with bacterial pneumonia. One patient with PMA died of exacerbation of the disease itself. None of the patients had reported complications, 5 patients had no complications and 6 patients were missing data. All data was sourced from single case studies.

Conclusions: Out the indications, outcomes and complications of HSCT in a case series of 4 patients with BS managed at a single centre of excellence.

Methods: Case notes were reviewed for 4 patients from the Liverpool Behçet's Centre of Excellence (LBCE) who have undergone HSCT.

Results: The primary indication for 3 of the 4 patients who have undergone autologous HSCT at LBCE was refractory BS. Patient 1 underwent HSCT for multiple myeloma, but suffered from severe BS with neurological and venous involvement and is now in partial remission with occasional mild muco-cutaneous ulceration, not requiring systemic immunosuppression. Patient 2 underwent HSCT for severe refractory neuro-Behçet's. This patient is now in complete remission after commencing azathioprine for oral ulceration. The indications for HSCT in patients 3 and 4 were severe muco-cutaneous ulceration and dermatological involvement refractory to numerous biologic agents with high ongoing steroid dependency. Patient 3 also had previous thrombophlebitis and patient 4 had previous gastro-intestinal ulceration. They are both currently in complete remission but follow up time is limited. Patient 3 had a post-HSCT complication of pneumonia and mucositis which resolved without persistent morbidity, patient 4 had an upper limb deep vein thrombosis (DVT) as an inpatient.

Conclusions: HSCT is an effective treatment modality for severe refractory BS and can result in medication free remission. However, the associated risks should be considered and alternative treatment options deliberated or exhausted before opting for this treatment modality.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2568

Abstract AB0574 – Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at HSCT (years)</th>
<th>Sex</th>
<th>Disease duration at HSCT (years)</th>
<th>BS manifestations</th>
<th>Treatment pre-HSCT</th>
<th>HSCT Indication</th>
<th>Follow up (months)</th>
<th>Complications</th>
<th>Outcome</th>
<th>Treatment post-HSCT</th>
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<tr>
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<td>47</td>
<td>M</td>
<td>6</td>
<td>OU</td>
<td>Tacroflex</td>
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<td>Nil</td>
<td>OU/GU (minor)</td>
<td>Pred 4mg</td>
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<td>29</td>
<td>M</td>
<td>5</td>
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<td>Neuro-Behçetts</td>
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<td>Nil</td>
<td>1x flare 2013 (OU)</td>
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<td>M</td>
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<td>DVT</td>
<td>Remission</td>
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<td>Pneumonia &amp; Mucositis</td>
<td>Remission</td>
<td>Pred 40mg</td>
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</tbody>
</table>

OU = oral ulceration, GU = genital ulceration, MSK = musculoskeletal, S = skin, N = neurological, V = vascular. AZA = azathioprine, CYCP = cyclophosphamide, MMF = mycophenolate motefil, MTX = methotrexate. ADA = adalimumab, IFX = Infliximab, ETN = Etanercept, ALN = Alentuzumab.
The most frequent vascular manifestation in BD. In this study, we looked at the pattern and outcome of venous events in BD.

Methods: Seventy-five patients, who fulfilled the criteria of the International Study Group for diagnosis of BD, were recruited. We studied the characteristics of patients with thrombotic venous events. Clinical data parameters were recorded, including age at onset, the vascular and extra-vascular manifestations of the disease.

Results: Twenty-six patients had vascular event. Twenty-three of these patients had a venous event. The mean age of the patients at the first venous event was 32 years. There were 22 males and 4 females. The first venous event occurred before BD diagnosis in one case (10.9%) and was the same time of onset of the disease in two cases. In the other cases, venous event occurred in patients followed for BD and the mean disease duration was 5, 82 years. The mean number of recurrence of venous events was 1.46. Deep vein thrombosis was the most frequent single vascular event (76, 92%). The most frequent localizations were in lower left leg (23 cases). Patients had cerebral vein thrombosis. A pulmonary venous involvement, a Budd-Chiari syndrome, an inferior and superior vena cava syndrome, and arm thrombosis were found in only one case each one. An arterial event was associated in 2 cases. An association with ocular manifestations was observed in 26, 9% patients and neurologic manifestations in 11, 53%.

Conclusions: Although there is no agreement on the frequency rate of the vascular lesions in the literature, most of the vascular lesions in the literature, most of the reported series indicate that the venous lesions are far more, by far more common than the arterial lesions. Kabba et al. reported 85% venous, 10% arterial and 5% miscellaneous with venous and arterial involvement which is similar to the reported frequency in our patients.

In conclusion, the frequency of vascular complications of BD in our patients is similar to those reported around the world.

References:

Disclosure of Interest: None declared


AB0575 RETROSPECTIVE SURVEY OF CONCOMITANT AUTOIMMUNE DISEASES AND AUTOANTIBODIES IN A Cohort OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIS (AAV)

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Background: Anti-neutrophil cytoplasmatic antibodies (ANCA) associated vasculitis (AAV) is a necrotizing vasculitits that predominantly affects small and medium arteries and has ANCA specificity for myeloperoxidase (MPO-AA) or proteinase 3 (PR3-ANCA). The major clinicopathologic variants of AAV include microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Recent studies have demonstrated the crucial role of complement activation in the pathogenesis of AAV. However, the clinical characteristics of AAV with hypocomplementemia (HC) still remain unclear.

Objectives: The aim of our study was to analyze the demographic, laboratory, treatment and clinical characteristics of AAV using medical records. To compare the AAV patients with and without HC.

Methods: Retrospective study of patients with AAV diagnosed and followed in a specific Systemic Autoimmune Diseases and Thrombosis Unit. We defined HC as the state in which at least one of the following was lower than the lower limit of the normal range: Complement C3 (C3), Complement C4 (C4). Demographic, clinical, treatment and evolution data were recorded and analyzed using SPSS 22.0.

Results: Thirty-six patients with AAV were included (94.4% MPO-ANCA, 5.6% PR3-ANCA). 8 patients were diagnosed of GPA, 21 of MPA and 3 of EGPA. 61% of the patients were males and the mean age at the onset of the disease was 63,1±14,38 years (30–85). 75% of patients had any vascular risk factors. Renal involvement occurred in 32 patients (88.9%); hematuria in 96.9%, proteinuria in 90.6% (>1 g/day), and gloomerular filtration decreased in 81,25%. Biopsy was performed in 22 patients and a focal and segmental necrotizing glomerulonephritis with extracapillary proliferation was the finding more common. Pulmonary disease (61,1%) included interstitial disease 40,9%, alveolar hemorrhage 22,7% and nodules 18,2%. Other clinical manifestations were constitutional syndrome 36,1% (the main symptom was asthenia); ear, nose, and throat manifestations 33.3%; neurologic involvement 27.8% (the main finding was polynyruropathy); articular manifestations 33.3% and skin lesions 16.7%. All the patients received prednisone in combination with cyclophosphamide (69.4%) or rituximab (13.9%). Azathioprine was used as glucocorticoid-sparing agent (41,7%). 83,3% of the patients needed hospital admission and 6 died (16,7%). Eleven patients (30.6%) had HC at their diagnosis of AAV. Compared to the AAV patients without HC (n=25), we found no significant differences in the frequency or severity of the manifestations (evaluated by Five factor score). The small sample size could in part explain these results.

Conclusions: Our patients with HC at diagnosis of AAV did not have different characteristics than those without HC. More studies are needed to determinate if HC is a predictor of poor prognosis in AAV patients.

Disclosure of Interest: None declared


AB0577 SYSTEMIC AUTOIMMUNE VASCULITIS IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPTHLOGIC STUDY OF 161 PATIENTS

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Background: Systemic vasculitis of autoimmune origin (A-SV) may be regarded as a basic histological manifestation of rheumatoid arthritis (RA) [1,2]. The aim of our study was to characterize the severity of systemic autoimmune vasculitis at death in RA patients.

Methods: A randomized autopsy population of 161 in-patients with RA was studied.

A-SV was confirmed clinically according to the criteria of the ACR [4]. The severity of vasculitis was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale in 12 organs (heart, lung, liver, spleen, kidney, pancreas, gastrointestinal tract, adrenal gland, skeletal muscle, peripheral nerve, skin and brain) at death) [1]. 0*: no vasculitis; **: sporadically (scattered) located gender (OR 2.710,95% CI 1.034–7.099,p=0.043), MPA syndrome (OR 3.578, 95% CI 1.334–9.523,p=0.011) and MPO carriers (OR 3.346, 95% CI 1.166–9.601,p=0.025).

Conclusions: A substantial percentage of AAV patients, particularly MPA and anti MPO carriers, have associated autoimmune diseases and autoantibodies. The high frequency of our study (retrospective assessment and lack of comparator) do not allow accurate estimation of prevalence. The severity of AAV and difficulties in management, may lead to overdiagnosis of associated autoimmune diseases which appear to be frequent. Associated autoimmune disease may contribute to additional burden in AAV patients. (Supported by SAF 2014 57708-R).

Disclosure of Interest: None declared

vasculitis, “2”: less than five, “3”: five or more involved blood vessels/microscopic
field with a x20 objective.

The age at death, and the onset and duration of RA with mild (<0.2/patient), or
severe (0.2A-SV, were compared by Student (Welch) t-probe.

Results: 16 (50.0%) of 32 patients had a “mild” degree of A-SV (females 11, avg
age of 70.91 years, range 68 – 90, onset of RA: 62.55, avg disease duration: 8.39
years at death; males 5, avg age of 71.6 years, range 83 – 58, onset of RA: 57.2, avg
disease duration: 14.4 years).

16 (50.0%) of 32 patients had “severe A-SV” (females 8, age of 60.88 years,
range 62–32, onset of RA: 52.67, avg disease duration: 13.5 years at death; males
8, avg age of 65.0 years, range 78–53, onset of RA: 53.25, avg disease duration:
11.75 years).

Four (12.5%) of 32 patients had “extremely severe A-SV” (with an average
cumulative value of severity/RA patient with SV >0.630) (females 1, age of 82.0
years, onset of RA: 62.0, average disease duration: 20.0 years at death; males 3,
average age of 69.7 years, range 78 – 59, onset of RA: 60.7, average disease duration:
duration: 9.0 years).

Severity of SV in 32 RA patients with A-SV – according to increasing average values
of vasculitis/patient – is summarized in Figure.

Conclusions: A-SV is caused by circulating immune complexes in RA. Immune
complexes spread via the bloodstream and provoke vasculitis throughout the
body.

We found no differences in the linear and basically parallel development of A-SV
between patient groups with mild and severe vasculitis.

The progression of vasculitis was the same in both patient groups suggesting
differences in production of circulating immune complexes.

Quantitative differences in the production of circulating immune complexes may
be related to a “benign” or “aggressive” clinical course of RA, which may be due
to genetical and other factors.

In 4 of 32 RA patients the severity of vasculitis showed a “step-wise” growth
with “extreme severe” A-SV (0.630 or <) according to increasing average values
of vasculitis/patient (Figure 1). There was no gradual transition between the
“extremely severe” and “severe” degrees A-SV. This profile of “step-wise”
general severity in patients with vasculitis may represent a subgroup of patients
with a different genetic-immunologic background.

References:

Disclosure of Interest: None declared


AB0578 ARTERIAL ANEURYSMS MOROCCAN EXPERIENCE STUDY OF 37 CASES.

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University hospital Ibn rochd, Casablanca, Morocco

Background: Behcet’s disease is a systemic vasculitis with a tropism for the
venous system. Arterial involvement is uncommon (1%) and mainly represented
by aneurysms that can be life-threatening.

Objectives: This retrospective study was conducted in the internal medicine
department of the University Hospital Ibn Roch of Casablanca, over a period
of thirty-five years between 1980 and 2016. Where included all the cases of
Behcet’s disease diagnosed in our service (1618 case).

Methods: We aimed to determine the epidemiological profile, the different
possible clinical manifestations and to discuss both prognosis and treatment
in such cases.

Results: 37 patients – 32 men and 5 women – presented arterial involvement
in type of arterial aneurysm, which represents a rate of 2.35%.

Mean age at diagnosis was 32 years old (ranges 17–54). This complication was
the revealing event for Behcet's disease in 2 cases, concomitant in 3 cases and
occurring after an average of 6-year-period evolution of the disease in 32 cases.

The aneurysm affected: the pulmonary artery (22 cases), the abdominal aorta
(5 cases), the femoral artery (5 cases), the internal carotid artery (2 cases), the
iliac artery (2 cases) and the middle cerebral artery (1 case). The aneurysm was
associated with venous disease (18 cases), pulmonary embolism (2 cases) and
intracardiac thrombus (1 case).

The management treatment has relying on anticoagulants (6 cases), anti-aggregating
agents (9 cases), corticosteroids (36 cases), immunosuppressive drugs –
cyclophosphamide (23 cases) and azathiope (12 cases), while 7 patients
underwent surgical intervention.

Evolution was favorable in 23 patients and with negative outcome in 14 patients
(9 relapses and 5 deaths).

Conclusions: Arterial aneurysms are the most common arterial complications in
the context of Behcet’s disease, while the prognosis remains poor in the absence of
early and appropriate management (anticoagulants, immunosuppressive agents,
surgery).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4064

AB0579 IMMUNE RELATED DIFFUSE ALVEOLAR HAEMORRHAGE: SINGLE CENTER EXPERIENCE AND LONG TERM OUTCOME – RHEUMATOLOGICAL PERSPECTIVE.

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Background: Diffuse alveolar haemorrhage (DAH) is a feature of several immune
and nonimmune disorders. Failure to diagnose and treat DAH syndromes in their
early stages may lead to acute respiratory failure, CKD and death. Prognosis is poor
with in-hospital mortality ranging from 20% to 100%. Immune related DAH
is monophasic and if treated early and achieved remission, long term outcome is
good.

Objectives: To evaluate the therapeutic response and long term outcome in
patients with Immune related (AAV & SLE) DAH.

Methods: A retrospective review of medical records of patients admitted under
Rheumatology and Clinical immunology department with Immune related DAH
was made with regards to their presentation, treatment & response, mortality,
 morbidity and long term outcome. Study was performed after approval and ethical
clearance from IRB.

Results: From June 2012 to August 2016, 18 patients (15 were AAV related &
3 as SLE related) were admitted. Amongst AAV patients, PR3 positive were
11 & MPO positive were 4. Fourteen patients were females and 4 males, age
 ranged from 14 – 68 yrs (median=54.5 yrs). Mean duration of disease before
onset of DAH was 3 months. Nine (50%) patients had associated kidney and
musculoskeletal involvement. Eleven (61.11%) patients were admitted under
ICU care requiring artificial ventilation. Pulse methylprednisolone injections were
given in 15 (83.33%), Cyclophosphamide in 13 (72.22%), IVig in 2 (11.11%),
plasmapheresis in 7 (38.88%) patients. Time from first consultation to pulse
methylprednisolone was in range from 1 to 5 days. Out of 18, 11 patients
achieved remission. In hospital mortality was seen in 5 (27.77%) patients, all
were AAV (MPO>3, PR3<2), all were complicated with sepsis with MODS
before death. Out of 7 who received plasmapheresis, 2 patients (28.4%) died, 2
patients developed CKD ( dialysis independent). Duration of ICU care
ranged from 3 to 28 days & 2 to 40 days respectively. Mean follow
up was 16 months (range 11–42 months) Two had relapse on follow up (1 nephritis, 1 persistant cavities with episcleritis) who were given
Rituximab. Total 5 (38.46%) received Rituximab out of which 2 were refractory
achieved remission. In hospital mortality was seen in 5 (27.77%) patients, all
were AAV (MPO>3, PR3<2), all were complicated with sepsis with MODS
before death. Out of 7 who received plasmapheresis, 2 patients (28.4%) died, 2
patients developed CKD ( dialysis independent). Duration of ICU care
ranged from 3 to 28 days & 2 to 40 days respectively. Mean follow
up was 16 months (range 11–42 months) Two had relapse on follow up (1 nephritis, 1 persistant cavities with episcleritis) who were given
Rituximab. Total 5 (38.46%) received Rituximab out of which 2 were refractory
achieved remission.

Conclusions: High index of suspicion with early diagnosis and treatment results
in low mortality and better long term outcome. All mortality was because of delay
in diagnosis. Rituximab is effective in achieving remission in refractory as well as
relapsed cases.

References:
and clinical outcome: results from affiliated hospitals of Catholic University of
Feb;30(1 Suppl 70):S77–S9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7012
Background: Behçet's disease is a kind of systemic vasculitis affecting multiple systems. Although symptomatic cardiac involvement in Behçet's disease is uncommon, the mortality rate may reach up to 29%. Conduction disturbances might lead to poor outcome and often need permanent pacemaker implanted. The clinical characteristics of conduction disturbances in Behçet's disease were rarely reported before.

Objectives: To investigate the clinical characteristics of Behçet's patients with conduction disturbances and explore the underlying risk factors.

Methods: We reviewed 57 medical records of Behçet's disease with cardiovascular lesions in Anzhen Hospital, Capital Medical University between January 2002 and July 2015, and analyzed the clinical characteristics.

Results: (1) There were 13 patients with conduction disturbances out of a total of 57 Behçet's disease cases (22.8%) in our research: three patients with first-degree atrioventricular block; one patient with Mobitz type I second-degree atrioventricular block; four patients with third-degree atrioventricular block; one patient with the left anterior branch block; one patient with complete right bundle branch block; three patients with first-degree atrioventricular block combined with the left anterior branch block or complete right bundle branch block. One patient (7.7%) died from infectious endocarditis and aortic root abscess during hospital stay.

(2) Hemoglobin level was significantly lower in cases than controls (111.23±23.06 vs. 127.16±19.66 g/L, P<0.017); the median of albumin level in cases was higher than controls (34.5 (14.2) vs. 27.6 (20.7) mg/L, P=0.024) (Table 1). C reactive protein level was higher in cases than controls [26.12 (21.3) vs. 6.7 (16.4) mg/L, P=0.045] (Table 1).

(3) The aortic valvular insufficiency presented more frequently in patients in the case group than the control group (92.3% vs. 47.7%, respectively; P=0.004). Heart reconstruction can be seen in Behçet's patients with cardiac involvement. The echocardiography showed the following parameters were significantly different between two groups: left ventricular end-diastolic diameter (64.85±10.96 vs. 52.5±10.13 mm, P=0.011); left ventricular end-contraction diameter (48 [15] vs. 31 [13] mm, P=0.001); left atrial diameter [50 [17] vs. 35.85 (13) mm, P=0.003]; outflow tract of right ventricle [26 (7) vs. 27 (6) mm, P=0.045] (Table 1).

(4) Aortic valvular insufficiency was an independent risk factor for Behçet's disease with conduction disturbances (OR =1.157, 95% CI 1.034, 1.293, P=0.011).

Conclusions: Behçet’s disease is one of the unusual etiologies of atrioventricular block. The evaluation of conduction disturbance should be kept in mind when diagnosing BD’s patient.

References:
factors, i.e. smoking history (6.3% vs 38.4%), hypertension (10.4% vs 30.5%) and diabetes (12.5% vs 17.9%). Instead these patients had more upper respiratory inflammations (chronic sinusitis, chronic otitis media and allergic rhinitis, 33.3% vs 6.6%) before the disease onset.

Conclusions: We found that MPA had more atherosclerotic risk factors, and MPO-GPA had more upper respiratory inflammations. These factors may determine MPA or GPA phenotypes in MPO-ANCA positive AAV.

References:

Acknowledgements: We gratefully acknowledge the work of people who helped to correct patients data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2839

AB0583 DIFFERENCES BETWEEN ISOLATED AORTITIS AND NON-INFECTIOUS AORTITIS SECONDARY TO OTHER ENTITIES. STUDY OF 93 PATIENTS FROM A SINGLE CENTER

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Background: Non-infectious aortitis is an inflammation of aortic wall which may be isolated or associated with a cluster of diseases.

Objectives: Our aim was to compare the clinical and laboratory findings of patients with isolated aortitis and patients with aortitis secondary to other underlying conditions.

Methods: Retrospective study of 93 patients with non-infectious aortitis diagnosed by PET/CT scan from a referral center from January 2010 to December 2016. We have considered two groups: group a) isolated aortitis; and group b) secondary aortitis. Distributions of categorical variables were compared by the Pearson Chi2 or Fisher exact test. Quantitative variables were analyzing using the Student t test or Mann-Whitney U test as appropriate.

Results: Ninety-three patients were diagnosed with non-infectious aortitis. One patient was excluded due to missing data. Group a) was composed by 54 patients (34 women/20 men) with a mean age of 67±11 years; group b) comprised 38 patients (28 women/10 men) with a mean age of 68±11 years. In this group, the underlying conditions we found were: giant cell arteritis (n=24), Takayasu arteritis (n=3), spondiloarthropathy (n=3), Sjögren’s syndrome (n=3), ulcerative colitis (n=2), sarcoidosis (n=1), rheumatoid arthritis (n=1), polyarteritis nodosa (n=1). The comparative study between both groups is shown in the TABLE. Only inflammatory low back pain and polymyalgic syndrome yielded statistical significance.

Conclusions: In this study, we observed that the presence of inflammatory low back pain and polymyalgic syndrome might have clinical relevance in the clinical suspicion of primary aortitis. However, larger studies are needed to corroborate these findings.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3233

AB0584 UTILITY OF PET/CT SCAN FOR THE DIAGNOSIS OF AORTITIS. A STUDY OF 170 PATIENTS FROM A SINGLE CENTER IN A 6-YEAR PERIOD

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Background: Aortitis is the inflammation of the aortic wall. This entity is often under-recognised due to its frequent presentation with non-specific symptoms. PET/CT scan represent a major breakthrough to establish an early diagnosis, but this is an expensive technique.

Objectives: Our aim was to compare the baseline characteristics of patients with a suspicion of aortitis and positive results on PET/CT scan, and those with a negative result, in order to search for predictive factors, that improve the clinical probability of diagnosis aortitis by this imaging technique.

Methods: Retrospective study on 170 patients and PET/CT scans ordered by suspicion of aortitis from a referral center from January 2010 to December 2016. According to a pre-specified protocol, baseline epidemiological and clinical variables of patients with positive and negative PET/CT scans results for aortitis were reviewed. Distributions of categorical variables were compared by the Pearson Chi2 or Fisher exact test. Quantitative variables were analyzing using the Student t test or Mann-Whitney U test as appropriate.

Results: In 170 patients, PET/CT scans were performed due to clinical suspicion of aortitis, and were positive in 93 (54.7%) cases. Patients (113 women/57 men) had a mean age of 67.7±13.1 years (range, 20–90 years). One patient was excluded because missing clinical or laboratory data. The underlying diseases at the moment of ordering the PET/CT scan were: giant cell arteritis (GCA) (n=28), spondiloarthropathies (n=7), connectivopaties (n=6), Takayasu arteritis (n=3), ulcerative colitis (n=3), other condition (n=11). The remaining 111 patients did not have any underlying condition suggestive of aortitis. Two out of 170 patients suspected an infectious aortitis (Brucella and Salmonella); however, PET/CT was negative in both cases.

Characteristics of patients with positive and negative PET/CT scans were summarized in the Table. Patients with GCA had a higher percentage of positive PET/CT scans, whereas they were negative more frequently in patients who did not have any condition suggestive of underlying aortitis. Only inflammatory low back pain and polymyalgic syndrome were significantly more frequent in patients with positive PET/CT scans. The remaining clinical and laboratory variables did not show differences between both groups.

Conclusions: In this study, we have found that the presence of inflammatory low back pain and polymyalgic syndrome, especially in GCA patients, may have clinical relevance in ordering a PET/CT scan when aortitis was suspected.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3368

AB0585 VASCULITIS DAMAGE INDEX IN LIMITED AND SYSTEMIC GRANULOMATOSIS WITH POLIANGIITIS IN MEXICAN PATIENTS

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Background: Granulomatosis with polyangiitis (GPA) has been transformed
from life-threatening conditions to chronic relapsing long-term diseases as a result of significant advances in immunosuppressive therapy. Structured clinical assessment using Vasculitis Damage Index (VDI) should form the basis of a treatment plan and be used to document progress.

Objectives: To investigate the Vasculitis Damage Index and clinical manifestations in localized and systemic polyangiitis in Mexican patients.

Methods: We enrolled 61 patients with GPA according to The American College of Rheumatology (ACR) criteria at a referral hospital during the period from 2005 to 2015. Clinical and laboratory data, organ involvement and the Vasculitis Damage Index (VDI) were recorded at baseline. Patients were divide into systemic and localized forms of vasculitis.

Results: There were 61 GPA patients (34 men and 27 women) mean age 42 years old at diagnosis. Systemic form was observed in 53% and localized form 47%. Chronic sinusalitis was the most frequent manifestation in 33% followed by oteological in 26%. Subglottic stenosis (n=3) (52,6%) involvement of peripheral muscle or bire nal hemorrhage 1.0%. Of the patients with the systemic form 22 presented focal and segmental glomerulonephritis and 10 patients (32%) rapidly progressive glomerulonephritis. Distal-symmetrical polyneuropathy and cranial neuropathy were present in 24%; scleritis 24.5% and propiosis in 16%, palpable purpura 26.2% and ulcers in 9 patients (14.8%). The VDI score in the systemic form was 3.8 and in the localized 2.6. p< NS. The disease related damage was pronounced in kidneys and upper airways. The majority of patients in the induction to remission phase received steroids plus cyclophosphamide, 7 patients also received plasmapheresis and in maintenance phase they were treated with methotrexate or azathioprine.

Conclusions: In the cohort of patients with GPA, a high chronic damage was found which was similar in both systemic and localized forms of this vasculitis. The VDI was more prominent in kidneys and upper airways in GPA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6690

AB0586 EVALUATION OF ASSOCIATION BETWEEN ANTIPHOSPHOLIPID ANTIBODIES OR LUPUS ANTICOAGULANT POSITIVITY AND SEVERITY OF VASCULAR INVOLVEMENT IN TAKAYASU ARTERITIS PATIENTS

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Background: Takayasu Arteritis is a rare large-vessel vasculitis variant that affects the aorta and its main branches and the pulmonary arteries. Antiphospholipid syndrome is characterized by obstetric and thrombotic complications in the presence of antiphospholipid antibodies, which consist of anticyclidapin antibody, lupus anticoagulant and anti-β2 glycoprotein 1. The association of antiphospholipid antibodies and Takayasu arteritis is very rare and few cases documented it, while others argued against such association.

Objectives: This study was planned to find out the prevalence of immunoglobulin-lgM anti-cardiolipin antibodies, anti beta 2 glycoprotein-1 antibodies and lupus anticoagulant in TA patients. In conclusion we can not suggest the routine evaluation of antiphospholipid antibodies or lupus anticoagulant test during the follow-up Takayasu arteritis patients. These antibodies may only be measured in the presence of clinical suspicion.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3529

AB0587 ANTINEUTROPHILIC CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS AND HYPOCOMPLEMENTEMIA: CLINICAL IMPACT AND OUTCOME

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Background: Although their pathophysiology are still largely unknown, there are growing evidences that complement (C) alternative pathway activation is implicated in antineutrophilic cytoplasmic antibody-associated vasculitides (AAV) pathogenesis.

Objectives: The aim of our study was to evaluate the clinical characteristics and outcome of AAV patients, according to their serum C levels at diagnosis.

Methods: A retrospective monocentric study carried out in Caen University Hospital led to identify proteinase-3 (PR3) or myeloperoxidase (MPO)-ANCA AAV patients (via an ELISA technique). All patients with available C3 and C4 levels (by nephelometry) at diagnosis were included, except for eosinophilic granulomatosis with polyangiitis (EGPA), which has a different pathophysiology. AAV were classified between granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), and limited or severe forms according to respectively European Medicines Agency vasculitis algorithm and WGET group. Patients were categorized in the hypocomplementemia group if the C3 or C4 level at diagnosis was below the lower limit of the normal range (respectively 750–1400 mg/l and 100–340 mg/l). Categorical variables were reported as percentages and compared using Fisher’s tests. Continuous variables were expressed as means and analyzed using Student’s t-test. Associations between survival, renal survival and relapse-free survival, and low serum C levels were evaluated by the log-rank test. A p-value <0.05 was considered to be statistically significant.

Results: Among the 157 AAV patients identified, 81 were excluded (8 EGPA, 73 without C3 and C4 determinations before treatment initiation). On the 76 AAV included (43 GPA, 33 MPA), median age at diagnosis was 65 years (M/F, 38/38). Clinical presentations included constitutional symptoms (56, 73.3%), pulmonary (52, 68.4%), renal (50, 65.8%), rheumatologic (43, 56.6%), and ear, nose or throat (37, 48.7%) involvements, without statistical differences between groups. Twelve (15.8%) deaths and 41 relapses in 25 (32.9%) patients were noted (median follow-up: 38 months). Four patients (5.3%) had hypocomplementemia: 1 patient had isolated low C3 level, 1 had isolated low C4 level, and 2 had both low C levels. All 4 patients had renal involvement. The G level, controlled in 1 patient, became normal 1 month later. No thrombotic microangiopathy (TMA) features were found on the 2 performed kidney biopsies.

Survival and renal survival were significantly lower in the hypocomplementemia group (p=0.0011 and p<0.001, respectively), but relapse-free survival was similar (p>0.05).

Conclusions: Hypocomplementemia at AAV diagnosis may be responsible for worse survival and renal prognosis. This particular phenotype may confer resistance to common immunosuppressive approaches as in thrombotic microangiopathy caused by abnormalities in the regulation of the C system. These results also argue for larger studies and for investigating C pathway targeting.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1293

AB0588 CONCOMITANT ASSOCIATION OF GIANT CELL ARTERITIS AND MALIGNANCY: A MULTICENTER RETROSPECTIVE CASE-CONTROL STUDY

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Scientific Abstracts
AB0589 THE ROLE OF ANCA SPECIFICITY IN THE CLINICAL MANIFESTATIONS AT DISEASE ONSET: COMPARISON BETWEEN PATIENTS WITH GRANULOMATOUS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS

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Background: ANCA specificity, rather than clinical diagnosis, has been suggested to influence the phenotype and clinical course of ANCA associated vasculitides (AAV) (1,2).

Objectives: To investigate differences in clinical presentation at disease onset between MPO-ANCA-positive granulomatosis with polyangiitis patients (MPO- GPA), PR3-ANCA-positive (PR3-GPA), and MPO-ANCA-positive microscopic polyangitis (MPO-MPA).

Methods: Clinical records of AAV patients from three tertiary rheumatologic centers in Northern Italy were retrospectively analyzed.

Results: Of the 133 AAV patients included, 84 were PR3-GPA, 24 MPO-GPA, and 25 MPO-MPA. Patients with MPO-MPA were significantly older at diagnosis compared to both PR3-GPA and MPO-GPA (average age 63±10, 49±15, 55±29, respectively) (Table 1). Patients with MPO-GPA experienced a significant diagnostic delay compared to PR3-GPA (17±30 vs 7±14, p<0.02). ENT involvement was equally frequent in both MPO-ANCA-positive AAV variants, whereas more represented than the MPO-MPA group (68%, 71% and 17% respectively; p<0.001). Figure 1. Renal involvement was significantly more frequent in MPO-MPA patients (100%) compared to GPA (p<0.001), without differences between MPO-GPA (46%) and PR3-GPA (46%), both with significantly lower renal involvement compared to GPA (53% vs 16% respectively; p=0.02). Cauterous manifestations, mainly purpura, were significantly more reported in PR3-GPA compared to MPO-GPA (29% vs 4%; p=0.03).

Conclusions: Clinical phenotype of GPA at disease onset did not seem to be influenced by ANCA specificity. Despite ANCA positivity (PR3 or MPO), GPA patients were significantly different from MPA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1291

AB0580 PERFORMANCE OF 2017 ACR/EULAR PROVISIONAL CLASSIFICATION CRITERIA FOR GRANULOMATOSIS WITH POLYANGIITIS IN CHILEAN POPULATION

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Background: Anca Associated Vasculitis (AAV), are a group of necrotizing primary vasculitis, with multisystemic manifestation, of unknown etiology. The variants are: Microscopic Polyangiitis (MPA), Granulomatosis with polyangiitis (GPA), Granulomatosis with Polychistitis and Eosinophilic Pneumonia (GPE) and AAV limited to one organ. Until now, there are no diagnostic criteria for AAV. Therefore definitions, as Chapel Hill consensus Conference Nomenclature, classification criteria and the physician judgement are used for diagnosis. Currently the DCVAS (Diagnosis and Classification Criteria in Vasculitis) project is developing diagnostic criteria for AAV, using data-driven methods. The preliminary DCVAS classification criteria for granulomatosis whith polyangiitis has been recently realased.

Objectives: To evaluate and compare the accuracy of ACR/EULAR 2017 provisional Classification Criteria for GPA whith the ACR 1990 Classification Criteria In Chilean patients with AAV.

Methods: All adult patients (>18 yo) with diagnoses of AAV according to their rheumatologist judgment, from 2000–2016 at the University of Chile, Clinical Hospital (UCHC), were included. Clinical variables of interest were extracted from medical chart and AAV database, which is kept for these patients at the Rheumatology Section of UCHC. Based on that data, the Classification criteria ACR 1990 and 2017/preliminary ACR/EULAR (DCVAS) classification criteria for GPA were applied to each individual. Sensibility, specifity, Likelihood ratio (LR +/-), predictive values (PPV/NPV) and accuracy were calculated for both sets of Criteria as compared to Clinical diagnosis.

Results: 93 patient were included in the study. 59 patients with GPA, 33 with...
Efficacy and Safety Profile of Intravenous Cyclophosphamide Treatment in Elderly Patients with Systemic Vasculitis

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Background: Intravenous cyclophosphamide is mainstay of remission induction and dose reduction of glucocorticoid in patients with systemic vasculitis. However, little evidence has yet shown the safety profile of intravenous cyclophosphamide, especially in elderly patients.

Objectives: To evaluate efficacy and safety of patients diagnosed as systemic vasculitis and treated with intravenous cyclophosphamide.

Methods: This retrospective study comprised the patients with active systemic vasculitis who were admitted to Kitami Red Cross Hospital and Obihiro Kosei General Hospital from April 2009 to March 2016. These patients were treated with intravenous cyclophosphamide plus conventional therapy (IVCY group) or only with conventional therapy (glucocorticoid/azathioprine/tacrolimus and methotrexate) (conventional therapy group). The patients treated with oral cyclophosphamide or rituximab were excluded. Primary endpoint was defined as death or serious infections. Prognostic factors in IVCY group were analyzed by multivariate Cox regression methods.

Results: This study comprised 90 patients with active systemic vasculitis (61 microscopic polyangiitis, 9 eosinophilic granulomatosis with polyangiitis, 10 granulomatosis with polyangiitis, and 10 polyarteritis nodosa). Fifty-one patients were over 70-year-old (26 patients in IVCY group). The mean observation period was 31.1±13 months. IVCY group had a trend for higher event-free survival rate as compared with conventional therapy group (p=0.19).

Conclusions: Intravenous cyclophosphamide treatment had acceptable safety profile even in elderly patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6732

AB0592 PULMONARY ARTERY ANEURYSM IN BEHÇET’S DISEASE: RETROSPECTIVE MONOCENTRIC TUNISIAN STUDY

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Background: Behçet’s disease (BD) is a chronic inflammatory disorder. Arterial inflammatory involvement includes predominantly aortic and pulmonary aneurysms, lesions affects about 10% of patients with BD. They account for the severity of the disease and a leading cause of death.

Objectives: To investigate the frequency of Behçet’s disease with pulmonary artery aneurysm (PAA). We aimed to review PAA and other systemic involvements associated with PAA in BD and to provide a review of diagnostic techniques, treatment and prognosis.

Methods: 243 BD patients were recruited for this study (152 men, 91 women, mean age 31.7±7 years). Diagnosis of BD was made according to the international study group for Behçet’s disease [International Study Group for Behçet’s Disease, Lancet 1990; 335: 1078–80]. All patients underwent full clinical examination, routine laboratory investigations. Chest X-rays and pulmonary CT angiography were performed on all patients with pulmonary involvement.

Results: Eight of the patients have pulmonary aneurysm, all of them are male, mean age 32.6±13. The mean disease duration until PAA appear was 2.8±3.5 years. The main pulmonary symptoms were as follows: dyspnea 87%, cough 50%, hemoptosis: 75%, fever 37%. Other systemic involvements associated PAA were as follows: bacular (100%) and genital (75%) ophthalmic 25%, neurological 50%, cardiac 25%. 3 patients presented with Hughes Stovin syndrome. The treatment includes corticosteroids, colchicine and immunosuppressant agents (Cyclophosphamid or azathiopeine), only two patients receive coil embolization. At follow up for a median of 4 years (1 to 25 years), three patients died because they stopped their medical treatment.

Conclusions: The prognosis of PAA is poorer than other lesions involved in BD, treatment (immunosuppressant agents, colchicine) seems to improve the prognosis. It is important to maintain the immunosuppressive therapy and a regular follow-up to prevent these complications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3338
ANCA-ASSOCIATED VASCULITIS WITH BOTH MPO-ANCA AND PR3-ANCA: Shares of Characteristics of ANCA-ASSOCIATED VASCULITIS WITH SINGLE ANCA

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Background: The anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides are heterogeneous group of necrotizing inflammation of small vessel and the presence of the ANCA. ANCA refers to the target antigens, leucocyte proteinase 3 (PR3) and myeloperoxidase (MPO). Recently, the ANCA specificity could be better for classification of ANCA-associated vasculitides than the clinical diagnosis. A few patients have both MPO- and PR3-ANCA. However, the clinical characteristics of these patients were not well described by ANCA type.

Objectives: To analyze organ involvement of patients with ANCA-associated vasculitides according to ANCA type focusing both MPO- and PR3-ANCA (both-ANCA) positive vasculitis

Methods: The medical records of the patients with positive ANCA and clinical diagnosis of the patients with positive ANCA and vasculitis diagnosis confirmed by biopsy were reviewed at two regional tertiary hospitals. The age at diagnosis, sex, and the organ involvement of kidney, lung, upper airway (nose/sinus/ear), skin, peripheral nervous system, central nervous system, and gastrointestinal tract were collected. The clinical variables were analyzed by ANCA type.

Results: Total 82 patients with positive ANCA and clinical diagnosis or the patients with positive ANCA and vasculitis diagnosis confirmed by biopsy were reviewed at two regional tertiary hospitals. The age at diagnosis, sex, and the organ involvement of kidney, lung, upper airway (nose/sinus/ear), skin, peripheral nervous system, central nervous system, and gastrointestinal tract were collected. The clinical variables were analyzed by ANCA type.

Conclusions: ANCA-associated vasculitides (AV) are a group of multi-system autoimmune diseases characterized by inflammation and necrosis in small and medium vessels. AV could respond to different therapeutic protocols depending on diverse levels of clinical severity and early treatment could improve the outcome of the disease. In spite of recognized efficacy of regimens consisting of cyclophosphamide and high-dose corticosteroids to control the AV efforts to minimize drugs-related toxicity led to consider targeted therapies. We identified the latest quality evidence in treatments novelly proposed to AV and the severity of renal disease presentation, we suggest new rational approaches targeting B-cells therapy and preventing disease relapse.

Methods: We identified the latest quality evidence in treatments novelly proposed to AV and the severity of renal disease presentation, we suggest new rational approaches targeting B-cells therapy and preventing disease relapse.

Results: Rituximab (RTX), a monoclonal anti-CD20 antibody, has emerged as the biologic agent more using in AV patients in current publications and unlike latest Guides and Recommendations published, RTX would be recommended in induction and maintenance AV with renal involvement treatment (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Therapy</th>
<th>AAV Induction</th>
<th>AAV Maintenance</th>
<th>AAV Relapse</th>
<th>VAA Refractaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTX + GC low-dose</td>
<td>6 months up (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Minor Relapse</td>
<td>RTX + GC, specially patients whose never received RTX (II, B)</td>
</tr>
<tr>
<td>GC &amp; RTX</td>
<td>Low-dose GC &amp; AZA up 18 months (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Increase GC dose (Ib, C)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>GC &amp; RTX</td>
<td>Low-dose GC &amp; MTX with GC ≤ 60 mg/dl (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Major Relapse + RTX + GC (Ia, A)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>GC &amp; RTX</td>
<td>Avoid use of GC long-term (higher relapse risk) (Ia, A)</td>
<td>≤ 60 mg/dl</td>
<td>Major Relapse with CFM cumulative dose ≤ 36 gr CFM + GC (II, B)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>CFM IV/PO + MPS (Ia, B)</td>
<td>Prophylaxis against Pneumocystis jiroveci (in CFM or RTX therapy)/Corticimazol PO (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Severe with RPGN: Plasma Exchange-adjuvant therapy (Ia, B)</td>
<td>plasma Exchange (II, B)</td>
</tr>
<tr>
<td>CFM IV/PO + MPS (Ia, B)</td>
<td>Generalised with concomitant to CFM/RTX + GC (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Avoid use of CFM (Ia, A)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>CFM IV/PO + MPS (Ia, B)</td>
<td>Severe with RPGN: Plasma Exchange-adjuvant therapy (Ia, B)</td>
<td>≤ 60 mg/dl</td>
<td>Avoid use of CFM (Ia, A)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>CFM IV/PO + MPS (Ia, B)</td>
<td>Prophylaxis against Pneumocystis jiroveci (in CFM or RTX therapy)/Corticimazol PO (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Avoid use of CFM long-term (higher relapse risk) (Ia, A)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>GC &amp; RTX</td>
<td>Prophylaxis against Pneumocystis jiroveci (in CFM or RTX therapy)/Corticimazol PO (Ib, B)</td>
<td>≤ 60 mg/dl</td>
<td>Avoid use of CFM (Ia, A)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
<tr>
<td>GC &amp; RTX</td>
<td>Avoid use of CFM long-term (higher relapse risk) (Ia, A)</td>
<td>≤ 60 mg/dl</td>
<td>Avoid use of CFM (Ia, A)</td>
<td>Plasma Exchange and/or MPS (Ib, C)</td>
</tr>
</tbody>
</table>

References:
Of the 175 BD patients, the positive rate of tuberculosis infection in BD patients between January 2010 and March 2015. Statistical analysis was carried out using IBM SPSS version 20.

Results: Of the 175 BD patients, the positive rate of tuberculosis infection in BD patients was 34.3%. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the T-SPOT.TB test for the diagnosis of ATB were 87.5%, 73%, 36.8%, 98.3%, respectively. Positive likelihood ratio (PLR) of ATB was 11.93, 95% CI 2.108–67.508, p=0.005. The kappa coefficient was poor (kappa = 0.37). Multiple logistic regression analysis revealed that BD patients with positive T-SPOT.TB had the highest likelihood of LTBI infection. The OR of BD patients having LTBI was 11.93, 95% CI 2.108–67.508, p=0.005. The rates of LTBI infection had no significant difference between BD patients and healthy controls. Agreement between T-SPOT.TB and TST in BD patients measured by the kappa coefficient was poor (kappa = 0.37). Multiple logistic regression analysis revealed that BD patients with positive T-SPOT.TB had the highest likelihood of ATB. Positive likelihood ratio (PLR) of ATB was 11.93, 95% CI 2.108–67.508, p=0.005. No significant difference was found in cumulative CR rate between HD and LD RTX (p=0.15). There was an negative correlation between circulating alpha defensin and Rodnan score (r=0.30) and CRP (r=0.34).

Conclusions: The combination of T-SPOT.TB and other diagnostic tests should be used to determine the LTBI and ATB in BD patients. The use of RTX in patients with BD may increase individual susceptibility of BD patients to LTBI and ATB. Immunocompromised BD patients should be closely monitored for LTBI and ATB infection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4149

AB0597

LOW-DOSE RITUXIMAB AS INDUCTION THERAPY FOR JAPANESE PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Four times of once-weekly doses of 375 mg/m² rituximab (RTX) are frequently used as remission induction therapy for ANCA-associated vasculitides (AAV). Since this regimen has been basically generated from experience of B-cell non-Hodgkins' lymphoma in the Europe and North America, appropriate dose and interval for patients with AAV in other population have been poorly investigated. Here we comprehensively analyzed the efficacy and tolerability of low or low dose regimen of RTX in Japanese patients with AAV.

Methods: We retrospectively examined AAV patients who met the 2012 Chapel Hill classification from 2006 to 2016. We divided them into 2 groups, those treated with high-dose (HD) and low-dose (LD) RTX. HD RTX was the original regimen and LD RTX consisted of twice of one-weekly dose of 375 mg/m². We evaluated cumulative complete remission (CR) rate and relapse-free rate for 1.5 years. CR was defined as BVAS=0 and relapse was defined as BVAS>1.

Results: We evaluated 17 patients with HD and 11 patients with LD RTX. Higher percentage of elderly patients was observed in LD group (p<0.01). No significant difference was found in BVAS (p=0.49) and VDI (p=0.15) before treatment. No significant difference was found in cumulative CR rate (p=0.90) (Fig. 1A), relapse-free rate (p=0.48) (Fig. 1B), B cells counts and serious adverse events. We found patients with nasal involvement and pulmonary module cavity formation had higher relapse rate in LD group than those with HD group (p=0.05, and p=0.09 respectively).

Scleroderma, myositis and related syndromes

AB0596

SERUM DEFENSIN LEVEL IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Scleroderma is an autoimmune disease characterized by fibrosis of skin and lung as well as involvement of kidney, gastrointestinal system and heart (1). Etiology and exact mechanism of disease is poorly understood. A small number of studies have examined the role of AMPs on autoimmune diseases. It has been demonstrated that the amount of alfa- and beta-2 defensin serum levels are increased in systemic lupus erythematosus patients (2, 3). Likewise, the association between AMPs and other diseases such as idiopathic pulmonary fibrosis, diffuse panbronchiolitis, pulmoner alveolar proteinosis and psoriasis has been reported (4).

Objectives: No study investigated the role of AMPs on scleroderma patients. Hence, we aimed to investigate AMP serum levels and their possible association in these patients.

Methods: There were 42 patients (40 female, mean age 42 years) and 38 healthy subjects (32 female, mean age 38 years) in the study. For SSc patients, the following data were recorded at enrollment: disease subset (limited/diffuse), autoantibodies (anti-nuclear, anti-centromere (ACA), and anti-scl DNA, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), modified Rodnan skin score, presence and history of digital ulcers, presence and history of interstitial lung disease, kidney and gastrointestinal system, intestinal blood detected by chest HRT and pulmonary function tests, estimated pulmonary arterial systolic pressure at echocardiography.

Results: There were 42 patients (40 female, mean age 42 years) and 38 healthy subjects (32 female, mean age 38 years) in the study. Twenty-nine of the patients had diffuse systemic sclerosis and thirteen of the patients had limited systemic sclerosis. Average disease duration is 5.5 years. Pulmonary involvement was detected in twenty patients. The levels of beta 1 and beta 2 defensin that are epithelial defensins were higher than control group but it has not reached statistical significance. (beta-1 defensin 235±178 vs 185±24 pg/ml, p=0.08 and beta2 defensin 253±453 vs 152±101 pg/ml, p=0.18). Alpha defensin levels in scleroderma patients were significantly higher than control group (563±415 vs 377±289 pg/ml, p=0.02). In sub-group analysis patients with interstitial lung disease had a higher level of alpha defensin than those without involvement (684±473 vs 430±299 pg/ml, p=0.04). There was a negative correlation between alfa defensin and Rodnan score (r=-0.30) and CRP (r=0.34).

Conclusions: Alpha defensin levels in scleroderma patients were significantly higher than control group. There may be an increase in the level of alpha defensin in a cause of vasulopathy in scleroderma patients

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5410
AB0599 COMBINATION OF CAPILLAROSCOPIC AND ULTRASONOGRAPHIC EVALUATIONS OF THE HAND TO DETECT SEVERE VASOPATHY IN SYSTEMIC SCLEROSIS: RESULTS OF A CROSS-SECTIONAL STUDY

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Background: Although micro-vein alterations have been largely described, macrovascular involvement is also frequent in Systemic Sclerosis (SSc). Macrovascular damages specifically involve narrowing or occlusions of proper palmar digital arteries and ulnar artery. On the contrary, radial artery is rarely concerned. Ulnar artery occlusion (UAO) assessed by power doppler ultrasonography has proven to be predictive of the onset of new ischaemic DUs in longitudinal studies (1). PDUS could also be a reliable tool to evaluate finger pulp blood flow (FPBF). Only few studies have explored the association between macrovascular damages evaluated by PDUS and microvascular involvement assessed by nailfold capillaroscopy (NC) (2). The association between macrovascular disease and calcinosclerosis or Acro-osteosclerosis is still to be determined in SSc.

Objectives: to confront microvascular damages on NC with macrovascular manifestations evaluated by PDUS in SSc patients. Micro and macro-vascular damages were confronted with the main digital manifestations of the disease: digital ulcers (DU), Acro-osteosclerosis and Calcinosis.

Methods: NC, hand X-Rays and PDUS were systematically performed in 64 unselected SSc patients. PDUS evaluation with assessment of Ulnar Artery Occlusion (UAO) and finger pulp blood flow (FPFB) was performed blinded for the results of X-Rays and NC.

Results: UAO and pathologic FPFB were associated with severe capillary loss (<4 capillaries/mm) on NC (respectively OR=4.04 (1.23–13.29); p<0.05 and OR=3.38 (1.03–11.05); p<0.05). UAO was significantly associated with Cutis laxa late NC pattern (OR=3.80 (1.31–11.01); p<0.05). A DU history was associated with UAO (OR=10.71 (3.36–34.13); p<0.0001), pathologic FPFB (OR=7.67 (2.52–23.28); p<0.0001), late pattern (OR=6.33 (2.03–19.68) and severe capillary loss (OR=8.52 (2.15–33.78); p<0.001). Acro-osteosclerosis was also associated with UAO (OR=15.15 (3.95–63.54); p<0.001), pathologic FPFB (5.52 (1.71–17.90) p=0.003), late NC pattern (OR=6.86 (2.18–21.53); p<0.001) and severe capillary loss (OR=7.20 (2.16–24.02); p<0.001). Calcinosis on X-rays were associated with late NC pattern (5.41 (1.82–16.12); p=0.002), severe capillary loss (OR=12.69 (3.14–51.26); p<0.0001) and UAO (3.19 (1.14–8.92); 0.025) but not with pathologic FPFB. Combination of UAO and severe capillary loss in a same patient was especially associated with DU history (OR=18.60 (2.24–154.34); p<0.001) and Acro-osteosclerosis (OR=10.83 (2.56–45.88); p<0.001).

Conclusions: The combination of macro and microvascular evaluations by PDUS and NC can help to detect patients with a more severe vasopathology.

References:

Disclosure of Interest: None declared

AB0600 CLINICAL RELEVANCE OF AUTOANTIBODY PROFILES IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease accompanied by immune abnormalities. A number of autoantibodies such as anti-centromere, anti-topoisomerase I, anti-RNA polymerase III and anti-U3 (fibrilin) antibodies were proven to be of great diagnostic and prognostic factors in patients with scleroderma. Certain studies have reported the presence of antinuclear, anti-SSA (Ro) and/or anti-SSB (La), anti-Pm/Sc, anti-endothelial cell and anti-nucleosome antibodies in patients with systemic sclerosis. However, the clinical relevance of these autoantibodies is yet to be fully elucidated.

Objectives: Our aim was to assess clinical features, capillaroscopic abnormalities and autoantibody titers in patients with systemic sclerosis as well as analyze relationships between these three parameters for the disease.

Methods: We conducted a prospective observational study on 36 adult patients who satisfied ACR/EULAR 2013 criteria for systemic sclerosis. We recorded disease duration, current symptoms and classified patients as limited cutaneous (lc) SSc and diffuse cutaneous (dc) SSc. Skin involvement was assessed using the modified Roden-Nolan skin score. We performed nailfold videocapillaroscopy using a FEDMED Digital 100N at a magnification of 200X. Thoracic Xrays were done to establish the presence of pulmonary fibrosis. Ultrasounds were performed by a single examiner to evaluate pulmonary artery pressure. Blood samples were drawn to measure anti-topoisomerase 1, anti-centromere, anti-SSA (Ro), anti-SSB (La), anti-U1RNP and anti-nucleosome antibody titers (ELISA). Patient characteristics were included in a database and analyzed using IBM SPSS Statistics v20.

Results: Our study group was composed of 20 dc SSc (55.6%) and 16 lc SSc (44.4%) patients. Severity of capillary changes correlated with mRSS values (p<0.01), anti-topoisomerase I (p<0.006), anti-SSA (p<0.01) and anti-nucleosome antibodies (p<0.02). We found positive associations between the presence of dyspahgia, anti-centromere (p<0.009) and anti-SSA (p<0.01) titers in patients with lc SSc. Anti-centromere antibody positivity also correlated with pulmonary hypertension (p<0.011) and pulmonary fibrosis (p<0.04) in these patients. Anti-SSA antibodies correlated with pulmonary hypertension (p<0.01) and capillaroscopic changes (p=0.024) in dc SSc.

Conclusions: Our findings support the relationship between autoantibody titers, systemic involvement and microvascular changes in scleroderma patients. Non-specific autoantibodies such as anti-nucleosome and anti-SSA antibodies were associated with microvascular changes in our study group. Further studies in this field may provide new information on SSc pathogenesis and possibly novel targets for treatment in scleroderma patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2577

AB0601 ANATOMIC AND FUNCTIONAL ASSESSMENT OF PERIPHERAL PERFUSION IN PATIENTS WITH SYSTEMIC SCLEROSIS. IS THERE ANY CORRELATION BETWEEN CAPILLAROSCOPIC FINDINGS AND ERGOSPIROMETRY?

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Background: Microvasculopathy of systemic circulation in patients with Systemic Sclerosis (SSS) is widely assessed by digital capillaroscopy (DC), a method that evaluates the architecture of capillary network and reveals changes of vascular anatomy. On the other hand, ergospirometry (ERG) reveals functional impairment of microcirculation by assessing indirect measures of peripheral tissue ischemia (1). Today, there has been an increase in the use of capillaroscopy in correlation with spirometric parameters (2). Nevertheless, no reports have been published correlating the same DC findings with ERG parameters (functional microvascular perfusion).

Objectives: To propose the use of DC as a screening tool for impaired functional microvasculopathy by investigating correlations between patterns of capillaroscopic findings with ergospirometric values of peripheral tissue blood perfusion.

Methods: 11 patients (11 women mean age 43±12 y) with SS were evaluated contemporarily with High Resolution Computed Tomography of the chest, ERG, and DC. Parameters were correlated using SPSS (3). Statistic significance was considered p<0.05.

Results: Patient data are shown in the table. Patients with late pattern in capillaroscopy had less endurance in exercise test (P=0.05) but no correlation was found between capillaroscopic pattern and ERG parameters (VE/VC02) (P=0.05).

Conclusions: The correlation of late pattern capillaroscopy findings with reduced ergospirometric endurance in 11 patients indicates that in a larger cohort, specific parameter associations between DC and ERG are probable to emerge.
We conducted a cross-sectional study that included 78 SSc patients. The aim of this study was to assess the presence of subclinical atheroma- tization by carotid Doppler ultrasound in SSc patients under 55 years. The background: In Systemic sclerosis (SSc), as in other autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus, cardiovascular events are one of the most frequent causes of mortality not attributed to the disease itself. The objectives: The aim of this study was to assess the presence of subclinical atherosclerosis by carotid Doppler ultrasound in SSc patients under 55 years. The methods: We conducted a cross-sectional study that included 78 SSc patients without cardiovascular events from H. Vall d’Hebron cohort (Barcelona). Carotid Doppler ultrasound was performed to measure the Carotid Intima Media Thickness (CIMT) of common carotid artery (CCA) and detection of cholesterol plaques in CCA, bulb and internal and external carotid arteries, according to Mannheim consensus criteria. The results were compared to a healthy cohort from Barcelona, adjusted to age and sex. We used SCORE for populations with low risk and REGICOR as cardiovascular risk assessment charts. The results: Risk factors and SSc related features are described in table 1. Twenty-three patients (29.5%) had carotid plaques (CP) being the presence of CP statistically significant compared to the healthy cohort (29.5% vs 15.6%; p < 0.05). The intermediate risk patients had CP. Carotid Intima Media Thickness mean (CIMTm) and maximum (CIMTmax), were statistically significant increased compared to the healthy cohort (CIMTm 0.57 vs 0.53; p < 0.05 and CIMTmax 0.74 vs 0.61; p < 0.05). We performed multivariate regression analysis. Age, CIMTmax, low High Density Lipid (HDL), the presence of pulmonary hypertension, and diffuse cutaneous SSc patients were independent factors for the presence of CP.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6599

### AB0602 CAROTID ATEROESCLEROTIC PLAQUES DETECTED BY ULTRASOUND IN SYSTEMIC SCLEROSIS PATIENTS UNDER 55 YEARS OLD

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**Background:** In Systemic sclerosis (SSc), as in other autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus, cardiovascular events are one of the most frequent causes of mortality not attributed to the disease itself. The objectives: The aim of this study was to assess the presence of subclinical atherosclerosis by carotid Doppler ultrasound in SSc patients under 55 years. The methods: We conducted a cross-sectional study that included 78 SSc patients without cardiovascular events from H. Vall d’Hebron cohort (Barcelona). Carotid Doppler ultrasound was performed to measure the Carotid Intima Media Thickness (CIMT) of common carotid artery (CCA) and detection of cholesterol plaques in CCA, bulb and internal and external carotid arteries, according to Mannheim consensus criteria. The results were compared to a healthy cohort from Barcelona, adjusted to age and sex. We used SCORE for populations with low risk and REGICOR as cardiovascular risk assessment charts. The results: Risk factors and SSc related features are described in table 1. Twenty-three patients (29.5%) had carotid plaques (CP) being the presence of CP statistically significant compared to the healthy cohort (29.5% vs 15.6%; p < 0.05). The intermediate risk patients had CP. Carotid Intima Media Thickness mean (CIMTm) and maximum (CIMTmax), were statistically significant increased compared to the healthy cohort (CIMTm 0.57 vs 0.53; p < 0.05 and CIMTmax 0.74 vs 0.61; p < 0.05). We performed multivariate regression analysis. Age, CIMTmax, low High Density Lipid (HDL), the presence of pulmonary hypertension, and diffuse cutaneous SSc patients were independent factors for the presence of CP.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6599

### AB0604 RITUXIMAB EXPERIENCE IN PATIENTS WITH LONGSTANDING SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: A SERIES OF 14 PATIENTS

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**Background:** Interstitial lung disease (ILD) is the leading cause of mortality in systemic sclerosis (SSc) patients. Treatment options are rather limited in SSc patients and in whom unsatisfactory response in lung functions was noted under conventional treatments.

**Objective:** The objective of this study was to report the experience of RTX treatment in a series of patients with longstanding SSc-ILD in whom unsatisfactory response in lung functions was noted under conventional treatments.

**Results:** A retrospective review of charts of 197 SSc patients evaluated between April 2015 and November 2016. 14 patients who received rituximab (RTX) for SSc-ILD participated in this analysis. The severity of ILD based on FVC was defined as follows; mild (FVC between 71% and 80% of predicted), moderate (FVC between 51% and 70% of predicted) and severe (FVC <50%). The extent of skin disease was clinically measured using Modified Rodnan Skin Score (mRSS) tool. End of follow-up was considered as six months after the last RTX dose.

**Results:** Median (IQR, interquartile range) age was 53.2 (46.8–55.5) and median disease duration was 9.1 (5.1–13.6) years. Median FVC was 52.5 (41.5–64.0)

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4612
prior to RTX. At the end of follow-up, no significant change was revealed in FVC when compared with pre-RTX values [58.0 (44.7–58.7), p=0.069]. FVC was improved in four patients and stabilized remaining ten patients. All of the patients with improvement of PFTs had moderate or severe restrictive lung disease. High resolution thorax computed tomography (HRCT) findings remained stable in 7 and improved in the remaining 3 patients. In total, mRSS remained stable at the end of follow-up when compared with baseline [8.0 (5.2–12.2) vs. 6.0 (4.0–12.2), p=0.026].

Table 1. Demographic, clinical and laboratory data of patients

<table>
<thead>
<tr>
<th>Age/ Sex</th>
<th>Disease duration, years</th>
<th>Cutaneous subset</th>
<th>Auto-antibodies</th>
<th>Previous immunosuppressive treatment</th>
<th>RTX cycles</th>
<th>Follow-up after RTX, months</th>
<th>FVC (predicted%) Before RTX</th>
<th>FVC (predicted%) After RTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>52/F</td>
<td>7.0</td>
<td>Diffuse</td>
<td>ANA, Scl-70</td>
<td>CYC, MMF</td>
<td>2</td>
<td>12</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>53/M</td>
<td>10.0</td>
<td>Diffuse</td>
<td>ANA, Scl-70</td>
<td>MMF</td>
<td>4</td>
<td>24</td>
<td>75</td>
<td>79</td>
</tr>
<tr>
<td>55/F</td>
<td>5.0</td>
<td>Diffuse</td>
<td>ANA, Scl-70</td>
<td>MMF</td>
<td>4</td>
<td>24</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>43/F</td>
<td>16.6</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>CYC, MMF</td>
<td>1</td>
<td>6</td>
<td>38</td>
<td>47</td>
</tr>
<tr>
<td>50/F</td>
<td>4.6</td>
<td>Diffuse</td>
<td>ANA, Scl-70</td>
<td>CYC, MMF</td>
<td>4</td>
<td>24</td>
<td>52</td>
<td>57</td>
</tr>
<tr>
<td>65/F</td>
<td>13.0</td>
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<td>ANA, Scl-70</td>
<td>MMF</td>
<td>1</td>
<td>6</td>
<td>42</td>
<td>41</td>
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<tr>
<td>48/B</td>
<td>5.7</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>CYC</td>
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<td>24</td>
<td>67</td>
<td>64</td>
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<tr>
<td>54/F</td>
<td>16.9</td>
<td>Diffuse</td>
<td>ANA, Scl-70</td>
<td>CYC, MMF</td>
<td>2</td>
<td>12</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>53/F</td>
<td>15.0</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>MMF</td>
<td>5</td>
<td>30</td>
<td>53</td>
<td>44</td>
</tr>
<tr>
<td>56/F</td>
<td>5.1</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>CYC</td>
<td>5</td>
<td>30</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>52/B</td>
<td>8.2</td>
<td>Limited</td>
<td>ANA</td>
<td>MMF</td>
<td>3</td>
<td>12</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td>51/F</td>
<td>11.2</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>MMF</td>
<td>1</td>
<td>6</td>
<td>63</td>
<td>72</td>
</tr>
<tr>
<td>62/F</td>
<td>4.6</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>CYC</td>
<td>3</td>
<td>18</td>
<td>51</td>
<td>61</td>
</tr>
<tr>
<td>54/F</td>
<td>13.1</td>
<td>Limited</td>
<td>ANA, Scl-70</td>
<td>MMF</td>
<td>5</td>
<td>30</td>
<td>54</td>
<td>67</td>
</tr>
</tbody>
</table>

FVC, forced vital capacity; ANA, antinuclear antibody; Scl-70, antiparaneoplasmin-1 antibody; CYC, cyclophosphamide; MMF, mycophenolate mofetil; RTX, rituximab.

Conclusions: In this case series of SSc patients treated with RTX, improvement or stabilization of pulmonary functions was observed in most of SSc patients. RTX may be useful in SSc-ILD patients with longer disease duration and resistant to conventional immunosuppressive therapies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5501

**AB0605 VITAMIN D SERUM CONCENTRATION IN EUROPEAN SYSTEMIC SCLEROSIS PATIENTS: CORRELATIONS WITH SEASONALITY, ORGAN INVOLVEMENT AND STANDARD ORAL SUPPLEMENTATION**

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Background: Vitamin D deficiency is reported to interfere with immune responses and to correlate with course and outcome in several autoimmune diseases. In systemic sclerosis (SSc), low 25-hydroxyvitamin D (25(OH)D) serum concentration has been recognized.

Objectives: To investigate relations between 25(OH)D serum concentration and seasonality, clinical parameters as well as standard oral supplementation, in SSc patients.

Methods: 154 SSc patients (mean age 59±15 years, 24.7% diffuse form and 75.3% limited form) were evaluated, at any time of the year, in a retrospective survey. Serum 25(OH)D quantification was performed using the LIAISON 25-OH vitamin D assay (DiaSorin, Italy). Pulmonary function test, chest x-ray, lung CT scan, electrocardiography, renal artery resistive index by eco color Doppler, Dual x-ray absorbtiometry, were performed at the time of sample collection. Disease severity scale (DSS) was performed according to Medsger. Drug assumption (glucocorticoids, calcium channel blockers, cyclic intravenous loop diuretics, endothelin receptor antagonists) and supplementation with vitamin D analogues, were recorded. Non-parametric tests were used for statistical analysis.

Results: Average 25(OH)D serum concentration was found to be 18.7±9 ng/ml (<20 classified as deficiency). A significant difference was observed among seasonal 25(OH)D serum concentration (winter: 14.6±7.8 ng/ml, spring: 17.2±7.9 ng/ml, summer 21.4±10 ng/ml, autumn 20.2±10; p=0.032) (Figure 1). A significant correlation was found between 25(OH)D serum concentration and presence/absence of bi-astral fibrotic changes at lung computed tomography (CT) scan (Pearson correlation coefficient 0.16, p=0.04). Peripheral vascular (p=0.03), kidney (p=0.02), gastrointestinal (p=0.05) Medsger’s DSS parameters also were found to correlate with 25(OH)D serum concentration (Figure 1). Interestingly, no influence of treatment with vitamin D analogues (1,000 UI daily) was found regarding 25(OH)D serum concentration in treated (18.8±10 ng/ml) and not treated (18.7±9 ng/ml) SSc patients (p=0.81).

Conclusions: In SSc is confirmed a serum 25(OH)D deficiency that we report to be associated with lung involvement, peripheral vascular, kidney and gastrointestinal Medsger’s DSS parameters, as well as with seasonality. Supplementation with vitamin D analogues did not influence present results.
Mortality was 22.5% (20/89 patients), CI95 (14.3–32.5). Mean time from diagnosis to the event was 18 months. The primary cause of death was sepsis 14/20 (70%).

Conclusions: Mortality of patients with inflammatory myopathies was 22%, and the primary cause was infectious. In the analysis of multiple variables, male sex, presence of neoplasms and serious infectious complications were significantly factors associated with mortality.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5243

AB0608 PREDICTIVE FACTORS FOR LONG-TERM SURVIVAL AND DISEASE PROGRESSION OF SYSTEMIC SCLEROSIS – A LONGITUDINAL ANALYSIS

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Background: Systemic sclerosis (ScS) has unpredictable course and high mortality. Generalised Estimating Equations (GEE) is a technique useful for longitudinal data analysis, using data from all time points and adjusting for within-patient correlation, and comparison between time points within the same patient. GEE does not require a normal distribution of dependent variables, making it attractive for analyzing ScS data.

Objectives: To identify predictive factors for death and unfavorable outcomes.

Methods: Data of ScS patients was collected from our EUSTAR centre in 2004–2016 were analyzed. GEE investigated the relationship over time between outcomes (death, digital ulcers (DUs), forced vital capacity (FVC), modified Rodnan skin score (mRSS)) and potential predictors (age, gender, disease duration, cutaneous subset, mRSS at baseline, DUs history, DLCO, left ventricle ejection fraction (LVEF), proteinuria), separately for each predictor and in combined models.

Results: 89 patients (12.4%males, mean±SD age 49.2±12.5years, disease duration 4.1±7.5years) were included, with a follow-up of up to 13 years. There were 14deaths, most due to lung involvement (7/14). In multivariable GEE analysis (Table 1), predictors of death were a shorter disease duration, DUs history, and a lower LVEF. Predictors for FVC decrease over time were diffuse cutaneous subset (dcSSc), younger age and lower DLCO. Younger age, shorter disease duration and higher baseline mRSS were the most important predictors for higher mRSS at follow-up. The only predictor for the development of new DUs was a history of DUs.

Table 1. Prediction factors for death and for evolution over time of parameters reflecting disease severity in ScS

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Death</th>
<th>DUs</th>
<th>FVC</th>
<th>mRSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>B (95% CI)</td>
<td>B (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>1.1 (0.9, 1.3)</td>
<td>0.9 (0.9, 1.0)</td>
<td>0.3 (0.1, 0.6)*</td>
<td>0.0 (0.2, 0.01)*</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.8 (0.7, 0.9)**</td>
<td>1.0 (0.9, 1.1)</td>
<td>-0.3 (0.3, 0.3)</td>
<td>0.1 (0.3, 0.03)**</td>
</tr>
<tr>
<td>FVC baseline</td>
<td>1.1 (0.9, 1.2)</td>
<td>1.0 (0.9, 1.1)</td>
<td>0.2 (0.2, 0.07)</td>
<td>0.2 (0.2, 0.00)**</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.9 (0.9, 0.98)**</td>
<td>0.9 (0.9, 1.0)</td>
<td>0.2 (0.2, 0.07)</td>
<td>0.0 (0.2, 0.02)**</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.0 (0.9, 1.1)</td>
<td>0.0 (0.1, 1.0)</td>
<td>0.7 (9.3, 10.7)</td>
<td>0.7 (9.3, 10.7)</td>
</tr>
<tr>
<td>dcSSc</td>
<td>6.8 (6.8, 81.7)</td>
<td>0.7 (0.2, 2.9)</td>
<td>-16.5 (28.9, 4.9)**</td>
<td>1.7 (9.3, 10.7)**</td>
</tr>
<tr>
<td>DUs history</td>
<td>13.1 (3.1, 55.8)**</td>
<td>28.4 (2, 356)**</td>
<td>3.2 (2.1, 8.4)</td>
<td>0.2 (1.4, 1.7)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>1.1 (0.6, 1.6)</td>
<td>0.9 (0.4, 1.9)</td>
<td>2.2 (2.5, 6.8)</td>
<td>0.7 (1.9, 3.5)</td>
</tr>
</tbody>
</table>

Additional predictors for DUs:
- p<0.05, **p<0.01, ***p<0.001.

Conclusions: Patients with shorter disease duration, dcSSc, higher mRSS, lower DLCO and LVEF and a history of DUs had a worse unfavorable course. GEE is a robust technique for longitudinal data analysis, excellent for identifying prediction factors in ScS.

Acknowledgements: This abstract is part of the QUANTICAP project, UEFIS-CDI PN-II-PT-PCCA-2013–41589 grant.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5783

AB0609 CORRELATION OF PSYCHOLOGICAL PROFILE (MMPI-II A BDI TESTS) OF SCLERODERMA PATIENTS WITH ORGAN MANIFESTATION AND IMMUNOLOGICAL PROFILE

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Background: There is high prevalence of mood disorders in patients with systemic scleroderma. Psychosocial distress can influence some of clinical manifestations and can worsen the course of the disease and socioeconomical status of patients.

Objectives: The aim of study is detection of correlations of depression and psychological profile measures by MMPI-II (The Minnesota Multiphasic Personality Inventory) and BDI-II (The Beck Depression Inventory-II) and organ manifestation and immunological profile of patients with systemic sclerosis.
Methods: From March 2015 to July 2017 we examined 42 patients with scleroderma, from which 37 filled the valorisation criteria of MPM-II test. The data of MPM-II scales and BDI-II was correlated with antropometric data, form of disease, disease duration, duration of RP, organ major manifestation, comorbidities, use of medication and immunological profile.

Results: Of 37 patients, 30 female patients (81%) and 7 male patients (19%) were included. Mean age was 58.8±10.6y, duration of disease 8.9±9.1y, duration of RP 13.9±13.4y. 10 patient have diffuse, 27 patient limited form. Subjective perceived depression detected by BDI II test was present in 11 patients (35%), mild 6, moderate 3 and 2 severe. Total BDI-II score correlated with anticontermon Abs (p=0.05), total cholesterol (p=0.008), LDL (p=0.05) and gastrointestinal manifestation (p=0.002).

Conclusions: In addition to well-known thermoregulatory abnormalities, clear psychometric and clinical manifestations of more abnormalities on NCM may occur independently of the presence or development of a CTD and may be unknown. The presence of more abnormalities on NCM, assessed by widefield videocapillaroscopy, was retrospectively correlated with primary RP. BMI was negatively associated with NCM pattern, number of dilated capillaries with primary RP. Patients were included when they had negative serology and did not develop any definite connective tissue disease. Disease duration and duration of RP correlated with psychometric retardation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6327

AB0610 NAILFOLD CAPILLARY MICROSCOPY AND LOW BODY MASS INDEX IN RAYNAUD’S PHENOMENON PATIENTS

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Background: Underweight patients develop Raynaud's phenomenon (RP) more frequently. [1] In a small study, skin temperature and perfusion in RP patients was positively associated with body mass index (BMI). [2] In clinical practice, we frequently observe an abnormal nailfold capillary microscopy (NCM) in underweight subjects with presumably primary RP, from which the implications are unknown.

Objectives: The aim is to study whether being underweight is associated with the presence of more abnormalities on NCM.

Methods: NCM, assessed by widefield videocapillaroscopy, was retrospectively assessed in consecutive patients with suspected RP. Patients were included when they had negative serology and did not develop any definite connective tissue disease or organ involvement after a maximum of 5 years follow-up. NCM pattern was classified as normal, non-specific, early, active or late, based on the Cutolo patterns. Weight and height were measured for clinical practice and patients were divided into BMI categories: underweight (BMI<18.5 kg/m²), normal weight (BMI 18.5–25 kg/m²), dilated and giant capillaries were counted as well as the number of capillaries.

Results: A total of 352 patients were included (median age 40.6 years (24.9–52.9)), male:female 11:1 (41%), of which 47 were underweight (BMI<18.5 kg/m²), 65 normal weight (BMI 18.5–25 kg/m²), and overweight (BMI >25 kg/m²). Dilated and giant capillaries were counted as well as the number of capillaries.

Conclusions: In addition to well-known thermoregulatory abnormalities, clear NCM pattern aberrations are more frequently observed in underweight patients with primary RP. BMI was negatively associated with the number of dilated capillaries (p=0.021) and positive with capillary density. These data potentially suggest that damage to the microvasculature in underweight patients with primary RP may occur independently of the presence or development of a CTD and may be explained by other mechanisms.

References:

AB0611 MYCOPHENOLATE MOFETIL FOR THE TREATMENT OF INFLAMMATORY MYOPATHY RELATED INTERSTITIAL LUNG DISEASE: A SYSTEMATIC REVIEW

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Background: Inflammatory myopathies (IMI) are a heterogeneous group of rare autoimmune rheumatic diseases in which extramuscular manifestations, especially interstitial lung disease (ILD), are common and may occur in the absence of muscle symptoms. ILD has been identified as a marker of poorer prognosis, with sparse, mainly observational evidence, supporting the use of immunosuppressant therapies. Despite the lack of clinical trial evidence, corticosteroids are considered first-line therapy. Ciclosporin is frequently used for severe disease and Azathioprine as maintenance therapy. Mycophenolate Mofetil (MMF) has emerged as a promising treatment, encouraged by data published from a randomised controlled trial comparing Ciclosporin with MMF in patients with systemic sclerosis and ILD, which showed similar efficacy and better tolerability in the MMF group compared with Ciclosporin.

Objectives: To examine the evidence supporting the use of MMF in patients with IMI associated ILD.

Methods: An electronic literature search was performed using the Ovid platform. Population: Adults diagnosed with IMI according to validated criteria (2, 3) or antistreptase syndrome (defined by the presence of anti-streptase antibodies), with ILD demonstrated by HRCT or lung biopsy and treated with MMF, with extractable outcomes regarding ILD. Outcomes were recorded as positive (improvement/stabilisation) and negative (deterioration) as defined by the American Thoracic Society consensus guidelines (4).

Results: 506 initial citations were identified, with 23 studies included in the review comprising a total of 82 patients. Median follow-up was 12 months, median age 55 years. There was sufficient data to apply American Thoracic Society criteria in 37 patients: improvement/stabilisation n=29, deterioration n=8. Although the criteria could not be applied in 45 patients, improvement/stabilisation was reported in 44 with deterioration in one patient. A non-significant trend to better outcomes was observed when MMF was prescribed as first line therapy, in Jo-1 positive patients and non-Usual Interstitial Pneumonia pattern. Mean Prednisolone dose reduced from 40 mg/day to 10.1 mg/day. No significant toxicity was reported.

Conclusions: Mycophenolate Mofetil is a promising drug with encouraging results, but randomised controlled clinical trials are needed to prove its efficacy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5243
AB0612 EFFICACY OF LOW DOSE AND SHORT-TERM IL-2 TREATMENT TO EXPAND ENDOGENOUS REGULATORY T CELLS IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE

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Background: The concept of Mixed Connective Tissue Disease (MCTD) was first proposed by Sharp and his colleagues in 1972.1 MCTD has overlapping features between at least two autoimmune diseases, such as SLE, SSC, PM/DM and RA. Regulatory T cells (Treg cells) play a critical role in the maintenance of immune tolerance and the regulation of immune responses. Treg cell dysfunction contributes to the initiation of pathogenesis and the maintenance of high disease activity in RA and SLE.2 Recently, some studies have indicated that the proportion of Treg cells was different from healthy controls in SSC patients.3 Therefore, MCTD may be associated with Treg cells.

Objectives: To explore the status of CD4+ T cells in peripheral blood of patients with MCTD; to explore the effect of low dose interleukin-2 (IL-2) treatment on the balance of Treg cells and Th17 cells in patients with MCTD; and to observe the short-term curative effect.

Methods: CD4+ T cells in the peripheral blood of 58 MCTD patients and 33 healthy controls were analyzed by flow cytometry. All of 58 cases were treated with standard therapy, including corticosteroids, NSAIDs, immunosuppressants, or combination therapy. Among them, 26 cases of MCTD without using immunosuppressant (CYC, MTX, LEF, MMF), were as untreated group, another 32 cases were as treated group. Then we compared the difference of CD4+ T cells between two groups. In 58 patients with MCTD, a total of 27 patients were treated with low-dose IL-2 (50WIU) on the basis of standard treatment for 5 days. The difference of CD4+ T cells before and after treatment with IL-2 was compared.

Results: The absolute count of CD4+CD25+FOXP3+ Treg cells in peripheral blood of patients with MCTD was significantly lower than those in healthy controls. There was no significant difference in the absolute count of CD4+CD25+FOXP3+ Treg cells in the peripheral blood of the treated group and the untreated group. The absolute count of CD4+CD25+FOXP3+ Treg cells significantly increased higher than those before treatment with IL-2.

Conclusions: The absolute count of CD4+CD25+FOXP3+ Treg cells in peripheral blood of patients with MCTD were significantly reduced, which may be the mechanism of immune imbalance in MCTD patients. The decrease of the absolute count of CD4+CD25+FOXP3+ Treg cells in peripheral blood of patients with MCTD was not associated with the use of immunosuppressive agents. Low dose and short-term IL-2 treatment may increase the absolute count of CD4+CD25+FOXP3+ Treg cells in the peripheral blood in patients with MCTD, so as to restore the immune balance in patients with MCTD.

References:

Disclosure of Interest: None declared


AB0614 ANTISYNTHETASE SYNDROME: AUTOANTIBODIES, CLINICAL PATTERN AND MANAGEMENT OF 17 SPANISH PATIENTS

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Background: Antisynthetase syndrome (ASS) is a heterogeneous rare inflammatory condition characterized by myopathy, interstitial lung disease (ILD), arthritis, mechanic hands and Raynaud phenomenon (RP). The hallmark of ASS is the presence of antibodies against aminoacyl-transfer RNA synthetases (anti-ARS). Eight different anti-ARS have been described: anti-Jo1, anti-PL7, anti-PL12, anti-EJ, anti-OJ, anti-KS, anti-Zo, anti-TyrYRS. Despite recent publications, correlation between autoantibodies clinical pattern and management in ASS is not entirely well-known.

Objectives: The aim of this study was to define clinical features, autoantibodies and outcomes of a series of ASS patients.

Methods: We retrospectively analyzed the epidemiology, clinical data, lung function parameters, muscle enzymes, electromyogram (EMG) and autoantibodies pattern and its relationship with clinical manifestations, treatment management and outcomes of 17 patients recruited between 2005 and 2016 from the Autoimmune Diseases Division of a Spanish hospital.

Results: A total of 17 patients were reviewed (15 female). Mean age at diagnosis was 55 years. Median time delay to diagnosis was 5 months. Median follow-up was 65 months. Main clinical symptoms were dyspnea (76.5%), polyarthritis (58.8%), muscle weakness and myalgias (52.9%), RP (41.1%) and mechanic

Conclusions: The CT determined MPAD correlates strongly with the presence of pulmonary hypertension in patients with systemic sclerosis.

Disclosure of Interest: None declared

hands (23.5%). Lung involvement was defined by HRCT compatible with ILD (64.7%) and abnormal functional exploration (47.1%); restrictive pattern (87.5%) and diminished DLCO (61%). Muscle involvement was defined by elevated CK (52.9%) with a median maximum value of 517 IU/L, myopathic pattern on 8 of 13 performed EMG (61.1%) with myositis found in 4 of them (50%), and inflammatory myositis in 5 of 8 performed biopsies (62.5%). Anti-ARS findings were anti-Jo-1 (11), PL-12 (2), PL-7 (1), anti-EJ (2) and one patient with both PL-7 and PL12. Anti-Jo-1 predominant clinical pattern was ILD (72.7%), followed by myopathy (63.6%) and concomitant myopathy and ILD (45.5%). Anti-PL12 was associated with ILD, RP, and esophageal involvement and no myopathy. Anti-PL7 patient showed mild muscle involvement and cutaneous association alone. A combination of anti-PL12 and PL7 was described in one patient who developed ILD with severe myopathy. Anti-EJ patients had pulmonary involvement but no evidence of muscle disease. There was no evidence of cancer in any of our patients. Corticosteroids therapy was administered in 20 patients (88.9%), and corticosteroids dependence was highlighted, being necessary at times to associate one or more immunosuppressants.

Conclusions: Regardless of ASS being a rare disease, 17 patients were collected. Anti-Jo-1 was the most described antibody. It is important to note that one patient was found to be positive for both anti-PL7 and PL12 meanwhile they were described as exclusive, showing overlap of clinical pattern with severe muscle injury. This finding suggests that positive results for more than one ASS antibody infer more severity. In contrast with previous literature, pulmonary was more frequent than muscle involvement. The coexistence of both was observed in a small group (35.3%), mostly in anti-Jo1 patients (45.5%). Therefore, we suggest the need to reevaluate the association in patients with pulmonary or muscle involvement at onset although classic clinical pattern is missing.

References:

Disclosure of Interest: None declared.
DOI: 10.1136/annrheumdis-2017-eular.5218

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Background: Persistent infection by high-risk oncogenic Human Papillomavirus (HPV) is the main cause of the development of dysplastic or malignant lesions of the cervix. Furthermore, a few life habits, such as smoking, sexual habits and hormonal contraception, are known risk factors for cervical HPV infection. Persistent infection or high-grade intra-epithelial lesion rates was anecdotally described in patients affected by immune-mediated diseases, such as systemic lupus erythematosus, rheumatoid arthritis and systemic sclerosis (SSc), in comparison with the general population.

Objectives: To determine the prevalence of persistent HPV infection in an SSc patients series and its possible correlation with the disease clinical features.

Methods: The study retrospectively evaluated 52 consecutive female SSc patients (age 56.7±11.2SD years, disease duration 12.1±7.4SD years), classified into three groups using the Bethesda system.

Results: Seventeen (32.7%) patients were diagnosed with high-grade intra-epithelial lesion. Only tabagism was significantly correlated to HPV infection; namely, smoking habit was observed in 41.6% of SSc patients with and in 21.7% of those without HPV infection, respectively; (p=0.008); moreover immunosuppressive therapies, namely melofen, mycophenolate, cyclophosphamide or rituximab, tended to be associated with HPV infection (presence/absence 21.4 vs 21.7%; p=0.055).

More interestingly, among SSc patients over 50, HPV infection was found in 9/38 (23.7%) individuals, a frequency markedly higher than that expected in age-matched general population from the same geographical area (5%).

Conclusions: Persistent HPV infection was observed in over a quarter of SSc patients, notably in women over 50. The HPV positivity was not related to SSc clinical features, while a significant association with tabagism and immunosuppressive therapies was evidenced. Considering the possible clonico-prognostic implication on the overall disease outcome, routine gynaecological screening of SSc female patients is highly recommendable.

Disclosure of Interest: None declared.
DOI: 10.1136/annrheumdis-2017-eular.5218

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Background: Intravenous Immunoglobulins (IVig) represent a relevant treatment option in various immune-mediated disorders such as idiopathic inflammatory muscle diseases (IMIDs), immune-mediated chronic neuropathies (IMCN), hema-toplogic autoimmune diseases, Still disease, Felty syndrome, systemic lupus erythematosus, vasculitis, some organ-specific autoimmune disease, and atopic diseases. The IVig treatment is expensive and need of hospital-based assistance for its administration; therefore, the use of home-thrapy and concomitant intravenous immunoglobulins (SCIg) may significantly reduce costs and improve the patient's quality of life.

Objectives: The primary objective was to perform an analysis of costs of SCIg administration in patients affected by IMID or IMCN compared to that of previous IVig treatments.

Methods: We prospectively evaluated 6 consecutive patients (3 males and 3 females, mean age 65.3 years, range 63 - 77), 2 affected by IMID in the context of polymyositis and 4 by IMCN, 3 in the context of vasculitis and 1 in the context of a Sjögren's disease. All patients were previously treated with IVig at the dosage of 2g/Kg monthly. (mean monthly dosage 143 g, range 98 – 160, average patient weight 71.5 kg, range 49 - 80), with good clinical and humoral response. After a mean therapy duration of 49.8 months (range 12 – 125) all patients were shifted to SCIg at the dosage of 10 g twice a week (80 g monthly).

Each patient was followed up by hemurgical and clinical evaluation, including Medical Research Council (MRC) score to quantify muscle strength and INCAT Sensory Score to evaluate sensory symptoms. The costs of the two therapeutic strategies were also compared, excluding indirect costs (absecces from work and productivity losses, transport and parking, health care sector cost for healthcare assistance).

Results: In 5/6 patients, we observed the maintenance of clinical and humoral status after a mean follow-up of 21 months (range 4 - 51), in particular we observed a stability in MRC score in patients presenting loss of strength and INCAT score in patients presenting sensory symptoms. Furthermore, the treatment with SCIg was well-accepted and preferred to IVig by all patients. In one patient SCIg were discontinued after 2 weeks, because of the appearance of a haemorrhagic lesions nearby the injection site (in the same patient IVig have been stopped because of a hypertensive crisis during the infusion). Direct cost associated to IVig amount to 25246 for 5 g of immunoglobulins (7.09€/g monthly, considering a protocol of 2 g/kg/monthly and a patient-weight of 70kg), while direct costs associated to SCIg (20g weekly) amount to 6,40€/month, with a saving of 656€/monthly and 7.872€/yearly.

In our case-series the annual saving was 9,686.40€/patient (from 86,846.40€ to 76,800€, for IVig and SCIg, respectively).

Conclusions: Our experience suggests that the shift to SCIg from IVig in patients affected by IMID and IMCN is feasible, cost-effective, safe and well-accepted by patients. Further studies are needed to evaluate the effectiveness of SCIg in first-line therapy of these diseases.

Disclosure of Interest: None declared.
DOI: 10.1136/annrheumdis-2017-eular.4336

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Background: Scleredema adultorum Buschke is a rare disorder characterized by multiple hardening of the skin around the neck, shoulders, occasionally the face and the trunk. The most frequent form of scleredema is associated with diabetes mellitus (DM). The histopathological features of scleredema are characterized by thickened collagen bundles within the reticular dermis that are separated by mucopolysaccharides (mainly mucin) containing fenestrations.

Objectives: To compare clinical data of patients with Buschke-scleredema DM to diabetic patients without skin involvement patients (Control-DM) with a focus on the late vascular and neurological complications.

Methods: Clinical data of 105 diabetic patients were investigated based on medical history, physical examinations. All subjects met the following inclusion criteria: each of their disease duration time of DM had to be more than three years. Twenty-eight patients with Scleredema-DM were collected (three of type 1 and 25 of type 2 diabetes, 19 female, nine male; their mean age (zSD) was 63.0±9.3 and mean DM-duration time was 17.9±9.6 years). Seventy-seven consecutive, age and DM-duration matched patients without skin involvement were investigated as controls (nine patients with type 1 and 68 with type 2, 50 female, 27 male, their mean age was 63.3±11.9 and mean DM-duration time was 17.4±10.7 years). For statistical analysis Pearson’s Chi-squared, Fisher and McNemar tests were used.

Results: In the medical history of the Scleredema-DM group stroke occurred more frequently (8 of 28 cases, 28.6%) compared to the Control-DM group (5/77, 6.5%, p<0.01). There were no significant differences in the occurrence of myocardial infarction (5/28, 17.9% vs. 10/77 cases, 13.0%), nephropathy (5/28, 17.9% vs. 10/77 cases, 13.0%), retinopathy (2/28 cases, 7.1% vs. 7/77 cases, 9.0%), nor in peripheral neuropathy (23/28 patients, 75.0% vs. 49/77, 63.6%) respectively. Higher level of cholesterol and triglycerides was present in the Scleredema-DM group compared to the Control-DM cases (mean cholesterol was: 5.7±1.5 mmol/l vs. 4.8±1.2 mmol/l, p<0.01; triglyceride: 2.3±1.1 mmol/l vs. 1.8±1.6 mmol/l,

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Background: Intravenous Immunoglobulins (IVig) represent a relevant treatment
A UNIQUE ULTRASOUND PATTERN OF ADIPOSE TISSUE IN CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASE TREATED WITH CYCLOPHOSPHAMIDE OR RITUXIMAB: A UNICENTRE, OPEN-LABEL AND COMPARATIVE STUDY


Background: To date, rheumatologists do not have curative treatments for connective tissue disease-associated interstitial lung disease (CTD-ILD). Therefore, an stabilization of the disease is considered as a therapeutic success. One of the most frequent drugs used for achieving this goal is Cyclophosphamide (CYC); however, in the last years there has been an increasing interest in the use of Rituximab (RTX) as a treatment for CTD-ILD.

Objectives: To compare long-term effectiveness of CYC vs. RTX as a treatment in patients with CTD-ILD.

Methods: Unicentre and retrospective study in which it was analyzed clinical and image data of 26 CTD-ILD patients treated with CYC or RTX between June 2004 and December 2016. Previously, we checked that baseline characteristics and baseline levels of Pulmonary Function Tests (PFTs) in both groups were similar by using Fisher and T-student tests.

The primary outcome of the study was the stabilization of PFTs or HRTC (High Resolution Tomography Computed Tomography) considering as relapse: a) a deterioration ≥10% in FVC ( Forced Vital Capacity), or b) a decrement ≥15% in DLCO (diffusing capacity of carbon monoxide), or c) a worsening in HRTC. The prognostic effect of each treatment on stabilization was evaluated using the Kaplan-Meier method and Long Rank test. The prognostic effect of each treatment on stabilization was evaluated using the Kaplan-Meier method and Long Rank test.

Results: The study includes 20 women and 6 men with an average age of 58.9±14.2 years. 14 patients had a diagnosis of Systemic Sclerosis whereas 12 had other types of CTD.

From the 26 patients, 15 received CYC and 11 RTX, according to the physician's decision. Both groups presented similar baseline characteristics and levels in PFTs. The Kaplan-Meier method showed that the treatment had an influence on the stabilization of CTD-ILD, although long Rank test was non-significative. The average of months without relapse in CYC and RTX group was 59.7±9.50 and 79.2±7.81 respectively.

Patients in the CYC group did not present any changes in FEV1, FVC, DLCO and DLCO/VA levels during the first year of treatment. In contrast, patients in RTX group showed an increase of all PFTs levels during the first year of monitoring, although these differences were non-significatives. A direct comparison between both treatment groups after 12 months showed lower levels of all PFTs in CYC vs RTX, been DLCO/VA (67.30±10.69 and 86.25±4.59, respectively) statistically significative.

Conclusions: This study suggests, in patients with ILD-CTD, that CYC treatment stabilizes the lung function, whereas RTX shows a tendency to improve it. Also, patients with RTX treatment shows a larger mean time of stabilization than CYC group. However, large scale randomized controlled trials are needed to confirm these results.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2072
**AB0620** ORAL HEALTH IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN EUSTAR CENTER EXPERIENCE

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**Background:** Although the orofacial manifestations are commonly reported among patients with systemic sclerosis (SSc), only few studies have adequately addressed the issue of oral health-related quality of life (QoL) in such pathobiological settings.

**Objectives:** The aim was to characterize the oral health status (OHS) of adults with SSc and to compare with the general population.

**Methods:** A cross-sectional prospective observational study in 37 consecutive SSc in a EUSTAR cohort (EUSTAR 162 center) and 37 gender and age-matched controls without SSc. A standardized oral exam meaning OHS (periodontal, dental, mucosal and microbial), oral health-related behaviors and oral HRQoL (Oral Health Impact Profile, OHIP) were evaluated in all recruited individuals, while oral manifestations such as size of oral aperture, oral dryness, manual dexterity for oral hygiene and HRQoL only in SSc.

**Results:** Multivariable regression analysis was done to evaluate association between SSc, oral abnormalities, oral health status and QoL.

**Conclusions:** SSc patients are at risk to develop impaired oral health and oral HRQoL compared with the general population.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.4115

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**AB0621** DEVELOPMENT OF SYSTEMIC SCLEROSIS IN TRANSGENDERED FEMALES: A CASE SERIES

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**Background:** Scleroderma (SSc) is an autoimmune connective tissue disease with a female preponderance (female to male ratio of 9.7:1) [1]. Sex hormones are thought to play a role in the susceptibility to autoimmune diseases [2].

**Objectives:** We report 3 cases of SSc in male-to-female transsexuals diagnosed following their male-to-female transition.

**Methods:** Medical records of 3 patients diagnosed with SSc after male-to-female transition were reviewed. Disease features, hormonal therapies and surgical interventions related to gender reassignment were collected.

**Results:** At our tertiary University Hospital clinical service, 3 male-to-female transsexual patients were diagnosed with SSc following their surgery between May 1997 and October 2016. All 3 patients had started their transition before the onset of the disease and had not been diagnosed with any autoimmune disease before either starting the hormonal therapy required for the transition or before underwent surgery interventions. The first case was diagnosed with anti-RNA Pol III +ve diffuse cutaneous SSc at the age of 35 years after the first surgical intervention for infected silicone buttlock implants and approximately 5 years of hormonal therapy with combination of mestranol and norethisterone (Norvestin®). She experienced scleroderma renal crisis 2 years after the diagnosis and severe vascular involvement with frequent and severe digital ulcers (DU), Raynaud’s phenomenon (RP), gastroesophageal reflux disease (GERD), pulmonary arterial hypertension and telangiectasiae. She required chronic dialysis and was treated with mycophenolate mofetil (MMF), raparacyn, bosentan and proton-pump inhibitors (PPI). She eventually died 8 years after the diagnosis. The second case was diagnosed at the of 49 years, approximately 6 months following her gender reassigment and 5 years after having started hormonal therapy initially with conjugated estrogen isolated from pregnant mares (Premarin®) and later with estrogen and progestin agents (Exemestane). She developed ANA +ve, anti-RNP, M2, Scl-70 antibodies and anti-centromere antibodies. Renal diffuse scleroderma pattern were associated with RRI (Figure 1). Pathologic and immunologic assessment for internal organ involvement were collected and analysed as appropriate with SPSS vers 20.0. Considering that age-adjusted mean values were higher in the SSc population in comparison to literature values for the general population, we created SSc-specific age-adjusted pathologic cut-offs in reflecting renal and other disease-related organ damage.

**Objectives:** to describe RRI in a larger scleroderma population and to test both the fixed 0.70 RRI cut-off and age-adjusted cut-offs in reflecting renal and other disease-related organ damage.

**Methods:** SSc patients attending classified according to ACR/EULAR 2013 criteria were enrolled. Data on renal arteriy Doppler ultrasound (RRI), autoantibodies status and biochemical tests for renal function/damage, subset and extent of skin fibrosis, instrumental assessment for internal organ involvement were collected and analysed as appropriate with SPSS vers 20.0. Considering that age-adjusted mean values were higher in the SSc population compared to literature values for the general population, we created SSc-specific age-adjusted pathologic cut-offs in reflecting renal and other disease-related organ damage.

**Results:** 190 SSc patients (age 56.3±15.0 years, disease duration 6±8.20 years) were eligible for the study. In the SSc population significant positive correlations between RRI and age, as well as significant associations between RRI and above mentioned general population comorbidities [1], were confirmed. When considering absolute value of RRI, the 0.70 pathologic cut-off and age-adjusted cut-offs validated in the general population [1], only renal function, systolic PAS and late nailfold scleroderma pattern were associated with RRI (Figure 1). Pathologic RRI identified among those who did not detect early renal damage, but was significantly associated with various fibrotic (interstitial lung disease [p<0.015], tendon friction rubs [p=0.032], skin fibrosis vs no skin involvement [p=0.001], disease-related organ damage.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.4115

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**AB0622** RENAL RESISTIVE INDEX (RRI): PROPOSAL FOR AGE-ADJUSTED CUT-OFF VALUES IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Renal resistive index (RRI) by Doppler ultrasound, reflects changes in both renal vascular and tubular-interstitial compartments and systemic vascular compliance related to physiological (age) and pathological conditions among which hypertension, diabetes mellitus, hyperuricaemia, dyslipidaemia and chronic kidney disease is a major role [1]. Because of the age-related changes in RRI reported in literature [2,3] the use of a 0.70 cut-off to detect renal damage, as proposed [4], was questioned: renal injury in younger decades (<60yrs) may occur also for RRI value < 0.70 and be underestimated. In systemic sclerosis (SSC), RRI was previously correlated with disease duration, glomerular filtration rate and nailfold videocapilloscopy pattern [5-7], although were collected on small samples and not investigating the possible confounding role of age-related RRI values.

**Objectives:** to describe RRI in a larger scleroderma population and to test both the fixed 0.70 RRI cut-off and age-adjusted cut-offs in reflecting renal and other disease-related organ damage.

**Methods:** SSc patients attending classified according to ACR/EULAR 2013 criteria were enrolled. Data on renal arteriy Doppler ultrasound (RRI), autoantibodies status and biochemical tests for renal function/damage, subset and extent of skin fibrosis, instrumental assessment for internal organ involvement were collected and analysed as appropriate with SPSS vers 20.0. Considering that age-adjusted mean values were higher in the SSc population compared to literature values for the general population, we created SSc-specific age-adjusted pathologic cut-offs in reflecting renal and other disease-related organ damage.

**Results:** 190 SSc patients (age 56.3±15.0 years, disease duration 6±8.20 years) were eligible for the study. In the SSc population significant positive correlations between RRI and age, as well as significant associations between RRI and above mentioned general population comorbidities [1], were confirmed. When considering absolute value of RRI, the 0.70 pathologic cut-off and age-adjusted cut-offs validated in the general population [1], only renal function, systolic PAS and late nailfold scleroderma pattern were associated with RRI (Figure 1). Pathologic RRI identified among those who did not detect early renal damage, but was significantly associated with various fibrotic (interstitial lung disease [p<0.015], tendon friction rubs [p=0.032], skin fibrosis vs no skin involvement [p=0.001], disease-related organ damage.

**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.2912

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**References:**


higher mRSS (p=0.001) and vasculopatric manifestations [late scleroderma pattern (p=0.002) and digital ulcers (p=0.006)] of the disease (Figure 1).

Conclusions: in clinical practice, different age-related or non-related RRI cut-offs must be used when looking for renal or extrarenal SSc-induced damages.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8420

AB0623 PROGNOSTIC VALUE OF RENAL RESISTIVE INDEX (RRI) IN SYSTEMIC SCLEROSIS: PRELIMINARY DATA FROM A SINGLE CENTRE

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Background: Renal Resistive Index (RRI—measured with Renal arteries Doppler ultrasound) is a useful technique to evaluate vascular and tubular-interstitial damage in both general and systemic sclerosis (SSc) population, where increased RRI values correlates with longer disease duration [1], lower glomerular filtration rate and more advanced naldiloid-vascularcapillaroscopy pattern [2]. Moreover, higher RRI values were seen in SSc patients with new occurrence of digital ulcers [3].

Objectives: to test the prognostic value of RRI (absolute, ≥ 0.70 and SSc age-adjusted pathologic value (Table1)) and RRI delta change in predicting general and organ-specific worsening in scleroderma patients.

Methods: SSc patients classified according to ACR/EULAR 2013 criteria were enrolled. Demographics, Doppler ultrasound and renal and cardiac data were collected. Data on clinical worsening had been collected as herewith specified: a) Skin worsening as an increase of mRSS≥5 units, b) Peripheral vascular worsening as the appearance of new digital ulcers or the worsening of naldiloid-vascularcapillaroscopy scleroderma pattern, c) Lung worsening as decline of FVC>15% or FVC<80% with new detection of ILD on chest HRCT or worsening of HRCT-ILD extent, d) Cardiac worsening as new onset of left ventricular failure requiring treatments or new onset of PAH confirmed on RHC or detection of severe ventricular arrhythmias on 24h EKG, e) Renal worsening as a new scleroderma renal crisis or reduction of creatinine clearance <30 ml/min. General worsening was recorded in case of death due to SSc or for any of the above organ-specific worsening.

Data were analysed as appropriate with SPSS vers. 20.0.

Results: 190 SSc patients (age 56±15.0 yrs, 170 women, disease duration 6±10 yrs) were followed up with a follow up RRI measurement after 2.8±0.9 years) were enrolled. After a mean clinical follow-up of 3.6±2.6 years, 89 (46.8%) pts showed general worsening (Table 1). wider RRI changes were associated with general worsening (p=0.029) and cardiac worsening (p=0.006). The significance of these associations increased when sub-analysis was repeated focused on patients with normal SSc age-adjusted RRI values at baseline (p=0.017 and p=0.001 respectively, Figure 1).

Disclosure of Interest: None declared

AB0624 INTERSTICIAL LUNG DISEASE IN SCLERODERMA: SEVERITY ASSOCIATED FACTORS. OBJECTIVES

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Background: Systemic sclerosis (SSc) can virtually affect any organ system (such as lungs, kidneys, gastrointestinal tract, and heart). However, it is the pulmonary manifestations that account for the majority of deaths, especially interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH).

Objectives: Our aim was to assess the differences between severe and mild-to-moderate ILD in SSc.

Methods: A descriptive study was performed, using the available data from the Spanish Scleroderma Study Group (RESCLE). ILD was deemed as serious when forced vital capacity (FVC) ≤ 50% capacity. Patients were classified attending the modified classification criteria proposed by LeRoy and Medgser.

Results: Fourteen referral centers for SSc participated in the registry. By April 2014, 1374 patients with SSc had been enrolled, 541 of whom (39.4 %) had ILD, 275 severe ILD. In detail, 91% had ILD they were severe ILD more frequently than those with limited SSc (57% vs. 35%, p=0.002), as well as those who had tested positive for ATA (51% vs. 33%, p=0.005).

Additionally, prevalence of FVC<50 was higher in patients with myopathy (22% vs. 15%, p=0.002). Mean FVC percentage was 62±16.4 in the severe ILD group, whilst it was 80.8±18.9 in the mild-to-moderate one (p<0.001), and mean DLco was 36.7±15.2 and 62.9±34.5, respectively (p<0.001). Likewise, DLco~70% was also more frequent among patients with severe ILD (100% vs. 69%, p<0.001), as well as mean DLco (56.2±24.2 vs. 74.2±42.0, p=0.002). PAH was equally higher when FVC~50% (42.2±18.2 vs. 35.1±13.4, p=0.034), and so was the frequency of PAPs~40mmHg (66% vs. 29%, p<0.001) and PAH by right heart catheterism (19% vs. 11%, p=0.050). Finally, by means of a multiple logistic regression, both ATA positivity [OR 0.17 (0.05–0.58), p=0.005] and low DLco [0.93 (0.91–0.95), p=0.000] were found to be related to ILD.

Conclusions: Patients with ACA positivity and with a limited variant of SSc seem to be at lower risk of severe interstitial lung involvement. Furthermore, the presence of myopathy may contribute to explain the decrease of FVC in SSc patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2545

AB0625 AUTOANTIBODY PROFILE IN PATIENTS DIAGNOSED WITH IDIOPATHIC INFLAMMATORY MYOPATHY: MULTICENTER REGISTRY ON INFLAMMATORY MYOSITIS FROM THE RHEUMATOLOGY SOCIETY IN MADRID, SPAIN

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Background: Inflammatory myopathies (IM) are a heterogeneous group of autoimmune rheumatic diseases characterized by muscle inflammation and progressive weakness. They include any kind of primary inflammatory muscle disease that is not otherwise better explained by metabolic, toxic, infectious, neurologic or inherited causes. The presence of autoantibodies (AA) in IM is variable and they can recognize linear and cytoplasmic cellular components. Objectives: To evaluate the AA profile in patients diagnosed with IM.

Methods: We evaluated 479 patients that included 12 hospitals belonging to the IM registry of the Rheumatology Society in Madrid (SORCOM-REMIMAC) with diagnosis from January 1980 to December 2014. All patients were diagnosed of IM according to Bohan and Peter criteria. The AAs evaluated were ANA (n=476), anti-Jo1 (n=457), anti-RNP (n=427), anti-Mi2 (n=159) and ACA (n=293), according to the standard techniques in the respective laboratories. The presence of ANA was considered valid with at least two positive determinations. The AAs were compared according to the classification I) as dermatomyositis (primary...
and secondary dermatomyositis) (DM) and polymyositis (PM) including the rest of the patients. Also, IIM were classified (II) as primary polymyositis (PPM) primary dermatomyositis (PDM), overlap syndrome (OSd), juvenile myopathies (JM), cancer-associated myopathies (CAM), autoimmune necrotizing myopathy and inclusion body myositis (these were grouped as other myositis; OM).

Results: In the PM and DM groups 250 and 229 (52.2% and 47.8%) patients were included respectively. Positive ANA, anti-Jo-1 and anti-RNP were higher in the PM than in the DM group (67, 22 and 19% vs. 56, 11 and 6% p<0.021, p=0.002, p=0.0001, respectively). The presence of anti-Mi-2 was higher in the PM group (p=0.024), according to the classification II, we found statistically significant differences in ANA, anti-Jo-1, anti-RNP and anti-CAM. The OSt group had the highest proportion of ANA, anti-RNP and ACA positive AA and the JM group had the lowest frequency of Anti-Jo1 (see Table 1).

Table 1. Autoantibodies profile in IIM according to classification II

<table>
<thead>
<tr>
<th>AA</th>
<th>Comparison between groups</th>
<th>Frequency</th>
<th>P</th>
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<tbody>
<tr>
<td>ANA</td>
<td>OsD vs.</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>PPM</td>
<td>91% vs. 54%</td>
<td>0.0001</td>
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<td></td>
<td>PDM</td>
<td>91% vs. 63%</td>
<td></td>
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<tr>
<td></td>
<td>JM</td>
<td>91% vs. 40%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CAM</td>
<td>91% vs. 63%</td>
<td></td>
</tr>
<tr>
<td>PDM</td>
<td>OsD vs.</td>
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<tr>
<td></td>
<td>PPM</td>
<td>40% vs. 6%</td>
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<tr>
<td></td>
<td>PDM</td>
<td>40% vs. 3%</td>
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<tr>
<td></td>
<td>JM</td>
<td>40% vs. 7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CAM</td>
<td>40% vs. 5%</td>
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<tr>
<td>Anti-Jo1</td>
<td>OsD vs.</td>
<td></td>
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<tr>
<td></td>
<td>PPM</td>
<td>3% vs. 25%</td>
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<tr>
<td></td>
<td>PDM</td>
<td>3% vs. 19%</td>
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<tr>
<td></td>
<td>JM</td>
<td>3% vs. 36%</td>
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<tr>
<td>Anti-RNP</td>
<td>OsD vs.</td>
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<tr>
<td></td>
<td>PPM</td>
<td>0%</td>
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<tr>
<td></td>
<td>PDM</td>
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<td>JM</td>
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<td></td>
<td>CAM</td>
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<tr>
<td>ACA</td>
<td>OsD vs.</td>
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<tr>
<td></td>
<td>PPM</td>
<td>18% vs. 3%</td>
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Conclusions: The AA associated with the IIM subtypes is consistent with published scientific evidence on other cohorts for ANA, anti-Jo1, anti-RNP and anti-Mi2, in spite of the small sample size. The OsD group showed higher ANA and anti-RNP frequencies which might be explained by the coexistence of SLE and MCTD patients. It could be interesting to follow up those PPM patients with positive AA because they could be in the future diagnosed with a connective tissue disease. Carrying out longitudinal studies that include a greater proportion of patients may help to evaluate and predict the clinical course of IIM. References:


Acknowledgements:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7050

AB0626

EPITOPE PROFILING OF ANTI-RO52 ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS, SYSTEMIC SCLEROSIS-ASSOCIATED PRIMARY BILARY CIRRHOSIS, AND PRIMARY BILARY CIRRHOSIS ALONE

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Background: Anti-Ro52 antibodies are detected in patients with Sjogren’s syndrome (SS), systemic sclerosis (SSc) and other autoimmune rheumatic diseases. Epitope mapping studies of anti-Ro52 in autoimmune rheumatic diseases have failed to find any difference on epitope recognition suggesting a common stimulus for the loss of tolerance to Ro52. Such epitope differences, however, were noted between SS and non-rheumatic IIM and in particular, SS-associated primary biliary cirrhosis (SS-PBC) or PBC alone (1).

Objectives: To assess whether or not the Ro52 epitope profile in anti-Ro52+ SSc patients differs from that of SSc-associated PBC (SSc-PBC) or PBC. Methods: Serum samples were obtained from 63 anti-Ro52 positive (by ELISA) patients with systemic sclerosis (33 SSc), systemic sclerosis (SSc) and other autoimmune rheumatic diseases. Antibody reactivity to full length Ro52 in autoimmune rheumatic diseases have failed to find any difference on epitope recognition suggesting a common stimulus for the loss of tolerance to Ro52. Such epitope differences, however, were noted between SS and non-rheumatic IIM and in particular, SS-associated primary biliary cirrhosis (SS-PBC) or PBC alone (1).

Objectives: To assess whether or not the Ro52 epitope profile in anti-Ro52+ SSc patients differs from that of SSc-associated PBC (SSc-PBC) or PBC. Methods: Serum samples were obtained from 63 anti-Ro52 positive (by ELISA) patients with systemic sclerosis (33 SSc), systemic sclerosis (SSc) and other autoimmune rheumatic diseases.

Results: Reactivity was present to: full length Ro52 in all anti-Ro52 positive patients differs from that of SSc-associated PBC (SSc-PBC) or PBC. Ro52–1 in 6/33 (18.2%) patients (33 SSc, 10 SSc-PBC, 20 PBC alone). Antibody reactivity to full length Ro52 in autoimmune rheumatic diseases have failed to find any difference on epitope recognition suggesting a common stimulus for the loss of tolerance to Ro52. Such epitope differences, however, were noted between SS and non-rheumatic IIM and in particular, SS-associated primary biliary cirrhosis (SS-PBC) or PBC alone (1).

Objectives: To assess whether or not the Ro52 epitope profile in anti-Ro52+ SSc patients differs from that of SSc-associated PBC (SSc-PBC) or PBC. Methods: Serum samples were obtained from 63 anti-Ro52 positive (by ELISA) patients with systemic sclerosis (33 SSc), systemic sclerosis (SSc) and other autoimmune rheumatic diseases.

Results: Reactivity was present to: full length Ro52 in all anti-Ro52 positive SSc, PBC-SSc, or PBC patients by line immunoassay; Ro52–5 in 0/33 (0%) SSc, 0/10 (0%) SSc-PBC, or PBC; Ro52–4 in 0/22 (0%) SSc, 0/22 (0%) SSc-PBC, or PBC; Ro52–3 in 0/33 (0%) SSc, 0/10 (0%) SSc-PBC and 0/20 (0%) PBC; Ro52–2 in 4/33 (12.1%) SSc, 2/20 (10%) PBC; Ro52–1 in 18/33 (54.5%) SSc, 18/20 (90%) PBC and 18/33 (54.5%) PBC. Swollen and tender joint counts were present in 38 (31.4%) and 25 (20.6%) patients, respectively, while 35 patients (28.9%) had tendon friction rubs. Digital ulcers were present in 15 patients (12.4%) at baseline.

Conclusions: RISE-SSc has a unique trial design with a cohort enriched for diseased progressed, which is reflected in the baseline characteristics of the randomised patients. Results of the RISE-SSc study will provide data to inform not only the efficacy, safety and tolerability of riociguat treatment in patients with dcSSc, but also the feasibility of a new trial design based on cohort enrichment.

References:


Disclosure of Interest: D. Kharra Grant/research support from: Bayer, BMS, Genentech/Roche, Sanofi-Aventis, NIH K24AR063120, Consultant for: Actelion, Bayer, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, Y. Allano Grant/research support from: BMS, Genentech-Roche, Inventiva, Pfizer, Sanofi, Consultant for: Actelion, Bayer, Biogen, Genentech-Roche, Galapagos, Medac, Pfizer, Sanofi, Servier, UCB, C. Denton Grant/research support from: CSL Behring, Bayer, GSK, Inventiva, Consultant for: Actelion, Bayer, GSK, Merck-Serono, Genentech-Roche, Inventiva, Sanofi-Aventis, Boehringer Ingelheim, M. Matucci-Cerinic Grant/research support from: BMS, Pfizer, Actelion, Lilly, J. Pope Grant/research support from: Bayer, Merck, Consultant for: BMS, Roche, Roche, Merck, Z. Yerou Employee of: Bayer Healthcare Company Ltd, Beijing, China, J. Curran Shareholder of: Bayer AG, Employee of: Bayer plc, J. de Oliveira Pena Employee of: Bayer US LLC, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Consultant for: Actelion, A. Gkoutzourelas Employee of: Active Biotec, Bayer, Biogenidec, BMS, Boehring Ingelheim, ChemomAb, EpifarmPh, eserfandation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, Medimimme, Mitsubishi Tanabe Pharma, Pharmacolitics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, IQone Healthcare, Mepha
MACROVASCULAR DYSFUNCTION OF UPPER AND LOWER LIMBS CORRELATES WITH DIGITAL ULCERATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic connective tissue disorder of unknown etiology characterized by tissue fibrosis and vascular damage [1]. Digital ulcerations (DUs) are common manifestations of vascular involvement [2]. Although the role of macrovascular disease of LoS and SSc has been considered mainly to affect the microvasculature [3], there is recent evidence showing that SSc is associated with the prevalence of large vessel disease [4]. However, only a few studies investigated the relationship between macrovascular disease and its role in the clinical manifestations of SSc such as ulcers.

Objectives: To assess the relationship between the Macrovascular dysfunction of upper and lower limbs with digital ulcerations in patients with systemic sclerosis.

Methods: Ninety patients with SSc (45 cases with DUs and 45 cases without DUs) enrolled in this study. Patients with other rheumatologic diseases and diabetics patients were excluded from the study. Data were collected from the patients, included age, sex, date of disease onset, history of cardiovascular disease and dyslipidemia, SSc disease duration, type of SSc (lcSSc or dcSSc), Raynaud’s phenomenon (RP), RP duration and digital ulcerations (DUs), Body weight (BW), Height, Waist circumference (WC), Body mass index (BMI), Blood pressure (BP), serum levels of SCL-70 antibody and Anti-Jo-1 microglobulin antibody. Then Doppler sonographies were performed. The outcome variables were the peak systolic velocity (PSV) and resistance index (RI) of ulnar, radial, popliteal, dorsalis pedis and tibial artery.

Results: The SSc patients with DUs have significantly lower PSV and higher RI in tibiopercal artery (PSV:52.1±7.9 vs 55.7±7.4, p=0.006 and RI: 0.58±0.15 vs 0.52±0.06, p=0.003), dorsalis pedis (PSV: 33.9±1.9 vs 34.5±0.4, p=0.027 and RI: 0.54±0.11 vs 0.50±0.04, p=0.045) and tibial artery (PSV: 32.6±3.1 vs 34.4±0.9, p=0.01 and RI: 0.62±0.16 vs 0.51±0.07, p=0.001) in comparison to SSc patients without DUs. PSV and RI of ulnar artery were significantly correlated with age (p=0.012 and p=0.019), disease duration (p=0.001 and p=0.001) and Raynaud’s phenomenon (RP) duration (p=0.048 and p=0.028), PSV and RI of tibial artery had significant correlation with age (p=0.038 and p=0.009), systolic blood pressure (p=0.022 and p=0.037) and diastolic blood pressure (p=0.015 and p=0.010).

Conclusions: We concluded that digital ulceration in patients with SSc might be frequently related to the macrovascular dysfunction in below the elbow and knee.

References:

Disclosure of Interest: None declared

Conclusions: Our study seems to indicate that clinical spectrum time course of anti PL-12 positive ASSD is different from that of anti PL7 and of anti EJ positive ASSD. The clinical pattern associated with these two latter antibodies was very similar. Furthermore, anti PL-12 positive patients seems to have a more stable disease, with a less common occurrence of ex-novo triad findings during the follow-up.

References:

Acknowledgements: To all members of the AENEAS collaborative group.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2592

AB0631 THE CLINICAL CONSEQUENCES PRESENCE OF ANTI-PM/SCL ANTIBODIES IN SYSTEMIC SCLEROSIS

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Background: Anti-PM/Scl (a-PM/Scl) antibodies are found in different systemic autoimmune disease such as polymyositis, dermatomyositis, systemic sclerosis (SSc), and overlap syndromes. According to literature they are detected in about 2% of patients with SSc, but their presence are more common in SSc with myositis overlap. Features positively associated with the presence of a-PM/Scl antibodies included younger age at disease onset, skeletal muscle involvement, calcinosis, inflammatory arthritis, and overlap disease. On the other hand interstitial lung disease and gastrointestinal symptoms were less frequent in SSc patients with a-PM/Scl.

Objectives: The aim of the study was to assess the clinical consequences presence of a-PM/Scl antibodies in patients with SSc.

Methods: The study was performed in 126 European Caucasian SSc pa-tients (98-female and 28-male) hospitalized consecutively in the Department of Rheumatology and Connective Tissue Diseases. Patients fulfilled the ACR classification criteria of SSc (59 have diffuse cutaneous SSc and 67 limited SSc). The study group were studied according to the presence of a PM/Scl antibodies applying commercial test – EUROLINE Systemic Sclerosis Profile. Detection and other cytokine and chemokine milieu in the tear of SSc patients has not yet been evaluated.

Conclusions: In SSc anti-PM/Scl antibodies are frequently associated with myalgia or myositis, contractures and overlap syndrome.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4393

AB0632 ASSESSMENT OF VEGF AND OTHER CYTOKINES IN THE TEAR OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease, characterized by widespread small vessel vasculopathy, immune dysregulation with production of autoantibodies, and progressive fibrosis. SSc may be associated with sicca syndrome. Changes in levels of proangiogenic and proinflammatory cytokines has already been determined largely in serum, however, the local inflammatory and cytokine milieu in the tear of SSc patients has not yet been evaluated.

Objectives: We wished to determine VEGF and other cytokine and chemokine levels in tear samples of SSc patients.

Methods: First, forty-three patients (40 female and 3 men, mean (SD) age 61 (48–74) years) with SSc and 27 healthy controls were enrolled in the VEGF study. Basal tear sample collection and tear velocity investigations were carried out followed by an ophthalmological examination. Total protein concentrations and VEGF levels were determined in tear samples. In the multiple cytokine study, unstimulated tear samples were collected from nine patients with SSc and 12 age and gender-matched controls. The relative levels of 102 different cytokines were determined by a cytokine array, and then absolute levels of four key cytokines were determined by a magnetic bead assay.

Results: In the first study, the mean collected tear fluid volume developed 10.4 L (1.0–20.6) in patients and 15.6 L (3.88–34.5) in control subjects. The mean total protein level was 6.9 g/L (1.8–12.3) and 4.1 g/L (0.1–14.1) in tear samples of SSc patients and controls, respectively. In patients with SSc, the mean VEGF tear concentration was 4.9 pg/L (3.5–8.1) compared to 6.15 pg/L (3.84–12.3) in healthy samples. Multicytokine-array studies revealed shifted cytokine profile characterization by predominant proinflammatory cytokines in the tear samples of SSc patients. Out of the 102 analyzed proteins, nine were significantly increased in tears of patients with SSc. Based on the multiplex bead results, CRP, interferon-inducible protein 10 (IP-10) and monocyte chemotractant protein-1 (mcp-1) levels were significantly higher in tears of patients with SSc compared to controls.

Conclusions: Impaired angiogenesis has been found by other investigators in SSc. This is reflected by lower VEGF levels in the tear samples of SSc patients compared to controls. The multi-cytokine array study revealed increased production of CRP and two important pro-inflammatory chemotaxins in the tears of SSc patients. Our current data depict a group of inflammatory mediators, which may play a significant role in ocular pathology of SSc.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3218

AB0633 RITUXIMAB IN SCLERODERMA RELATED INTERSTITIAL LUNG DISEASE: A SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

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Background: Pulmonary involvement is one of the major causes of morbidity and mortality in patients with progressive systemic sclerosis (PSS). Clinically significant interstitial lung disease (ILD) is noted in 25% of patients and accounts for 33% of deaths in PSS patients [1, 2]. Cyclophosphamide (CYC) and mycophenolate mofetil (MMF) have been shown to retard progression of ILD [3, 4]. The limited data on rituximab indicate that rituximab might be effective in PSS related ILD [5].

Objectives: To study the efficacy of rituximab in patients with PSS related ILD.

Methods: The clinical details of all patients of PSS related ILD who were treated with rituximab were noted from the case files. EULAR criteria were noted respectively from the case files. Forced vital capacity (FVC) value before and 1 year after administration of rituximab were noted. Increase in FVC by 10% from baseline was considered as improvement and fall in FVC by 10% or absolute value less than 40% of predicted was considered as worsening. Patients with FVC ±10% from baseline were considered to have stabilized lung functions.

Results: A total of 11 patients received rituximab between 2013 and 2016. Six (54.5%) patients were females. Median age of the subjects was 44 years (range: 31–75 years). All patients received intravenous CYC at least 1 year before rituximab. Rituximab was given either not responded to CYC or worsened after initial response to CYC. All patients received 2 doses of rituximab (1g each) at 2 weeks interval. Median FVC before rituximab was 57% of predicted. Two patients did not have post rituximab FVC values. Median FVC 1 year after rituximab was 54% predicted. Out of the remaining 9 patients, 2 (22.2%) patients had improvement in FVC 6 (66.7%) patients had stabilization of FVC and 1 patient worsened. One patient, who had stabilization of FVC with rituximab expired after 2 years of receiving rituximab.

Conclusions: Rituximab was effective in stabilization of lung functions in patients of PSS with ILD who did not have favourable outcome with intravenous CYC.
Efficacy of rituximab in treatment naïve PSS related ILD patients needs to be studied.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5384

AB0634
RITUXIMAB IN SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE, A CASE SERIES OF 18 PATIENTS
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Background: Interstitial lung disease (ILD) is a severe complication of systemic sclerosis (SSc). Immunosuppressives such as cyclophosphamide (CYC) and mycophenolate mofetil (MMF) are used in its treatment with no proven efficacy (1). Rituximab (RTX) appears to be an emerging agent according to case series.

Objectives: This retrospective study aims to evaluate the efficacy of RTX on SSc-ILD in a group of patients followed in our center.

Methods: A chart review revealed 18 patients (16 women, 2 men; mean age 50.3±12.1 SD years (range 30–72), mean disease duration 8.3±9.3 SD years) with SSc who have been diagnosed as having ILD (confirmed by high-resolution thorax computed tomography and pulmonary function tests) and have been treated with one or more cycles of RTX. Efficacy was evaluated according to the criteria of the American Thoracic Society: Improvement= an increase in FVC>10% or DLCO>15%; worsening= a decrease in FVC>10% or DLCO>15%; stabilization= changes in FVC less than 10% or DLCO less than 15% (2).

Results:

Table 1 Demographic findings of the patients and their response to RTX treatment

![Table 1](image)

Four patients were treatment naïve for ILD when they received RTX (Group 1). The mean duration between the diagnosis of ILD and RTX treatment in Group 1 was 3.5 months (range 6–14 months). The average RTX cycle in this group was 3.5 months (range 0–14 months). The average RTX cycle in this group was 3.5 months (range 0–14 months). The average RTX cycle in this group was 3.5 months (range 0–14 months). The average RTX cycle in this group was 3.5 months (range 0–14 months). The average RTX cycle in this group was 3.5 months (range 0–14 months). The average RTX cycle in this group was 3.5 months (range 0–14 months).

Conclusions: RTX appears to be modestly effective for ILD of SSc. The duration of ILD as well as the presence or absence of previous immunosuppressive therapy do not appear as playing a role in response.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4908

AB0635
THE CLINICAL FEATURES AND PROGNOSIS OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SCLERODERMA AND OTHER CONNECTIVE TISSUE DISEASE DURING THE MODERN MEDICAL ERA IN JAPAN
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While PAH has been recognized as a serious adverse event in patients with systemic sclerosis (SSc), the incidence and the clinical features of SSc-related PAH have been reported from diverse populations. This study intends to clarify the clinical features and prognosis of SSc-PAH in modern era where multiple PAH drugs are available, in addition, compare between SSc-PAH and PAH associated with other CTD-PAH (non SSc-PAH). Methode: Fifty-seven consecutive CTD-PAH patients were enrolled to this study, who received hemodynamic examination with right heart catheterization between 2004 and 2016. Thirty of 57 patients were SSc-PAH patients and other 27 patients were non SSc-PAH patients (11 mixed connective tissue disease, 8 systemic lupus erythematosus, 5 primary scleroderma, 1 polymyositis, 1 rheumatoid arthritis and 1 Still's disease were included). We retrospectively analyzed the relationship between clinical parameters at baseline and the prognosis of CTD-PAH patients.

Results: Mean age at entry were 65±10.3 and 48±15.5 years old each other (SSc-PAH vs non SSc-PAH P<0.05). Twenty-eight SSc-PAH patients (96%) took at least one vasodilator, among them, 18 SSc-PAH (60%) and 13 non-SSc-PAH (48%) patients took multiple vasodilators at the end of follow-up period. Comparing the baseline clinical parameters between two groups, vital capacity and diffusing capacity of the lung for carbon monoxide (DLCO) were significantly lower in SSc-PAH patients than non SSc-PAH patients and brain natriuretic peptide and creatinine level were higher in SSc-PAH patients than non SSc-PAH patients (P<0.05). However, there were no significant differences in hemodynamic indices between two groups. During a mean follow-up period of 42.5±31.5 months, 22 patients (18 SSc-PAH and 4 non SSc-PAH) died or received lung transplantation. The SSc-PAH patients had worse prognosis than non SSc-PAH patients (figure: P<0.001). Only 6 of 18 SSc-PAH patients and 1 of 4 non SSc-PAH patient died of PH related cardiovascular event and other principal causes of death included interstitial lung disease (ILD), neoplasm and infection. Applying multivariable Cox-proportional hazard regression, mean pulmonary arterial pressure, right atrial pressure, creatinine level and %DLCO were extracted as the independent risk for all-cause mortality.

Conclusions: SSc-PAH patients had poor prognosis among CTD-PAH patients despite the progression of PAH drugs. As well as the report from REVEAL registry, not only PAH severity but also respiratory dysfunction may predict the prognosis of CTD-PAH patient. Scleroderma is multorgan disease affected by complex pathology of vasoconstriction (ischemia), proliferation, inflammation, autoimmune disorder and fibrosis. Our data suggest that vasodilator alone is not enough to improve the prognosis of CTD-PAH patients. Comprehensive therapeutic strategy for SSc-PAH is needed.

References:

DOI: 10.1136/annrheumdis-2017-eular.4271

A COMPARISON STUDY OF PREVALENCE OF TRADITIONAL CARDIOVASCULAR RISK FACTORS AND FRAMINGHAM RISK SCORE IN SYSTEMIC SCLEROSIS PATIENTS AND MATCHED CONTROLS

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Background: In Systemic Sclerosis (SSc), data on prevalence of traditional cardiovascular (CV) disease risk factors is scarce and conflicting (1). Therefore, SSc patients CV risk attributed to traditional CV risk factors remains an issue of debate.

Objectives: To evaluate if patients with SSc have a higher prevalence of traditional CV disease risk factors and a higher risk of long-term CV events based on the risk prediction tool of the Framingham risk score (FRS) in comparison with age, race and sex matched control subjects.

Methods: The study comprised patients diagnosed with SSc, fulfilling both the 1980 ACR and the 2013 ACR/EULAR criteria for the disease, and followed-up at our institution for 1 year using a group of age, race and sex-matched controls. Inclusion criteria were age 30 to 74 and no history of CV events in order to calculate FRS. In total, 46 out of 62 patients were eligible for the study. Traditional CV disease risk factors (diabetes, arterial hypertension and smoking) were compared among the 46 patients with SSc and 51 matched controls. Systolic blood pressure (SBP) values and total and high-density lipoprotein (HDL) cholesterol levels were also collected. The 10-year risk for CV events according to FRS was calculated and means of patients and controls were compared. Subjects’ distribution into 3 categories of risk – low (<10% risk), medium (10–20% risk) and high (>20% risk) was also compared. Parametric and nonparametric tests were used for comparison between groups. P value <0.05 was defined as statistically significant.

Results: Mean risk for CV events in 10-years assessed by FRS was 10.00%±8.61 for SSc patients and 7.76%±8.30 for matched controls. Differences were not statistically significant (p=0.196). Additionally, prevalence of diabetes, arterial hypertension and smoking did not differ significantly between the two groups (p=0.890, p=0.443, p=0.651, respectively). Total and HDL cholesterol levels were also similar between groups (p=0.963 and p=0.506, respectively). Only SBP values (mmHg) of SSc patients were significantly higher (128.50 mmHg [113.5 to 139.3]) (median [interquartile range]) compared with controls (120.00 [110 to 130]), p=0.031. Subjects’ distribution into the 3 groups of risk defined was similar for both groups (p=0.205).

Conclusions: In our study, prevalence of traditional CV disease risk factors and 10-year risk for CV events based on FRS assessment tool did not differ significantly between SSc patients and age, sex and race matched controls.


Disclosure of Interest: None declared


SUBCLINICAL AtherosMATosis and Vitamin D DeficienCy In PaTients with Scleroderma

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Objectives: To study whether patients with systemic sclerosis (SSc) have an increased cardiovascular risk (CVR), measured on the basis of analytical, angiodynamic and/or vascular lesions on carotid ultrasound. The carotid IMT is a marker of cardiovascular morbidity and mortality, allowing measurement and monitoring of atherosclerosis in asymptomatic individuals, being surrogate markers of future coronary disease, stroke and general death in the general population and in inflammatory rheumatologic diseases.

Methods: Epidemiological and analytical data were collected, including the determination of the CRV SCORE index. Vascular ultrasound protocol included assessment of carotid intima-media thickness (IMT), presence of atheromatous plaques, and exploration of peripheral arteriopathy using the ankle arm index (ABI).

Results: Seventy adult patients with ES diagnosis (ACR-EULAT 2013 criteria) were included. 94% of the women had a mean age of 50.2±12.5 years, and an average evolution time of 3.0±4.4 years. The distribution by subgroups was: limited SSc (48%), diffuse SSc (34%), pre-SSc (4%), sine SSc (2%), MCTD (5%) and overlap syndrome 4%). The mean SSRm was 9.3±7.0 (range 0–42).

The ANA were positive in 91.4%, ACA (51.4%), ATA (10%), RNA polymerase (42%), 4% were DM, 7% were obese, 11% were active smokers, 13% were HTN, and 28% were ex-smokers. 28% had hypercholesterolemia with a mean total cholesterol of 192.5 ± SD (31 ± 9) and LDL of 102.4 (SD ± 29.4 mg/dL).

57% received vasodilators, most of them APA-II. 10% bosentan, 4.2% sildenafil, and a 2.8% combination therapy.

The percentage of immunosuppressive drugs was corticoid (50%), MTX (34%), mycophenolate (3%), AZA (11%), HCQ (14%), CP %.

The IMT presented pathological values (>0.9 mm) in 39% of the sample, 23% had atherothrombotic plaques (being bilateral in 40%). Subclinical atherosclerosis affected 41.4% (patients without cardiovascular events, pathological IMT and/or atheroma plaques). The ABI had pathological values (<0.9) in 17% of the patients.

In the bivariate analysis, the pathological GIM was related to the presence of ACA antibodies (OR =3.80, 95% CI: 1.15–12.52, p=0.028) and with the SCORE index of CVR (OR =2.93, 95% CI: 1.12–7. 64, p=0.028); And the presence of atherothrombotic plaques was associated with increased SSRm score (OR 1.09, 95% CI 1.00–1.19, p=0.046), and the highest CVR SCORE index (OR 3.90, 95% CI: 1.31–11.56, p=0.014).

In the multivariate analysis, the serum vitamin D concentration showed a protective effect on IMT (OR =0.94, 95% CI 0.89–0.99, p value =0.025). And the main determinant of atheromatous plaques is the SCORE index, since the increase of one unit in SCORE index multiples by 4 the probability of presenting plaques (OR =4.06, 95% CI: 1.31–12.60, P=0.015), once the effect of SSRm was controlled.

Conclusions: 40% of the patients had pathological IMT values, showing association with the presence of positive AAC and the SCORE risk index.

The serum concentration of 25-OH-vitamin D showed a protective effect on IMT. Sixty percent of the sample had vitamin D deficiency.

The presence of atheromatous plaques (23% of patients) was associated with higher SSRm indexes and SCORE cardiovascular risk.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6995

CARDIAC TRANSPLANT IN SYSTEMIC SCLEROSIS-ASSOCIATED CARDIOMYOPATHY: MONOCENTRIC EXPERIENCE OF 3 CASES

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Background: Cardiac involvement in systemic sclerosis (SSc) is a frequent complication, but end-stage cardiac failure remains uncommon and represents a poor prognosis. Heart-lung and lung transplant is an established treatment option for SSc-related pulmonary disease. Due to the limited published data, no recommendations exist for cardiac transplant in the context of SSc.

Objectives: We present our monocentric experience of 3 patients with SSc who underwent cardiac transplant for SSc-related end-stage heart disease (multiple hospitalisations due to failure of medical therapy and life-threatening complications).

Results: Case 1 is a 59-year-old male with limited cutaneous SSc. Antinuclear antibody (ANA) was negative. He had vascular (digital ulcers) and cardiac (heart failure (left ventricular ejection fraction (LVEF) 20%, NYHA class IV)) involvement, without major gastrointestinal or pulmonary involvement (no interstitial lung disease (ILD) or pulmonary arterial hypertension (PAH; assessed by right heart catheterization (RHC))). He underwent a cardiac transplant at the age of 51, after a disease duration of 6 years. Post-transplantation immunosuppressant therapy consists of tacrolimus and mycophenolic acid, initially associated with methylprednison, which is the standard immunosuppression protocol at our institution.

Case 2 is a 55-year-old male with limited cutaneous SSc. ANA was positive,
SUPERIOR TREATMENT RESPONSE OF INTERSTITIAL LUNG DISEASE IN INFLAMMATORY MYOPATHIES COMPARED TO OTHER CONNECTIVE TISSUE DISEASES – A PROSPECTIVE COHORT STUDY

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Background: Intersitial Lung Disease (ILD) associated to Connective Tissue Disease (CTD) represent a challenge for clinicians and researchers because of their significant morbidity and mortality. Although the different types of ILD associated to CTD are often studied and managed as one because of their autoimmune background, there are considerable differences in their etiopathogenesis and therefore it can be assumed that there are differences in their response to treatment (1). Even though previous studies have analyzed the impact of immunosuppression in ILD secondary to scleroderma, additional studies are needed in order to determine the response to treatment of the different forms of ILD associated to CTD (2–3).

Objectives: To characterize and analyze the response to treatment of different types of ILD associated to CTD. The primary endpoint is the Functional Vital Capacity (FVC) change at 6 months and 1 year, and secondary endpoints are the change in Diffusion Capacity of the Lung for Carbon Monoxide and in a 6 Minute Walk Test.

Methods: A prospective cohort study is being carried out where all patients who present to the Mayo Clinic Florida pulmonary clinic, age 18 to 80, with established ILD and with ILD who meet the criteria for immunologic mediated process, are being followed for a year in order to evaluate their clinical and functional outcomes to treatment. Patients with moderate or severe Pulmonary Hypertension and, and active smokers with bronchiolitis pattern are being excluded. Exploratory analysis were performed on the first group of patients enrolled in the study, continuous variables were described with central tendency measures and the mean absolute difference in adjusted 12-month FVC was analyzed between the different types of CTDs using student’s t-test.

Results: Thirteen patients with ILD were enrolled in the study’s initial phase. Five of the patients had been diagnosed with an Inflammatory Myopathy (IM), 2 with Rheumatoid Arthritis, 1 with an Undifferentiated Connective Tissue Disease, 1 with Churg-Strauss Syndrome, and one with Systemic Sclerosis. One patient was treated with Rituximab only, 2 with Rituximab and a steroid; 3 with Myophenolate Mofetil (MMF) only; 2 with steroids, MMF, and Rituximab; 1 with a TNF inhibitor and MMF; 1 with MMF and steroids; 1 with Azathioprine and steroids; and 1 received only steroids. IMs were compared to the rest. At year 4, after a disease duration of 7 years Standard immunosuppressants were initiated.

At present, 1.5 years (case 2 and 3) and 8 years (case 1) after transplant, the donor hearts are still functioning well. No other SSC-related organ manifestations have been observed nor signs of rejection.

Conclusions: We present 3 patients with SSC who successfully underwent cardiac transplant for SSC-related end stage heart disease. None had other major SSC-related organ involvement. This supports the limited published data that cardiac transplant is feasible and can be considered in end-stage SSC-related cardiomyopathy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4251

AB0640 DOES MIXED CONNECTIVE TISSUE DISEASE WITHOUT ANTI-U1RNP EXIST?

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Background: Mixed Connective Tissue Disease (MCTD) is a systemic autoimmun rheumatic disease (SARD) characterized by clinical manifestations of systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and polymyositis (PM) with the presence of anti-U1RNP antibodies. Objectives: To determine whether there are patients with symptoms of MCTD in the absence of anti-U1-RNP antibodies.

Methods: This was a monocentric, prospective, observational study of patients with SARD. All patients diagnosed of MCTD according to Kasukawa and/or Alarcón-Segovia’s criteria, SLE, SSc, PM, overlap syndromes (simultaneous or sequential criteria of 2 or more SARD), Sjögren’s syndrome, Antiphospholipid syndrome, systemic vasculitis and undifferentiated or incomplete SARD (at least one clinical criterion of the classification criteria and a related antibody of any of the SARD) were included. The data was collected in the Immunology and Systemic Rheumatic Diseases Registry of the Hospital General Universitario Gregorio Marañón Rheumatology Department from 1986 to 2012. The registry includes 2406 patients diagnosed with SARD. Patients with rheumatoid arthritis were excluded. Patients with clinical MCTD criteria were divided into seropositive (MCTD, with anti-U1RNP) and seronegative (possible MCTD, without anti-U1RNP). The registry counts with the local Institutional Ethics Board approval.

Results: A total of 692 patients were recruited, 608 women (87.9%), Seventy (70, 10.1%) patients were classified as seropositive and 75 (10.8%) as seronegative by Kasukawa’s criteria. Sixty-two (62, 8.9%) patients were classified as seropositive and 54 (7.8%) as seronegative according to Alarcón-Segovia’s criteria. There were no significant differences in age at disease onset, age at diagnosis or disease duration (p=0.05) between seropositive and seronegative patients. Seropositive patients with Kasukawa’s criteria presented more frequently: lymphadenopathy, malar rash, leucopenia, Raynaud’s phenomenon, muscle weakness and increase of muscle enzymes (Table 1). By Alarcón-Segovia’s criteria, patients who developed myositis were more frequent in the seropositive group (p=0.007, OR 3.25, 95% CI, 1.44–7.32).

Conclusions: Some patients with SARD manifestations fulfill MCTD clinical criteria, both Kasukawa’s and Alarcón-Segovia’s, in the absence of anti-U1-RNP antibodies from the onset of the disease and throughout its evolution (seronegative MCTD). The frequency of seronegative MCTD was similar to the frequency of seropositive MCTD. Patients with seropositive MCTD presented more frequently manifestations of SLE (lymphadenopathy, malar rash and leucopenia) when using Kasukawa’s criteria and of PM when using both criteria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5192

AB0641 ARTERIAL STIFFNESS AND CLINICAL ASSOCIATION IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis is an autoimmune disease characterized by microvascular damage and fibrosis. There are several studies that shown microvascular damage with arterial stiffness (AS) and the risk of cardiovascular complications. Carotid-femoral pulse wave velocity (CF-PWV) and augmentation index (AIx) are two competent methods to determine AS and predictors of macrovascular damage with arterial stiffness (AS) and the risk of cardiovascular complications. Carotid-femoral pulse wave velocity (CF-PWV) and augmentation index (AIx) are two competent methods to determine AS and predictors of macrovascular damage. Carotid-femoral pulse wave velocity (CF-PWV) and augmentation index (AIx) are two competent methods to determine AS and predictors of macrovascular damage. Carotid-femoral pulse wave velocity (CF-PWV) and augmentation index (AIx) are two competent methods to determine AS and predictors of macrovascular damage.

Objectives: To determine the frequency of arterial stiffness in patients with systemic sclerosis and its association with clinical manifestations.

Methods: We performed a cross-sectional study; patients with diagnosis of systemic sclerosis according to ACR/EULAR 2013 criteria were included and the control group was selected from a database of mechanical vascular service. AS
TTHICKNESS OF THE INTIMA-MEDIA COMPLEX AND DOPPLER FINGERPRINT ABNORMALITIES IN SYSTEMIC SCLEROSIS:

Objectives: The aim of the study was to determine if there is any difference in the intima-media complex thickness as well as in blood flow parameters measured using Doppler ultrasound examination in scleroderma patients and the general population.

Methods: 215 patients, aged 19–75, with diagnosed systemic scleroderma were examined using a Doppler ultrasound examination. Thickness of intima-media complex (IMT) approximately 2 centimeters from the carotid bulb was assessed for both right and left common carotid artery (CCA). The standard parameters of blood flow were measured – including peak systolic velocity (PSV), end diastolic velocity (EDV), as well as resistive index (RI), pulsatile index (PI) and standard deviation (SD) was measured in the common carotid arteries, internal carotid arteries (ICA) as well as in the vertebral arteries (VA).

Results: The mean IMT value in CCA was approximately 0.68 mm (0.35–0.9 mm).

Conclusion: A positive correlation between the age of examined subjects and the IMT was found (p<0.002; R=0.49). Additionally, a negative correlation between the IMT and the EDV was found (p=0.058; R=0.44).

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.6296

AB0643 MALIGNANCY SCREENING IN AUTOIMMUNE MYOSITIS AMONGST AUSTRALIAN RHEUMATOLOGISTS

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Background: The association between cancer and autoimmune myositis is well established and has led to the common practice of malignancy screening in asymptomatic individuals. The international literature advocates widely for cancer screening in autoimmune myositis however no consensus or guideline has been published to set forth a process for screening standardisation.

Objectives: To explore the current trends in malignancy screening in autoimmune myositis amongst Australian Rheumatologists using an online questionnaire.

Methods: Research approval was granted by The Townsville Hospital. An invitation containing the survey link was sent twice to 386 Australian Rheumatologists between August 2015 and August 2016. Voluntary participation and anonymity were guaranteed. The questionnaire contained a fixed set of multiple choice questions that requested data on respondent demographics, practice setting and screening preference, practice and concerns. Open entry comments allowed an option to provide any other questions.

Results: 58 respondents (N=58) were in private (67%) and/or public practice (33%). The majority (72%) performed cancer screening independent of patient characteristics. Determinants that triggered screening (in descending order of popularity) were: tobacco use (N=11), history of cancer (N=10), age ≥ 40 (N=7), cancer family history (N=7), age ≥ 50 (N=3) and age ≥ 60 (N=1). The majority (N=57) indicated that cancer screening was problematic due to a lack of clinical practice consensus & guideline (77%), test selection knowledge (37%) and knowledge regarding appropriate frequency of screening (53%). The potential for harm in conducting screening was identified to be a problem by most respondents (62%).

Conclusions: The practice of malignancy screening in autoimmune myositis amongst Australian Rheumatologists is highly variable. Practice is driven by patient factors and clinician preferences. The cancer screening process is felt on several fronts to have inherent problems. Guideline, consensus and further research is needed in this area to address the challenges and evidence gap.

References:

Disclosure of Interest: None declared.


AB0644 FINGERPRINT ABNORMALITIES IN SYSTEMIC SCLEROSIS: A SINGLE CENTER SURVEY FROM INDIA

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Background: Fingerprint [FP] abnormalities are known in patients with Systemic Sclerosis [SSc]. Little has been described about their frequency, systemic associations and social impact in literature.

Objectives: To study the fingerprint abnormalities in Systemic Sclerosis patients.

Methods: Raynaud’s phenomenon [RP] was taken as the inclusion criteria. Patients with SSc [limited LcSSc and diffuse DcSSc], SSc overlap with other Connective Tissue Diseases [CTDs] and other CTDs with RP were screened for FP abnormalities using a Standardization Testing and Quality Certification (STQC) approved and certified fingerprint scanner. FP quality assessments were done by recording The National Institute of Standards and Technology [NIST] fingerprint image quality [NFIQ] scores1. NFIQ’s 5 levels of quality are intended to be predictive of fingerprint matching. NFIQ<1 indicates high quality samples and NFIQ>5 indicates poor quality samples. Other associated systemic features of
the disease were noted. Also the social difficulties due to fingerprint abnormalities were noted. Healthy controls with no RP were included for comparison.

Results: 40 consecutive patients with RP attending Rheumatology outpatient services of our institute were screened for FP abnormalities. 29 with SSc [20- DsSSc, 9-LcSSc], 8 with overlap syndromes and 1 each of SLE, Unilateral Diffuse Vasculitis and Undifferentiated Connective Tissue Disease. It was noted prior to screening that 15 patients experienced some difficulty in the past with biometric recognition of their FPs at various times. On screening with biometric scanner, 15 of 40 [37.5%] had FP abnormalities in the form of non recognition of at least one finger with a median of 2 [range 1–6 fingers]. Of these 15, seven had DsSc, six had LcSSc and two had overlap syndromes. The mean NFIQ score of these 15 patients was 4.5 [poor] and the mean NFIQ scores in SSc was 3.8. Eleven [27.5%] patients could not get government identity cards based of FP scanning, four could not avail various government benefit schemes which needed their fingerprints as identity. Sixteen [40%] had history of digital vasculopathy in the form of livedo, digital ischemia or ulcers. PAH was found in one and eight had interstitial lung disease. Among the 10 controls all FPs were recognized and the mean NFIQ score was 2.2 indicating a better quality of FPs.

Conclusions: Fingerprint abnormalities occur frequently in patients with systemic sclerosis causing social disabilities in few. The quality of FPs in SSc patients is poor. Raynaud's phenomenon and vasculopathy are frequently associated. Documentation of this abnormality should allow the use of other biometric tools for personal identification.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3860

AB0645 LYMPHOCYTE SUBSETS T, B AND NK CELLS IN SYSTEMIC SCLEROSIS
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Background: Systemic sclerosis (SSc) is a rare multisystem disease with underlying immune mechanisms, whose pathogenesis remains unclear. Few previous reports have evaluated lymphocyte subpopulations in SSc and your results are conflicting.

Objectives: The present study aimed to analyze the lymphocyte subsets in SSc patients in comparison to healthy individuals.

Methods: Peripheral blood (PB) samples to analyze lymphocyte subsets were obtained from a non-random convenience sample of 20 SSc patients. Twenty healthy individuals recruited from the blood bank were used as sex and age-matched controls. Blood samples were analyzed by flow cytometry for total T cells, CD4+ and CD8+ T cells subsets, CD19+ B cells and total NK cells. Statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS 18.0). Data are expressed as mean ± SD and median and range. Non-parametric Mann–Whitney U test was used for analyses of the flow cytometry. A probability p<0.05 was considered statistically significant.

Results: The mean (SD) age of SSc patients was 57.9 (14.2) years; 95% were female and 31.6% presented diffuse cutaneous SSc (dcSSc). Patients presented Raynaud’s phenomenon and vasculopathy are frequently associated. Documentation of this abnormality should allow the use of other biometric tools for personal identification.

Conclusions: Fingerprint abnormalities occur frequently in patients with systemic sclerosis causing social disabilities in few. The quality of FPs in SSc patients is poor. Raynaud's phenomenon and vasculopathy are frequently associated. Documentation of this abnormality should allow the use of other biometric tools for personal identification.

References:

Conclusions: Our data support previous reports indicating that depletion of lymphocyte in the PB of SSc patients. However, we found no significant difference in relation to lymphocyte subtypes, which differs from the literature data.

References:

AB0646 DETERMINANTS OF QUALITY OF LIFE IN SYSTEMIC SCLEROSIS AND PATIENT’S PERCEPTION OF THEIR ILLNESS
L. Groseanu 1, 2, A. Balanescu 1, 2, D. Predeteanu 1, 2, D. Opris-Belinski 1, 2, V. Bojinca 1, 2, I. Saulescu 1, 2, A. Borangiu 1, 2, D. Mazilu 1, 2, C. Constantinescu 1, 2, F. Berghera 1, 2, R. Ionescu 1, 2 .1, 2Internal Medicine and Rheumatology, St Maria Clinical Hospital; 2Department 5- Internal Medicine, University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

Background: Systemic sclerosis (SSc) is a chronic multi-system autoimmune disease associated with disability and reduced quality of life. Objectives: The purpose of this study was to assess health-related quality of life and disease perception in a group of SSc patients.

Methods: We performed a case-control study on 50 SSc patients from EUSTAR cohort 2016. Socio-demographic data, disease characteristics and self-assessment questionnaires: Health assessment questionnaire (HAQ), EuroQol-5D (EQ5D) and the Brief Illness Perception Questionnaire were collected.

Results: The group included 41 females, 31 limited SSc subsets. None of the mean EQ-5D value was 0.66. Baseline HAQ score was 0.02. synovitis (p<0.02), late capillaroscopic pattern (p<0.03), muscle weakness (p<0.01), gastrointestinal involvement (p<0.01) and those on immunosuppressants (p<0.02) have a poor quality life. According to EQ-5D, the quality of life was related to specific organ involvement. 48% of the patients had some mobility problems, 8% were confined to bed; mobility was influenced by lung involvement (p=0.008), digital ulcers (p<0.03) and Medsger score (p<0.01). 48% of the patients had some self-care problems and 8% were not able to wash/dry themselves; self-care was influenced by the Rodnan score (p<0.02), diffuse subset (p<0.02), muscle weakness (p<0.03) and gastrointestinal involvement (p<0.02). 64% of the patients do not feel they have a good control on their disease, 6.3 (3.3/10) and unfortunately they do not think that the treatment is very helpful 7.9 (2.7)/10. The intensity of the symptoms is quite severe 7.5 (2.7)/10, related to digital ulcers (p<0.04) and gastrointestinal involvement (p<0.02). Patients are very concerned about their disease 9.1 (2.3)/10, most of them feel emotionally affected 7.6 (2.6). Conclusions: This study confirms the presence and magnitude of impaired quality of life in patients with SSc with impact on mobility, self-care, usual activities. The major determinants were the extend of skin involvement, muscularoarticular, gas- trointestinal involvement and arthritis. Often patients are anxious/depressed, had a high pain intensity and the perception of this illness is pessimistic.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7032

AB0647 DIAGNOSIS OF SYSTEMIC SCLEROSIS – “A TANGLED STORY”
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Background: Proper diagnosis of scleroderma is often long and difficult, since it is a rare disease, and one which few doctors or patients are familiar with. Objectives: To establish the interval between the symptoms’ onset of systemic sclerosis and the final diagnosis of a rheumatologist Methods: This is a cross-sectional study that included randomly selected patients with diagnosis of SSc which were evaluated based on a questionnaire about symptoms at onset, specific consuls and investigations. Descriptive statistics were used.

Results: The study group included 47 patients, of which only 5 were males and 17 from rural areas. The medium age was 53 (14.4) years.


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4178
DISEASE-RELATED AUTOANTIBODY PROFILE IN SYSTEMIC SCLEROSIS IN GREECE

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Background: Anti-Topo I abs were strongly associated with dcSSc, interstitial lung disease (ILD) and pulmonary hypertension.

Methods: Twenty two patients with primary Raynaud phenomenon and 113 SSc patients were positive against 13 SSc-related antigens. Twenty two patients with SSc. Excluding anti-Ro52, 113 (89.3%) SSc patients were positive with ILD.

Results: Anti-Topo I abs were strongly associated with dcSSc, interstitial lung disease (ILD) and pulmonary hypertension (PH): PSAP>25 mmHg by right heart catheterization; Interstitial Lung Disease (ILD): compatible HRCT or >70% predicted FVC or 40% predicted DLCO; Heart: ventricle dysfunction without PH or anterior hypertension, pericardial effusion; Digital ulcers and pitting scars; History of scleroderma renal crisis (RSC); calcinosis. Anti-Scl-70 was determined by ELISA and anti-Centromere (ACA) by RIPA.

Conclusions: The median duration from the first symptom until the correct diagnosis was 39.2 (74) months. The first investigations recommended were blood tests in almost all of the patients (95.7%), but only a third of them included specific scleroderma autoantibodies. The first capillaroscopy was performed as an initial diagnostic test in only 6 patients (12.8%). The mean interval from disease onset until the patient was referred to the first capillaroscopy was 13.5 (28.8) months, to specific autoantibodies was 40.17 (61.3) month, to echocardiography was 36.36 (54) months, to lung function tests and lung CT – 41.76 (65.8) months.

There were no significant statistical differences between patients coming from rural environment and those coming from urban environment. The only significant statistical difference between diffuse and limited subset was the time the patient was referred to echocardiography (19.8 (47.6) months for the diffuse subset, 66.8 (94.1) months for the limited subset, p=0.04).

Conclusions: Scleroderma is a less well-known disease. This lack of awareness contributes to delayed diagnosis and delayed onset of therapy. Often such diagnostic uncertainty and frustration takes a huge toll on the psychological well-being of these patients, who describe their journey to diagnosis as being one of the most difficult part of their illness. One of our missions as rheumatologist is to increase recognition of this disorder.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3954

AB0649 SYSTEMIC SCLEROSIS IN ARGENTINA: EVALUATION OF A SINGLE CENTER COHORT AND COMPARISON WITH INTERNATIONAL SERIES

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Background: Systemic sclerosis (SS) is an autoimmune disease with generalized vascular dysfunction and a myriad of clinical and laboratory manifestations. Spreading of thickening of the skin, serological characteristics and the pattern of compromise of the internal organs help to classify them as diffuse scleroderma, localized scleroderma and systemic sinus scleroderma. Reports of Latin American cohorts published to date are scarce.

Objectives: To describe the clinical and serological data for a single center cohort and to compare those with national and international cohorts.

Methods: Descriptive, observational, cross-sectional study. We analyzed our SS database. Patients were evaluated since 01/15 to 05/2016 and fulfilled SS classification criteria (ACR 1980/ACR-EULAR 2013). Patients were classified according to Le Roy criteria in Limited Systemic Sclerosis (ISS), Diffuse Scleroderma (dSS), Systemic Sclerosis sine scleroderma (SSnS) and pre-systemic sclerosis (pSS). Organic compromise was defined as follows: Gastrointestinal (GI): esophageal dysmotility by manometry or esophagitis by endoscopy; Lungs: Pulmonary hypertension (PH): PSAP>25 mmHg by right heart catheterization; Interstitial Lung Disease (ILD): compatible HRCT or >70% predicted FVC or 40% predicted DLCO; Heart: ventricle dysfunction without PH or anterior hypertension, pericardial effusion; Digital ulcers and pitting scars; History of scleroderma renal crisis (RSC); calcinosis. Anti-Scl-70 was determined by ELISA and anti-Centromere (ACA) by RIPA.

Results: 123 patients were included: 74% with ISS, 24% dSS and 2% SSnS; age at diagnosis (years): 49.7 (18–79; DS: 12.27) and 48.7 (27–79; DS: 13.01) in ISS and dSS respectively. Raynaud’s phenomenon previous to diagnosis (years): 7.7 (0–54 DS: 12.81) in ISS and 4.03 (0–22; DS: 5.5) in dSS. 49.5% ISS were ACA positive vs 17% in dSS as well also 41.4% had Scl-70 positive (p<0.05). Lung:58.6% of dSS presented ILD and 3.4% RSC, according to published reports. No statistically significant differences were found between the presence of calcinosis, digital tip ulcers or PH between ISS and dSS. ISS: GI was studied in only 39/123 patients with 84.6% affected among those.

Table 1. Comparison of main variables among different cohorts

<table>
<thead>
<tr>
<th>Country</th>
<th>Diffuse (n=119)</th>
<th>Limited (n=238)</th>
<th>Spain (n=11)</th>
<th>Germany (n=568)</th>
<th>Argentina (n=91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
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<td>119</td>
<td>208</td>
<td>11</td>
<td>244</td>
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<tr>
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<td>128</td>
<td>293</td>
<td>12</td>
<td>448</td>
<td>484</td>
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<tr>
<td>Spain</td>
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<tr>
<td>Germany</td>
<td>2838</td>
<td>4841</td>
<td>28</td>
<td>674</td>
<td>29</td>
</tr>
<tr>
<td>Argentina</td>
<td>448</td>
<td>484</td>
<td>93</td>
<td>674</td>
<td>29</td>
</tr>
<tr>
<td>US/Argentina</td>
<td>259</td>
<td>498</td>
<td>93</td>
<td>674</td>
<td>29</td>
</tr>
<tr>
<td>(%)</td>
<td>21.5%</td>
<td>49.7%</td>
<td>6.6%</td>
<td>15.3%</td>
<td>12.9%</td>
</tr>
<tr>
<td>Osseous dysmotility (%)</td>
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<td>67</td>
<td>70</td>
<td>66</td>
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<tr>
<td>ILD (%)</td>
<td>63</td>
<td>37</td>
<td>52</td>
<td>11</td>
<td>70</td>
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<td>PH (%)</td>
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<td>31</td>
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<td>RSC (%)</td>
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<td>Digital ulcers (%)</td>
<td>ND</td>
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<td>33</td>
<td>64</td>
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<tr>
<td>Calcinosis (%)</td>
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<td>42</td>
<td>ND</td>
<td>ND</td>
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</tr>
</tbody>
</table>

Conclusions: Our data showed similar results to the local and european cohorts. We found fewer calcinosis and digital tip ulcers in both ISS and dSS than international cohorts. A lower prevalence of PH was reported in ISS respect to other series, and it might be atributed to the method wich it was measured. (right heart catheterism).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3520

AB0650 ANTI-TOPOISOMERASE POSITIVE SYSTEMIC SCLEROSIS PROGNOSIS INFIAUT?

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Background: Anti-topoisomerase antibodies (ATA) in systemic scleroderma (SSc) have been associated with poorer prognosis including diffuse skin involvement, pulmonary fibrosis, cardiac involvement and increased mortality. However, 30–60% of ATA-positive SSc patients demonstrate limited skin involvement and some have only mild disease course. In SSc, optimal risk stratification is of utmost importance for tailored clinical care management at the patient level.

Objectives: We aimed to determine the prevalence of mild disease among ATA positive patients and to investigate which readily available clinical parameters best identify patients with highest disease severity.

Methods: Clinical baseline data from SSc patients included in the Combined Care In Systemic Sclerosis (CCIS) cohort of the Leiden University Medical Center were collected. Patients fulfilling ACR 2013 criteria and ATA positive were included. Descriptive statistics were used to summarize sociodemographic, clinical and serological features. Patients with grade 3 or 4 disease on any of the Medsger severity subscales were considered to be severely diseased. We compared presence of diffuse cutaneous involvement, Raynaud’s, pitting scars, calcinosis, proximal muscle weakness, >10% weight loss, interstitial lung disease and pro-BNP between the severity groups and corrected for confounding by disease duration (time since non-Raynaud) by stratifying into quartiles.
Results: Of 422 SSc patients in the database, 344 patients had SSc meeting ACR criteria. 89 patients were exclusively ATA-positive, of which n=42 with mild disease and n=47 with severe disease. Patients with severe disease appeared to be younger (mean age 50 vs 55 yr), more often non-caucasian (51 vs 12%), with a longer time since non-Raynaud (median 4 vs 2 yr) and more often diffuse skin involvement (dSSc, 65% vs 41%), calcinosis (6 vs 0%) and weight loss (23 vs 7%). Stratification by disease duration, however revealed there are no real differences between mild and severe disease. Overall 47% of ATA+ patients in our cohort presented with mild SSc. When stratifying patients according to time of non-Raynaud, 55% of ATA+ patients presented with mild disease in the first disease duration quartile (median follow-up 12,7 years, range 8.2–44.1) the percentage with mild disease was still 27% (Figure 1).

Conclusions: In our cohort, 47% of ATA-positive patients presented with mild systemic sclerosis, which could not be explained by disease duration. This suggests that solely the presence of ATA is of limited clinical relevance. Readily available sociodemographic and clinical parameters including type of skin involvement seem to have only limited value in identifying ATA patients with more severe SSc. More complex serological findings as antibody titers and fine-specificity of ATA should be defined for optimal serological subsetting.

Disclosure of Interest: None declared


AB0651 THE EFFECT OF CYCLOPHOSPHAMIDE ON PULMONARY FUNCTION AND DEPENDENCE ON DISEASE ACTIVITY OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: The pathogenesis of interstitial lung disease associated with systemic sclerosis (SSc-ILD) is not completely elucidated, although it is believed that chronic alveolar inflammation leads to increasing fibrosis. Treatment strategies using cyclophosphamide (CYC) have been focusing on the inflammatory pathway of SSc-ILD. We hypothesized that CYC is more effective in the early phase of SSc-ILD.

Objectives: To assess the occurrence of organ involvement and death in a large, unselected cohort of Dutch SSc patients at the moment of diagnosis and during 5 years of follow-up, stratified by disease subtype and auto-antibodies.

Methods: Up to 2015, 690 SSc patients were included in the Nijmegen SSc cohort. Occurrence of interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), cardiac involvement (CI), scleroderma renal crisis (SRC) and occurrence of death were determined using survival analysis, stratified by disease subtype (limited cutaneous SSc and diffuse cutaneous SSc) and auto-antibodies (ACA, ATA, anti-RNP).

Results: Organ involvement was already present at SSc diagnosis in 32% of patients. In 25%, organ involvement developed during follow-up, mostly ILD (22%). Significant differences between lcSSc and dcSSc were found in CI at baseline and ILD, PAH and SRC during follow-up. Between the autoantibody subgroups, the occurrence of ILD, PAH and SRC at baseline and ILD during follow-up differed. There were no differences in survival between subtypes and auto-antibodies. The overall 5-year survival rate was 89%. Patients without organ involvement at SSc diagnosis had a better 5-year survival rate than patients with organ involvement at SSc diagnosis: 95% versus 73% respectively (p<0.001). (figure 1)

Conclusions: In many SSc patients, organ involvement is already present at diagnosis or develops in the first 5 years after diagnosis. Survival is significantly worse in patients who already have involvement at the moment of SSc diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3426

AB0653 EFFICACY OF AN INTENSIVE 24-WEEK PHYSIOTHERAPY PROGRAMME IN MYOSITIS PATIENTS - PRELIMINARY DATA FROM A SINGLE-CENTER CONTROLLED STUDY

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Background: Involvement of musculoskeletal system (inflammation, atrophy and permanent damage to the muscle) in idiopathic inflammatory myopathies (IIM) leads to impaired function and reduced muscle strength, endurance, aerobic capacity and decreased quality of life. Data on efficacy of non-pharmacologic care in IIM is very limited due to rarity, is not studied in sufficient detail.

Objectives: To address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24-week intervention, 24-week follow-up), intensive (1h physiotherapy twice weekly, and home-exercise for 1h 5x weekly), tailored physiotherapy program to improve muscle strength, endurance and deep stabilizer system, and quality of life/disability in cohorts with a substantial number of IIM patients.

Methods: All patients fulfilled the Bohan and Peter 1975 diagnostic criteria for dermatomyositis (DM) or polymyositis (PM), had skeletal muscle involvement, and were consecutively recruited from 2014 to 2016 at the Institute of Rheumatology in Prague. Both groups received educational materials and instructions for home exercise at baseline, however, only intervention group underwent the intensive physiotherapy programme. At months 0,3,6,12 all patients were assessed by a physician [physical examination, Myositis intention to treat index (MITAX), Myositis disease activity assay, visual analogue scale (MVACT), and Myositis damage index (MDI)], and a physiotherapist blinded to intervention [standardized tests evaluating the level of muscle strength [Manual muscle test-8 (MMT-8)], and endurance [Functional index-2 (FI-2)], patients filled out patient reported outcomes (PROM/questionnaires [HAQ, SF-36, Beck’s depression inventory-II].
AN ULTRASOUND ASSESSMENT OF THE HAND AND WRIST IN EGYPTIAN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc, scleroderma) is a systemic disease characterized by fibrosis, progressive vascular obliteration and the production of autoantibodies. Ultrasound (US) imaging has advantages of simplicity, low cost, non-invasiveness, real-time capability and portability compared with traditional EDX. US imaging also offers high temporal and spatial resolutions, and can potentially provide diagnostic, anatomical information regarding local structures and kinesiology, few studies evaluate joint and tendons involvement in SSC by US study.

Methods: Randomly selected 50 Egyptian SSC patients were enrolled in the study in outpatient clinic Rheumatology department, Assuit university hospital. Consecutive patients were assessed by US evaluation (Sonostar Scale and Power doppler PD) of the tendons and joints of hands and wrists, were performed bilaterally on both dorsal and palmar sides. Joint assessment was performed on all MCP and PIP joints as well as the wrist and tendon assessment included finger flexors and extensors, wrist extensors and flexors. The Scoring for synovitis was based on the EULAR/OMERACT scoring system.

Results: Within the cohort, 100% of the patients were female; mean age and range disease duration were 40.93±11.71 (20–61) years and 8.13±5.56 (0.5–25)years, respectively. Modified Rodnan Skin Score mean and range were 40.93±11.71 (20–61) years and 8.13±5.56 (0.5–25)years, respectively. Modified Rodnan Skin Score mean and range were 23.17±9.14 (13–43), 22 patients were diffuse type (44%) and 28 patients were limited type (56%), 67% had inflammatory arthritis as reported by patients. US examination revealed abnormalities in 76% of all cases. Synovitis was present in 74% of patients (22% wrist; 15% MCP/PIP, 63% both); with a grade 2 and 3 synovitis in 29% of cases. The grade 2 or 3 synovitis was associated with a higher age (p<0.05) and disease duration (p<0.03) but not with inflammatory markers (CRP, ESR) and C3 nor with anti-CCP antibodies.

Furthermore, patients with US proven grade 2 or 3 synovitis had interstitial lung disease involvement (ILD) (74%) and elevated systolic pulmonary artery pressure (>35 mmHg in 46%). Grade 1 synovitis did not correlate with tenderness or joint swelling. Synovitis using PD abnormalities were present in 20% patients, but only a 25% had concomitant clinical synovitis. Bone erosions (≥1mm) were observed in 15%, which located at the second and third MC heads and at the styloid processes of the ulna. The presence of bone erosions was associated with the presence of grade 2 or 3 synovitis. US identified tenosynovitis in 40% of patients, involving the wrist extensors in the vast majority of cases (70%), especially of the 2nd extensor compartment.

Conclusions: US examination detects significant synovitis of the hand and wrist in the absence of clinical findings, and reveals structural damage in a number of patients. The grade 2 or 3 synovitis was associated with a higher age, and ILD involvement. Tendon involvement is frequent with specific pattern of wrist extensors. Thus, US seems to be a valuable tool to identify subclinical joint manifestations in Egyptian SSC patients.

Disclosure of Interest: None declared

NAILFOLD VIDEOCAPILLAROSCOPY FEATURES OF PATIENTS WITH ANTISYNTHETASE SYNDROME

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Background: Antisynthetase syndrome (ASSD) is an autoimmune disease characterized by the clinical triad arthritis, myositis, and interstitial lung disease (ILD). As in inflammatory myopathies, nailfold videocapillaroscopy (NVC) alterations have been sporadically described also in ASSD patients, but no elucidating data are available.

Methods: Within the framework of a multicenter study, we retrospectively analyzed NVC images of ASSD patients, after excluding patients with overlap syndrome with systemic sclerosis. Two operators in a blind manner re-evaluated all the cut-off points with the greatest positive likelihood ratio (12.52) for the presence of SSC-ILD.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6828
patients with at least one image per finger. For each patient, we examined number of capillaries (mean number of capillaries per mm in the distal row), enlarged and giant capillaries, micro-hemorrhages, avascular areas, ramified capillaries, and the presence of a scleroderma (SSc)-like pattern. In particular, eight patients were observed in 53.6% of ASSD patients. Nineteen patients (35.2%) showed a SSc-like pattern; the main features were disarrangement of hairpin and angiogenetic aspects (42.6%), avascular areas (39.8%), giant capillaries (27.6%), and microhemorrhages (20.4%). Finally, the mean number of capillaries was reduced (7.8±2/mm). No significant association was recorded between SSc-like pattern and the presence of arthritis, myositis, and ILD, nor with RP. Among other NVC features, angiogenetic was significantly associated to female gender (p=0.031), while microhemorrhages were inversely associated to the presence of arthritis (0.033). No association was observed between NVC features and autoantibodies profile. Of interest, in 56% of patients with IJD we observed at least a NVC alteration vs no patients without IJD (p=0.04). Finally, in patients with RP NVC alterations were recorded in 15/28 patients (53.6%) and a SSc-like pattern in 11/28 (39.3%), while only 57.9% of patients with SSc-like pattern had clinically manifest Raynaud’s phenomenon.

**Conclusions:** Despite the brevity, the present is the first study concerning NVC in ASSD patients. Regardless of the presence of Raynaud’s phenomenon, NVC alterations are frequently observed; in particular, a SSc-like pattern is recorded in more than 1/3 of patients. NVC should be performed in all ASSD patients at diagnosis regardless of the presence of RP in the patient history and duration of ASSD syndrome. ASSD should be always considered in the screening of RP. A prospective multicenter study has been planned to identify specific patterns and possible associations between NVC findings and clinical and serological features of ASSD.

**References:**

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5376

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### AB0657 SMALL INTESTINAL BACTERIAL OVERGROWTH IN RELATION TO GASTROINTESTINAL SYMPTOMS IN SYSTEMIC SCLEROSIS

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**Background:** Autonomic dysfunction, smooth muscle fibrosis and vascular damage lead to small intestinal bacterial overgrowth (SIBO) in Systemic Sclerosis (SSc). SIBO is characterized by diarrhea, abdominal pain, bloating, malabsorption and malnutrition.

**Objectives:** To evaluate NIH PROMIS® gastrointestinal symptoms scales and SIBO by hydrogen breath test (HBT) in patients with SSc.

**Methods:** We include 68 patients with SSc (ACR-EULAR 2015) who signed informed consent. NIH PROMIS® questionnaires was applied to evaluate gastrointestinal symptoms and classified in not symptomatic, light, moderate and most symptomatic. Glucose HBT was applied after 14 hours fast, oral hygiene and 24 hours free of antibiotics. Patients who have a negative HBT with symptoms associated to glucose ingestion we repeat test with lactulose.

**Results:** We applied questionnaire to 58 SSc patients, age 52 (±75) years, 65 (98%) female and 3 (4%) males, disease duration 13 (1–40) years, limited SSC 41 (59%) and diffuse SSC 24 (38%). They are using prednisone (28%), micofenolate (14%), methotrexate (19%), azathioprin (5%), amldopine or nifedipine (33%). Patients had continuous and very high increase of parts per million (ppm) of exhaled Hydrogen: min0: 13 ppm (5–21), min15: 17 ppm (5–43), min30:17 (3–49), min45:18ppm (7–103), min 60:22ppm (5–145), min90:19ppm (2–250), min120:25ppm (3–212), males/females (ppm (3–253). Normal values: <10 ppm during total test (Figure1). Frequency of gastrointestinal symptoms were flatulence (7.5±9±12%), nausea/vomiting (72.7±37.6%), constipation (65.6±40%), diarrhea (45.2±33.4%), abdominal pain (%) and constipation (39.4±3.1%) respectively between SCB (+) positive and negative. Hyperproduction of hydrogen in breath had a direct correlation to severity of their symptoms (p<0.05). The severity of diarrhea was in close relation to the severity of its rectal incontinence (r=0.73,p<0.001), and greater abdominal pain with flatulence (r=0.72,p<0.001).

**Conclusions:** Gastrointestinal symptoms are common in SSc regardless of whether they have SIBO. However, a higher Row Score SGI or moderate severe status (NIH PROMIS) correlates with high H scores from the 30th minute, therefore, the questionnaire is useful within the SSC assessment.
**Conclusions:** Time to diagnosis from onset of RF is significantly shorter in diffuse SSc. Although mRSS is typically higher in diffuse SSc, no correlation has been found between mRSS and time to diagnosis. Therefore, duration of diagnosis may be affected by other organ involvement and other complications rather than skin changes due to lack of awareness of physicians about SSc related early skin changes. Referral to a proper physician by a familiar healthcare practitioner decreased the number of physicians attending till the diagnosis, although it did not affect the time to diagnosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6465

### AB0659

**ASSOCIATION BETWEEN -12518A/G GENE POLYMORPHISM ENCODING MONOCYTE CHEMOTACTANT PROTEIN 1 (MCP-1) AND SERUM LEVEL OF C-REACTIVE PROTEIN IN DIFFERENT CLINICAL AND SEROLOGICAL PHENOTYPES OF SYSTEMIC SCLEROSIS IN THE RUSSIAN COHORT OF PATIENTS**


**Research Institute of Rheumatology, Moscow, Russian Federation**

**Background:** Immune system activation with associated up-regulation in the production of extra-cellular matrix proteins by fibroblasts are known specific features in the pathogenesis of systemic scleroderma (SSc). Most recent data indicate that MCP-1 and MCP-3 chemokines from the family of monocyte chemotactic proteins are also involved into SSc pathogenetic process. C-reactive protein (CRP) is known as the marker of acute-phase inflammation. The association between increased CRP levels and SSc clinical and serological parameters has been reported recently.

**Objectives:** To study the association between -2518 A/G gene polymorphism encoding MCP-1, and CRP levels in different clinical SSc phenotypes in the Russian cohort of pts.

**Methods:** PCR-RFLP method was used to identify MCP-1 genotype in 81 SSc pts aged 49±12.6 years, with mean SSc duration 11±5.0 years. CRP concentrations were measured with highly sensitive immunoturbidimetry method.

**Results:** CRP levels were correlated with MCP-1 genotypes in pts with limited (cSSc) and diffuse (dSSc) phenotypes, with interstitial lung disease (ILD+), with SSc duration >3 years, with increased CRP level (>5 mg/L), with positive antibody titers to DNA topoisomerase I (ATA+) and antibody to centromeres (ACA+). A total cohort analysis showed that carriers of -2518AA genotype had higher mean CRP level versus G allele carriers (12.6±7.5 mg/L vs 5.5±4.4 mg/L, respectively, p=0.040). In pts with -2518AA genotype and SSc duration >3 years mean CRP level was significantly higher than in G allele carriers (11±1.67 mg/L vs 4.5±4.4 mg/L, respectively, p=0.025). In (ILD+) and (ATA+) subgroup pts with -2518AAAA genotype demonstrated higher mean CRP levels as compared to G allele carriers (12.4±15.6 mg/L vs 5.5±4.1 mg/L, respectively, p=0.018; and 17.6±20.9 mg/L vs 5.5±5.5 mg/L, respectively, p=0.010). CRP levels (>5 mg/L) were found in 31 (38%) pts and were significantly different between AA genotype carriers and G allele carriers (27.4±19.2 mg/L vs 10.4±3.8 mg/L, respectively, p=0.003). No associations between genetic variations in the MCP-1 gene and CRP levels in lcSSc phenotype, SSc duration <3 years, CRP levels ≤5mg/L and (ACA+) pts were established.

**Conclusions:** Our data demonstrate that -2518A/G MCP-1 gene polymorphism is closely associated with CRP levels, thus, it can be considered as a new marker, reflecting the severity of the disease and unfavorable SSc prognosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3130

### AB0660

**CHARACTERISTICS OF AL-I LIGHT-CHAIN AND AMYLOID A DEPOSITION IN PROGRESSIVE SYSTEMIC SCLEROSIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 12 PATIENTS**

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**Background:** Different types of amyloid deposits may be present in systemic sclerosis (SSc), as consequences (complications) of basic or associated diseases.

**Objectives:** The aim of this study was to determine the type, prevalence and extent of amyloid deposits on different tissue structures in various organs in SSc.

**Methods:** We studied histopathologically 12 SSc patients (females 11, average age: 54.82 years, range 66–32, onset of SSc: 48.86, average disease duration: 6.43 year, one male, age 65.0 years at death, onset of SSc and average disease duration not known, who died at the National Institute of Rheumatology. SSc was diagnosed clinically according to the criteria of the ACR [1]. In 1 (8.0% of 12) 67 year old female patient (onset of SSc: 66 years, disease duration: 1 year) SSc was accompanied by B-cell lymphoma and complicated by systemic AL-I light-chain amyloidosis. In 1 (8.0% of 12) 53 year old female patient (onset of SSc: 41 years, disease duration: 12 years) SSc was complicated by systemic amyloid A (AA) deposition.

**Amyloid deposits on different tissue structures [arteriole, small artery, medium size artery, venule, small vein, medium size vein, interstitial collagen fiber, reticulin fiber (collagen IV), and nerve] of 6 organs [heart, lungs, kidney, gastrointestinal tract, skin and brain] were determined histologically. The extent of amyloid deposition was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [2].

The prevalence and extent of amyloid-I light-chain and amyloid A deposits on different tissue structures were compared by Student (Welch) t-probe.

**Results:** The involvement of different tissue structures (prevalence in %) and the average extent of AL-I light-chain and amyloid A deposits (absolute value) are summarized in Table 1.

**Table 1.**

<table>
<thead>
<tr>
<th>Tissue structures</th>
<th>SSc-I Prevalence in %</th>
<th>SSc-aaA Prevalence in %</th>
<th>p&lt;</th>
<th>SSc-I Average extent</th>
<th>SSc-aaA Average extent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arteriole</td>
<td>83.33</td>
<td>66.67</td>
<td>0.2749</td>
<td>0.0000</td>
<td>0.2749</td>
</tr>
<tr>
<td>Small artery</td>
<td>83.33</td>
<td>66.67</td>
<td>0.2749</td>
<td>0.0000</td>
<td>0.2749</td>
</tr>
<tr>
<td>Medium size artery</td>
<td>83.33</td>
<td>66.67</td>
<td>0.5000</td>
<td>0.0000</td>
<td>0.5000</td>
</tr>
<tr>
<td>Medium size vein</td>
<td>50.00</td>
<td>50.00</td>
<td>0.2749</td>
<td>0.0000</td>
<td>0.2749</td>
</tr>
<tr>
<td>Small vein</td>
<td>50.00</td>
<td>50.00</td>
<td>0.5000</td>
<td>0.0000</td>
<td>0.5000</td>
</tr>
<tr>
<td>Vein</td>
<td>33.33</td>
<td>33.33</td>
<td>0.5000</td>
<td>0.0000</td>
<td>0.5000</td>
</tr>
<tr>
<td>Collagen IV</td>
<td>33.33</td>
<td>16.67</td>
<td>0.7479</td>
<td>0.33</td>
<td>33.33</td>
</tr>
<tr>
<td>Average/Structure</td>
<td>53.70</td>
<td>44.44</td>
<td>0.2322</td>
<td>1.00</td>
<td>0.61</td>
</tr>
</tbody>
</table>

**Conclusions:** In SSc patients the prevalence and extent of I light-chain and amyloid A deposits on different tissue structures changed parallel.

The higher prevalence and extent of I light-chain deposits in contrast to amyloid A may be explained with qualitative differences of I light-chain and amyloid A; I light-chain seems to have greater affinity for tissues than amyloid A protein. Infiltration of the vessel walls – regarding the amount of I light-chain and amyloid A deposits in arterioles and arteries in contrast to the veins – showed a converse tendency in SSc patients with AL-I or AAa. This may be related to sluggish blood flow or stasis (backward congestion and accumulation of circulating precursors) in both diseases.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1222

### AB0661

**ORAL HEALTH-RELATED QUALITY OF LIFE MEASURED WITH OHIP 49 HIGHLY CORRELATES WITH DISEASE ACTIVITY AND SEVERITY IN SYSTEMIC SCLEROSIS PATIENTS**

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**Background:** Systemic sclerosis (SSc) is associated with decreased salivary production and interincisal distance, more missing teeth, and periodontal disease. Orofacial manifestations of SSc contribute greatly to overall disease burden and still are regularly overlooked and under-treated. Previous studies did not confirm correlation between disease severity and oral health-related quality of life in SSc patients.
**Objectives:** The aim of this study was to determine possible correlation of the SSC clinical parameters with oral health-related quality of life measured with the Oral Health Impact Profile 49 (OHIP 49).

**Methods:** Subjects were recruited from the Center of excellence for systemic sclerosis in Croatia cohort. Detailed dental by the same dentist and clinical examination was performed according to ACR EULAR criteria. The results between oral health-related quality of life and disease characteristics were examined. We evaluated the disease severity using clinical and laboratory parameters according to the Mediger Severity Scale. The level of SSC activity was evaluated according to the Vdiff activity score. Oral quality of life was measured using OHIP-49 and the relationship was evaluated by Spearman's rank coefficient. (p=0.016, r=0.4303, Spearman's rank coefficient).

**Results:** Forty-seven SSC patients (Male to female ratio 12 (25.5%) to 35 (74.5%) (Duration 47 SSc patients (Male to female ratio 12 (25.5%) to 35 (74.5%) (Duration 4 years) were consecutively enrolled for this study between January 2014 and December 2015. All patients fulfilled the ACR criteria for the diagnosis of SSC. The distinction between limited cutaneous SSC (lcSSC) and diffuse cutaneous SSC (dcSSC) was made according to the Leroy et al. (28 dcSSC, 3 lcSSC). OHIP 49 scores highly positively correlated with disease activity (p=0.005, r=0.4872, Spearman's rank coefficient) and severity (p=0.016, r=0.4303, Spearman's rank coefficient). Furthermore, oral health-related quality of life positively correlated with disease severity and activity (p=0.02, r=0.391 for skin, gastrointestinal and joint/tendon involvement, p=0.003, r=0.506 for general involvement, p=0.003, r=0.511, p=0.001, r=0.5207, Spearman's rank coefficient). Impaired quality of oral health positively correlated with the severity of general involvement, skin, gastrointestinal and joint/tendon involvement in SSC patients. Disease subset and autoantibodies profile could play a role in the oral manifestation of SSC. Better collaboration between rheumatologists and the dental team is required to improve access to dental care and oral health outcomes for SSC patients.

**Conclusion:** Contrary to previous studies to MRSS study disease severity and activity were related to OHIP 49 scores. Our data suggest that OHIP scores correlate with severity of general involvement, skin, gastrointestinal, and joint/tendon involvement in SSC patients. Disease subset and autoantibodies profile could play a role in the oral manifestation of SSC. Better collaboration between rheumatologists and the dental team is required to improve access to dental care and oral health outcomes for SSC patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6267

**AB0663**

**SYSTEMIC SCLEROSIS (SSC) COHORT IN ABU DHABI: FOCUS ON DIGITAL ULCERS (DU)**

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**Background:** DU are a significant burden for SSC patients affecting approximately 40–50% of patients (1). No data are available on the frequency of DU on SSC patients living in the United Arab Emirates.

**Objectives:** To identify the frequency of DU in a cohort of SSC in Abu Dhabi which is the capital city of the United Arab Emirates (UAE).

**Methods:** SSC patients identified according to ACR EULAR criteria through the hospital electronic medical records system, which was implemented from January 2011 for medical documentation in all public hospitals in Abu-Dhabi and districts. Using the International statistical classification of diseases and related health problems, usually called by the short form name international classification of Diseases (ICD), version 9 (710.1) from 1st of January 2011 to 31st of December 2016. Retrospective review of electronic medical records and paper case notes was performed on patients who presented during this period. The frequency of DU was searched. DU were defined (1) and categorised (2) (no digital ulcers, early (rarely recurrent), frequent (rarely recurrent) and chronic (>1 DU every follow up). Results and the incidence of gangrene were compared to data from DUO registry (3).

**Results:** 47 SSC patients (Male to female ratio 12 (25.5%) to 35 (74.5%) (Duration of disease from 2 to 24 years with peak age for ulcers between 40–50 years) were identified. No ulcers were detected in 34 patients (72.3%) while DU were found in 13 patients (27.7%): they were episodic in 9 patients (19%) and chronic in 4 patients (8.5%) of the total patients. No recurrent ulcers were found. Only one patient (2%) evolved to gangrene (she was a smoker). The other 12 patients were evaluated at the end of the follow up and the third of them were under 16 years of age.

**Conclusions:** In Abu Dhabi SSC population, the incidence of DU is 27.7%. This differs from the incidence in the western literature where it peaks from 40 to 50% (3). Our patients had episodic (19%) and chronic (8.5%) of the total patients. The incidence of gangrene in our cohort was lower when compared to the data reported in the DUO registry (20%) (2). Although patients live in a very warm climate, DU are still experienced in SSC in Abu Dhabi. Likely, the chronic exposure to air conditioning may explain this paradox.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4828

**AB0664**

**THE RELATIONSHIP OF SERUM LEVEL OF ANTICCP ANTIBODY WITH SEVERITY OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS PATIENTS REFERRED TO TOHID HOSPITAL**

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**Background:** Systemic sclerosis is a chronic systemic disease of unknown etiology. There are a number of autoantibodies that correlated with disease severity and severity of skin involvement (1). Various studies have shown that AntiCCP Ab can also be seen in other autoimmune diseases such as systemic sclerosis (2–4). Results Polimeni et al (4) and Morita et al (3) showed that AntiCCP Ab may be result from overlapping with RA.

**Objectives:** This study aimed to determine the relationship between serum levels of AntiCCP Ab with severity of skin involvement in systemic sclerosis patients referred to Tohid Hospital.

**Methods:** This study is a cross-sectional study, in the study population included all patients diagnosed with systemic sclerosis according to ACR 1980 criteria and subtypes according to Le Roy, that between 2013 and 2014 referred to Tohid hospital. We used from MRSS index to determine the extent of skin involvement. Sampling was available and we used to determine this association from chi-square statistics and to determine the amount of the connection from Phi statistics. Serum antibodies directed against CCP were assessed by ELISA.

**Results:** The results showed that the patients who were evaluated at the end of study were 50 patients, of whom 48 were women (96%) and 2% were male. The mean age of subjects is 38±10 years. The subtype of systemic sclerosis in 15 (%30 percent) of the patients were diffuse systemic sclerosis and 35 patients (%70 percent) have limited systemic sclerosis. Serum Anti CCP Abtivity was positive in 10% (5 patients). Also, there is no statistically significant relationship between the severity of skin involvement with AntiCCp Ab (p=0.164).Severity of skin involvement in both groups was more severe form, and there is no statistically significant relationship between the severity of skin involvement and subtypes of systemic sclerosis (p=0.233). Also we didn’t find no association between levels AntiCCP and joint symptoms and other symptoms.

**Conclusions:** In this study wasn’t observed a significant correlation between serum levels of Anti CCP Antibody with severity of skin involvement in patients with systemic sclerosis (p=0.164), also serum level of AntiCCP Antibody couldn’t be a predict factor to determine the severity of the disease. It seems that the relationship between other symptoms of systemic sclerosis and serum level of AntiCCP Antibody may be result from overlapping with RA.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1159

**AB0665**

**LEVEL OF SATISFACTION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES**

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**Background:** Idiopathic Inflammatory Myopathies (IIM) are the group of rare diseases that carry a significant impact on patient’s quality of life, influenced by the level of patient's satisfaction regarding medical services.

**Objectives:** To assess the patient's satisfaction and quality of life.

**Methods:** A cross-sectional study was performed from December 2015 to December 2016. There were included consecutive patients who fulfilled the Bohan and Peter1 criteria for IIM. The collected information was about demographic data, clinical and laboratory findings. The patient's satisfaction was assessed by self-administered Patient Satisfaction Questionnaire (PSQ III)2, which is a 50-item tool, covering 7 domains: general satisfaction, technical quality,
interpersonal aspects, communication, financial aspects, time spent with doctor, access/availability/convenience. To estimate the quality of life we applied Short Form-8 questionnaire with 8 items for 8 domains and two components: mental and physical.

**Results:** There were 32 patients enrolled in the study, including 23 females and 9 males, mean age 52.6±14.26 (range 25–78), the disease duration was 8.3±5.3 (range 0.5–12) years. The physical component was lower 37.49±8.49, than the mental component 44.96±6.24 points, we determined that the quality of patient’s life was reduced. The PSQ III results were: general satisfaction 12.9±2.72 (range 7–21), technical satisfaction 20±2.93, and high indirect costs.

**Conclusions:** Patients with idiopathic inflammatory myopathies have reduced quality of life; however they are satisfied of the medical attendance. The dissatisfaction was with the financial aspect, due to the long-term disease course and high indirect costs.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4844

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**AB0665 ASSOCIATION BETWEEN MICROVASCULATURE CHANGES AND PULMONARY INVOLVEMENT IN SYSTEMIC SCLEROSIS: A FOLLOW-UP STUDY**

**N. Novakova 1, 2, M. Cichova 3, H. Vastova 4, 5, 6, 7, 8, L. Kusnirova 1, 7, 8, M. Nosikova 1, 7, 8, A. Trouillet 1**, 9 **Department of Rheumatology; 2Institute of Rheumatology; 3Department of Dermatovenerology; 4Department of Pneumology, General Teaching Hospital, Praha 2, Czech Republic

**Background:** Lung involvement is the major cause of mortality in patients with systemic sclerosis (SSc). Gas transfer (DLCO) and FVC levels have traditionally been used as measures of disease severity and reductions of both parameters have been associated with increased mortality. In SSc repeated attacks of Raynaud’s phenomenon lead to the reduced capillary density leads with reduced blood flow and tissue ischemia. Raynaud’s phenomenon can occur also in the lungs. Tissue hypoxia usually initiates the formation of new blood vessels from the pre-existing microvasculature. Nailfold capillaroscopy is a safe, noninvasive routine way for the microvascular investigation.

**Objectives:** The aim of this study was to assess the correlation between capillaroscopic abnormalities and parameters of interstitial lung involvement at baseline and after one year follow-up in patients with SSc.

**Methods:** All patients underwent routine clinical examination (dyspnea, cough, crepitus), pulmonary function tests, DLCO (alveolar grade and fibrosis), blood gases and HRCT scan of chest (1). Microvascular changes were assessed using nailfold videocapillaroscopy (NVC) which was performed by two independent examiners. The obtained images were analysed anonymously by two investigators using nailfold videocapillaroscopy (NVC) which was performed by two independent examiners. The obtained images were analysed anonymously by two investigators using two independent examiners using Poisson’s correlation coefficient and T-test were used. All examinations were performed at baseline and after 12 months.

**Results:** Total 42 patients (38 females) were investigated: 30 individuals with limited form, 7 with diffuse form, 3 patients with scleroderma sine scleroderma, 1 with overlap syndrome and 1 with undifferentiated connective tissue disease. The mean age ± standard deviation (SD) of the whole cohort was 51±22 years and the mean disease duration ± SD was 10±7 years. In SSc patients with diffuse (>5% of the skin involved) involvement was quite low than reported in other cohort series, the results are similar to the more recent publications [3]. We showed that myopathy occurred more often in anti-Scl70 positive patients and that anti-centromere wasn’t present at all. All patients should be carefully assessed for muscle involvement in the first years of SSc diagnosis and screened for lung fibrosis, regardless of cutaneous subtype of the disease.

**Conclusions:** This study emphasizes the fact that male SSc patients are at increased risk of developing myopathy. Although the prevalence of muscle involvement was quite low than reported in other cohort series, the results are similar to the more recent publications [3]. We showed that myopathy occurred more often in anti-Scl70 positive patients and that anti-centromere wasn’t present at all. All patients should be carefully assessed for muscle involvement in the first years of SSc diagnosis and screened for lung fibrosis, regardless of cutaneous subtype of the disease.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1579
Objectives: To characterize the disease in a Colombian cohort with idiopathic inflammatory myopathy, assessing differences in its classification, cutaneous and systemic manifestations, laboratory results, and therapeutic approach, according to the type of myopathy.

Methods: A cross-sectional study was conducted in 112 patients, in whom sociodemographic, clinical and therapeutic characteristics were analyzed based on the type of myopathy. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses.

Results: From the 112 patients recruited, 59 had polymyositis (PM) and 53 had dermatomyositis (DM). The patients were classified with Peter & Bohan criteria as: “definite” diagnosis 67 (60%), “probable” 35 (31%) and “possible” 9 (10%). A high proportion of males were found in this cohort. Our most notable findings included in Table 1, reporting for this population a high rate of polyautoimmunity and seropositivity to PM (OR 3.85 95%IC 2.1-7.3) and DM (OR 7.03 95%IC 1.8-28.3), and an association between ANA antibodies positivity and PMso (OR 7.03 95%IC 1.8-28.3). Patients with PM presented higher values of CK, LD and transaminases. Also, according to the therapeutic approach, PM was positively associated with the use of azathioprine and immunoglobulins (OR 2.59 95%IC 1.18-5.69 and OR 3.21 95%IC 1.19-8.19, respectively), while chloroquine and hydroxychloroquine were mainly used in DM patients.

Table 1. Sociodemographic and clinical characteristics of Colombian patients with idiopathic inflammatory myopathy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Polymyositis N=59</th>
<th>Dermatomyositis N=53</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>41 (69.5%)</td>
<td>35 (66%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.3 (49.4)</td>
<td>49.4 (49.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symmetrical muscle weakness</td>
<td>59 (100)</td>
<td>50 (100)</td>
<td>0.13</td>
</tr>
<tr>
<td>Gottron’s papules</td>
<td>0 (0)</td>
<td>49 (92.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heliotrope rash</td>
<td>0</td>
<td>35 (66)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Shawl/ V sign</td>
<td>0</td>
<td>29 (54.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Polysymmetry</td>
<td>11 (18.6)</td>
<td>3 (5.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Muscle enzymes in serum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CK (median)</td>
<td>3825 (1012)</td>
<td>51 (60)</td>
<td>0.006</td>
</tr>
<tr>
<td>LD (median)</td>
<td>554 (433)</td>
<td>33 (33)</td>
<td>0.003</td>
</tr>
<tr>
<td>ALT (median)</td>
<td>87</td>
<td>46.3</td>
<td>0.01</td>
</tr>
<tr>
<td>AST (median)</td>
<td>72</td>
<td>38</td>
<td>0.005</td>
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<tr>
<td>Aldolase</td>
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<td>Autoantibodies</td>
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<tr>
<td>ANA (+)</td>
<td>27</td>
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<td>Anti-Jo1 (+)</td>
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<tr>
<td>Myopathic changes</td>
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<tr>
<td>Biopsy-proven myopathy</td>
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</tbody>
</table>

Conclusions: In this Colombian sample, a high proportion of patients were classified as definite diagnosis, high frequency of male-gender compromise, low autoantibodies frequency and low serum creatinine levels. The idiopathic inflammatory myopathies (IIM) are a group of immune-mediated systemic conditions characterized by chronic muscle inflammation, resulting in muscle weakness [1].

References:

Disclosure of Interest: None declared
ized in SSC. Patients fulfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in the ongoing observational cohort study. Patients filled in the ScleroID questionnaire (Figure 1), as well as selected comparators SHAQ, EC52, SF36. Additionally, they weighted the 10 dimensions of the ScleroID by dividing among 100 points according to the perceived impact on their health. The final score calculation will be based on the ranking of the weights. The study includes a reliability arm (follow-up questionnaire 7–10 days from baseline), as well as a longitudinal arm, looking at sensitivity to change at follow-up visits after 6 and 12 months from baseline.

Results: As of 01/2017 the study cohort included 224 patients with valid baseline data, 44 also had a reliability visit and 6 a 6-months follow-up visit. 84.4% of patients were female, 54.4% had limited SSC, median age 58, and median disease duration 8 years. The highest preliminary median weights for ScleroID domains were for Raynaud, impaired hand function, fatigue and pain (Table 1).

Except for pain, these dimensions were also scored most highly in the ScleroID questionnaire at baseline.

Conclusions: The EULAR ScleroID score is a novel tool designed for use in clinical practice and clinical trials to display the disease impact of SSC. In this preliminary analysis, Raynaud syndrome, impaired hand function, and fatigue were the main patient reported drivers of disease impact, however, further recruitment and validation of this new instrument is ongoing.


Background: Among patients, who meet the classification criteria for systemic sclerosis (SSc), there are the patients without specific SSc anti-nuclear antibodies and who are positive for antibodies to ribonucleoprotein (RNP). The clinical significance of the RNP antibodies in SSc is not clear.

Objectives: To investigate clinical and laboratory characteristics of SSc patients positive for antibodies to RNP.

Methods: The study included 52 patients (49 women and 3 men, mean age 44±15 years, median disease duration from the beginning of Raynaud’s phenomenon 11.2±7years) who met the criteria for mixed connective tissue disease (MCTD) proposed by Kasukawa et al. (1987).

Results: All the patients met the criteria for classification of SSc ACR/EULAR 2013 (table 1). Other prevalent clinical manifestations were gastroesophageal reflux in 63, 5% of patients, joints involvement in 58%, myositis in 30, 7%, serositis in 27.5% (including 23% of pericarditis). All patients were positive for antinuclear factor (Hep-2) and in some cases RF, anti-SS-A, anti-SS-B, anti-Sm and anti-dsDNA antibodies were identified. The increased levels of GRP and/or ESR were found in 56% of cases. Among the SSc patients, there were 38 (73%) who satisfied for the classification criteria for mixed connective tissue disease (MCTD) proposed by Kasukawa et al. (1987).

Table 1. Frequency of items of SSc classification criteria (ACR/EULAR 2013) in the group under study

<table>
<thead>
<tr>
<th>Items</th>
<th>52 patients</th>
</tr>
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<tbody>
<tr>
<td>Skin thickening of the fingers extending proximal to the metacarpophalangeal joints</td>
<td>9 (17,3%)</td>
</tr>
<tr>
<td>Skin thickening of the fingers</td>
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<tr>
<td>Puffy fingers</td>
<td>29 (55,7%)</td>
</tr>
<tr>
<td>Sclerodactyly</td>
<td>14 (27%)</td>
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<tr>
<td>Fingertip lesions</td>
<td>22 (42,3%)</td>
</tr>
<tr>
<td>Telangectasia</td>
<td>25 (48%)</td>
</tr>
<tr>
<td>Abnormal nailfold capillaries</td>
<td>45 (85,6%)</td>
</tr>
<tr>
<td>Lung involvement</td>
<td>37 (72%)</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension</td>
<td>2 (4%)</td>
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<tr>
<td>Interstitial lung disease</td>
<td>35 (68%)</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>52 (100%)</td>
</tr>
<tr>
<td>SSc related autoantibodies:</td>
<td></td>
</tr>
<tr>
<td>ACA</td>
<td>12 (23%)</td>
</tr>
<tr>
<td>Anti-Scl-70</td>
<td>4 (7,7%)</td>
</tr>
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Conclusions: In the group under study the limited form of SSc dominated, with high frequency of the different manifestations of vasculopathy, esophagus, joint and muscle disorders symptoms. A subtype of RNP-positive SSC patients often met the criteria for MCTD. This fact makes it reasonable to discuss the possibility of overlap-syndrome between these two diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4975

AB0671 INCREASED BODY FAT BUT DECREASED LEAN BODY MASS AND BONE MINERAL DENSITY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES ARE ASSOCIATED WITH DISEASE DURATION, INFLAMMATORY STATUS, STELLATE MUSCLE INVOLVEMENT AND PHYSICAL ACTIVITY

S. Orssea,1 M. Spirito1,2, P. Cesak2, O. Marecek2, H. Storkanov2, K. Kubinova1, M. Klein1, L. Vernoiva1, O. Ruzickova1, R. Becvar1, K. Pavlev1, L. Senoil1, H. Mann1, J. Vencovsky1, M. Tomick1.1Department of Rheumatology, 1Medical Faculty, Charles University, Institute of Rheumatology, 2Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic

Background: Idiopathic inflammatory myopathies (IM) are characterized by inflammation and atrophy of skeletal muscles, pulmonary and articular involvement, which limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.

Objectives: To assess body composition and physical activity of IM patients and healthy controls (HC).

Methods: 54 patients with IM (45 females/9 males; mean age 57.3; disease duration 5.8 years; polymyositis (PM,22)/dermatomyositis (DM,25)/necrotizing

Conclusions: The EULAR ScleroID score is a novel tool designed for use in clinical practice and clinical trials to display the disease impact of SSc. In this preliminary analysis, Raynaud syndrome, impaired hand function, and fatigue were the main patient reported drivers of disease impact, however, further recruitment and validation of this new instrument is ongoing.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5297

AB0670 CLINICAL AND LABORATORY MANIFESTATIONS OF RNP-POSITIVE PATIENTS WITH SYSTEMIC SCLEROSIS


Background: Among patients, who meet the classification criteria for systemic sclerosis (SSc), there are the patients without specific SSc anti-nuclear antibodies and who are positive for antibodies to ribonucleoprotein (RNP). The clinical significance of the RNP antibodies in SSc is not clear.

Objectives: To investigate clinical and laboratory characteristics of SSc patients positive for antibodies to RNP.

Methods: The study included 52 patients (49 women and 3 men, mean age 44±15 years, median disease duration from the beginning of Raynaud’s phenomenon 11.2±7years) who met the criteria for mixed connective tissue disease (MCTD) proposed by Kasukawa et al. (1987).

Results: All the patients met the criteria for classification of SSc ACR/EULAR 2013 (table 1). Other prevalent clinical manifestations were gastroesophageal reflux in 63, 5% of patients, joints involvement in 58%, myositis in 30, 7%, serositis in 27.5% (including 23% of pericarditis). All patients were positive for antinuclear factor (Hep-2) and in some cases RF, anti-SS-A, anti-SS-B, anti-Sm and anti-dsDNA antibodies were identified. The increased levels of GRP and/or ESR were found in 56% of cases. Among the SSc patients, there were 38 (73%) who satisfied for the classification criteria for mixed connective tissue disease (MCTD) proposed by Kasukawa et al. (1987).

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Conclusions: In the group under study the limited form of SSc dominated, with high frequency of the different manifestations of vasculopathy, esophagus, joint and muscle disorders symptoms. A subtype of RNP-positive SSC patients often met the criteria for MCTD. This fact makes it reasonable to discuss the possibility of overlap-syndrome between these two diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4975

AB0671 INCREASED BODY FAT BUT DECREASED LEAN BODY MASS AND BONE MINERAL DENSITY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES ARE ASSOCIATED WITH DISEASE DURATION, INFLAMMATORY STATUS, STELLATE MUSCLE INVOLVEMENT AND PHYSICAL ACTIVITY

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Background: Idiopathic inflammatory myopathies (IM) are characterized by inflammation and atrophy of skeletal muscles, pulmonary and articular involvement, which limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.

Objectives: To assess body composition and physical activity of IM patients and healthy controls (HC).

Methods: 54 patients with IM (45 females/9 males; mean age 57.3; disease duration 5.8 years; polymyositis (PM,22)/dermatomyositis (DM,25)/necrotizing
myopathy (IMMFT).) and 30 age-sex-matched HC (25 females/5 males, mean age 54.9) without rheumatic/tumor diseases or manifest cardiovascular event were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. Anthropometric status. Compared to HC, IIM patients had significantly lower bone mineral density (BMD: 1.16±0.10 vs 1.05±0.11 g/cm², p=0.0010), and were currently able to perform less energetically demanding physical activities according to HAP score (86.3±5.9 vs 49.0±20.2, p<0.001). Disease duration negatively correlated with BMD (r=-0.292, p=0.032) and BIA (r=-0.236, p=0.05). CRP was positively associated with BMD assessed both by DXA (r=0.27, p=0.035) and BIA (r=0.306, p=0.025). MMT-8 score negatively correlated with BMD/BCM ratio (r=-0.385, p=0.006), and physical activity (HAP) negatively correlated with BMD/BCM ratio (r=-0.385, p=0.006).

Conclusions: Compared to healthy age-sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease duration, inflammatory status, skeletal muscle involvement, and physical activity, and could reflect their impaired nutritional status, compromised aerobic exercise, and decreased fitness and performance.

Acknowledgements: Supported by AZV-16-33574A, GAUK-214615.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4824

AB0673 TESTING FOR ANTIBODIES SPECIFIC TO FIBRILLARIN (U3 RNP) SHOWS ADDED VALUE FOR DIAGNOSIS OF SYSTEMIC SCLEROSIS

I. Gehring 1, S. Sjölander 2, P. Höfäl 3, L. Swiniarski 1, L. Vinderslev Iversen 2

Methods: Blood samples from 187 female patients with established diagnosis of SSc were obtained. Antibodies against Fibrillarin (U3 RNP), a helicase found in both PM III and Fibrillarin using the ELIA platform (Thermo Fisher Scientific, Freiburg, Germany).

Results: In 149 out of the 187 patients one or more of the tested parameters were detected. Fibrillarin was identified in 7 out of the 149 patients including 6 women with SSc (17%).

Conclusions: Increased diagnostic sensitivity was shown in this cohort of 187 patients with SSc by adding the analysis of antibodies against Fibrillarin. Testing allowed additional identification of 6 SSc patients which correlates to an increase of 3.74% in sensitivity.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4865

AB0674 YKL-40 IS THE BIOMARKER FOR THE PRESENCE OF INTERSTITIAL PNEUMONIA AND PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS

T. Furukawa, K. Matsui, M. Kitano, Y. Yokoyama, M. Sekiguti, N. Azuma, H. Sano. Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan

Background: SSc is a refractory of connective tissue disease that causes fibrosis of the skin and various organs. Recently, it is attention to 2013 ACR/ESR classification criteria because can diagnose early phase before causing skin involvement in SSc. Thus, we considered that YKL-40 which is known to be involved in inflammation, tissue fibrosis and remodeling, is useful marker for evaluating early diagnosis and complications in SSc. YKL-40 is a chitinase-like protein and expressed in the synovial membrane and cartilage fibroblast cells in Rheumatoid Arthritis. Several cases of relationship between SSc and YKL-40 have been reported overseas, but it is unclear. Our report is the first in Japan.

Objectives: We investigated serum YKL-40 levels and examined immunohistochemistry (IHC) with YKL-40 of cutaneous tissue in SSc patients. To clarify YKL-40 is useful biomarker in early diagnosis in the presence or absence of complications in Japanese SSc patients.

Methods: Between August 2014 and March 2016, we treated 57 SSc patients in our department. We excluded infection, malignant disease, and other active complication may be a factor that increases YKL-40 levels. The patients were divided into 4 groups depending on whether suffered IP or PAH, which can affect the prognosis. Group1 (n=30) did not suffer from either IP or PAH, Group2 (n=12) suffered from IP, Group3 (n=7) suffered from PAH, and Group4 (n=8) suffered from both IP and PAH. YKL-40 levels in 4 groups and a control group of healthy individuals (n=13) were measured by ELISA. And age percentile strata of YKL-40 were calculated because serum YKL-40 levels have reported to rise with age; YKL-40 age percentile = 100/(1 + (Serum YKL-40 levels-3) / 5000).

Results: YKL-40 levels in 4 groups and a control group of healthy individuals (n=13) were measured by ELISA. The patients were divided into 4 groups depending on whether suffered IP or PAH, which can affect the prognosis. Group1 (n=30) did not suffer from either IP or PAH, Group2 (n=12) suffered from IP, Group3 (n=7) suffered from PAH, and Group4 (n=8) suffered from both IP and PAH. YKL-40 levels in 4 groups and a control group of healthy individuals (n=13) were measured by ELISA. And age percentile strata of YKL-40 were calculated because serum YKL-40 levels have reported to rise with age; YKL-40 age percentile = 100/(1 + (Serum YKL-40 levels-3) / 5000).

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References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4865

AB0672 RISK FACTORS AND TREATMENT OF RECURRENT DERMATOMYOSITIS AND POLYMYOSITIS

S. Yamada, H. Yamashita, Y. Takahashi, H. Kaneko. Division of Rheumatic Diseases, National Center for Global Health and Medicine, Tokyo, Japan

Background: Patients with polymyositis (PM) and dermatomyositis (DM) often have repeated exacerbations of myositis. Sometimes immunosuppressive agents are added to induce remission in steroid-resistant cases, with steroid reduction in maintenance therapy, and to prevent exacerbations. However, comparative clinical studies are difficult to conduct and the appropriate immunosuppressive agents are not known [1-2]. There are also no studies of the treatment in recurrent cases with repeated relapses.

Objectives: In this study, we defined myositis that relapses more than once as recurrent myositis and examined its risk factors and re-inductions treatments.

Methods: Patients from our PM and DM database who were hospitalised between January 1991 and September 2016 were reviewed. We included only patients who had followed longer than 1 year.

Results: There were 14 cases (13.1%) with recurrent myositis. The average observation period was 11.3 and 8.0 years in the relapsing and non-relapsing groups, respectively (P =0.18), and the average ages at onset were 46.2 and 55.0 years (P =0.17). The myositis relapse rate was significantly higher in the anti-aminoacyl-tRNA synthetase (ARS) antibody-positive group than in the group with other antibodies [8/24 (33.3%)] vs. 0/14 (0.0%) cases; P =0.02]. The myositis relapse rate was significantly lower in the group in which one more immunosuppressive agent was combined in the initial treatment than in the group without any [3/33 (5.7%) vs. 11/48 (22.9%) cases; P =0.02]. The myositis relapse rate did not differ significantly between DM and PM, men and women, the groups with or without malignancy, the groups with or without interstitial pneumonia (IP), and groups with or without the following initial findings: fever, joint pain, dysphagia, constipation, bedridden, muscle pain, distal muscle weakness, respiratory symptoms (Hagen-Zanker), V-signs, Raynaud's phenomenon, skin ulcers and necrosis, and itching sensation), cardiac complications, hypertension, diabetes, and smoking history. There was no significant difference in the serum creatine kinase and C-reactive protein between the relapse and non-relapse groups. Only 3 of 14 cases (21.4%) had successful re-remission induced and were on maintenance therapy. In two of these cases, two immunosuppressive agents other than glucocorticoid were added: tacrolimus and methotrexate in one and tacrolimus and mycophenolate mofetil in the other. The other 11 patients were treatment-resistant.

Conclusions: The presence of anti-ARS antibody and initial treatment with glucocorticoid only (without any other immunosuppressive agent) were the only two risk factors for recurrent myositis; none of the other factors examined were significant. Recurrent myositis is often treatment-resistant; if one immunosuppressive agent cannot introduce remission, it is worth trying two drugs.

References:

Acknowledgements:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2529
a significant difference was found between the other groups (p<0.05). IHC with YKL-40 revealed staining of the vessels in the superficial dermis in SSC and normal skin remained un stained. The ROC curve for PAH showed an AUC=0.959, and the most valid cut-off levels of YKL-40 age percentile was 85.2 (sensitivity 86.7% and specificity 92.8%).

Conclusions: Our report is the first report of IHC with YKL-40 in SSC. IHC suggest that YKL-40 may be further elevated by angiogenesis caused by microcirculatory damage in SSC. Our results suggest that YKL-40 may be very useful biomarker for diagnosing SSC and complications associated with microvascular lesions.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5684

AB0675 ANTI-MDA5 POSITIVE DERMATOMYOSITIS: AN EMERGING ENTITY
V. Ortiz-Santamaria, A. Ponce, N. Busquets, N. Del Castillo, X. Suris, Rheumatology Unit, Granollers General Hospital, Granollers, Barcelona, Spain

Background: Hypo or amyopathic dermatomyositis (DM) represent about 20% of the classic DM. Melanoma differentiation-associated gene 5 antibody or anti-MDA5 antibody, formerly known as anti-CADM140 antibody, has been reported in the last decade. This antibody is detected in more than 50% of patients with hypo or amyopathic DM and it has specific features such as the presence of ulcerative vascular lesions and rapid progression of the interstitial lung disease.

Objectives: To report anti-MDA5 positive DM cases diagnosed at a university county hospital, between 2012 and 2016.

Methods: Design: Retrospective descriptive study. Location: University county hospital. Reference area: 750,000 inhabitants. Clinical manifestations, analytical results, diagnostic approach, treatment administered and follow-up have been exposed.

Results: We report four anti-MDA5 positive DM with a mean age at diagnosis of 54 years (35–77), Caucasian origin in 2 men and Maghreb origin in 2 women. They had no relevant medical history neither neoproliferative process was detected. ANA were negative and CK values were normal in all the cases. Naiifold capillaroscopy was characteristic of DM pattern. Case B did not present cutaneous manifestations and he was diagnosed as anti-MDA5 DM after his death.

Discussion: B and C cases showed abnormal heart rhythm that could be related to myocardial involvement, as suggested in a recent publication of anti-MDA5 DM (1). In case C, sinus tachycardia was resolved with the clinical response to treatment. In the literature reviewed, anti-MDA5 positive DM has been reported as a dermatomyositis syndrome, but probably the clinical profile of these patients remains to be defined. In our cases, one of them did not present skin lesions and another case did not develop pulmonary involvement 18 months after the diagnosis.

Conclusions: Keep in mind anti-MDA5 antibody in patients with cutaneous manifestations of DM with vasculopathy lesions, minimal or absent muscular disease, heart rhythm abnormalities not explained by other causes and/or rapidly progressive pulmonary involvement. Anti-MDA5 positive DM may have a poor response to treatment and fatal outcome. It remains to be seen if early diagnosis could improve the life expectancy of these patients.

Abstract AB0675 – Table 1

<table>
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<th>B</th>
<th>C</th>
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AB0676 RELATIONSHIP BETWEEN BIOLOGICAL BIOMARKERS AND CHANGES IN RIGHT VENTRICLE THAT PRECEDE PULMONARY HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS
V. Márquez Fernández1, C. Soto1, A. Robles1, A. Noblejas1, E. Martínez1, G. Guzmán2, C. Busca1, F. Arnalich1, J.J. Rios1, 1 Internal Medicine; 2 Cardiology; Hospital Universitario la Paz, Madrid, Spain

Background: A higher prevalence of Pulmonary Hypertension (HP) has been described in patients with Systemic Sclerosis (ES) diagnosis, so this fact significantly overshadows the prognosis, since it leads to the failure of the right ventricle (RV). In this context, it could be very useful to identify ES patients who are at greater risk of developing PH in the future to make an early diagnosis of this complication, and prescribing an early therapy to improve their prognosis.

Objectives: The purpose of this study is to investigate if certain fibrosis, inflammation and vasculopathy biomarkers could be associated to early functional changes in RV, assessed by echocardiography and cardiac nuclear magnetic resonance (MRI) in ES patients.

Methods: A cross-sectional study was performed on a cohort of ES patients diagnosed according to the LeRoy modified criteria, who were being follow-up in the Systemic Autoimmune Diseases Unit of the Internal Medicine Service of La Paz University Hospital. Serum levels of inflammation (IL-13, IL-6, TNF alpha), vasculopathy (VEGF), fibrosis biological markers (endoglin, PDRFR, TGFβ1, TGFβ2, TGFβ3) and cardiac biomarkers (NP-PROBNP, High sensitivity T troponin) were determined as well as hemodynamic and cardiac morphological variables, were measured by transthoracic echocardiography (systolic and diastolic eccentricity index, E/E' ratio, E/A, pulmonary artery systolic pressure, RV thickness) and cardiac MRI (Mean pulmonary artery velocity). We investigated how many patients had these markers elevated and how many of them had hemodynamic and morphological cardiac altered measurements.

Results: Twenty patients with a diagnosis of ES (18 females/2 males) aged between 41 and 77 years, with a mean of 56 years, were included. A control group of 9 patients with similar demographic characteristics was included. ES subjects had higher levels of PDRFR (fibrosis marker) compared to the control group. In addition, in the group of ES patients, two statistically significant associations were observed: troponin T levels (hs-cTnT), endoglin and TGFβ2 had higher levels in patients with a systolic eccentricity index >1, a negative correlation was evidenced between levels of NT-proBNP and the mean pulmonary artery velocity measurement (VELAP).

Conclusions: Hs-cTnT, Endoglin and TGF beta are biomarkers that could appear...
AB0677 INDIVIDUAL IMMUNOLOGICAL PREDICTORS OF THE RISK OF LUNG DAMAGE IN PATIENTS WITH SYSTEMIC SCLEROSIS

V. Hayevsky, V. Chopyak, V. Hayevsky on behalf of Chopyak Valentina, Hayevsky Volodymyr. Department of clinical immunology, Liviv National Medical University named by Danylo Halytsky, Liviv, Ukraine

Background: A significant role in the formation and development of systemic sclerosis (SSc) belongs to immunogenetic factors and immunopathological mechanisms, so nowadays become important to find immunological predictors of early diagnosis of the disease. An urgent task is timely diagnosing the pulmonary complications as the main causes of high mortality and appointment of adequate therapy and objective assessment of its effectiveness.

Objectives: The main purpose was to develop a personal way of forecasting the risk of damage of the lungs, including its subtype – pulmonary fibrosis (PF) and pulmonary hypertension (PH) in patients with SSc.

Methods: To address this goal, the following studies performed: clinical, general laboratory, instrumental, immunological, molecular genetics, statistical methods. Adequacy and reliability of the results of mathematical model of the risk of damage lungs were using criteria Wald and Xi-square. The results show that our model is correct with a probability of error less than 1% (p<0.001).

Results: We found that among the analyzed complex interrelated factors in the development of lung damage in patients with SSc significantly influenced: the duration of the disease, mRNa2b, expression levels in the blood concentration of IL17 in serum and blood, neutrophil phagocytic index 1 that we include in the predictive model.

We know that the most significant complications associated with damage to their lungs are pneumofibrosis and pulmonary hypertension, which threatened the rapid development of respiratory failure and a high mortality of these patients. In this regard analyzed immunological and molecular genetic parameters of patients with SSc depending on the development of PH and LH.

Conclusions: The application withdrawn prognostic clinical and immunological and molecular genetic criteria of lungs damage (pulmonary hypertension and pneumofibrosis) will enable medical practitioners to verify early visceral lesions in patients with SSc in time and justified the appointment of basic therapy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4123

AB0679 THE CLINICAL VALUE OF NAILFOLD CAPILLAROSCOPY IN THE EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS

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Background: Vascular changes was early pathological changes of SSc, gradually appearing with irreversible fibrosis of the skin and internal organs. Early diagnosis and assessment of the development and efficacy timely, could improve survival in patients with SSc.

Objectives: To assess the value of nailfold capillaroscopy in the early diagnosis of systemic sclerosis (SSc).

Methods: 60 patients with SSc and 55 patients with other connective tissue diseases.Data were extracted on clinical and laboratory parameters.2013 ACR/EULAR classification criteria and 1980 ACR criteria for SSc were evaluated.

Results: The sensitivity of the 2013 criteria was 91.7% compared to 56.7% for the 1980 criteria (P<0.001). The specificity of two criteria was no significant difference. This sensitivity of the 2013 criteria was higher compared to the 1980 criteria among those with icSSc (95.5% versus 50%),The pattern was consistent among those with disease duration <3 years (90.5% versus 57.1%, P<0.05) and disease duration ≥3 years (92.3% versus 82.4%, P<0.05). The sensitivity and specificity of nailfold capillaroscopy to determine SSc were 86.7% and 43.6%. Patients not fulfilling the two classification criteria were met the very early diagnosis of systemic scleroderma, and often suffering from RP, and had an SSc pattern on nailfold capillaroscopy.

Conclusions: The sensitivity of 2013 ACR/EULAR classification criteria was higher compared with 1980 ACR classification criteria. The specificity of two classification criteria was no significant difference. This sensitivity of two criteria was higher among those with icSSc and short disease duration.Scleroderma pattern were significantly associated with the development of systemic sclerosis.

References:
ANALYSIS THE CAUSES AND COUNTERMEASURES OF IGNORING SWALLOWING DYSFUNCTION IN PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS

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Background: The patients with Polymyositis and Dermatomyositis always ignored swallowing dysfunction and most of them eventually had no enough knowledge of this. For this situation, to find out the reasons and take appropriate measures was necessary.

Objectives: To analyze the causes of ignoring swallowing dysfunction in patients with Polymyositis and Dermatomyositis and to explore the corresponding preventive measures.

Methods: The clinical data of 47 patients with Polymyositis and Dermatomyositis in hospital from September 2012 to December 2013 was analyzed retrospectively. The swallowing function was evaluated by the water swallow test, and the patients’ knowledge of swallowing dysfunction was surveyed.

Results: Only 2 patients complained of choking during swallowing, with ignorance rate of 95.74%. Positive rate was 40.43% in water swallow test, of which grade II dysphagia proposition was 58%, III grade was 32%, IV grade was 10%. 100% of patients believed that sternal obstruction or dysphagia as swallowing dysfunction. 89.36% of patients didn’t think drinking water with bucking as swallowing dysfunction.

Conclusions: The symptoms of limb weakness in patients with Polymyositis and Dermatomyositis may obscure the presence of dysphagia. In addition, the patients do not have enough knowledge about dysphagia that to neglect the swallowing dysfunction. To improve detection rate of swallowing dysfunction in patients with Polymyositis and Dermatomyositis, earching detailed history by listing dysphagia performance and providing water swallow test is necessary.

References:

Disclosure of Interest: None declared


AB0682

THE INCIDENCE RATE OF INFLAMMATORY MYOPATHIES IN SLOVENIA

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Background: Annual incidence rates of inflammatory myopathies (IM) vary widely from 1.16–19.0 per 106 of adults.1 Our aim was to, for the first time, determine the incidence rate of IM in our population.

Objectives: To determine the incidence rate of IM in our population.

Methods: We retrospectively collected incident cases of IM from 1 January 2005 to 31 December 2016 at our department of rheumatology which is a part of an integrated secondary/tertiary university teaching hospital that is the only referral center for two well defined regions representing roughly a third of the national adult population. Tertiary cases are referred to our department from the entire country. We identified the cases by searching the electronic patient records (PRs) for ICD-10 codes M05, M33–35, M60, G73.7, G72.4. The paper and electronic PRs were scrutinized to assess clinical, laboratory and histopathological data. Descriptive statistics was used to describe our group of patients. The adult population size of the two regions served by our department was obtained from the national statistics institute database. The annual incidence rate for IM was then calculated.

Results: During the 12-year observation period we identified 117 new cases of IM from a well defined adult white Caucasian population aged 18 or above. 38 cases were excluded from analyses since they were referred to our department from outside the two regions we serve on the secondary and tertiary level. Thus, we analyzed 79 cases of IM (63% female; median (IQR) age 67 (55–75) years; 44% ever smokers). The median time to diagnosis was 5 (IQR 3–12) months. We diagnosed 29% patients with dermatomyositis, 25% with anti-synthetase syndrome, 18% with polymyositis, 9% with statin induced necrotizing autoimmune myopathy, 9% with concomitant myositis as a part of connective tissue disease, 6% with paraneoplastic myositis, and 4% with undifferentiated myositis. The IM cases were most often diagnosed in the summer months (32.9%), followed...
Spinal Involvement - treatment

**AB0683** TROUGH INFlixIMAB LEVELS AND ANTI-INFlixIMAB ANTIBODIES IN SPONDYLOARTHRITIS PATIENTS ON TREATMENT WITH LOW DOSE INFlixIMAB: A SINGLE CENTRE CROSS-SECTIONAL STUDY

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**Background:** Infliximab (IFX) is an anti-TNF chimeric, monoclonal antibody approved for use in refractory spondyloarthritis (SpA). Studies done in patients with Rheumatoid arthritis and Inflammatory bowel disease have demonstrated the clinical utility of the measurement of serum trough IFX and antibodies to IFX (ATI). In India, many centres including ours use IFX at lower doses of 3–5 mg/kg and on demand IFX treatment without the use of the loading dose IFX in SpA patients. Data on the utility of measuring trough IFX and ATI levels and their correlation with disease activity in such group of patients is lacking.

**Objectives:** To evaluate the co-relation between trough Infliximab levels and disease activity measures, viz ASDAS ESR and ASDAS CRP in SpA patients on low dose IFX therapy

**Methods:** Thirty-nine adult spondyloarthrtitis patients in the age group of 18–70 years, meeting the ASAAS classification criteria for peripheral and/or axial negative patients were quantitated using ASDAS ESR and ASDAS CRP scores.

**Correlation between the mean ASDAS scores and the trough IFX levels was analysed by Pearson’s product moment correlation assay. The difference in mean trough IFX and ASDAS scores between the ATI positive and ATI negative patients was assessed using Welch two sample t-test.**

**Results:** There was a moderately significant negative correlation between the trough IFX levels and the ASDAS ESR (r = -0.69, p<0.001), ASDAS CRP scores (r = -0.67, p<0.001) (Fig 1). ATI positive patients in comparison to ATI negative, had significantly higher ASDAS ESR and ASDAS CRP scores (Table 1).

**Conclusions:** SpA patients from India on low dose, on demand IFX therapy, have both the trough IFX and ATI correlate significantly with the measures of disease activity. Therefore, these may be used in addition to clinical activity scores for a more cost effective on demand IFX therapy in SpA patients, especially in an expense constrained country like India.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2688

**AB0684** CLINICAL RESPONSE AND RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS PATIENTS UNDER ANTI-TNF THERAPY: IMPACT OF HIP INVOLVEMENT

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**Background:** Hip involvement is considered an important prognostic factor associated with radiographic progression in ankylosing spondylitis (AS) patients. However, there are no studies regarding hip involvement impact on clinical response and radiographic progression in AS patients under anti-TNF therapy.

**Objectives:** Compare clinical and radiographic progression in AS patients receiving anti-TNF therapy with and without moderate-severe hip involvement.

**Methods:** Forty-seven AS patients referred to receive anti-TNF treatment were included and classified according to baseline hip involvement based on Bath Ankylosing Spondylitis Radiology Hip Index (BASRI-Hip); none-minimal hip disease (hip grade <3) or moderate-severe disease (hip grade ≥3). Demographic data, presence of HLA-B27, extra-articular involvement, DMARD and NSAID use, clinical and laboratory disease parameters (BASDAI, BASMI, BASFI, ASQoL, mSASSS and inflammatory markers) were assessed at baseline and two years after anti-TNF treatment.

**Results:** Thirty-four (72.3%) patients were classified as none-minimal hip disease and 13 (27.7%) as moderate-severe hip involvement. Both groups were similar at baseline considering age, HLA-B27, extra-articular involvement and comedication use. Laboratorial markers (ESR, CRP) and disease parameters (BASDAI, BASMI, BASFI, ASQoL, mSASSS and inflammatory markers) showed no difference at baseline. Moderate-severe group had longer disease (10.0±7.6 vs. 4.9±3.3, P=0.002) and lower BASMI (3.8±2.4 vs. 6.5±2.5, P=0.002) and ASQoL (13.7±4.6 vs. 9.9±4.9, P=0.007). After two-years of anti-TNF therapy, both groups presented similar BASDAI response (delta BASDAI, p=0.134; final BASDAI, p=0.324) and an increase in mSASSS (13.6±18.3 vs. 16.1±19.4, P=0.02), despite similar delta BASDAI and final BASDAI.

**Conclusions:** Our study provides evidence that hip involvement did not impact on clinical response in AS patients under anti-TNF therapy but may have an effect on radiographic progression of these patients.
SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN WORK PRODUCTIVITY AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: LONG-TERM RESULTS FROM MEASURE 1 AND MEASURE 2

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Background: Patients (pts) with ankylosing spondylitis (AS) experience significant restrictions in work productivity and health-related quality of life (HRQoL). Secukinumab (SEC) demonstrated rapid improvements in signs, symptoms and physical functioning in pts with AS.

Objectives: To assess whether the beneficial effects of SEC on AS signs and symptoms were reflected in improvements in work productivity and HRQoL in the overall population and in TNF inhibitor (TNF)-naive pts and pts with an inadequate response or intolerance to TNF inhibitors (TNF-IR) for up to 52 weeks (wks) in MEASURE 2 and 104 wks in MEASURE 1.

Methods: 371 and 219 pts were randomized to SEC or placebo (PBO) in MEASURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and MEASURE 2 (150 or 75 mg SC). At Wk 16, PBO pts were re-randomized to SEC 150 or 75 mg SC (PBO pts with ASAS20 response at Wk 16 were switched to SEC at Wk 24 in MEASURE 1). Productivity was measured using the Work Productivity and Activity Impairment-General Health (WPAI-GH) questionnaire, which includes questions to assess absenteeism, presenteeism and overall work productivity and health-related quality of life (HRQoL).

Results: At baseline (BL), 77 of 125 and 45 of 72 randomized pts were employed and working in the SEC-groups in MEASURE 1 and 2, respectively. Improvements in all WPAI domains were observed with SEC in the overall, TNF-naïve and TNF-IR populations at Wk 16 in both studies, and effects were generally sustained through Wks 52 and 104 (Table). In MEASURE 1, activity impairment in the overall population was improved by 49% and 44%, respectively, and was significantly improved by 45% from BL at Wk 104. Improvements were 51%/49% in TNF-naïve and 42%/19% in TNF-IR pts, respectively. In MEASURE 2, activity impairment and work productivity improved by 43% and 40% vs BL, respectively, at Wk 52; improvements in activity impairment/work productivity in TNF-naïve and TNF-IR pts were 49%/34% and 32%/16%, respectively. Similar responses were seen in the other WPAI scores across both studies. Early improvements in ASQol were sustained through Wk 104 in MEASURE 1 and Wk 52 in MEASURE 2. At Wk 104 of MEASURE 1, ASQol scores had improved by 48% vs BL with SEC; improvements were 50%/37% in TNF-naïve and TNF-IR pts, respectively.

Conclusions: SEC provides sustained improvements in work productivity and ASQol for up to 104 wks among AS pts, regardless of prior TNF exposure.

References:

Disclosure of Interest: A. Deodhar Grant/research support from: Amgen, Abbvie, GSK, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Speakers bureau: Eli Lilly, Janssen, Novartis, Pfizer, UCB, P. Conaghan Consultant for: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, Speakers bureau: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, V. Strand Consultant for: Abbvie, Amgen, BMS, Celgene, Celltrion, CORRONA, Gilead, Genentech/Roche, Lilly, GSK, Novartis, Pfizer, Regeneron, Samsung, Sanofi, and UCB. A. Boonen Grant/research support from: Merck, Pfizer, Abbvie and Amgen, Speakers bureau: Sandocz, Janssen, Lilly G. Ferraccioli Grant/research support from: BMS, Roche, MSD, Speakers bureau: Abbvie, Pfizer, UCB, Roche, Lilly, GSK, Novartis, F. Van den Bosch Consultant for: Abbvie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, V. Bhosekar Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Jugil Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.1856
STATEMENTS

The asAS NSAID index. 1 year after baseline — 9 (13.8%) pts started treatment with anti-TNF because of high activity of the disease and absence of effect from 2 NSAIDs. 2 years after baseline number of pts with anti-TNF equal - 15 (23.0%).

Results: Compared with baseline characteristic after 2 years have significantly reduced disease activity and increased the number of asAS partial remission (PR) in patients with axSpA (Table 2).

There were no statistical differences between the frequency of NSAIDs intake and early axSpA disease activity (Table 2).

Conclusions: Long reception of NSAIDs in patients with early axSpA reduces disease activity; however, the receive frequency does not affect the activity of the disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3646

AB0689 METABOLIC SYNDROME IN ANKYLOSING SPONDYLITIS AND THE EFFECT OF ANTI-TNF THERAPY

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Background: Metabolic syndrome (MeS) is a cluster of cardiovascular (CV) risk factors (obesity, dyslipidemia, hypertension, alterations in glucose metabolism, and insulin resistance) whose prevalence is increasing particularly in developed countries. In comparison with the general population, patients with ankylosing spondylitis (AS) are at increased risk of cardiovascular (CV) disease, which is one of the main causes of mortality among them.

Objectives: The aim of this study was to identify the relationship between MeS and disease activity in AS patients, and evaluate the effect of anti-tumour necrosis factor (TNF) therapy.

Methods: The study involved 30 outpatients who met the New York diagnostic criteria for AS: 14 males and 16 females; mean age 53.07±10.73 years; mean disease duration 5.03±2.07 years. All of the patients were being treated with DMARDs and anti-inflammatory drugs, but none had received any biological agents or steroids at baseline. The patients underwent laboratory tests (lipid profile and glucose levels), a clinical and standard echocardiographic examination, carotid ultrasonography (including the assessment of intima-media thickness and pulse wave velocity), and speckle tracking echocardiography (STE) of the left ventricle (LV) using Philips CLAB software to evaluate their CV risk profiles. Functional impairment and disease activity were assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI). All of the patients were evaluated at baseline and after 12 months of anti-TNF treatment. The data were statistically analyzed using non-parametric chi-squared and McNemar tests, and the Wilcoxon-Mann-Whitney test.

Results: Before starting anti-TNF therapy, the cohort was divided into two groups: those with MeS (25%) and those without. The patients with MeS higher BASDAI scores (chi-squared test: 4.85; p=0.03). After 12 months of follow-up, there was a statistically significant improvement in global functional impairment (QoL) in both groups: from a baseline median of 19.94 (IQR 18.66–20.78) to a median of 21.46 (IQR 20.37–22.69) (p=0.02) in the non-MeS group, and from a baseline median of 18.88 (IQR 16.00–19.35) to 19.54 (IQR 18.21–19.98) (p=0.04) in the MeS group. No other changes in CV parameters were observed. The improvement in BASDAI scores was greater in the MeS group, but the difference was not statistically significant. The prevalence of MeS decreased after 12 months of anti-TNF therapy, although the McNemar test showed that the decrease was of borderline significance (p=0.048).

Conclusions: AS patients affected by MeS. The effects of anti-TNF drugs on MeS are still controversial, but our findings suggest that they improve CV markers such as GLS as well as disease activity. The main limitation of this study is its small sample size and short follow-up; further studies are required in order to clarify the influence of MeS on clinical therapeutic outcomes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1792
Background: The regulatory phase III trial supporting the approval of biosimilar infliximab (BOW015) in India included only rheumatoid arthritis patients. Consequent-ly, there is paucity of data on the effectiveness of BOW015 in Ankylosing Spondylitis (AS).

1,2,3 Hence, we decided to objectively quantify the effectiveness and safety of BOW015 in AS patients.

Objectives: To determine safety, efficacy and tolerability of BOW015 in Indian AS patients.

Methods: We retrospectively collected data from seven centres to get a comprehensive picture of the Indian population. The protocol along with data collection form was designed by the investigators and ethics committee approval was obtained. Biologic naïve patients diagnosed with AS as per Assessment of SpondyloArthritis International Society criteria who were having six months of follow up data during January-November 2016 were included in the study. Percentage of patients achieving major clinical improvement (Ankylosing Spondylitis Disease Activity Score C-reactive protein (ASDAS-CR) ≥2.1 from the baseline to six months of follow up) was the primary variable. Secondary variables included: clinical improvement criteria (ASDAS-CR ≤1.1 from the baseline to six months of follow up), change in ASDAS-CRP, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), CRP and Erythrocyte Sedimentation Rate (ESR) from the baseline to six months. Variables were reported as mean ± Standard Deviation (SD), absolute change in variable were reported along with their Confidence Interval (CI) and data was analyzed using Statistical Package for the Social Science V.22.

Results: A total of 68 patients treated with BOW015 having follow up data for six months were analyzed. Mean age of patients was 32.63±11.73 (SD) years. BASDAI, ASDAS-CRP, ESR and CRP which continued till the end of six months. There was an absolute change of -2.54 (95% CI -1.92, -3.17) in BASDAI and -1.77 (95% CI -1.43, -2.11) in ASDAS-CRP right from first follow up corresponding to post 1st dose visit which was statistically significant (see Table-1). This trend was observed in the subsequent visits in BASDAI, ASDAS-CRP, ESR and CRP which continued till the end of six months. One patient developed pulmonary tuberculosis and marginally elevated liver enzymes were seen in two patients.

Conclusions: BOW015 showed significant improvement in ASDAS-CRP and BASDAI in patients with AS on a six month follow up period and the clinical benefits were apparent as early as first dose of BOW015.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5865
Table: Summary of mean (standard deviation) changes in SF-36, EQ-5D, and ASQoL.

<table>
<thead>
<tr>
<th>GOLIMUMAB</th>
<th>2mg/kg</th>
<th>PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) change from baseline in SF-36 PCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>6.89 (6.90)</td>
<td>2.07 (5.56)</td>
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<tr>
<td>Week 16</td>
<td>5.72 (5.74)</td>
<td>2.87 (6.11)</td>
</tr>
<tr>
<td>Week 28</td>
<td>8.08 (6.02)</td>
<td>9.28 (7.09)</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in SF-36 MCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>5.56 (9.26)</td>
<td>1.67 (8.60)</td>
</tr>
<tr>
<td>Week 16</td>
<td>6.47 (3.12)</td>
<td>0.84 (3.92)</td>
</tr>
<tr>
<td>Week 28</td>
<td>10.16 (10.93)</td>
<td>5.60 (9.90)</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in EQ-5D VAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>17.61 (24.02)</td>
<td>6.63 (19.081)</td>
</tr>
<tr>
<td>Week 16</td>
<td>20.32 (23.47)</td>
<td>4.75 (23.47)</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in ASQoL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>-4.5 (4.71)</td>
<td>-1.5 (3.90)</td>
</tr>
<tr>
<td>Week 16</td>
<td>-5.4 (5.01)</td>
<td>-1.8 (4.50)</td>
</tr>
<tr>
<td>Week 28</td>
<td>-5.3 (5.24)</td>
<td>-5.3 (4.84)</td>
</tr>
</tbody>
</table>

Conclusions: Adult psA/w active AS treated w/IV GLM showed marked improvements in physical functioning, mental health functioning, health state, & HRQoL.


DOI: 10.1136/annrheumdis-2017-eular.3408
DOSE TAPERING OF INFIXIMAB IN PATIENTS WITH SPONDYLOARTHROPATHIES

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Background: Infliximab have proven to be effective in spondyloarthritis. Previous studies suggest that patients in clinical remission may benefit from dose reduction or pharmacological tapering without relapse.

Objectives: To study the evolution of clinical activity and physical function in patients with spondyloarthritis, ankylosing spondylitis (AS) and psoriatic arthritis (PsA) under Infliximab (IFX) tapering strategy.

Methods: This is a prospective single-centre observational study of patients diagnosed with AS and PsA treated with IFX (5 mg/kg/infusion) between January 1, 2012 and December 31, 2015. We included patients who achieved clinical remission or low activity index (expressed with BASDAI and BASFI) and decided to lower the dose of 5 mg/kg/infusion, maintaining the periodicity of the treatment in each patient. Demographic data (age, gender, time with IFX) daily activities, physical activity (BASDAI and BASFI) and laboratory data (ESR and CRP) were collected at the baseline visit prior to tapering, at the next infusion following dose reduction and the last infusion (between November 1st 2014 and December 31st, 2016).

Results: We included 18 patients (16 men) on IFX treatment with EA (16) or axial APs (2). The medians of age and time of evolution were 50.79 years (41.8–55.1) and 9.5 years (7.2–11.9), respectively. Table 1 shows the clinical and laboratory data obtained at the baseline visit, the next infusion and the last infusion. Fourteen patients (87.9%) continued with the dose of 4 mg/kg/infusion and are maintained in clinical remission. Four patients returned to the dose of 5 mg/kg/infusion due to loss of efficacy at dose reduction, with a mean follow-up of 17.6 months (17.0–19.1). Clinical remission was again achieved in 4 patients, although one of them changed biological therapy due to loss of efficacy of IFX after 3 infusions with 5 mg/kg/infusion.

Conclusions: In our patients with spondyloarthritis dose reduction of IFX was well tolerated and safe, maintaining the clinical response measured by BASDAI and BASFI. In 3 out of 4 patients who worsened upon dose reduction, the 5 mg/kg/infusion dose recovered clinical remission.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4730

IMPACT OF THE BASELINE BATH ANKYLOSING SPONDYLITIS RADIOLOGY HIP INDEX ON THE STRUCTURAL HIP JOINT PROGRESSION AFTER TNFα BLOCKING THERAPY IN SPONDYLOARTHROPATHIES PATIENTS

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Background: One of the major goals of treatment of spondyloarthritides (SpA) is to prevent, slow the radiographic damage. The TNFα inhibitors – Infliximab have proven to be effective in spondyloarthritis. Previous studies suggest that patients in clinical remission may benefit from dose reduction or pharmacological tapering without relapse.

Objectives: To compare, in real-life settings, the retention rates of the initial anti-TNF therapy between 2001 and 2015. Nevertheless, the randomized studies were of short duration and included a selected population that differed from patients treated in daily practice.

Methods: To compare, in real-life settings, the retention rates of the initial anti-TNF therapy between 2001 and 2015. Nevertheless, the randomized studies were of short duration and included a selected population that differed from patients treated in daily practice.

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conditions like ankylosing spondylitis (AS). Despite good treatment options such as tumor necrosis factor alpha (TNFα) inhibitors in AS, it is seen that patients have applied for CAM use for many reasons including local regulatory funding requirements, potential risks and accessibility of biological treatments. Few studies have examined the frequency of CAM use, and associations between demographic and disease-related factors in it in AS.

**Objectives:** To investigate the CAM usage of patients with AS and to determine the associated factors.

**Methods:** Total of 123 patients with AS, who were being followed in a tertiary rheumatology outpatient clinic, were included to the study. The demographic and clinical characteristics along with the behaviors about the CAM usage of the patients agreeing to participate were recorded to the “Patient Assessment Form”. The activity of the disease were determined with doctor global assessment (numeric visual analog scale (nVAS); 0–10), and Routine Assessment of Patient Index Data (RAPID)-3 score. The treatment adherence of the patients was assessed with the Morisky Green Levine Scale.

**Results:** One hundred eleven patients (%90.2) were male, and mean age was 36.5±8.8 years. The mean disease duration and mean delay in diagnosis were 10.9±6.4, and 3.7±3.9 years, respectively. The mean RAPIDS score, doctor and patient global assessment were, 9.9±5.3, 2.8±1.9, and 4.6±2.7, respectively. While 79 patients (%64.2) were on anti-TNF treatment, 76 patients were receiving NSAIDs, and 35 patients (%28.5) reported an adverse event related with the treatment. Forty-five patients (%36.6) reported to use any CAM (previous or current) (Table1). The reasons reported by the patients for the usage of CAM were: for disease activity – Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), for functionality – Bath Ankylosing Spondylitis Functional Mobility Index (BASMI), and for depression – Beck depression Inventory (BDI). All patients were evaluated before treatment and at 3 months.

**Results:** The demographic characteristics of the patients were compared and there was no significant difference between the groups. The improvements in all parameters were better in both groups receiving exercise and anti-TNF therapy than in the control group after treatment compared with baseline. The Anti-TNF + GPR exercise therapy resulted in greater improvements than the anti TNF+ conventional exercise therapy in pain, and mobility parameters.

**Conclusions:** Anti-TNF therapy and exercise were efficient in both groups on improving pain, disease activity, fatigue, sleep quality, and depression. However, the improvements in pain and mobility were greater in the active AS patients with GPR exercise method. Therefore motivated patients should be encouraged to perform this exercise program.

**References:**


**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.6379

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**AB0700**

**EFFECTIVE DRUG AND SURVIVAL OF ANTI-TUMOUR NECROSIS FACTOR-ALPHA THERAPIES IN PATIENTS WITH SPONDYLO-ARTHRITIS: ANALYSIS FROM THE THAI RHEUMATIC DISEASE PRIOR AUTHORIZATION (RDPA) REGISTER**

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**Objectives:** To evaluate the long-term efficacy and safety of the first TNFi in real-life practice and to identify the risk factors related to drug discontinuation in Thai patients with SpA from the RDPA registry.

**Methods:** Patients who fulfilled the 1984 Modified New York criteria for ankylosing spondylitis (AS), CASPAR criteria or Moll and Wright criteria for psoriatic arthritis (PsA) and the European Spondyloarthropathy Study Group Criteria for Modified Amor criteria for undifferentiated SpA (uSpA), and were prescribed the first TNFi between December 2009 and October 2014 in the RDPA registry were enrolled. Baseline demographic and clinical data were retrieved. A Cox proportional hazard model was used to identify the factors associated with discontinuation. The P-value of <0.05, two-sided was considered statistically significant.

**Results:** Of the 142 patients included, 97 had AS, 41 had PsA, and 4 had uSpA. Most AS patients were male (54.6%) with mean (SD) age of 44.6 (10.6) years, median (IQR) delay in diagnosis 6.5 (5.6, 8.2) [from a 10-cm visual analog scale (VAS)], and median baseline patient global assessment (bPGA) was 7.2 (6.0, 9.8) [from a 10-cm visual analog scale (VAS)]. For PsA patients, patients were female (68.3%) with mean age of 52.6 (SD 12.2) years, median (IQR) delay in diagnosis 6.6 (5.8, 7.4, 9.7) years in patients active axial involvement and median baseline number of joint involvement was 13.5 (IQR 8.5, 6, 18.3) joints per patient with active peripheral joint involvement. The Efficacy of the TNFi treatment was good and it was increased over time in AS and PsA patients (figure 1). During the 5-year follow-up, AS, PsA, and uSpA patients had comparable discontinuation rate of their first TNFi treatment [25% (26%) in AS, 14% (34%) in PsA, and 1% (25%) in uSpA; P=0.82]. In univariate analysis, leflunomide use, and bFGF use -3 comparing to >-6 (from a 10-cm VAS) were associated with the discontinuation of TNFi in AS patients with hazard ratio (HR) (95% CI) of 2.56 (1.13, 5.81) and 8.59 (1.82, 40.65), respectively. For the patients with PsA, only infliximab use was associated with TNFi discontinuation with HR of 4.79 (95% CI 1.33, 17.20) in univariate analysis. The reason for TNFi discontinuation were good response (38%), serious adverse effects (SAE) (30%), non-adherence (20%), and lack of efficacy (13%). Among SAE, 58% was infectious causes (57% tuberculosis and 43% non-mycobacterium infections). The others were non-infectious causes.

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**AB0699**

**EFFECTS OF GLOBAL POSTURAL REEDUCATION EXERCISE AND ANTI-TNF TREATMENTS ON DISEASE ACTIVITY, FATIGUE, MOBILITY, SLEEP QUALITY AND DEPRESSION IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS (PROSPECTIVE-CONTROLLED TRIAL)**

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**Background:** Ankylosing spondylitis (AS) is chronic inflammatory disease that affects primarily the spine and the sacroiliac joints. ASAS/EULAR guidelines describe regular exercise as the cornerstone of non-pharmacological treatment and non-pharmacological treatments including non-steroidal anti-inflammatory drugs as first-line therapy, and a tumour necrosis factor (TNF) alpha inhibitor (anti-TNFα) as second-line medication in patients with persistently high disease activity despite conventional pharmacological treatment in patients with AS.

**Objectives:** The purpose of this study was to investigate the effects of combination therapy with global postural reeducation exercise (GPR) and Anti-TNF treatments on pain, disease activity, mobility, fatigue, sleep quality, and depression in patients with active AS.

**Methods:** 60 active AS patients who meet the criteria of Modified New York and/or AS ASAS axial spondyloarthropathy were included in the study. Patients were divided into 3 groups. The first group was given anti-TNF therapy plus GPR exercise program. The 2nd group was given anti-TNF and conventional exercise therapy. The 3rd group was given routine exercise program along with their existing treatments (NSAIDs and/or SLZ). Following inventories are used for clinical evaluation: for disease activity – Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), for functionality – Bath Ankylosing Spondylitis Functional Index (BASFI), for mobility – lumbar Schober, chest expansion, hand-finger to floor distance, for fatigue – fatigue Multidimensional Assessment Questionaire (MAF), for sleep quality – Pittsburgh sleep quality index (PSQI), for depression

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**Disclosure of Interest:**

None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.6196
**AB0701** THE REAL-LIFE USE OF GOLIMUMAB IN PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISEASES: ONE YEAR RESULTS OF THE GO-PRACTICE STUDY

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**Background:** The GO-PRACTICE study was initiated to describe the use of Golimumab (GLM), a human anti-TNFα monoclonal antibody, in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) in French clinical practice.

**Methods:** Observational, multicenter, prospective, national study. Adult patients with RA, PsA and AS were included consecutively after GLM decision for treatment. The primary outcome was the M0-M4 change of VAS-F. The secondary outcomes included: 1) the M0-M4 change of VAS-M; 2) the proportion of patients with a 50/100 change of VAS-F; 3) the proportion of patients with a 50/100 change of VAS-M; 4) the proportion of patients with a 25/100 change of HAQ.

**Results:** A total of 754 patients (134 sites) were included between January 2015 and March 2016. Most of them had AS (64%), and 22% and 13% had RA and PsA, respectively. Mean age was 46±13 years and 61% were female. Almost 37% had received prior biotherapy. Nearly all patients (99%) were prescribed GLM as 50 mg-monthly injections. GLM was mostly co-prescribed with other anti-rheumatic treatments (84%). Of the 163 patients with available data at strictly 1-year, 56.4% were still treated with GLM; (61.8% in biotherapy-naïve patients); the persistence rate was similar across the three groups. The Kaplan-Meier duration curves of GLM are presented in figure 1. The main reason for GLM discontinuation was primary non-response, reported in 42% of patients. Among patients who continued GLM treatment, a meaningful improvement in disease activity was observed at 1-year in 71.9% of RA, 63.2% of PsA and 68.0% of AS patients. Patients-reported outcomes, including pain and functional disability, also showed improvement.

**Conclusions:** In real-life practice in France, GLM was prescribed according to recommendations in terms of dosage and therapeutic strategy. One-year interim analysis, performed in one third of the cohort, suggests that GLM treatment is associated with clinical improvements leading to persistence of treatment. These results need to be confirmed in the final overall analysis planned in 2018. 


**AB0702** IMPROVEMENT OF FATIGUE IN PATIENTS WITH SPONDYLOARTHRITIS TREATED WITH ANTI-TNF THERAPY: PROSPECTIVE STUDY IN A REAL-LIFE SETTING


**Background:** Besides randomized controlled trials evaluating biologic agents on fatigue, the impact of anti-TNF therapy on this crucial symptom has been poorly assessed in a real-life setting.

**Objectives:** To assess the early effect of etanercept (ETN) on fatigue-related outcomes in spondyloarthopathies (SpA) patients in a real-life setting.

**Methods:** This prospective study included patients with active SpA fulfilling ASAS axial or peripheral criteria, requiring an anti-TNF. All patients were treated with ETN 50mg weekly. BASDAI, BASFI, functional assessment of chronic illness therapy-fatigue (FACIT-F) (0 maximum and 52 the minimum of fatigue) and visual analogic scale of fatigue (VAS-F) (0 the minimum -100 maximum of fatigue) were assessed at inclusion at the time of ETN beginning (M0) and 4±1 months later (M4).

**Results:** The primary outcome was the M0-M4 change of VAS-F. The secondary outcomes were: i) the M0-M4 change of FACIT-F; ii) the frequency of patients who met improvement according to FACIT-F (defined as the minimal clinically important difference of FACIT-F corresponding to a 4-points decrease). To determine whether fatigue change was related to disease activity improvement, a correlation between M0-M4 changes of BASDAI and VAS-F or FACIT-F was determined.

**Conclusions:** This real-life study investigating the early effect of etanercept therapy on fatigue in SpA patients showed that fatigue (according to VAS-F) significantly improved while effect on FACIT-F was less pronounced. This improvement was explained, in part, by disease activity improvement.

**References:**


**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.2735

**AB0703** IMPACT OF ANTI-TNF AGENTS ON PATIENT-REPORTED OUTCOMES IN SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW OF THE LITERATURE AND META-ANALYSIS

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**Background:** Disability, alteration in quality of life and fatigue are frequently reported in spondyloarthritis (SpA). Anti-TNF demonstrated clinical efficacy in SpA. However efficacy on patient-reported outcomes (PROs) may differ from medical assessment.

**Objectives:** To assess the impact of anti-TNF on quality of life, disability and fatigue reported by SpA patients.

**Methods:** Design: systematic review and meta-analysis of the literature. Data sources: two authors (SL and YD) independently screened PubMed-Medline, Cochrane library and EMBASE databases until November 2016. Key words: (“Patient reported” OR “quality of life” OR fatigue OR FACIT) AND (spondyloarthritis OR “psoriatic arthritis” OR “ankylosing spondylitis”) AND (anti-TNF OR certolizumab OR etanercept OR adalimumab OR infliximab OR golimumab).

**Articles selection:** randomized controlled trials (RCTs), published in English, assessing efficacy of anti-TNF on PROs, in ankylosing spondylitis (AS), psoriatic arthritis (PsA) or SpA according to the ASAS criteria. Data collected: fatigue assessed by FACIT score, quality of life assessed by Short Form 36 (SF36) mental and physical component or by Health Assessment Questionnary Disability Index (HAQ). Data analysis: Article quality was evaluated by the Jadad scale. For SF36 and HAQ outcomes, pooled variations at 12 and 24 weeks were computed by meta-analysis. Heterogeneity was measured by I² index.

**Results:** Of the 604 articles identified, 37 references were eligible for systematic review and 13 for meta-analysis. Our systematic review identified 10 RCTs concerning AS, 20 concerning PsA and 7 concerning axial SpA. However due to the heterogeneity in available statistical data, references eligible for meta-analysis were mainly related to PsA.

HAQ assessment was available for a meta-analysis in 8 studies. HAQ was significantly improved at 12 and 24 weeks with anti-TNF. The impact on HAQ variation at week 24 was -0.29 points [95% CI: -0.37, -0.22]. Heterogeneity was important (I² = 57%; see figure).

Ten studieswere eligible for a meta-analysis of anti-TNF effect on SF36 mental form. An improvement was observed at 12 and 24 weeks, although superior at 24 weeks. The effect at week 24 was 2.78 [95% CI: 1.87 - 3.68], without heterogeneity (I² = 0%; see figure).
Twelve studies were eligible for a meta-analysis of anti-TNF effect on SF36 physical form. We observed a similar and significant improvement at 12 and 24 weeks. The effect at week 24 was 6.74 [95% CI: 5.34 – 8.13], with an important heterogeneity (I² = 84%; see figure). Fatigue was evaluated in 3 studies. Adalimumab induced a significant improvement in FACIT score at 12 and 24 weeks in one study. Two studies using different scores (Fatigue Assessment Scale, BASDAI fatigue item) to assess cetolizumab effect highlighted similar findings: an early improvement in fatigue at week 12, remaining significant and stable at week 24.

Conclusions: Anti-TNFs agents significantly improve disability, quality of life and fatigue in patients with PsA.

Acknowledgements: France pharmaceutical company provided logistic support by organizing a meta-analysis methods workshop, but played no further role in the project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5268

AB0704 HIP ARTHROPLASTY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: CLINICAL AND FUNCTIONAL EFFICIENCY

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Objectives: To evaluate the results of the hip joint replacement in patients with SpA under the dynamic supervision of a rheumatologist and orthopedist within the first year after the operation.

Methods: As part of special program for rheumatology patients hip endoprosthesis was done in 12 patients (mean age - 44±15.3 years) with SpA, 8 of them with ankylosing spondylitis (AS) and 4 with psoriatic arthritis (PsA). Duration of the disease - 13±7.9 years, positive for HLA B27 in 9 (75%) patients. High activity for AS-DAS was at 58.3% of the patients. Took NSAIDs at the time of the operation - 11 (91.6%) patients, salsalazine 5 (41.6%), methotrexate - 2 (16.7%). 1 (8.3%) patient received etanercept, 1 (8.3%) patient - infliximab. Dynamic observation of rheumatologist and orthopedist was carried out before, just after surgery, after 6 months, 1 year and 2 years, with the assessment of VAS, BASDAI, ASDAS, BASFI.

Results: The reduction of pain intensity on the VAS was observed in the first month after the surgery (47.3±18.6 mm), initially it was 74.0±24.1 mm, 42.5±9 mm after 6 months (p<0.05), after 12 months - up to 22.5±19.9 mm (p<0.05). ASDAS significantly (p<0.05) reduced from 2.9±0.01 to 1.6±0.35 - in 6 months and 1.26±0.88 - 12 months after operation; BASDAI: from 6.2±3.91 to 2.7±2.20 - 6 months, 2.6±1.53 at 1 year follow-up. BASFI index before surgery - 5.4±5.29, 6 months - 2.7±2.31, 1 year - 2.3±2.60 points. No complications after surgery were registered.

Conclusions: Hip joint endoprosthesis in patients with SpA is effective not only in improving functional ability and pain relief, but also a reduction of disease activity. Dynamic rheumatologist observation in perioperative period leads to positive dynamics in relation to the activity of SpA and quality of life of patients during the first year after surgery.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3966

AB0705 CONTINUED EFFECTIVENESS OF A BIOSIMILAR ADALUMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS AFTER STOPPAGE OF INITIAL TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Adalimumab, an anti TNF-α agent, has been proven to be safe and effective in treatment of ankylosing spondylitis (AS). A biosimilar adalimumab was approved for use by Indian regulators in 2014. It is a ‘first in market’ of the reference adalimumab in terms of purity, potency, safety and clinical efficacy. In the absence of availability of adalimumab in India, this biosimilar adalimumab currently serves as an accessible, cost-effective option for treatment of AS patients.

Objectives: This retrospective analysis evaluates effectiveness of biosimilar adalimumab (bADA), in terms of disease activity, safety and outcomes in real-life Indian AS patients treated for initial 24 weeks and then followed for next 24 weeks off biologic treatment.

Methods: Medical records of AS patients with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) >4, who were prescribed bADA therapy between January to December 2015 were analysed. For patients, who stopped bADA treatment after 24 weeks, standard AS outcome-measurement scores including ESR, CRP, BASDAI, BASFI, and Health Assessment Questionnaire (HAQ) at baseline, week 24 and at week 48 were measured to evaluate ongoing efficacy, were compared using paired Student’s T-test. Patients were allowed to continue methotrexate and salazopyrin as part of routine medical care.

Results: During the study period, 52 AS patients were prescribed bADA 40 mg every 2 weeks. Of these patients, 10 (19.2%) patients had stopped treatment after 6 months, were considered for this analysis. Mean age for this group was 36.5±71.08 years; 10 females. At the end of 24 weeks' treatment, there were significant reductions in levels of inflammatory markers ESR, CRP, as well as in BASDAI, BASFI and HAQ scores. Eight patients continued to receive methotrexate and 8 patients sulfasalazine as concomitant medications. After week 48 (24 weeks post stoppage), BASDAI and BASFI scores did not deteriorate despite discontinuation of bADA treatment. The patients' HAQ scores were also indicative of similar trends of continuing improved health status post therapy.

Table 1. Disease activity scores and patient outcomes at 24 weeks after completion of biosimilar adalimumab therapy

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>Week 24 (last dose)</th>
<th>P value (baseline – week 24)</th>
<th>Week 48 (24 weeks bADA free period)*</th>
<th>P value (baseline – week 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASFI</td>
<td>8.3±0.72</td>
<td>2.87±0.77</td>
<td>p&lt;0.001</td>
<td>2.55±0.65</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>BASDAI</td>
<td>7.7±0.84</td>
<td>2.45±0.58</td>
<td>p&lt;0.001</td>
<td>2.41±0.58</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>ESR</td>
<td>49.5±28.78</td>
<td>13.97±11.19</td>
<td>p&lt;0.001</td>
<td>30.3±10.24</td>
<td>p&lt;0.002</td>
</tr>
<tr>
<td>CRP</td>
<td>19.7±12.24</td>
<td>3.56±3.6</td>
<td>p&lt;0.001</td>
<td>6.13±1.94</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HAQ (Pain)</td>
<td>77.6±7.22</td>
<td>27.0±8.2</td>
<td>p&lt;0.001</td>
<td>28.1±9.42</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HAQ (Heal)</td>
<td>60.8±3.43</td>
<td>28.1±3.45</td>
<td>p&lt;0.001</td>
<td>25.6±10.56</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Data presented as Mean±standard deviation. *p = not significant for any parameter when compared for changes from week 24 to week 48. **p=0.006 as compared to week 24 for rise in ESR during the bADA free period.

Conclusions: Biosimilar adalimumab therapy was effective in treating AS patients. The disease activity and health assessment scores continued to remain stable with no worsening after the stoppage of treatment for 6 months, indicating a post-therapy effectiveness in these patients with no reported adverse event.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3825

AB0706 ANKYLOSING SPONDYLITIS PATIENTS WITH UVEITIS HAD A HIGHER ADALUMAB RETENTION RATE: HUR-BIO REAL LIFE RESULTS

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Background: Retention of biological drugs in inflammatory arthritis may be affected by many different obvious and unknown factors. It is also important to explore the characteristic or disease features in ankylosing spondylitis (AS), retention rate of biological drugs may be related with extra-articular presentation of AS such as uveitis, as well.

Objectives: The objective of this study was to assess whether uveitis affected retention of adalimumab in AS patients in our single center biological cohort.

Methods: Hacettepe University Biological registry is single-center biological registry since 2005. HURBIO had 2165 spondyloarthritids patients of which 1190 patients had AS according to NY criteria. Until now, in 510 of 1190 patients had used adalimumab and 350 of 510 patients had available for uveitis. Patients

None declared

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3996
were assessed for demographic characteristics, disease duration, HLA-B27, DMARD and biological usage, biological switch ratio. Baseline disease activity was assessed with BASDAI, BASFI VAS (pain, fatigue and patients global assessment), ESR and CRP. Patients were compared according to having uveitis or not. Retention rate of adalimumab assessed by Kaplan-Meier survival analysis. For routine practice, adalimumab could be considered for not. Our biological cohort supported that AS patients with uveitis had better survival. For routine practice, adalimumab could be considered for AS patients with uveitis.

Conclusions: Determination of possible risk factors for retention of TNFi drugs is one of the treatment option for uveitis whether uveitis related with SpA or not. Our biological cohort supported that AS patients with uveitis had better adalimumab survival. For routine practice, adalimumab could be considered for AS patients with uveitis.

Disclosure of Interest: None declared

COMPARATIVE EFFECTIVENESS OF SECUKINUMAB AND GOLIMAB IN ANKYLosing SPONDYLITIS ASSESSED BY MATCHING-ADJUSTED INDIRECT COMPARISON USING PIVOTAL PHASE 3 CLINICAL TRIAL DATA

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Background: No data are available from head-to-head RCTs between secukinumab 150 mg (SEC; an anti-IL-17A) and golimumab 50 mg (GOL; a TNFi) in patients with active ankylosing spondylitis (AS). Matching-Adjusted Indirect Comparison (MAIC) can be used to estimate comparative effectiveness and enables treatment outcomes to be compared across effectively balanced trial populations. MAIC is an established method in health technology assessments and NICE have published guidance on appropriate methodology, and especially for assessing imbalances in observed covariates between trials.

Objectives: To assess the comparative effectiveness of SEC and GOL up to week 24 using MAIC with pooled individual patient data (IPD) from the RCTs MEASURE 1 (M1) and MEASURE 2 (M2) and published aggregate data from the RCT GO-RAISE.

Methods: Pooled M1 and M2 data were used to maximize the effective sample size (ESS) for SEC. IPD from the SEC arms of M1 and M2 (n=197) were weighted to match the published baseline characteristics of the GOL arm of GO-RAISE (n=138). Placebo arms were matched in the same way; placebo-comparisons were possible only until week 16 because patients could receive active treatment from this time onwards. Logistic regression was used to determine weights for age, sex, BASFI, disease duration, CRP and previous TNFi therapy. Recalculated outcomes from M1 and M2 (SEC, ESS=102; placebo, ESS=81) were compared with data from GO-RAISE (GOL, n=138; placebo, n=78). Pairwise comparisons – reported as odds ratios (ORs [95% CIs]) – were performed for ASAS 20, ASAS 40 and ASAS PR responses at nearest-equivalent time points across trials: week 12 (SEC)/14 (GOL), week 14 (GOL)/16 (SEC) and week 24 (SEC and GOL). Non-responder imputation (NRI) was available for all binary outcome data. Strict thresholds were avoided when interpreting p values, in line with American Statistical Association 2016 guidance.

Results: There was no evidence of differences in ASAS 20 and ASAS 40 responses between SEC and GOL at weeks 12/14 and 14/16 (both placebo-adjusted). At week 24, non-placebo-adjusted ASAS 20 and ASAS 40 responses using NRI were higher with SEC than GOL (OR [95% CI]: 1.58 [0.93–2.69], p=0.089 and 1.58 [0.94–2.64], p=0.089, respectively). There was no evidence of differences in ASAS PR responses between SEC and GOL at weeks 12/14, 14/16 and 24. A sensitivity analysis conducted after adding BASDAI score to the matching parameters yielded similar results.

Conclusions: There was no evidence of differences in ASAS responses between SEC and GOL in placebo-adjusted analyses. In non-placebo-adjusted analyses, SEC showed higher ASAS 20 and ASAS 40 responses than GOL at week 24.

References:

AB0708 TRANSITION FROM ONGOING INFlixIMAB REFERENCE PRODUCT TO ITS BIOSIMILAR: CAN WE TALK ABOUT A FAILURE?

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Background: Some recent publications support the fact that there is no clinically meaningful difference between infliximab biosimilar and the originator in naïve patients, but sole a few of them actually assessed the transition itself. Since May 2016, according to the European guidelines, the French Health Authorities have allowed interchangeability between a biotherapy reference product and its biosimilar. According to the last studies focusing on the safety and efficacy issues, avoiding the transition to biosimilar looks no longer justified.

Objectives: This work aimed to understand to which extent the use of infliximab biosimilar may result in the failure of the switch strategy in spondyloarthritis patients.

Methods: This is a retrospective study conducted from June to December 2016, according to the European guidelines. The French Health Authorities have allowed interchangeability between a biotherapy reference product and its biosimilar.
2016. Only were included the adult patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) or psoriatic arthritis (PsA) having accepted the transition from Infliximab reference product (IFXR) to its biosimilar (IFX B). For SpA patients, transition monitoring was based on the end-of-dose “wearing off” (WO) phenomenon assessment before and after the switch, disease activity score BASDAI and also the inflammatory marker CRP. Transition was considered as unsuccessful after 2 IFX® infusions with patient complain. In this case, the drug level was determined using ELISA before switching back to IFX®, and any spacing infusions because a concomitant health disorder was sought.

Results: Of the 99 patients treated with IFX® for more than 2 years, 91% (90/99) infusions because a concomitant health disorder was sought. The level was determined using ELISA before switching back to IFX®, and any spacing infusions because a concomitant health disorder was sought. Only were included the adult patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) or psoriatic arthritis (PsA). Fourteen patients (12 SpA, 2 RA) didn’t reach the 3rd IFX® administration. SpA patients reported the occurrence of arthralgia (12/12) and a partial (8/12) or total (4/12) efficacy loss. Only 5 patients reported a 2 point-increase or more regarding the BASDAI score, and only 3 patients had an increase in the CRP level (in Table 1). Except for P1, the efficacy loss was associated in each case with WO phenomenon already reported before the transition (8/12) or undetectable IFX® level (3/12). For these 3 last patients, the IFX® drug administration rate was increased by at least 2 weeks than usual because of a concomitant infection.

Table 1: SpA patients discontinued IFX® outcomes

<table>
<thead>
<tr>
<th>SpA patients</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
<th>P5</th>
<th>P6</th>
<th>P7</th>
<th>P8</th>
<th>P9</th>
<th>P10</th>
<th>P11</th>
<th>P12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Partial or total efficacy loss</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>CRP</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
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<tr>
<td>Existing WO</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Undetectable IFX level</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
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<tr>
<td>Spacing infusions</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</tr>
</tbody>
</table>

Conclusions: This observational study showed a transition failure rate at 16% (76/99) in global, which reached 23% (12/53) if limited to SpA. All SpA patients with supposed transition failure reported either a disease escape beforehand or a concomitant infection requiring to spacing infusions. In order to complete these results, an anti-IFX antibodies monitoring is in progress to so highlight any IFX activity loss. Any failure observed with the transition would be actually more complex than the presumably inefficacy of the biosimilar IFX® especially for SpA patients. So, it seems difficult to assess robustly the inefficacy of the transition to IFX® in SpA patients only according to patient complain. References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5869

Spondyloarthritis - clinical aspects (other than treatment)

**AB0709 THE RELATIONSHIPS BETWEEN THORACIC REGION INVOLVEMENT AND FUNCTIONS OF UPPER EXTREMITY, SCAPULAR KINEMATICS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: PILOT STUDY**

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that mainly affects the axial skeleton. As the disease progresses, increased thoracic kyphosis can be seen in these patients. Because of increase in thoracic kyphosis, the orientation of the scapula on the thorax and thus the functions of upper extremity may change.

Objectives: The aim of the study is to investigate the relationships between thoracic region involvement and functions of upper extremity, scapular kinematics in patients with AS.

Methods: Fifteen (15) patients with AS and eleven (11) healthy control were participated in the study. Thoracic kyphosis angle and shoulder range of motions were assessed by using digital inclinometer, scapular and shoulder muscle strength were assessed by using digital dynamometer. Three dimensional (3D) scapular kinematics were assessed by using electromagnetic tracking system, disability level of upper extremity was assessed by Turkish Version of Disability of Arm, Shoulder and Hand Questionnaire (DASH-T). Spearman correlation coefficient, Pearson correlation coefficient, Mann-Whitney U Test and Independent Sample T-Test were used for statistical analysis.

Results: DASH-T, thoracic kyphosis angle, shoulder abduction, internal rotation, external rotation of dominant side, shoulder abduction, internal rotation of non-dominant side, anterior deltoid, middle deltoid, serratus anterior, downward trapezius muscle strengths of dominant and non-dominant side, upward rotation of scapula during 30.60.90 degrees humeroracohal elevations at sagittal plane, and anterior deltoid, middle deltoid, serratus anterior, muscle strength of dominant and non-dominant side showed significantly differences between two groups. Thoracic kyphosis angle showed correlations with DASH-T (p<0.05, r=0.619), shoulder flexion, abduction, internal rotation, external rotation of dominant side (p<0.05, r=0.687), middle deltoid (p<0.05, r=0.657), p<0.05, r=0.599) and shoulder flexion, abduction, internal rotation of non-dominant side (p<0.05, r=0.858). P<0.05, r=0.805), (p<0.05, r=0.791), (p<0.05, r=0.691), (p<0.05, r=0.877). (p<0.05, r=0.796), (p<0.05, r=0.884), (p<0.05, r=0.724), (p<0.05, r=0.673). Correlations between thoracic kyphosis angle and anterior tilt of scapula during 90 degree humeroracohal elevations at sagittal plane of dominant side were obtained (p<0.05, r=0.522).

Conclusions: Scapulohumoral joint biomechanics and functions of upper extremity were affected by kyphotic posture in patients with AS. One of the most important causes of biomechanical impairment in AS patients is the deterioration of scapular kinematics with kyphosis. For preventing functional impairment, treatment programs should be supplemented with scapular kinetic exercises.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4823

**AB0710 REVIEW OF PREGNANCY OUTCOMES IN SPONDYLOARTHROPATHY IN A UNIVERSITY TEACHING HOSPITAL**

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Background: Spondyloarthropathy (SpA) is a chronic inflammatory condition of the spine affecting mainly the male population however the incidence amongst the female population is increasing. The peak incidence of SpA is in the reproductive age group. There has been a lack of focus on pregnancy in SpA as compared to other autoimmune condition such as Lupus and Rheumatoid arthritis, but this is changing. There is a paucity of information (1) on fertility and pregnancy outcomes in this condition compared to other diseases and this may lead to inequality in healthcare delivery.

Objectives:

• To review the pregnancy outcomes in women with SpA in our unit
• To review ankylosing spondylitis activity during pregnancy
• To improve the quality of care in this group of patients by developing local pathways and appropriate MDT involvement

Methods: This is a retrospective case review of pregnancies in women with SpA booked at a large tertiary teaching hospital over three years between January 2014 and December 2016. We have an annual delivery rate of 11,000 maternities. The maternity electronic database and clinic diaries were used to identify the cases. A standardised proforma was used to collect and collate the data for demographics, pre pregnancy counselling, disease activity and pregnancy outcome.

Results: Six pregnancies were identified in the study period. All patients were under the care of a Rheumatologist. The maternal age range was between 28 and 35 years. The BMI ranged between18 and 37. Ethnicity included 5 caucasian and one Asian woman. Five women had previous pregnancies and one was in her first pregnancy. Two of the multiparous women had previously delivered by caesarean section. Three of the six women suffered from anxiety and/or depression and one had antiphospholipid syndrome. Two of the patients were not on any medcations at the time of pregnancy and didn’t require any during pregnancy. Four women needed various analgesics and one patient was on sulfasalazine but stopped this at 5 weeks’ gestation. NSAIDs was stopped in 3 women after confirmation of pregnancy. One patient who was on Anti TNF therapy discontinued the drug preconception. We observed 50% attended specialist maternal-fetal medicine and anaesthetic services. One patient saw a physiotherapist and accessed hydrotherapy during pregnancy.

Two of six patients delivered preterm (<37 weeks) and 4 delivered at term (>37 weeks). Of the preterm deliveries, 1 went into spontaneous, labour not related to disease flare and the other was delivered electively for fetal concerns. All the women delivered by caesarean section. One was planned as an elective caesarean for maternal request due to difficulty abducting legs. All the remaining caesarean deliveries were for obstetric indications not related to SpA.

Conclusions: This small observational case series did not highlight any worsening SpA disease activity or poor pregnancy outcome. Further larger studies are required. However a care pathway for managing this group of patients would help to standardise the care during pregnancy. A multidisciplinary approach is essential to optimise the quality of care for these patients.
AB0711 REVIEW OF MANAGEMENT OF HLA B27 POSITIVE UVEITIS PATIENT ATTENDING A TERTIARY HOSPITAL – HOW GOOD ARE WE?

B Kapoor1, K Periyasamy1, M Babington1, A Moorthy1, B. Kapoor1

Objectives:

• To assess the ophthalmologist practice in evaluating patients with AAU for inflammatory back pain or other Rheumatological diagnoses.
• To identify the number of HLA B27 requests made for uveitis patients.
• To identify the referral rate of HLA B27 uveitis patients to Rheumatologists for evaluation.

Methods:

We conducted a retrospective pilot study to assess all patients with AAU presenting over a period of one-week to our busy teaching hospital eye casualty which serves over one million population. All patients with iritis were identified from eye casualty records and medical case notes were obtained. A standard proforma was designed and piloted with few case notes initially. Modified proforma was subsequently used to collect the data which was collated and analysed using EXCEL spread sheet.

Results:

A total of 62 patients (n=62) with AAU presented to eye casualty over a one-week period. Case notes of 49 patients could be procured. Majority of the patients were Caucasians (n=35) while the rest were Asians (n=12) and blacks (n=2). Sex ratio was nearly equal with 25 patients being males and the rest were females. Most of our patients’ age ranged between 20 to 60 years. 60% patients had a history of recurrent iritis. Out of these 9 patients had bilateral uveitis and 14 were unilateral. In 6 patients, the laterality was not documented. A history for spondyloarthropathy was elicited in only 14 patients by the ophthalmologist at the time of initial assessment. Out of these 14 patients inflammatory back pain history was positive in 10 patients. Only 17 out of 62 (27%) patients had HLA B27 checked and it was noted to be positive in 5. Among the 5 HLA B27 positive patients 2 patients were referred to rheumatology whereas 2 patients were already under rheumatologist.

Conclusions: We observed that there is a clear lack of understanding in eliciting effective rheumatology history in patients with recurrent anterior uveitis and requesting HLA B27 appropriately. Therefore, a need for a clear pathway for managing patients presenting with recurrent uveitis and HLA B27 positivity for evaluation of Inflammatory back pain. Clear local guidelines and pathway need to be developed to provide effective care. Good communication between the Ophthalmologist and Rheumatologist is key in early diagnosis and effective management of this deforming condition.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3842

AB0712 CLINICAL CHARACTERISTICS OF SPONDYLARTHROPATHIES (SPA) WITH AND WITHOUT PERIPHERAL ENTEHESITIS – DATA FROM THE DESIR COHORT

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Background: Peripheral enthesitis, mostly in the lower limbs, is a major feature of spondylarthropathies. Its prevalence is highly variable depending on the population studied, estimated between 10% and 70%. The probability to develop a peripheral enthesitis over time and the factors associated with it are mostly unknown.

Objectives: The aims of the present study were: 1) To describe the prevalence and characteristics of peripheral enthesitis in early axial SpA population, at the inclusion in the DESIR cohort; 2) to estimate the incidence of peripheral enthesitis over time; 3) to determine the factors associated with the presence of peripheral enthesitis.

Methods: We used data from the DESIR cohort, a prospective multi-center, longitudinal French cohort of 708 patients with inflammatory back pain suggestive of early axial SpA (~3 years since axial symptoms onset). We performed a descriptive analysis to evaluate the prevalence and characteristics of the peripheral enthesitis at time of inclusion (location, number of entheses, and mean time between first entheses and axial symptoms). We also estimated the incidence of peripheral entheses over a follow up period of 80 months, using Kaplan-Meier curves. Finally, we determined the baseline characteristics associated with the presence of a peripheral enthesis by multivariable analysis (logistic regression, including the variables significantly associated in the univariable analysis).

Results: At inclusion, 399 patients (56.4%) had peripheral enthesis in their past medical history. The locations were mainly the plantar fascia (212/395, 53.7%) and the Achilles tendon (152/395, 38.5%). Seventy-seven (19.4%) of these patients developed peripheral enthesis before their axial symptoms, with a mean time interval of 773 days. During the 5-year follow-up period, 109/708 (15.4%) patients developed new peripheral enthesic symptoms, resulting in 504/708 (71.2%) patients who had presented with at least one episode of peripheral enthesitis at 5 years. Variables associated to peripheral enthesitis according to the univariable analysis were: older age, male gender, HLA B27 positivity, MRI sacroiliitis, Modified NY criteria fulfilled, presence of either anterior chest wall pain, peripheral arthritis, dactylitis or psoarisis, high BASDAI, BASFI or mean score ASAS-NSAID. Only the history of anterior chest wall pain and of peripheral arthritis were significantly and independently associated with the presence of peripheral enthesis in the multivariable analysis (Odds Ratio (OR) = 1.6 [95% Confidence interval 1.6–2.3], and OR=2.1 [1.4–3.0], respectively)

Conclusions: This prospective study highlights the high prevalence of peripheral enthesitis in early axial SpA and stresses the importance of researching any signs and symptoms of enthesitis, especially in those patients with anterior chest wall pain and peripheral arthritis.

References:


Disclosure of Interest: V. Nadon: None declared, A. Molto: None declared, A. Ethcheto: None declared, L. Michel: None declared, P. Claudepierre: None declared, D. Wendling: None declared, C. Tkaczyk Grant/research support from: This projet was partly supported by an unrestricted grant from Janssen Canada, B. Harauzi: None declared, M. Dougados: None declared

DOI: 10.1136/annrheumdis-2017-eular.4511

AB0713 UVEITIS SECONDARY TO SPONDYLARTHROPATHIES IN AN OCULAR INFLAMMATION INTERDISCIPLINARY UNIT

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Objectives: To describe the characteristics of ocular involvement in spondyloarthropathies in an ocular inflammation interdisciplinary unit.

Methods: This descriptive study include the patients with uveitis secondary to spondyloarthropathy or inflammatory bowel disease (IBD) treated by the rheumatologist from January 2012 to December 2016 in an ocular inflammation multidisciplinary unit. Demographic characteristics, aetiology, ocular involvement pattern, and systemic therapy data were collected and analysed.

Results: From 276 patients evaluated by the rheumatologist, 111 (40.2%) were uveitis secondary to systemic inflammatory diseases. Within this group, the uveitis
associated with spondyloarthritis (including also IBD) were the most frequent (68 patients, 61%). Focusing on this group, 57.4% were male with a mean age of 49±15.8 years. 73.5% were HLAB27 positive and 76% had radiologic sacroiliitis.

In 24 patients (35.3%) the diagnosis of spondyloarthritis was made after the anamnesis in the uveitis unit. The diagnosis was already known in the other cases. The spondyloarthritis subtypes are described in the table.

According to the anatomical distribution, 95.6% were anterior uveitis (AU), followed by the intermediate and posterior ones (1.5% both), 85.3% has unilateral involvement and 10.3% bilateral. Relapsing acute AU was the most frequent pattern (73.5%), followed by non-relapsing acute AU (16.2%) and chronic AU (7.4%).

27 patients (35.3%) required treatment with DMARD to achieve uveitis control. The most commonly used drugs were salazopyrine (7 patients), methotrexate (6 patients), mycophenolate (1), and in another 6 patients anti-TNF treatment was started or the previous dose of the biological was adjusted. The visual acuity (VA) was not perfect (VA<1 in both eyes) in 35% in the first collected visit. 19 patients had cataract, and 19 (13%) had ocular hypertension. Only 1 patient had bilateral ciliary macroedema. Follow-up data were available for 43 patients and VA was stable in 47%, worsening in 23% and improving in 30% (median follow-up time 23 months, IQR: 6–41).

Conclusions: Our work confirms that in spondyloarthritis the most frequent pattern of ocular involvement is relapsing acute AU. Spondyloarthritis diagnosis was made at the uveitis unit in 35% of patients. More than one-third of patients required systemic therapy for ocular involvement control. Thirty-five percent of the patients had a reduced VA, remaining stable or improving in most, during the follow-up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6521

AB0714 DIFFERENTIATING CHARACTERISTICS IN PATIENTS WITH SPONDYLOARTHRITIS WHO HAVE RECEIVED DIFFERENTS ANTI-TNF THERAPIES
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Background: The term spondyloarthritis (SpA) encompass a group of chronic inflammatory disease with predominant axial involvement. Anti-TNF therapy (AT) has collected a high patient visit. From 19 patients has cataract, and 19 (13%) had ocular hypertension. Only 1 patient had bilateral ciliary macroedema. Follow-up data were available for 43 patients and VA was stable in 47%, worsening in 23% and improving in 30% (median follow-up time 23 months, IQR: 6–41).

Conclusions: Our work confirms that in spondyloarthritis the most frequent pattern of ocular involvement is relapsing acute AU. Spondyloarthritis diagnosis was made at the uveitis unit in 35% of patients. More than one-third of patients required systemic therapy for ocular involvement control. Thirty-five percent of the patients had a reduced VA, remaining stable or improving in most, during the follow-up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6566

AB0715 DIFFERENCES IN THE CO-MORBIDITIES DESCRIBED FROM SPONDYLOARTHRITIS PATIENTS WITH OR WITHOUT CONCOMITANT FIBROMYALGIA
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Objectives: To assess the differences in the occurrence of co-morbidities from cardiovascular, respiratory, renal/urological and Central nervous systems (CNS) between patients with spondyloarthritis (SpA) not having headache as presenting symptom and those having headache as presenting symptom.

Methods: Data obtained through a questionnaire from 776 patients seen in clinic with SpA was analysed with reference to headache as symptom at presentation. From the total 776 patients 13 patients did not record an answer to the question and were hence excluded. The remaining 763 patients were divided in 2 groups: Those having headache at presentation (n=117) considered having sFM, and those not having headache at presentation (n=656).

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>No headache (n=656)</th>
<th>Headache at presentation (n=117)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>121/100 (12.3%)</td>
<td>154/117 (13.5%)</td>
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</tr>
<tr>
<td>Respiratory</td>
<td>108/117 (9.3%)</td>
<td>132/117 (11.2%)</td>
<td>0.120</td>
</tr>
<tr>
<td>Renal/urological</td>
<td>113/100 (11.3%)</td>
<td>137/117 (11.7%)</td>
<td>0.833</td>
</tr>
<tr>
<td>Central nervous systems</td>
<td>118/100 (11.8%)</td>
<td>137/117 (11.7%)</td>
<td>0.833</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>No headache (n=656)</th>
<th>Headache at presentation (n=117)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artritis</td>
<td>135/100 (13.3%)</td>
<td>165/117 (14.3%)</td>
<td>0.173</td>
</tr>
<tr>
<td>Migraine</td>
<td>122/100 (12.2%)</td>
<td>144/117 (12.4%)</td>
<td>0.833</td>
</tr>
<tr>
<td>Angina</td>
<td>109/100 (10.9%)</td>
<td>133/117 (11.4%)</td>
<td>0.235</td>
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<tr>
<td>Hypertension</td>
<td>114/100 (11.4%)</td>
<td>127/117 (11.0%)</td>
<td>0.733</td>
</tr>
</tbody>
</table>

24% of the nonresp-AT were ADA + at drug discontinuation, while only 0.7% of the AT- (resp-AT) were ADA + (p=0.001) at last visit.

Conclusions: In our cohort of patients with axial SpA, a significant improvement in BASDAI, ASDAS and ASDAS after 6 months of treatment is associated with a lower frequency of drop-out of the first AT. Moreover a lower BMI, DMARDS at baseline and absence of ADA determine a better response to AT treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6566
The data of patients with sFM were compared with the data of patients who did not report headache as a presentation symptom therefore not having FM with regards to age, disease duration, delay in diagnosis, disease activity (BASDAI) functional ability (BASFI), ESR, CRP and associated comorbidities from cardiovascular, respiratory, renal/urinary, and CNS systems. Central nervous system was evaluated by symptoms of dizziness and numbness. Independent sample T test was used to explore differences between the 2 groups and confidence intervals obtained.

Results: Table shows demographics and disease characteristics as well as differences between SpA patients presenting with headache (indicating secondary FM), and those not presenting with headache. A greater proportion of patients with SpA and headache (sFM) report cardiovascular and CNS co-morbidities. There was no significant difference noted in the respiratory or renal/urological co-morbidities amongst the 2 sub-groups.

Conclusions: A significantly higher proportion of patients described cardiovascular and CNS co-morbidities in the sFM group of SpA. No significant difference was noted in the 2 sub-groups with regards to the respiratory or renal systems.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5474

AB0716 PREVALENCE OF STRUCTURAL LESIONS TYPICAL FOR AXIAL SPONDYLOARTHRITIS IN YOUNG MILITARY RECRUTS BEFORE AND AFTER MECHANICAL STRESS

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Background: Magnetic resonance imaging (MRI) has become the imaging modality of choice in early SpA. Not only has this imaging technique proven useful in the identification of inflammatory lesions on T2 FS/T2R sequences, also structural lesions such as erosions, sclerosis, fat infiltration and ankylosis can be seen on T1 sequences. There is still ongoing debate concerning the possible inclusion of any structural lesion in the definition of a positive MRI in order to improve specificity. However, erosions and fat infiltration have also been found in respectively more than 10% and 17% of non-SpA patients on MRI of the sacroiliac joints. [1]

Objectives: To evaluate the presence of structural lesions on MRI of the sacroiliac joints (MRI-SIJ) in young, asymptomatic subjects.

Methods: Twenty-five military recruits volunteered to perform a MRI-SIJ before and after 6 weeks of physical training, of which 22 recruits underwent imaging at both time points. The MRIs were scored for structural lesions by 3 trained readers MdH, GV and TR, blinded for time sequence and clinical findings. Regarding the number of lesions a consensus was made by agreement of 2 out of 3 readers.

Results: At baseline, structural lesions were present in 36.4% (8/22) of subjects of which 5 subjects presented with at least 1 erosion, one subject with sclerosis and 3 subjects presented fatty lesions. This increased to 50% subjects (11/22) with structural lesions on MRI-SIJ after 6 weeks of mechanical stress, of which 8 subjects with at least 1 erosion, one subject with sclerosis and 3 subjects presented fatty lesions (P=0.453). The change scores for sclerosis, erosions and fatty lesions were respectively 0.0 (±0.0), 0.2 (±0.1) and 0.3 (±0.2). None of the subjects displayed ankylosis. The lesion distribution is visualized in Table1.

Table 1. Number of structural lesions in young military recruits before and after intensive training

<table>
<thead>
<tr>
<th></th>
<th>N=22</th>
<th>Baseline</th>
<th>Week 6</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sclerosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>0.05 (±0.05)</td>
<td>0.05 (±0.05)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Median (25, 75 percentile)</td>
<td>0.0 (0.0, 0.0)</td>
<td>0.0 (0.0, 0.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Erosions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>0.32 (±0.14)</td>
<td>0.55 (±0.17)</td>
<td>0.096</td>
<td></td>
</tr>
<tr>
<td>Median (25, 75 percentile)</td>
<td>0.0 (0.0, 0.25)</td>
<td>0.0 (0.0, 1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fatty lesions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>1.0 (±0.86)</td>
<td>1.3 (±1.0)</td>
<td>0.285</td>
<td></td>
</tr>
<tr>
<td>Median (25, 75 percentile)</td>
<td>0.0 (0.0, 0.0)</td>
<td>0.0 (0.0, 0.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Although not prevalent, structural lesions such as erosions, sclerosis and fatty lesions can be found in young asymptomatic subjects. However, these lesions do not seem to increase after 6 week of intense physical training.


Acknowledgements: ASAS research grant 2017.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5967

AB0717 CONDUCTION DISTURBANCES IN A GROUP OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Cardiac conduction disturbances are known to be one of the many extra-articular manifestations of Ankylosing Spondilitis but not as well related to axial spondyloarthropathies.

Objectives: Description of conduction disturbances found in a group of patients with Axial Spondyloarthropathy (AxSpa) that met ASAS criteria.

Methods: Clinical and demographic variables of 78 patients with AxSpa were registered. It included cardiovascular risk factors as well as cardiovascular adverse events. All of them had a routine electrocardiogram done which were analyzed by a cardiologist.

Results: 48 of the 78 patients were men, with a mean age of 61 with standard deviation (SD) of 14. The mean time of evolution of the disease was 23 years (SD ±16). HLA-B27 was prevalent in 54 (69.2%). The sacroiliitis was found in radiologic examination of 72 (92.2%), and 6 (7.7%) of them presented edema in magnetic resonance imaging. Other clinical traits were: 43 (55.1%) peripheric arthritis 43, 8 (10.3%) dactylitis, 33 (42.3%) enthesitis, 16 uvulitis (20.5%), 2 (2.6%) inflammatory bowel disease and psoriasis 34 (43.3%). The following cardiovascular risk factors were registered: 25 (32%) smokers, 42 (53%) hypertension, 32 (41%) dislipemia, 9 (12%) diabetes, 9 (12%) hyperuricemia and 20 (26%) obesity. 14 patients had structural cardiac (11 ischemic cardiopathy and 3 aortic valvulopathy). The electrocardiographic register showed conduction disorders in 20 patients (25.6%). The details of these findings are specified in table 1.

Table 1. Cardiac conduction disturbances in a group of patients with AxSpa

<table>
<thead>
<tr>
<th></th>
<th>N=78</th>
</tr>
</thead>
<tbody>
<tr>
<td>First grade auriculoventricular block</td>
<td>5</td>
</tr>
<tr>
<td>Second and third grade auriculoventricular block</td>
<td>2</td>
</tr>
<tr>
<td>Left anterior fascicular block</td>
<td>1</td>
</tr>
<tr>
<td>Right bundle branch block</td>
<td>2</td>
</tr>
<tr>
<td>Unspecific intraventricular conduction disorder</td>
<td>4</td>
</tr>
<tr>
<td>Bachmann intertrial conduction disorder</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusions: A quarter of our series of presented conduction disturbances in electrocardiography. The relation with disease evolution, as in Ankylosing Spondilitis remains yet to be analized.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4140

AB0718 PREVALENCE OF RISK FACTORS FOR FRACTURES IN AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW

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Background: Spinal fractures occur more than expected in axial spondyloarthritides (AxSp). However, it is not totally clear whether fracture risk depends solely on biomechanical problems of the spondyloarthritic spine or whether the prevalence of risk factors for fracture is larger than expected in these patients.

Objectives: To describe the prevalence of risk factors for osteoporotic fractures (both axial and peripheral) in AxSp.

Methods: A systematic literature search was conducted. Medline, Embase and Cochrane Library databases were searched with a sensitive strategy including type of study and synonyms of AxSp. All contemporary cross sectional studies or baseline results from representative cohorts of AxSp published between January 2006 and 2016 were selected for detailed review. Only studies that fulfilled a minimum quality for survey data were included. Data on bone mineral density, prevalence of osteoporosis, and risk factor for fractures in AxSp patients were collected.

Results: After screening 3597 titles and abstracts, only 43 studies (34 cross-sectional, 3 prospective and 6 retrospective) were reviewed in detail. Of these, 20 studies compared AxSp patients with a control group, either healthy individuals (17 studies) or subjects with other diseases (6 studies). Reported prevalence of osteoporosis varied from 2% to 39.6%. Alcohol intake (58–61%), use of corticosteroids (11.7–87%), and 25-OH vitamin D deficit (25–76%) were unexpectedly high in AxSp patients. All other factors were within expected frequencies for a not too old population.

Conclusions: Our systematic review found that alcohol intake, steroid use and 25-OH vitamin D deficit should be taken into account when assessing comorbidity in AxSp in order to avoid excess fractures.

Acknowledgements: this project was funded by Merck Sharp & Dohme of Spain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3539
AB0719 BASELINE CHARACTERISTIC OF NEWLY DIAGNOSED PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SINGLE CENTRE LITHUANIAN COHORT

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Background: The prevalence rates for spondyloarthropathies has been investigated in an epidemiological study in Lithuania (1), but no studies are analysing the demographics, clinical characteristics of SpA in Lithuania. Changes in spondyloarthritides (SpA) concept and application of the new criteria for classification should improve spondyloarthritides diagnostic standards in routine clinical practice.

Objectives: To assess demographics and clinical manifestations of firstly diagnosed axial spondyloarthritides, to compare arkyloising spondylitis (AS) with non-radiographic axial spondyloarthritides (nr-axSpA) using standardized clinical assessment tools.

Methods: In September 2014 our centre began to collect a cohort of patients with newly diagnosed axial spondyloarthritides, according to ASAS criteria. Statistical analysis was performed with SPSS 20.0. A p<0.05 was considered statistically significant.

Results: 97 patients (60 men, 37 women) have been included. All of them (100%) suffered from chronic back pain. Inflammatory back pain (according to ASAS criteria) was present in 77%, 34 (35,1%) patients already had definite radiographic changes in the sacroiliac joints (SIJ), therefore based on modified New York criteria was diagnosed. The mean age at first visit was similar: 35.5±15.7 (AS) versus 33.5±14.0 (nr-axSpA). BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) was significantly less in AS group (mean 106.6 months in AS versus 44.8 months in nr-axSpA). The prevalence of HLA-B27 was similar: 74.6% vs 91.2% for nr-axSpA and AS, respectively. There were more males in AS group (76.5% vs 54.0%, p<0.05). The frequency of clinical features (peripheral arthritis, dactylitis) and extra-articular manifestations (enthesitis, uveitis, psoriasis, inflammatory bowel disease, preceding infection) was similar between the two subgroups (p>0.05).

Mobility was slightly more impaired in AS patients, but it did not reach a significant level.

No differences in the level of global pain, patient’s global assessment were found. BASDAI did not show the significant difference between AS and nr-axSpA (mean 4.5±2.1 vs 3.9±2.0), as well CRP (mean CRP 17.3±19.0 vs 17.5±17.0), due to the fact that ESR.

Conclusions: Diagnosis of axial SpA in Lithuania remains delayed. The proportion of patients with AS among newly diagnosed axial SpA is high. There are more women in the nr-axSpA group. Both groups do not differ regarding clinical features, disease activity.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6944

AB0720 CHARACTERISTICS OF TUNISIEN SPONDYLOARTHRITIS PATIENTS WITH HIP DISEASE

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Background: spondyloarthritides (SpA) is characterized by inflammation of spine and sacroiliac joints. Hip involvement is the most frequent extra spinal arthritic manifestation of SpA and may lead to a worse functional outcome.

Objectives: The objective of this study was to assess clinical, biological and radiological characteristics of SpA patients with hip disease.

Methods: This is a transversal multicenter study, including SpA patients (satisfying ASAS criteria2009) with hip disease. Demographic, clinical, radiographic, and laboratory data were collected and analyzed. Radiographic forms of hip disease were assessed according to Netter classification (early, condensing, destructive, and synostosante forms). Radiographic severity was assessed by the modified Stokes Ankylosing Spondylitis Spine Score (mSASSS) and BASRI (Bath Ankylosing Spondylitis Radiologic Index).

Methods: Patients with hip disease were enrolled. In all patients, X-ray of both hips was performed. The presence of mSASSS and BASRI were calculated.

Results: Ninety-five patients were evaluated (77men). The mean age was 41.53±1.97 years. The median age at disease onset was 26.23±10.29 years. The mean disease duration was 6.48 years. 46% of patients were smoker. HLA-B27 was positive in 50% of cases. A peripheral joint involvement was found in 33% of cases. Extra-articular manifestation was seen in 57% of patients: uveoprosis (16 patients), uveitis (15 patients), psoriasis (10 patients), chronic inflammatory bowel disease (12 patients). 5% of patients had bilateral hip involvement and 147 hips were evaluated. The median BASDAI and BASFI scores were respectively 5.4 and 5.5.

The mean index of severity for osteoarthritis for the hip (ISH) was 12.24 (±6.84). Patients had an early form of hip disease in 22% of cases. Condensing form was in 3% of cases, combined forms in 22% of cases and destructive form in 53% of cases. The mean mSASSS score was 15.34±16.22.

Conclusions: Our finding confirm previous observation that clinical and radiological hip involvement is associated with a more severe disease with a high activity and pronounced functional impairments.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5099

AB0721 THE EVALUATION OF ULTRASONOGRAPHIC AND CLINICAL ENTHESOPATHY IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: Enthesitis is considered as the primary anatomical lesion in spondyloarthropathy (SpA) but it can be seen in other rheumatic diseases. Its locations and clinical relationships have not been studied well in the literature.

Objectives: We aimed to investigate the frequency of ultrasonographic, clinical enthesopathy and the relationship between enthesopathy and disease activity, functional status in patients with rheumatoid arthritis (RA) and axial SpA.

Methods: Thirty three axial SpA, 21 RA patients and 30 healthy subjects were included in the study. The clinical and functional evaluations relied on the BASDAI, BASFI, ASQoL, DAS28, and HAQ, and on aVAS for enthesal pain, as well as on the RMDQ. Knee, ankle and elbow were examined with US bilaterally in 172 joint regions.

Results: The physical examination scores for enthesis were 1.97±2.68, 2.43±1.80, 0.23±0.12 in axial SpA, RA and healthy subjects, respectively. There was a significant difference between axial SpA and RA about enthesitis physical examination scores (p=0.123). A statistically significant difference was not found between axial SpA and RA in quadriceps tendon enthesis and distal patellar ligament enthesis according to MASEI index (MASEI 3.45, p=0.993, p=0.124, p=0.652). Other MASEI enthesis scores were statistically higher in axial SpA group than RA and healthy subjects (p<0.008). Positive correlations were found between BASDAI scores and enthesis pyhsical examination scores, MASEI total scores (p=0.739, p=0.0001, p=0.516, p=0.002).

Conclusions: Ultrasonographic enthesis was associated with impaired quality of life in axial SpA. MASEI 1 and 2 was specific enthesal regions in MASEI index for axial SpA. Different from RA, the calcaneal enthesis region for clinical investigation and ultrasonographic enthesisopathy should be focused on in axial SpA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6834
Results: 92 primary care practices were randomized. 679 patients participated (64% women, mean age 36.2 years (SD7.5) and median CLBP duration 9 years (IQR 4–15 years). 333 patients were randomized to the intervention group, both groups had similar characteristics at baseline. Sixty percent of participants had a positive referral rule. RMDQ scores are shown in table 1. Sub scores are shown for patients with a positive outcome of the referral rule (PRP) and a negative outcome of the referral rule (NRR). The change in RMDQ score after 4 months in the intervention group was -0.74 (95% confidence interval (CI) -1.31 – -0.18) and in the control group -0.46 (95% CI -0.98 – 0.05). There was no significant difference between groups.

Conclusions: Compared with usual care, use of the CaFASpA referral rule in CLBP patients in a primary care setting did not significantly impact disability in these patients, 4 months after a referral advice was made. Results after 12 and 24 months should be awaited before definitive conclusions about the impact of the CaFASpA referral rule for axSpA in CLBP patients can be made.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6041

AB0723 TECHNICAL AIDS AGREED AMONG SPECIALISTS FOR THE MANAGEMENT OF COMORBIDITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: THE GEOCAO PROJECT

C. González 1, R. Curbelo 2, J.C. Torre-Alonso 3, E. Collantes 4, S. Castañeda 5, M.V. Hernández 6, A. Urruticoetxea-Aranza 7, J.C. Nieto 8, J. García 9, M.A. Abad 10, J. Ramírez 11, J.C. Torre-Alonso 12, R. Dalmáu 13, M.D. Martín-Amor 14, L. Leon 15, J.C. Hermosa 16, J.C. Obaya 17, T. Otón 18, L. Carmona 19, 1 Rheumatology, HU Gregorio Marañón; 2 InMuse, Madrid; 3 Rheumatology, HU Monte Naranco, Oviedo; 4 Rheumatology, HU Reina Sofia, Córdoba; 5 Rheumatology, HU la Princesa, IIS-IP, Madrid; 6 Rheumatology, HU Clinic i Provincial, Barcelona; 7 Rheumatology, H U Can Misses, Ibiza; 8 Rheumatology, HU 12 de Octubre, Madrid; 9 Rheumatology, H U de Plasencia, Plasencia; 10 Internal Medicine, HU la Princesa, IIS-IP; 11 Cardiology; 12 Gastroenterology, HU la Paz; 13 Psychology, UCJC, Madrid; 14 Centro de Salud Ciudadanos, Getafe; 15 Centro de Salud Alcobendas, Alcobendas, Spain

Background: The management of comorbidity in patients with axial spondyloarthritis (AxSpA) needs improvement; the implementation of clinical practice guidelines is still deficient and heterogeneous.

Objectives: To prioritise comorbidities in AxSpA and to elaborate practical aids for their identification and follow-up.

Methods: A multidisciplinary panel [10 rheumatologists (6 experts in AxSpA), 2 family doctors, 1 internist, 1 cardiologist, 1 gastroenterologist, 1 psychologist and 3 methodologists] prioritised, in a discussion group, a list of comorbidities based on frequency and impact. Each comorbidity was discussed largely and systematically. A list of items was prioritised, in a discussion group, a list of comorbidities based on frequency and impact. Each comorbidity was discussed largely and systematically. A list of items was prioritised, in a discussion group, a list of comorbidities based on frequency and impact. Each comorbidity was discussed largely and systematically.

Conclusions: These checklists are intended to facilitate the systematic evaluation of co-morbidity associated with AxSpA, thus allowing an earlier detection and better control and management of these patients by the rheumatologist.

Table 1. Estimated RMDQ scores with linear mixed effects regression model in young chronic low back pain patients by application of the CaFASpA referral rule versus usual care

<table>
<thead>
<tr>
<th>RMDQ at baseline</th>
<th>RMDQ after 4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of referral rule, mean (95% CI)</td>
<td>0.38 (0.38–0.51)</td>
</tr>
<tr>
<td>PRP†, mean (95% CI)</td>
<td>0.51 (0.56–0.64)</td>
</tr>
<tr>
<td>NRR, mean (95% CI)</td>
<td>0.77 (0.68–0.86)</td>
</tr>
<tr>
<td>Use of care, mean (95% CI)</td>
<td>0.61 (0.53–0.69)</td>
</tr>
<tr>
<td>PRP†, mean (95% CI)</td>
<td>0.68 (0.56–0.79)</td>
</tr>
<tr>
<td>NRR, mean (95% CI)</td>
<td>0.73 (0.62–0.77)</td>
</tr>
</tbody>
</table>

There were no significant differences between use of the referral rule and usual care; RMDQ–Rahmed Morán’s Disability Questionnaire; †Not positive referral rule, table below normal reference.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5325
AB0725 USING A REDUCED JOINT COUNT IN MEASURING DISEASE ACTIVITY IN PSORIATIC ARTHRITIS, IS IT LEGIT?

M. Vis1, K. Wervers2, I. Tchetverikov3, A. Gerards 4, M. Koek5, C. Appels6, K. Wervers2, I. Tchetverikov3, A. Gerards 4, M. Kok5, C. Appels6.

Newly diagnosed PsA patients were included in the Dutch Early Methods:

Objectives: To evaluate the effect of using a 28, 44 or 66/68 joint count on Minimal Disease Activity (MDA).

Methods: Newly diagnosed PsA patients were included in the Dutch Early south-west Psoriatic Arthritis Registry (DEPAR) study between August 2013 and January 2017. Joint scores at baseline and 6 months were calculated using a 28, 44 and 66/68 joint count. Consequently MDA was calculated using each of these joint counts. MDA is defined as minimal disease activity in 5 out of 7 domains (swollen joints, tender joints, PASI, patient vas pain, patient vas global, HAQ, emotional state).

Results: In total, 413 patients were included into the study, of which 320 had reached 6 months follow-up at the time of this abstract. Half of the patients were male (49%), and mean age was 50 years (SD 13.8).

The percentage of patients with at least one involved joint (swollen or tender) at baseline decreased from 91% using the 66/68 score to 86% with 44 joints and then to 80% with a 28 joint count (Table 1). At 6 months these scores were 66% 63% and finally 56% respectively for the 66/68, 44 and 28 joint count. After 6 months, 96 patients (30%) had achieved MDA using the original 66/68 joint count. Using a 28 joint count, 10 more patients (10% of the MDA population) were classified as having achieved MDA.

Table 1. Joint scores and MDA at baseline (n=421) and 6 months (n=320) using 66/68, 44 and 28 joint counts in a population of newly diagnosed PsA patients

<table>
<thead>
<tr>
<th>Joint Count</th>
<th>T0</th>
<th>T6</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMA</td>
<td>66/68</td>
<td>66/68</td>
</tr>
<tr>
<td>Swollen joint</td>
<td>44</td>
<td>44</td>
</tr>
<tr>
<td>Tender joint</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>MDA (%)</td>
<td>56 (14)</td>
<td>65 (16)</td>
</tr>
</tbody>
</table>

Conclusions: Using reduced joint counts in PsA misclassifies around 10% of patients as having no joint involvement. It also misclassifies about 10% of the MDA population of having achieved MDA while they have not. Full 66/68 joint counts remain recommended for measuring disease activity in PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6851

AB0726 SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Systemic inflammatory response of various autoimmune diseases has been reported as a cause of accelerated atherosclerosis which is a risk factor for cardiovascular complications.

Objectives: This study aimed to evaluate atherosclerosis in patients with ankylosing spondylitis (AS) and its relation to disease activity.

Methods: The study was carried out on thirty AS patients, who fulfilled the modified New York criteria. Thirty apparently healthy normal volunteers, age and sex matched served as control. Complete History taking, General and systemic examination, Body mass index (BMI), Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI), lipid profile, inflammatory markers and serum glucose level were done. Based on BASADI score, patients were then classified to active and inactive groups comprised 11 patients (37%) and 19 patients (63%) respectively. Carotid intima-media thickness (CIMT) was measured using real-time gray-scale sonography. The intima-media thickness (IMT) of common carotid artery, carotid bulb and internal carotid artery was determined.

Results: 25 males (83.3%) and 5 females (16.7%) with mean age 39.1±12.38, their mean disease duration 13.13±8.03 while controls were 21 males (70%) and 9 females (30%) with mean age 39.7±12.6.

While IMT was found significantly increased in patients (0.87±0.49) versus controls (0.5±0.12) (P<0.001), there was no significant difference regarding the presence of plaques and there was no stenosis found in cases or controls. No significant difference was found between active and inactive cases as regard to components of lipid profile. The mean IMT in active and inactive cases was 0.76±0.11 and 0.72±0.17 respectively with no significant difference, we found no significant correlation between IMT and different disease scores, ESR or CRP.

Conclusions: AS patients have a higher risk for developing atherosclerosis. IMT of common carotid artery could be added as a further investigation for detection and follow up of atherosclerosis in AS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3439
RHEUMATIC MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASES, STUDY FROM MIDDLE EAST

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Background: Musculoskeletal symptoms accompanying the diagnoses of Inflammatory bowel diseases (IBD), are seen in 6-46% of cases.

Objectives: The goal of this study is to examine the prevalence of rheumatic manifestations among patients diagnosed with IBD.

Methods: Between 1/2/2015 and 30/7/2016 all consecutive IBD patients were approached. A total of 127 adult patients signed the consent form. The diagnosis and the clinical course of inflammatory bowel disease (IBD) of Crohn’s or Colitis (UC) had to be confirmed by a colonoscopy and histopathology. Patients were then interviewed and examined by one of two expert rheumatologists. A set of questions were used, complete rheumatological examination, X-rays of the lumbosacral and SI joints, and HLA-B27 test were done.

Results: Among our sample; 66% were Arabs and 34% are Asians. 58.3% were males, 52% fell in the age category of 30–49 years, 83.1% were married, 25.6% had a graduate degree, 36.5% had a history of smoking, and 15.2% had a family history of IBD.

In our study, it was seen that 36.9% had Crohn’s disease, and 64% had ulcerative colitis.

Any type of rheumatic manifestations were present in 57.5% with no significant differences between the the two types of IBD diseases (p>0.05).

The majority of these patients had peripheral manifestations (arthritis, arthralgia, enthesitis) (43.3%), while only 3.1% had axial alone, and 11% had both types. Among those with peripheral manifestations; 7.2% had type 1 arthritis (Psoriatic), while 1.4% had type 2 arthritis (Polyarticular).

There were no significant differences between the two types of IBD diseases in regards to the presence of peripheral manifestations (p>0.05).

However, the two diseases were significantly different in the presence of axial manifestations as more people with Crohn’s have axial manifestations. Combined with Ulcerative colitis (12.3%). Those with Crohn’s had more people with rheumatic manifestations 4–7 years before the diagnosis of IBD. HLA-B27 was positive in 5 patients with Crohn’s and 2 with ulcerative colitis.

Logistic regression analysis of the data did not reveal any significant predictor or potential risk (type of IBD, gender, age group, BMI, smoking, family history, duration or extent) for the development of musculoskeletal manifestations in our patients.

Conclusions: In this study of musculoskeletal manifestations of patients with IBD from the Middle East 57.7% of them have any rheumatic manifestations. Peripheral manifestations occurred in 43%, axial alone in 3.1%, axial and peripheral manifestations in 11.5%, type 1 arthritis in 7.2% and type II in 1.4%. More patients from the Middle East 57.7% of them have any rheumatic manifestations. Peripheral manifestations in our patients.

Disclosure of Interest: None declared.

References:

SPONDYLOARTHRITIDES AND ITS RESPONSE TO ANTI-RHEUMATIC DRUGS

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Background: Spondyloarthritis is associated to accelerated atherosclerosis, possibly due to chronic inflammation and lipid metabolism disturbances. Circulating lipoprotein function may be more important than concentration. In particular, cholesterol efflux capacity (CEC) of high density lipoproteins (HDL) opposes foam cell formation and cholesterol esterification, which in turn represents a cardiovascular risk.

Objectives: Our aim was to compare CEC and CLI in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA). We also aimed to evaluate CEC and CLI modulation upon anti-rheumatic therapy and their relationship to lipid profile levels.

Methods: Patients with AS (n=24) and PsA (n=36) were from the observational PSARA study. Treatment was: anti-TNF agents for AS; MTX alone or in combination with an anti-TNF agent for PsA.

Results: Serum was drawn before, after 6 weeks and after 6 months of anti-rheumatic therapy to measure CEC with a validated cell model (radioisotopic technique to measure % cholesterol efflux on total cell cholesterol) and CLI with a macrophage model and fluorometric measurement of cell cholesterol.

Conclusions: At baseline serum LDL and total cholesterol were higher in PsA than in AS patients. LDL, total cholesterol and HDL increased after treatment in AS, but not in PsA. In AS, CEC increased after 6 weeks of treatment (4.9±0.3 vs. 5.5±0.3, 95% CI: −1.09 to −0.03, p<0.05), in parallel with HDL serum levels. In PsA, CEC did not differ between any of the time points.

Cqc did not change with treatment in AS nor in PsA, but was overall higher in PsA than in AS patients. Despite the LDL serum level increase in AS, after 6 months of treatment the difference between CLC in PsA and AS was the most significant (34.0±1.8 in PsA vs 27.8±1.5 in AS, CI 95%: 3.28 to 6.67, p<0.05). In addition, after 6 months of therapy the correlation of CLC with LDL levels, present before treatment, was lost in the AS group. In the PsA group CLI did not correlate with LDL serum levels at any time point.

References:

BENEFITS OF ADDITIONAL SPINAL MAGNETIC RESONANCE IMAGING COMPARED TO SACROLIAC JOINTS IMAGING ALONE IN THE DIAGNOSIS OF Spondylarthropathy

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Background: Axial spondyloarthritis (AxSpA) is a chronic inflammatory condition predominantly involving the axial skeleton including the spine and sacroiliac joints. Magnetic resonance imaging (MRI) demonstrates inflammation and structural changes in patients with both ankylosing spondylitis and non-radiographic (nrAxSpA) forms of SpA and has become widely used in diagnosing SpA.

Objectives: To determine the additional diagnostic benefit of including limited spine MRI in the whole spine imaging with SU MRI to SU MRI alone in patients with suspected SpA.

Methods: MRI scans performed for suspected SpA over twelve months from November 2015 to November 2016 were reviewed retrospectively (n=203).

Results: MRI scans from 203 patients with suspected SpA were reviewed. 81 (40%) were male and 122 (60%) were female. The age range was 13 to 78 years (mean ±41). 130 (64%) were less than 45 years of age. 157/203 (77%) patients had inflammatory changes involving both SpA and Spine and 4/43 (9%) had spinal inflammatory changes only with normal SIJs (Table 1). In these four patients the sacro-iliacum spine was involved. In HLA-B27 positive patients (n=46), 25 (54%) had a positive MRI.

Conclusions: The majority of patients with SpA can have their diagnosis confirmed on SU MRI. However a proportion of patients (9%) had spinal changes only. Additional spinal MRI has been shown to increase the diagnostic yield for axial spondyloarthritis in our cohort.

References:
In AS, CEC improved significantly during anti-TNF therapy, probably due to increase in anti-atherogenic HDL. Despite the LDL increase associated with the anti-TNF therapy in AS patients, CLC stayed constant, standing against a hypothetical pro-atherogenic effect of such LDL increase. These data may be useful for atherosclerosis prevention and treatment with tailored strategies for AS and PsA patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5776

AB0731 OVERCOMING THE PROBLEMS OF UNTRANSLATABILITY: A MOBILE PHONE APPLICATION IN THE EXAMPLE OF TURKİSH VERSION OF BASDAI

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Background: Patient-reported outcomes (PROs) are important in monitoring and making treatment decisions. Recently, we reported that the translation of “tender points” in the fourth question of the Turkish version of BASDAI was not correctly understood, and replacing this question with an enthesis examination (BASDAI-Q4) decreased the score (ΔBASDAI-Q4:p<0.0001, 95CI:0.54–1.44).

Objectives: We report here the results of an investigator initiated clinical trial using a self-developed mobile phone application (MPA) to overcome the problem of untranslability.

Methods: Out of 135 invited 95 axSpA patients participated. Initially, BASDAI self-report forms (BSRF) were administered. Thereafter, patients were randomized into two groups and completed a second set of BSRF after using the MPA with embedded videos defining terms and grading for each domain. Group B completed a second set of BSRF under guidance of an inexperienced family physician (FP). A third set of BSRFs were completed by Group B with the same FP after going through the MPA. Afterwards, an enthesis examination (EE) was performed by a blinded rheumatologist and patients graded enthesis pain between 0–10. Standard Q4 was replaced with the EE scoring (BASDAI-Q4). Patients older than 45 years of age were excluded.

Results: Fifth three male (%55.7) and 42 female (%44.3) patients, with a mean age ±SD at the onset of the disease was 41.3±12.4 years. Non-radiographical axial disease (21.1%) 12 years (SD=8.7) were studied. Sixty-four and 31 patients were randomized to Groups A and B, respectively. Nine patients reported the Q4 as “not understood.” 32 patients had no enthesis on EE, but of those only 21 scored “0” for Q4 during the unassisted PRO. Eleven reporting no enthesis had so on EE.In Group A, 9 patients reported enthesis after MPA assistance and four had enthesis at the final EE. Nineteen patients had no enthesis on physical examination, but of those only 12 scored “0” for Q4 during the unassisted PRO, and an additional nine scored “0” for Q4 after MPA assistance. Six out of seven patients reporting no enthesis, but with enthesis on EE reported enthesis after MPA assistance. In Group B, scoring for Q4 was similar after both the unassisted- and FP’s first assistance PRO. Out of four “not understood” responders for Q4, two reported enthesis after the second assistance of FP and both had enthesis at the final EE. Six patients had no enthesis on EE, but one scored “0” for Q4 during the unassisted PRO, and an additional two scored “0” for Q4 after second FP assistance. Two out of four patients reporting no enthesis, but with enthesis on EE, reported enthesis after second FP assistance. Mean BASDAI was significantly higher in both groups than BASDAI-Q4 (Group A:3.97±1.95 vs. 2.84±1.98, p<0.0001, 95% CI:0.58–1.52; Group B:3.91±0.25 vs. 2.98±2.25, p<0.0001, 95% CI:0.48–1.31). In both groups, MPA, both patients, and FPs resulted in more reliable overall BASDAI scores with BASDAI-Q4 as the gold standard (Group A:3.05±2.25 vs. 2.84±1.98, p=0.081, 95% CI:0.71–1.45; Group B:3.21±1.87 vs. 2.98±2.25, p=0.075, 95% CI:0.01–1.63).

Conclusions: Mobile applications may improve the quality of collected data in cases of untranslatability even in previously validated PROs.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4231

AB0732 SPONDYLOARTHRITIS IN THE DEMOCRATIC REPUBLIC OF CONGO

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Background: While spondyloarthritis (SpA) is intensively studied in the Western world, data are scarce in sub-Saharan Africa.

Objectives: To determine the spectrum of SpA in outpatients with rheumatological complaints attending two rheumatology practices in Kinshasa, Democratic Republic of Congo.

Methods: A descriptive cross-sectional study over six months (December 1st, 2010 until May 31th, 2011). We included consecutive patients attending to the two rheumatology practices of Kinshasa; diagnosis was based on the Amor or the ESSG criteria, and a clinical evaluation by a rheumatologist. Sacroiliac joint radiographic lesions were scored with the modified New York criteria. BASDAI and BASFI were evaluated in axial SpA.

Results: One hundred five patients (10.7%) were diagnosed among 984 rheumatologic outpatients with a sex ratio (male to female) of 1.4. The average age at the onset of the disease was 41.3±12.4 years. Non-radiographical axial spondyloarthritis was the most frequent subtype (49.8%) followed by reactive arthritis (25.0%). Other subtypes were: ankylosing spondylitis (1.02%), psoriatic arthritis (0.1%), SAPHO syndrome (0.1%) and IBD associated arthritis (0.1%). Mean BASDAI and BASFI in axial SpA were 42.7±100 and 46.4±100 respectively.

Conclusions: These data may be useful for atherosclerosis prevention and treatment with CBD and CoA clinical trials.

References:

Acknowledgements: The authors would like to thank Dr Thierry Lusienie for helping with acquisition of data from the Rheumatology unit at Provincial General Hospital Kinshasa.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4642

AB0733 ASSOCIATIONS OF SERUM OSTEOPROTEGERIN AND IL-18 CONCENTRATIONS WITH CARDIOVASCULAR RISK IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS

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Background: Inflammatory spondyloarthropathies (SpAs), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are associated with cardiovascular (CV) disorders. In both diseases cytokines of IL-17/IL-23 axis are thought to play a pathogenic role. PsA, but not AS, is usually preceded by psoriasis, suggesting contribution of skin inflammation-related cytokines to disease manifestation and CV risk.

Objectives: To search in AS and PsA patients for the association between CV risk and serum concentrations of select cytokines, i.e. of IL-17/A23 axis, IL-18 and osteoprotegerin (OPG) with skin and cardiovascular (CVD) pathogenesis, respectively.

Methods: Twenty patients with AS (15M/5F) and 18 patients with PsA (10M/8F) of similar age (meansSD: 42±7 vs 46±10 years) and disease duration (6.5±10 vs 6.1±7 years) were evaluated. A group of 38 sex and age-matched healthy volunteers was used as a control. Routine laboratory tests, i.e. measurement of serum C-reactive protein (CRP) concentrations were performed. Clinical data, including evaluation of disease activity by ASDAScore and BASDAI indices, calculation of SCORE (Systemic Coronary Risk Evaluation) index and atherogenic index (AI=total cholesterol/HDL) were collected. Serum concentrations of IL-17A, IL-21, IL-23, IL-27, IL-18 and OPG were measured by specific commercially available enzyme-linked immunosorbent assays (ELISA) and were expressed in pg/ml. The Mann-Whitney U-test was applied for intergroup comparison, and correlation was assessed using a Spearman’s Rank two-tailed test (R value is shown).

Results: Compared with control, total group of SpAs patients was characterized by significantly elevated serum concentrations of OPG (1757±852 vs 464±100 pg/ml), IL-18 (273±235 vs 164±195 pg/ml) and IL-21 (68±127 vs 20±49 pg/ml). Interestingly, while up-regulation of OPG (1517±387) and IL-18 (324±291)
EVALUATION OF CARDIOVASCULAR RISK PROFILES IN A POPULATION OF PATIENTS WITH ANKYLOSING SPONDYLITIS: A CROSS-SECTIONAL STUDY


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Background: ankylosing spondylitis (AS), like the other chronic inflammatory rheumatic diseases, is considered to have higher cardiovascular (CV) risk (1). The pathogenesis is not clearly defined.

Objectives: assess the early biological markers of atherosclerosis in Tunisian patients with AS compared with healthy controls and evaluate the relationship between systemic Coronary Risk Evaluation (SCORE) for CV-related mortality and biological markers (2).

Methods: This was a cross-sectional study conducted since June 2015 until October 2016 including patients with AS in the South of Tunisia and matched controls with sex, age group, body mass index (BMI) and smoking. Patients diagnosed with AS should fulfill the modified New York criteria. For patients and controls, we measured total cholesterol (TC), high density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein (Apo) AI, ApoB, lipoprotein (a) [Lp(a)] and C-Reactive Protein (CRP). Low-density lipoprotein (LDL) cholesterol was calculated with the Friedewald formula. SCORE was calculated through the use of sex, age, systolic pressure, smoking and TC. Comparisons were performed using two sample t-tests for parametric values and Wilcoxon Mann-Whitney Test for non-parametric values. Correlation analyses were performed with Spearman rank.

Results: Overall 85 patients with AS and 79 controls were included. The mean age was (43.81±14.29 vs 44,27±14 years). The sex ratio (M/F) was 2/1 and the age was (43.81±14.29 vs 44,27±14 years). The sex ratio (M/F) was 2/1 and the age was (43.81±14.29 vs 44,27±14 years). The sex ratio (M/F) was 2/1 and the age was (43.81±14.29 vs 44,27±14 years).

Conclusions: Risk factors of CV disease in AS patients are similar to markers of vascular pathology and traditional cardiovascular disease risk. In addition, we showed that CRP is significantly higher in AS patients than in controls.

Disclosure of Interest: Supported by the NIHRG, Warsaw, Poland (grants No S/16 and S/2).

DOI: 10.1136/annrheumdis-2017-eular.3475

AB0735 EVALUATION OF PSYCHOLOGICAL STATE OF PATIENTS WITH ANKYLOSING SPONDYLITIS: REGIONAL REGISTRY AS A TOOL FOR IMPROVEMENT OF MANAGEMENT

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Background: According to modern conception “T2T” a patient with ankylosing spondylitis (AS) takes an active part in the disease treatment that determines the importance of his psychological state.

Objectives: To evaluate interconnection between the psychological state of the patient with AS and the disease course.

Methods: Within the regional registry which is a part of epidemiological study of clinical diversity of AS in Russian population, 40 patients (32 males and 8 females) at the age of 21 to 56 years (average age 40.3±10.0) were examined. The average disease duration on the day of examination was 12.7±9.9 years, BASDAI - 5.4±1.8, BASFI – 5.3±4.2, Functional status (range of motion) was determined by applanation tonometry by SphygmoCor, Australia. For statistical analysis we used Mann-Whitney criteria and Spirmen correlation method. The study was based on GCP principles.

Results: A total of 17 (42.5%) patients had anxiety and depression: moderate – 15 (88.2%), severe – 2 (11.8%) responders. With the disease duration of less than 5 years propensity for depression and anxiety was noted by 6 out of 11 (54.5%) patients, 5 to 10 years – 2 out of 12 (16.7%), more than 10 years – 9 out of 17 (52.9%).

Conclusions: Among the patients without limitation of motion (BASFI) anxiety and depression was revealed in 2 out of 11 (18,2%), with moderate limitation –6 out of 18 (33,3%), with severe limitation –9 out of 11 (81.8%) patients. According to BASMI 1 out of 2 patients without limitation of motion had anxiety and depression, 6 out of 19 (31,5%) – with moderate limitation and 10 out of 19 (52.6%) with severe limitation. The direct correlation was revealed between EQ-5D score and BASFI (r=0.996) and between EQ-5D and BASDAI (r=0.855), concurrently such correlation was also revealed between BASMI and BASDAI (r=0.803).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3959

AB0736 THE DATA OF CENTRAL AORTIC PRESSURE AND PULSE WAVE VELOCITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Pulse Wave Velocity (PWV) is the main determinant of arterial stiffness. In recent years the increased arterial stiffness in Ankylosing Spondylitis was shown [1]. The most of investigations of arterial stiffness in ankylosing spondylitis were performed on the treatment by anti TNF-therapy [2]. However, today this issue has not been adequately studied.

Objectives: To evaluate the data of central aortic pressure and PWV and their relationship with Ankylosing Spondylitis.

Methods: 49 patients with Ankylosing Spondylitis aged between 19 and 60 (mean age 39.6±10.6) were examined. This group (group 1) included 38 men, 11 woman. Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) was 3.1±0.55. Duration of Ankylosing Spondylitis was from 0.5 to 20 years (mean 5.8±4.76 years). X-ray stage sacroiliac joints (according Modified New York Criteria) was 2.9±1.42. The control group included 33 healthy individuals. The groups were similar in age and sex. 10 patients with ankylosing spondylitis have history of arterial hypotenison, however, at the time of inclusion in this study their blood pressure was stabilized. The groups did not differ by office blood pressure parameters and heart rate. Indicators of central aortic pressure and PWV were determined by applanation tonometry by SphygmoCor, Australia. For statistical analysis we used Mann-Whitney criteria and Sperm correlation method.

The study was based on GCP principles.

Results: Increased levels of central systolic blood pressure (118.0±14.02 vs 111.1±10.2, p=0.0001), mean blood pressure (80.2±11.86 vs 78.1±7.3, p=0.001) were determined in patients with Ankylosing Spondylitis.

Conclusions: Increased levels of central systolic blood pressure, central diastolic blood pressure, central mean pressure were determined in patients with Ankylosing Spondylitis. The relationship between clinical data, X-ray stage and PWV was demonstrated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6936
Psoriatic arthritis

AA AMYLOIDOSIS IN RHEUMATOID ARTHRITIS AND IN PSORIATIC ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 173 PATIENTS

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA), like all chronic autoimmune arthritides, may be complicated by AA amyloidosis (rAA).

Objectives: The aim of this study was to determine the prevalence and extent of AA in RA and PsA patients, and to appraise the extent of amyloid A deposits in various organs.

Methods: At the National Institute of Rheumatology 11860 patients died between 1968 and 1998; among them 161 patients with RA and 12 with PsA. All of them were autopsied. RA and PsA were diagnosed clinically according to the criteria of 1987 and 1998; among them 161 patients with RA and 12 with PsA. All of them were autopsied.

Results: The prevalence (in %) and the average extent of amyloid A deposits (absolute value) in various organs of RA and PsA patients are summarized in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Organs</th>
<th>RA-Aa</th>
<th>PsA-Aa</th>
<th>p&lt;</th>
<th>RA-Aa</th>
<th>PsA-Aa</th>
<th>p&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>48.49</td>
<td>68.18</td>
<td>0.0611</td>
<td>0.99</td>
<td>1.41</td>
<td>0.0706</td>
</tr>
<tr>
<td>Heart</td>
<td>56.97</td>
<td>38.89</td>
<td>0.0651</td>
<td>0.97</td>
<td>0.67</td>
<td>0.1065</td>
</tr>
<tr>
<td>Liver</td>
<td>19.17</td>
<td>38.89</td>
<td>0.0314</td>
<td>0.60</td>
<td>0.67</td>
<td>0.9781</td>
</tr>
<tr>
<td>Lung</td>
<td>29.80</td>
<td>15.00</td>
<td>0.0852</td>
<td>0.44</td>
<td>0.13</td>
<td>0.0002</td>
</tr>
<tr>
<td>Skin</td>
<td>10.83</td>
<td>50.00</td>
<td>0.0000</td>
<td>0.18</td>
<td>1.00</td>
<td>0.0027</td>
</tr>
<tr>
<td>Brain</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Average/Organ</td>
<td>29.21</td>
<td>35.16</td>
<td>0.332</td>
<td>0.529</td>
<td>0.645</td>
<td>0.341</td>
</tr>
<tr>
<td>Average/Patient</td>
<td>32.77</td>
<td>36.21</td>
<td>0.244</td>
<td>0.585</td>
<td>0.668</td>
<td>0.198</td>
</tr>
</tbody>
</table>

Conclusions: Based on the nearly same 0.585 versus 0.668, significantly not different: p<0.198 average amount of amyloid A deposits/patient, the immune processes (producing amyloid A deposit) of our RA and PsA patients may be similar.

The more prominent amyloid deposition in the lungs of RA patients (in contrast to PsA patients) may be associated with more frequent and pronounced pulmonary complications of RA (vasculitis, interstitial pneumonitis and fibrosis, etc.), than by PsA.

Extreme severe amyloid deposition in the skin of PsA patients may be due to local factors, namely severe systemic dystrophic changes of the skin in psoriasis.
MHAQ RESPONSE AMONG PATIENTS WITH PSORIATIC ARTHRITIS INITIATING A TNFI

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Background: Improved functional ability is among the most relevant outcomes for patients with psoriatic arthritis (PsA). The modified health assessment questionnaire (mHAQ) is one of the most commonly used patient reported outcome measures used in PsA and addresses the domains of disability and physical function.

Objectives: We examined the change in mHAQ over one year among patients with PsA initiating a TNFI and examined predictors of a clinically meaningful improvement in disability and physical function, as measured by the mHAQ.

Methods: Patients with PsA enrolled in the Corona Registry between 2005–2013 were followed from initiation of a TNFI (etanercept, adalimumab, infliximab, certolizumab, or golimumab) to the visit closest to 12 months. Patients were required to have at least three tender or swollen joints for inclusion for this study (this is not an inclusion criteria for Corrons). The mHAQ within six months prior to TNFI initiation was included, and at least one follow up visit 5–13 months after TNFI initiation with mHAQ. The mean change in mHAQ score was the change in percentile of 0.35 or more in the mHAQ score, the minimal clinically important improvement in PsA2. Predictors of mHAQ response were measured in the six months before TNFI initiation. Covariates with p-value <0.10 in univariable logistic regression models and -10% missing values were included in a multivariable model and removed individually until all remaining variables were significant (p<0.05).

Results: Among 1742 TNFI initiations, 721 initiations (623 patients) met inclusion criteria. Mean age at initiation was 51.5 years (SD 12.3), 56% were female, mean PsA duration was 5 years (IQR 2–11), and median baseline mHAQ was 0.375 (IQR 0.125–0.875). The mean change in mHAQ was -0.086 (SD 0.38) and median change in mHAQ was 0 (IQR: -0.25 to 0.125); 23% had a mHAQ decrease of 0.35 or more. In univariable models, college education and being married or partnered were inversely associated with mHAQ response (baseline decrease of 0.35 of more. In univariable models, college education and being married or partnered were inversely associated with mHAQ response (baseline decrease of 0.35 or more). In multivariable models and -10% missing values were included in a multivariable model and removed individually until all remaining variables were significant (p<0.05).

Conclusions: A clinically meaningful change in mHAQ occurred in 23% of patients and was strongly associated with age and baseline mHAQ score. In this real world population, there was little change in mHAQ scores over one year, despite treatment with TNFis and other biologics. These analyses are limited by the mHAQ score in patients with PsA. Despite having at least 3 tender and 3 swollen joints, many patients in this cohort had a low mHAQ at baseline which did not allow for sufficient change to meet the MCII.


Acknowledgements: This work was funded by the Corona Research Foundation.

Disclosure of Interest: A. Ogdie Grant/research support from: Pfizer (co-investigator); Consultant for: Pfizer; Novartis; Lilly; Pfizer; Novartis; L. Palmer: None declared; D. Solomon Grant/research support from: Grants to BWH from amgen, lilly, bristol myers squibb, and pfizer; Consultant for: Corona, LLC, A. Kavanagh: None declared; J. Greenberg Shareholder of: Corona, LLC, Consultant for: Genentech, Janssen, Novartis and Pfizer; Eli Lilly, Employee of: Corona, LLC; J. Curtis: None declared; J. Harrold, Shareholder of: Corrona Research Foundation; J. Kremer, Consultant for: Pfizer (to UMass); Consultant for: Roche, Employee of: Corona LLC, UMass Medical School; J. Kremer Shareholder of: Corona, LLC, Employee of: Corona, LLC; P. Mease: None declared

DOI: 10.1136/annrheumdis-2017-eular.3547
OBJECTIVES: The aims of this study were to culturally adapt the questionnaire for Portugal, and evaluate its reliability and validity in patients with PsA.

Methods: The original UK English version of PsAQoL was translated into Portuguese by a bilingual translation panel. An independent lay panel reviewed the instrument’s item phrasing to ensure appropriateness in colloquial European Portuguese. Structured cognitive debriefing interviews were conducted with ten PsA patients to assess the acceptability, the understanding and the redundancy of ambiguity of the questionnaire. The Portuguese PsAQoL was subsequently applied to PsA patients followed at the Rheumatology Department of Centro Hospitalar do Baixo Vouga, E.P.E. To assess reproducibility, thirty patients with PsA completed the Portuguese PsAQoL on two occasions, two weeks apart. A larger sample was recruited to determine internal consistency and construct validity. Descriptive statistical analysis was used to characterize the data. The Nottingham Health Profile (NHP) was used as a comparator instrument.

Results: Translation and adaptation were successful. The validation sample included 104 patients, 67% of whom were men. Their median age was 50.2 (SD=12.1) yrs and most were married. Cronbach’s alpha for the Portuguese version of the PsAQoL was 0.91 and the test-retest reliability 0.92, indicating that the measure has good internal consistency and produces low random measurement error. The PsAQoL could distinguish between groups of patients defined by self-reported general health status, self-reported severity of PsA and fibromyalgia. Differences in arthritis did not influence PsAQoL scores. There was a positive correlation between the total score of ApAQoL and each of the dimensions of the NHP.

Conclusions: The Portuguese version on the PsAQoL was found to be relevant, understandable and easy to complete, reliable and valid. It should be considered for use in clinical practice and research settings to assess PsA-specific QoL.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3297
While Tumor Necrosis Factor inhibitors (TNFi) are effective agents for PsA, the relationship between early treatment and patient reported outcomes in a real world setting has not been reported previously.

**Objectives:** To assess whether timely treatment with TNFi leads to better improvement in quality of life outcomes than delayed treatment.

**Methods:** This was a retrospective analysis of patients with PsA and/or Psoriasis (PsO) using TNFi with or without methotrexate, and who had a minimum of 2 visits at the Center of Excellence for Psoriasis and Psoriatic Arthritis at our university. Detailed demographic and clinical characteristics of this cohort have been published previously\(^1\). Demographics, quality of life measures (e.g. Routine Assessment of Patient Index Data – RAPID3; Psoriasis Quality of Life – PqOQ12. Short Form 12 – SF-12), and clinical data (percent of body surface area involved with PsO – BSA%) were collected from patient-reported questionnaires and electronic medical records. Only those patients who had a chronological overlap of treatment exposure and QoL measures such as RAPID3, SF-12 and PqOQ were included. To ascertain treatment effects, a mixed-effects model was fitted to estimate the effect of each QoL outcome of a patient separately. Then, for all estimated trends of an outcome, a linear regression model was employed to explore the association between the magnitude of estimated trends and timeliness of TNFi treatments.

**Results:** The quality of life measures were not affected by how early after the disease onset TNFi treatment was started (in other words, no statistically significant associations between the effectiveness of TNFi treatment and disease duration) for RAPID3 (p=0.285), SF-12 (p=0.674), or BSA (p=0.078). For PqOQ, there was a significant association between the trend of treatment effects and timeliness of treatment. A day of delay into treatment was reached in a reduction of 4.4x10^-6/day in the trend of PqOQ scores (p=0.007).

**Conclusions:** In this sample of PsA & PsO patients, timing of starting TNFi in patients with PsA had significant impact on improvements in the PqOQ, but not other quality of life measures such as RAPID3, SF-12 and BSA. A relatively short treatment history might have led to the negative correlations.

**References:**


**Disclosure of Interest:** None declared.

DOI: 10.1136/annrheumdis-2017-eular.1535
AB0746 PRELIMINARY RESULTS OF A TWO-YEAR FOLLOW UP OF SUBCLINICAL Atherosclerosis IN PATIENTS WITH PSORiATiC ArTHRiTS

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Background: Psoriatic arthritis (PsA) is a disease associated with an increased cardiovascular (CV) risk, due to early atherosclerosis, which is comparable to a rheumatoid arthritis population. However, there is a lack of studies that evaluate the progression of subclinical atherosclerosis over a year in these patients.

Objectives: To explore the progression of the vascular damage by different techniques in patients with PsA and the factors related with these changes.

Methods: Pre-post study with analytical components. 44 patients with PsA (CASPAR criteria) and peripheral joint involvement of more than one year since diagnosis were consecutively included. We gathered demographic (age, gender, BMI), clinical (traditional CV risk factors, previous CV event), and analytical variables (atherogenic index, GFR [MDRD], fibrinogen, glycated hemoglobin, CRP, ESP, ultrasensitive CRP, apolipoprotein A1 ratio) and baseline CV risk was estimated with SCORE tool. Other variables were collected retrospectively from patients electronic medical record. The extracranial branches of carotid artery were explored by ultrasonography (US) using an Esaote MyLab70XVG with a 7–12 MHz linear transducer and an automated program measuring intima-media thickness (IMT) through radiofrequency (RFQIMT), and the presence of atheroma plaques, as per the Mannheim consensus, was registered. Pulse wave velocity (PWV) was determined, as an arterial stiffness marker, by a validated MobileOCTraphy device.

Patients were followed during a 2-year period between may 2015 until december 2016. All of the tests were repeated after 2 years. Statistical analysis was performed using SPSS 17.0 software.

Results: We analyzed 38 patients, excluding those with high CV risk (previous CV event, diabetes, hypertension, dyslipidemia, smoking, age ≥60 years). At baseline, the mean and median of age was 59.2 and 60.5 years (39–88), respectively, mostly women (65.8%). The median BMI was 28 (17–35). 28.9% were smokers and 36.8% had hypertension. 26.3% received glucocorticoids, 57.9% NSAIDs, 64.2% DMARDs and 31.6% biologic therapies. The median SCORE, ESP and MDA28 were 5.8mg/L (1–19.1), 7mmHg (23–28) and 2.17 (1.24–3.7), respectively. The median SCORE was 1 (0–7), the PWV was 8 m/s (5.6–13.5) and basal IMT was 728 (462–1087); the presence of atheroma plaques was detected in 35.1% of the patients.

After 2 years, plaque appearance was seen in 15% more of patients, as well as worsening of PWV and IMT in 38.9% of patients, respectively. These changes were not significant. No patient developed a CV event. In the bivariate analysis, PWV progression at 2 years related with advanced age, female gender, higher CV risk factors, and smoking. It demonstrated that CZP treatment inhibits radiographic progression over 96 weeks (wk).

It demonstrated that CZP treatment inhibits radiographic progression over 96 weeks (wk).

Objectives: We report the long-term effect of CZP treatment on radiographic progression in pts with PsA over 4 years.

Methods: The RAPID-Psa phase 3 trial was double-blind and placebo-controlled to Wk4, dose-blind to Wk48, and open-label (OL) to Wk216. Pts had active PsA and had failed ≥1 DMARD. Pts randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wk0, 2, 4) continued their assigned dose in the OL period. Radiographs taken at baseline (BL), and at Wk96, 168, 216, were read in a single reading campaign using the modified Total Sharp Score (mTSS) for PsA by 2 readers, blinded to patient information and time point sequence. The mean of the scores of the 2 readers was used. Outcomes reported are the least squares (LS) mean mTSS score, change from BL (CFB) in mTSS score, and the percentage of pts assessed for radiographic damage who achieved mTSS non-progression (defined either as CFB in mTSS score <0.5 or <0), for all Wk60 CZP-treated pts, irrespective of dose regimen. mTSS score and CFB were estimated using Mixed Model Repeated Measures (MMRM) estimates; proportions of pts with radiographic non-progression are presented as observed cases.

Results: 409 PsA pts were randomized, of whom 273 received CZP from Wk0. The LS mean BL mTSS score was 16.0 and there was little increase from BL in mTSS score to Wk216 (Table). Amongst those who completed the study to Wk216, the majority of CZP-treated pts achieved radiographic non-progression to Wk216, both with non-progression defined as CFB in mTSS score <0.5 or <0 (Table). The change in LS mean mTSS score over time for Wk0 CZP-treated pts was consistently low throughout the trial: 0.14 (95% CI: 0.02–0.26) per 48 wks from BL to Wk96, and 0.18 (95% CI: 0.08–0.28) per 48 wks from Wk96 to Wk216.

Table: mTSS score and radiographic non-progression to Wk216 for patients treated with CZP from Week 0

<table>
<thead>
<tr>
<th>Week</th>
<th>mTSS score, LS mean (SE)</th>
<th>CFB</th>
<th>mTSS score, LS mean (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>16.0 (2.2)</td>
<td>0.0 (0.0)</td>
<td>16.0 (2.2)</td>
</tr>
<tr>
<td>Week 60</td>
<td>16.6 (2.3)</td>
<td>0.6 (0.2)</td>
<td>16.2 (1.9)</td>
</tr>
<tr>
<td>Week 168</td>
<td>16.7 (2.3)</td>
<td>0.7 (0.2)</td>
<td>16.2 (2.1)</td>
</tr>
<tr>
<td>Week 216</td>
<td>16.5 (2.3)</td>
<td>0.7 (0.2)</td>
<td>16.2 (2.1)</td>
</tr>
</tbody>
</table>

Conclusions: There was little radiographic progression in CZP-treated PsA pts, as measured by mTSS, throughout the 4-year RAPID-Psa trial.
**AB0748**  HYPERURICEMIA IN PSORIATIC ARTHRITIS: A NEW LOOK AS A RISK FACTOR FOR CARDIOVASCULAR EVENTS

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**Background:** According to various authors, the prevalence of hyperuricemia in patients with psoriatic arthritis is higher than the general population. This is consistent with the total patient population. Thus, seronegative spondyloarthritis patients, as it is known, possess a higher incidence of cardiovascular mortality than the population in general, in particular due to life-threatening cardiac arrhythmias.

**Objectives:** To study the effect of hyperuricemia on the development of ventricular extrasystole in patients with psoriatic arthritis and the interrelation of uric acid levels and gradation of ventricular extrasystole.

**Methods:** The study involved patients with psoriatic arthritis, confirmed by CASPAR criteria (2006), n=59. The average age – 57.15±11.12 years. All patients underwent the study, including record of cardiac contractility and treadmill test. Inclusion criteria - the presence of psoriatic arthritis for the period of at least one year, uric acid levels over 360 mmol/l for women and more than 420 mmol/l for men. The exclusion criteria included the presence of coronary heart disease, myocardial contractility disorders and decreased ejection fraction according to Simpson less than 55%. For all patients was recorded Holter ECG for the period of 24 hours on an outpatient basis. The level of uric acid was measured by means of the standard method of biochemical analyzer.

**Results:** The prevalence of ventricular extrasystole in patients with psoriatic arthritis and age are shown in Table 1. Moreover, there has been discovered a direct correlation of medium strength between the uric acid levels and frequency and Lown-Wolf gradation of ventricular extrasystole (Table 1).

<table>
<thead>
<tr>
<th>Low-Wolf gradation</th>
<th>Percentage of patients with ventricular extrasystole</th>
<th>Average level of uric acid</th>
<th>Coefficient of correlation, r</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>25.40%</td>
<td>546.52±12.24</td>
<td>0.54</td>
</tr>
<tr>
<td>II</td>
<td>22.03%</td>
<td>622.15±28.11</td>
<td>0.47</td>
</tr>
<tr>
<td>III</td>
<td>1.69% (1 patient)</td>
<td>511.21</td>
<td>Small sample</td>
</tr>
<tr>
<td>IV a</td>
<td>20.34%</td>
<td>784.22±55.16</td>
<td>0.68</td>
</tr>
<tr>
<td>IV b</td>
<td>25.42%</td>
<td>774.13±22.60</td>
<td>0.33</td>
</tr>
<tr>
<td>V</td>
<td>5.08%</td>
<td>894.23±13.90</td>
<td>0.50</td>
</tr>
</tbody>
</table>

**Conclusions:** 1. Hyperuricemia in patients with psoriatic arthritis by exclusion of cardiogenic causes of cardiac extrasystole is an independent risk factor for ventricular extrasystole.

2. The level of hyperuricemia correlates directly with the Lown-Wolf gradation of ventricular extrasystole.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.7042

**AB0749**  AXIS INVOLVEMENT IN THE RUSSIAN COHORT OF EARLY PERIPHERAL PSORIATIC ARTHRITIS PATIENTS AND ITS ASSOCIATION WITH ARTHRITIS ACTIVITY, PATIENT’S ASSESSMENT AND SEVERITY OF SKIN LESION


**Background:** The association of axial involvement with peripheral arthritis activity and skin lesion severity in early psoriatic arthritis (ePsA) patients (pts) has not been studied properly.

**Objectives:** To study the prevalence of axial involvement detected by magnetic resonance imaging (MRI) and X-ray of sacroiliac joints (SJs) and its correlation with peripheral arthritis activity and skin lesion severity in peripheral ePsA pts.

**Methods:** 79 pts (M/F–42 /37) with peripheral ePsA criteria (NCT02065713) were included; mean age 36.5±10.9 yrs, disease duration 12.1±10.1 mo., disease activity index (DAS28) 8.8±1.7, patient’s pain VAS 55.0±17.9, patient’s global disease activity VAS 56.9±17.1, C-RP16.1 [8.6; 31.0] mg/l, ESR 22.5±19.2 mm/h. All pts were examined by an independent reader. Radiographic sacroiliitis (R-SI) was defined at 2 grade changes, at least in one SIJ, while definite radiographic sacroiliitis (MRI-SI) was evaluated by an independent reader. Radiographic sacroiliitis (MRI-SI) was considered according to New York criteria (unilateral grade ≥3 or bilateral grade >2). Skin lesion area was measured according to BSA. BSA ≥10% was defined as extensive.

**Results:** IBP was found in 58 out of 89 (65.1%) pts, 35 (60.3%) of them had short-term (episodic) IBP, and 23 (39.7%) pts had long-term IBP. MRI-SI was observed in 28 out of 79 (35.4%) pts. R-SI was determined in 42 out of 89 (47.2%) pts, while dR-SI was found in 27 out of 89 (30.3%) pts. 34 (38.2%) pts were HLA-B27 positive. In pts having IBP disease activity measured by DAS28 was 4.5±1.6. An association was detected between the presence of MRI-SI and activity of peripheral arthritis by DAS28 (r=0.25; p=0.03). Correlation was detected between the presence of MRI-SI and the value of patient’s global disease activity (r=0.23; p=0.047) as well as patient’s pain (r=0.31; p=0.007).

**Acknowledgements:** This investigator initiated trial was supported by a research grant from Meck Sharp and Dohme.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5482

**AB0750**  THE GO-DACT PROTOCOL: A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF GOLUIMAB IN COMBINATION WITH METHOTREXATE (MTX) VERSUS MTX MONOTHERAPY, IN IMPROVING DACTYLITIS AND ENETHESIS, IN MTX NAIVE PSORIATIC ARTHRITIS PATIENTS

E_Vieira-Sousa 1, H. Canhão 2, J.E. Fonseca 1 on behalf of GO-DACT research team. 1Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa and Rheumatology Department, Hospital de Santa Maria, Lisbon, Portugal, 2Academic Medical Centre, CEDOC, NOVA Medical School, Universidade Nova de Lisboa, Lisbon, Portugal

**Background:** Dactylitis is a hallmark manifestation of psoriatic arthritis (PsA) and a key feature for PsA diagnosis. Active dactylitis is associated with a higher risk of erosions and can severely impact function. The therapeutic strategies for dactylitis are however largely empirical, with a profound absence of knowledge regarding efficacy, as primary endpoint, and impact on disease progression. The use of biologic disease modifying anti-rheumatic drugs (DMARDs) in patients with dactylitis, refractory to non-steroidal anti-inflammatory drugs (NSAIDs) or local corticosteroids, is recommended by EULAR guidelines, over the use of conventional DMARDs, based in the scarcity of evidence and properly designed studies in this field.

**Methods:** GO-DACT is an investigator initiated ongoing multicentric trial, involving 13 national Rheumatology departments. Patients older than 18 years, with the diagnosis of PsA and active dactylitis (tenderness score ≥1), refractory to NSAIDs for <3 months, were included. Patients were randomized on a 1:1 ratio, to either MTX in combination with golimumab or placebo, for a period of 24 weeks. The primary aim of this trial is to determine differences of efficacy between the two treatment arms, in improving dactylitis (and enthesis), as assessed by the dactylitis severity score (DSS) at 24 weeks. Key secondary outcomes include: Leeds dactylitis index (LDI), Leeds enthesis index (LEI), joint counts, psoriasis area and severity index (PASI) and nail psoriasis severity index (NAPSI), health assessment questionnaire (HAQ), Dermatology life quality index (DLQI) and composite indexes for disease activity. The effect of treatment arms, on different tissue compartments, will be assessed by contrast-enhanced magnetic resonance imaging (MRI), with high resolution images for dactylitis, at baseline and 24 weeks.

**Results:** The results from GO-DACT are expected to have implications in clinical practice, bringing robust and valid data for the definition of dactylitis treatment stratification and algorithm GO-DACT will also contribute to understand dactylitis pathogenesis through the assessment of treatment efficacy, namely in distinct tissue compartments as defined by MRI. https://www.clinicaltrials.gov (NCT02065713)

**Acknowledgements:** This investigator initiated trial was supported by a research grant from Meck Sharp and Dohme.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3047

**AB0751**  THE DIFFERENCES AND SIMILARITIES BETWEEN PATIENTS AND PHYSICIAN GLOBAL ASSESSMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis, axial involvement, enthesis, dactylitis and uveitis. The differences and similarities between patient’s global assessment (PGA) and physician’s global assessment (PhGA) were not assessed clearly in PsA.

**Objectives:** The aim of this study was to assess differences and similarities between patient’s and physician’s perspective of global assessment in patients with PsA.
AB0752  CONSENSUS STATEMENT ON THE USE OF METHOTREXATE IN PSORIATIC ARTHRITIS PATIENTS

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Background: Methotrexate (MTX) is the cornerstone in rheumatic diseases, including psoriatic arthritis (PsA), but the complexity of PsA and the paucity of randomised controlled studies and strategic trials need a clear analysis.

Objectives: To develop recommendations for the management of MTX in PsA (musculoskeletal manifestations) based on best evidence and experience.

Methods: The coordinators formulated 14 questions about MTX use (indications, efficacy, safety) in patients with PsA. A systematic literature review was performed to answer these questions. Using this information, inclusion and exclusion criteria were established as well as the search strategies (Medline, Embase and the Cochrane Library), that were designed by an expert librarian. Two different reviewers selected the articles, first by title and abstract, then by detailed review, and collected data independently. Evidence tables were produced. With this evidence the coordinators proposed 12 preliminary recommendations that will be discussed and voted in a nominal group of expert meeting. The level of evidence and grade of recommendation will be defined using the Oxford Centre for Evidence Based Medicine. Agreement will be stabilised if at least 80% of the experts voted yes (yes/no).

Results: A total of 12 preliminary recommendations on the use of MTX in PsA were proposed (see table).

Conclusions: This document aims to help to answer usual clinical questions and facilitate decision making when treating PsA patients with MTX.

Disclosure of Interest: None declared

AB0753  ARTERIAL STIFFNESS INCREASE IN THE EARLY PHASE OF ARTHROPATHY RELATED TO PSORIATIC ARTHRITIS IS NOT FURTHER MODIFIED BY STABLE PROLONGED RETENTION OF A MINIMAL DISEASE ACTIVITY CONDITION

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Background: Increased large arteries wall stiffness (AS) is a well known independent morbidity and mortality cardiovascular risk factor, not only related to hypertension and diabetest, but also induced by long standing systemic inflammation, as observed in inflammatory rheumatic or gut chronic diseases. Psoriatic arthritis (PsA) was also shown to increase cardiovascular morbidity, but this observation was commonly related with the associated occurrence of long term arthritis, disease activity and CV traditional risk factors

Objectives: To assess whether in a selected group of PsA patients, affected by recent onset (4–12 months) arthritis, not suffering from CV disease risk factors, evidence could be obtained of an early alteration of arterial wall function as expressed by an increased arterial pulse wave velocity (aPWV) and secondary reduced tonometric subendocardial viability ratio (tSEVR).

Further, we evaluated if a 18 months (Mth) treatment with synthetic disease modifying antirheumatic drugs (sDMARD) other than cyclosporine, leading to a demonstrable target of clinical “minimal disease activity”(MDA) could modify such possible modifications

Methods: Conclusive data were obtained in a selected group of 12 PsA patients (PsA disease criteria classification JCA 2010; M/F 6/6; mean age 50.8; range 40-70) not suffering from axial spondylitis who firstly underwent (without any previous treatment) aPWV measurement (PulsePen, Diatecne Srl, Milan) and tSEVR calculation, and then were re-evaluated for the same calculations after a 18 mth time of sDMARD treatment. Each of the PsA Pts had a 3–4 Mth follow up and showed to reach the target of stable MDA (with also ultrasound confirmed remission of active synovitis) after a 4–8 Mth treatment. Before treatment, the group of PsA Pts was compared with an age, body weight, CV parameters and risk factors–matched control group of voluntary 22 healthy subjects (M/F 11/11; mean age, 51.3; range, 41–87).

Results: Before any treatment, aPWV was higher in the group of patients with PsA than in control subjects (median, 8.667 m/s vs 6.963 m/s, p<0.02) while tSEVR was decreased (median, 1.44 vs 1.50, p<0.05). Aortic PWV was not modified after the sDMARD treatment (median m/s, before=8.691, after=8.691, p=0.55), despite statistically significant improvements of the disease activity scores (DAS28; modified CDAI; DAPSA) as well as cutaneous PASI, and stable retention of a MDA condition. A direct correlation (Spearman rank) between aPWV and DAS28 (rho=0.70; p-value=0.04), BASDAI (rho=0.77; p-value=0.01), and RA 28 Score (rho=0.66; p-value=0.005) was found, not instead between aPWV and ESR or CRP. Pts with PsA, at the end of the follow up, had increased levels of systolic (134,1±14,3 vs 122±11,2, p<0.05) and diastolic (82±7,4 vs 73,5±6,6, p<0.05) blood pressure, with unmodified heart rate.

Conclusions: Early onset of PsA seems to be associated with already established and stable increase of AS. Sub-clinical previous inflammation and length of psoriatic disease could be addressed as possible causes

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5528
COMPARISON OF COMPOSITE INDICES TAILORED FOR PRIMARY EFFICACY AND SAFETY OF ADALIMUMAB IN NAIL PSORIASIS vs PsA

AB0754

COMPARISON OF COMPOSITE INDICES TAILORED FOR PRIMARY EFFICACY AND SAFETY OF ADALIMUMAB IN NAIL PSORIASIS vs PsA

FM. Perrotta, A. De Socio, E. Lubrano. Medicina e scienze della salute, Università degli studi del Molise, Campobasso, Italy

Background: Remission or low disease activity should be the target of therapy in chronic inflammatory arthritis as well as in Psoriatic arthritis (PsA). In a complex disease such as PsA, several methods are available to define remission that comprise the assessment of different clinical features.

Objectives: The aim of this study was to compare the composite indices tailored for PsA in both patients treated with csDMARDs and bDMARDs.

Methods: Adult PsA patients classified with CASPAR criteria and with >6 months follow up treated with first csDMARDs and bDMARDs were consecutively enrolled in our recent clinic. To assess disease activity, composite indices tailored for PsA namely DAPSA, cDAPSA, PASDAS, MDA (5/7) and MDA (7/7) were used. DAPSA and cDAPSA score ≤4, MDA 7/7 and PASDAS ≤1.9 identified remission while MDA 5/7 and PASDAS ≤3.2 the minimal disease activity and inactive disease criterion

Results: One hundred nine PsA patients were enrolled. Of this, 79 patients were in stable treatment with bDMARDs and 30 with csDMARDs. Overall, 28 (25.6%), 23 (21.1%), 19 (17.4%), 54 (49.5%), 13 (11.9%) and 35 (32.1%) PsA patients were in cDAPSA remission, DAPSA remission, MDA 7/7, MDA 5/7, PASDAS ≤1.9 and PASDAS ≤3.2. Patients in bDMARDs had a significantly low median DAPSA, cDAPSA, PASDAS and PASDAS score than patients treated with csDMARDs (table 1). Overall, the concordance between the ratios ranging from slight to good.

Conclusions: PsA patients in bDMARD are more likely to reach a status of MDA and remission in respect to csDMARDs. PASDAS ≤1.9 and MDA 7/7 seem to be stringent remission criteria.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6825

AB0755

DEPRESSON AND ANXIETY MAY CONTRIBUTE TO HIGHER DISEASE ACTIVITY AND WORSE QUALITY OF LIFE IN PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease with variable types of joint involvement, extra-articular features, including skin psoriasis, and with well-known comorbidities such as depression and anxiety. Composite Psoriatic Disease Activity Index (CPDAI) adequately assesses disease activity in this complex condition. To date, no study has evaluated the relationship between depression/anxiety scores and CPDAI in PsA.

Objectives: The aim of this study was to compare 1) depression/anxiety scores; 2) physician-assessed and patient-reported outcome measures (PROMs) between patients with CPDAI≤4 suggesting low disease activity versus with CPDAI>4 reflecting moderate or severe disease activity in PsA.

Methods: PsA patients fulfilling the CASPAR criteria were recruited. Patients underwent musculoskeletal and skin assessments (TCJ68, SJUC66, Leeds enthesitis index, dactylitis digit score and PASI) and they have completed questionnaires on physical function and health-related quality of life (HAQ, PsAQoL, DLQI; EQ-SD, BASDAI, BASFI, ASQoL, Braf-NRS, pain and general health VAS). Patients were assessed for depression/anxiety using the Hospital Anxiety and Depression Scale (HADS-A and HADS-D) and Penn State Worry Questionnaire (PSWQ). Data were analyzed using Mann Whitney, Chi-square tests and linear regression model.

Results: 100 PsA patients were recruited; 57 presented with CPDAI≤4 (age 52.7±9.46 years) and 43 with CPDAI>4 (age 52±11.82 years). Patients with CPDAI>4 had significantly higher TCJ68 (p<0.001), Leeds enthesitis index (p<0.015) and significantly worse HAQ, BASDAI and ASQol scores. There was no significant difference in other items of CPDAI between the two groups. Patients with CPDAI>4 had significantly higher HADS-D, HADS-A and PSWQ scores (p<0.001; p<0.001, respectively) and significantly worse PROMs, including PsAQoL, EQ-SD score, BASFI, Braf-NRS, pain and general health VAS (Table 1). Multiple regression analysis revealed significant relationship between PsAQoL, BASFI and CPDAI (B=0.311, p=0.0093; B=0.568, p<0.0001, respectively).

Conclusions: This is the first study assessing the relationship between depression/anxiety and CPDAI in PsA. We have found significantly higher HADS-D, HADS-A, PSWQ scores and worse PROMs in patients with CPDAI>4 compared to those with CPDAI≤4. Based on our results there is significant relationship between depression/anxiety, physical function, quality of life and disease activity in psoriatic arthritis.

References:

Disclosure of Interest: F. Farkas: None declared, N. Ikumi: None declared, A. Szentpetery: None declared, B. Kirby Grant/research support from: Abbvie, O. FitzGerald Grant/research support from: Abbvie, Pfizer, BMS, Consultant for: Abbvie, Pfizer, BMS, Novartis, Celgene, Janssen, UCBe, Eli Lilly
DOI: 10.1136/annrheumdis-2017-eular.6825

AB0756

PRIMARY EFFICACY AND SAFETY OF ADALIMUMAB IN NAIL PSORIASIS FROM THE FIRST 26 WEEKS OF A PHASE-3, RANDOMIZED, PLACEBO-CONTROLLED TRIAL WITH SUBANALYSIS IN PATIENTS WITH AND WITHOUT PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) disease burden for patients (pts) with psoriasis (Ps) and concomitant fingernail Ps plus psoriatic arthritis (PsA) is higher compared with pts with Ps alone.

Objectives: We report safety and efficacy of originator adalimumab (ADA) in pts with fingernail Ps, and also for pts with or without concomitant PsA.

Methods: Results are reported from the double-blind PBO-controlled, Period A in which 217 pts with moderate to severe plaque Ps and fingernail Ps were included and randomized 1:1 to receive 40 mg ADA every other week (eow) from wk 1 (initial 80 mg dose at wk 0), or matching PBO, for 26 wks. The primary endpoints were the proportion of pts with ≥75% improvement in modified Nails Ps Severity Index (mNAPSI 75) and the proportion of pts with Physician’s Global Assessment of Fingernail Psoriasis (PAGA-F) of (clear) or (minimal) (1) with ≥2 grade reduction from baseline (primary in US only; for regulatory purposes). Missing data were handled by multiple imputation. Safety was assessed using treatment-emergent adverse events (AEs).

Results: Of the 217 randomized pts (108 PBO, 109 ADA), 84.3% were male; mean age (SD) was 46.7 years (17.8); 66% completed 26 wks of treatment, or early escaped to Period B according to protocol. Both primary endpoints were met: total fingernail mNAPSI 75 was achieved by 3.4% PBO vs 46.6% ADA (p<0.001), and PAGA-F 0 or 1 with ≥2 grades improvement was achieved by 6.9% vs 48.9% (p<0.001). At baseline, 28.6% had PsA (29.6% PBO, 27.5% ADA) with mean

Table 1. Comparison of patient-reported outcome measures between CPDAI ≤4 and CPDAI >4 groups

<table>
<thead>
<tr>
<th>PROMs</th>
<th>CPDAI ≤4</th>
<th>CPDAI &gt;4</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HADS-D</td>
<td>2.32±2.53</td>
<td>5.27±3.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HADS-A</td>
<td>3.44±2.74</td>
<td>5.98±2.81</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PSWQ</td>
<td>38.71±2.23</td>
<td>46.95±2.22</td>
<td>0.001</td>
</tr>
<tr>
<td>PASDAS-VAS</td>
<td>2.04±2.52</td>
<td>4.41±2.07</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>gVAS</td>
<td>76.73±20.95</td>
<td>66.6±20.15</td>
<td>0.005</td>
</tr>
<tr>
<td>Braf-NRS</td>
<td>12.35±6.51</td>
<td>16.41±4.76</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PsAQoL</td>
<td>1.6±4.47</td>
<td>6.17±3.15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EQ-SD SCORE</td>
<td>0.82±0.15</td>
<td>0.66±0.19</td>
<td>0.0001</td>
</tr>
<tr>
<td>BASFI</td>
<td>1.51±3.13</td>
<td>4.26±1.74</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mann-Whitney test. Results are presented as mean ± SD.
impact of disease activity on physical function and health-related quality of life in patients with psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic progressive inflammatory disease characterized by peripheral arthritis, dactylitis, axial joint involvement and enthesitis. Disease consequences such as chronic pain, severe joint damage and fatigue may adversely affect on patient’s physical function and health-related quality of life (QoL) to perform daily activities.

Objectives: The aim of this study was to investigate the potential relationship between physical function and health-related QoL and disease activity measures in patients with PsA.

Methods: For all participating patients, quality of life, functional and disease activity measures were measured by different ways: Nottingham Health Profile (NHP), psoriatic arthritis quality of life (PsQoL), Antirheumatic Drugs Survey, Health Assessment Questionnaire (HAQ), BASFI, VAS pain, BASDAI, and ESR. CRP. Patients with PsA were discriminated into low and high disease activity (NHP), psoriatic arthritis quality of life (PsAQoL), Ankylosing Spondylitis Quality of Life (ASQoL) and Disease Activity Score 28 (DAS28). Baseline measurements of disease activity and health-related QoL were performed in all patients. Disease activity measures were found correlated with all important QoL measurements including NHP, SF36, PsQoL, HAQ and ASQoL. In patients with PsA, high disease activity may lead to severe impairments in daily activities and influence on participation in society.

Conclusions: Psoriatic arthritis has a major impact on patients’ lives. Variable disease activity measurements were found correlated with all important QoL measurements including NHP, SF36, PsQoL, HAQ and ASQoL. In patients with PsA, high disease activity may lead to severe impairments in daily activities and influence on participation in society.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2148

AB0757

IMPACT OF DISEASE ACTIVITY ON PHYSICAL FUNCTION AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS

Table 1. Correlation coefficients between disease activity and various health related QoL measurements in patients with PsA

<table>
<thead>
<tr>
<th>VAS</th>
<th>BASFI</th>
<th>BASDAI</th>
<th>ESR</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>NH-Pain</td>
<td>0.571 (-0.001)</td>
<td>0.326 (-0.001)</td>
<td>0.644 (-0.001)</td>
<td>0.250 (-0.003)</td>
</tr>
<tr>
<td>NHP-physical activity</td>
<td>0.599 (-0.001)</td>
<td>0.335 (-0.001)</td>
<td>0.652 (-0.001)</td>
<td>0.277 (-0.001)</td>
</tr>
<tr>
<td>NHP-fatigue</td>
<td>0.425 (-0.001)</td>
<td>0.324 (-0.001)</td>
<td>0.530 (-0.001)</td>
<td>0.287 (-0.001)</td>
</tr>
<tr>
<td>NHP</td>
<td>0.236 (0.003)</td>
<td>0.119 (0.162)</td>
<td>0.308 (-0.001)</td>
<td>0.113 (0.018)</td>
</tr>
<tr>
<td>NHP-social isolation</td>
<td>0.214 (0.008)</td>
<td>0.299 (-0.001)</td>
<td>0.272 (-0.001)</td>
<td>0.080 (0.345)</td>
</tr>
<tr>
<td>NHP-emotional reaction</td>
<td>0.315 (-0.001)</td>
<td>0.281 (-0.001)</td>
<td>0.326 (-0.001)</td>
<td>0.085 (0.315)</td>
</tr>
<tr>
<td>SF36 physical component</td>
<td>0.581 (-0.001)</td>
<td>0.333 (-0.005)</td>
<td>0.439 (-0.001)</td>
<td>0.346 (0.004)</td>
</tr>
<tr>
<td>SF36 mental component</td>
<td>0.439 (-0.001)</td>
<td>0.232 (0.057)</td>
<td>0.366 (-0.001)</td>
<td>0.250 (0.038)</td>
</tr>
<tr>
<td>PsAQoL</td>
<td>0.451 (-0.001)</td>
<td>0.285 (-0.001)</td>
<td>0.484 (-0.001)</td>
<td>0.103 (0.223)</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.428 (-0.001)</td>
<td>0.294 (-0.001)</td>
<td>0.498 (-0.001)</td>
<td>0.097 (0.246)</td>
</tr>
<tr>
<td>ASQoL</td>
<td>0.459 (-0.001)</td>
<td>0.459 (-0.001)</td>
<td>0.459 (-0.001)</td>
<td>0.220 (0.081)</td>
</tr>
</tbody>
</table>
previous exposure to anti-TNF agents to which they have either been intolerant or found ineffective. More research into drug survival and persistence should be considered as real-world data may not reflect RCT results.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4003

AB0760 EFFICACY OF USTEKINUMAB IN A COHORT OF PATIENTS AFFECTED BY PSORIATIC ARTHRITIS IN REAL-LIFE


Background: Psoriatic arthritis (PsA) is a chronic inflammatory joint disease, that can be treated effectively with synthetic disease modifying anti-rheumatic drugs (DMARDs) and biological agents. Ustekinumab is a monoclonal antibody that inhibits IL-12 and 23 that has recently demonstrated efficacy and safety for the treatment of patients with PsA in the PSUMMIT 1 and PSUMMIT 2 studies.

Objectives: To evaluate the efficacy of Ustekinumab in our patients with psoriatic arthritis with peripheral involvement in clinical practice conditions.

Methods: Descriptive, prospective, longitudinal and open study including patients diagnosed with psoriatic arthritis with peripheral involvement. All patients were given ustekinumab at an initial dose of 45 mg administered subcutaneously followed, by another dose 4 weeks later then every 12 weeks. Clinical scores (DAS28, MASES, Pain Vas, Clinicians Vas) were assessed and CRP was measured at baseline and after 6 months of treatment.

Results: 52 patients were included, 25 were female (48.1%) and 27 male (51.9%). They had a mean age of 46.9±11.39 years, a disease duration of 5.03±5.08 years, and moderate disease activity (DAS 28 of 3.95±0.87), the number of tender and swollen joints were 6.24±4.9 and 2.82±2.36, respectively. The patients had received an average of 1.42±1.75 biological therapies previously. Ustekinumab was prescribed as a first line treatment in 42.3% of patients, 19% after failure of a TNF inhibitor and 38% of patients had received 2 or more biological therapies previously. Ustekinumab was administered alone in 51% of the patients, 36.5% in combination with methotrexate and 11.5% in combination with leflunomide. 23.1% of the patients had dactylitis and 36.5% had enthesitis (mean MASES 1.31±0.86). At 6 months of treatment, there were improvements in the number of tender and swollen joints (mean NAD 4.84±6.4 and NAT 2±4 at 6 months, respectively) and MASES index (mean at 6 months, 0.35±0.96). 15 patients completed at least 6 months of treatment. Improvements in DAS28-CRP scores were observed at 6 months of treatment (3.26±1.62), with a mean DAS28 change after 6 months (ΔDAS28) of -0.65±1.88. At month 6, 71.4% of the patients had low disease activity, and 35.7% were in clinical remission according to the DAS28 index.

Conclusions: Ustekinumab is effective in patients with psoriatic arthritis with peripheral involvement in routine clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6153

AB0761 THE BIOLOGIC THERAPY USE FOR ENTEHISIS AS A PREDICTOR OF PSORIATIC ARTHRITIS IN PSORIATIC PATIENTS

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Background: According to ACR data 15–20% patients (PTN) with psoriasis are developed with psoriatic arthritis (PsA). Herewith the enthesitis (ETS) as usual is the first signs of PsA manifestations. It is usually asymptomatic at the beginning of the disease. However it is successfully diagnosed with Doppler ultrasound (DU). In average, it takes about 2 years from beginning of the disease till diagnosis PsA is established. PsA treatment is low effective with DMARD, and middle effective with biologic therapy. Wherein no treatment restores the articular changes that have occurred. Thus the actual is to find some resolution to the effective therapy for PTN with psoriasis and also to identify the factors preceding the development of the PsA.

Objectives: Consider the application of biologic therapy before the articular changes in PTN with psoriasis and predictors of psoriatic arthritis.

Methods: Observed 82 PTN with pustular psoriasis without clinical manifestations of PsA. A physical examination (including PASI), a series of laboratory tests (hematology, CRP, RF, anti -icp, HLA-B27, uric acid), DU to identify the PsA, its activity, as well as to the exclusion of other types of arthritides were used.

Results: 3.7% PTN were diagnosed with PsA with articular changes. 23.1% PTN were founded with enthesitis. The remaining 73.2% PTN had no signs of enthesitis during physical examination and DU. PTN with enthesis were divided into 2 groups. I – 47% PTN (22% of them had clinical manifestations of enthesis; the average group PASI= 42.4±8.2) received a 52-weeks course of ustekinumab (45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks), II group – 53% people (20% PTN had clinical manifestations of enthesis; the average group PASI= 43.6±9.0) did not receive biological therapy, but only standart treatment for psoriasis. After 1 year follow-up after completion of the treatment course – 11% PTN from group I developed PsA with articular changes. From the group II in 80% PTN developed PsA with articular changes. The average group I PASI= 7.6±1.5; the average group PASI= 6.2±1.3. (p < 0.05)

Conclusions: Thus, the ustekinumab use in pustular psoriasis with enthesitis possibly may be reasonable and will hinder the development of PsA. Ustekinumab is also high effective for the improving of the psoriasis skin symptoms. DU is the high effective diagnostic method for detecting enthesitis without clinical manifestations. Frequency of screening DU in PTN with psoriasis, for the early detection of enthesis is the perspective for further study.

Disclosure of Interest: None declared
Methods: There was no statistically significant difference between groups in terms of hypertension, LDL levels, and smoking status (p=0.775, p=0.228, p=0.136 respectively). PsA patients had higher BMI scores (p=0.03). Insulin levels and HOMA-IR scores were significantly higher among PsA patients compared to controls (p=0.001, p=0.005). There was a statistically significant difference between groups in terms of PTX 3 (p<0.001). PTX 3 was significantly correlated with HOMA-IR and cIMT (r=0.243 p=0.043 and r=0.421 p=0.001 respectively). However, no correlation between PTX 3 and disease activity parameters such as ESR, CRP, SJC, TJC, and VAS-pain was detected (p=0.824, 0.662, 0.922, 0.924, 0.410 respectively). There was no significant difference in terms of PTX 3 levels between PsA patients on biologic treatment or other treatment strategies (p=0.27).

Conclusions: Elevated levels of PTX 3 may be associated with cardiovascular involvement in PsA patients independent from the disease activity. This marker might be used for risk prediction for CMD or may represent a target for new therapies.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3757

AB0763 USTEKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS – RESULTS OF THE FIRST INTERIM ANALYSIS OF THE NON-INTERVENTIONAL STUDY SUSTAIN


Objectives: SUSTAIN is a prospective, multi-center non-interventional study in Germany to observe long term efficacy and safety, quality of life and further patient reported outcomes in patients with active psoriatic arthritis under treatment with Ustekinumab in routine clinical care.

Methods: In this study treatment with Ustekinumab is according to the label (Stelara®). It is planned to observe 400 patients at 75 centers for 160 weeks with documentation intervals at week 0 and then every 12 weeks. Besides demographic data, the following data will be documented: Amount of swollen and tender joints, joint entheses, skin symptoms (BASI and PASI), patient reported outcomes concerning disease activity and pain, Health Assessment Questionnaire (HAQ), quality of life (SF-12), sleep quality (VAS), satisfaction with therapy of patient and physician, safety (adverse events [AE]/serious adverse events [SAE]), pharmacoeconomic aspects, number of patients with “Minimal Disease Activity” (MDA), number of patients with MDA at week 28 and 52.

Results: Overall, there have been 189 patients (56% women) at 59 centers documented after 11 months. At week 4 154 patients and at week 16 112 patients. At baseline, the patients had a mean age of 56 years (29–85), body weight 87 kg (50–147), BMI 30 (19–47), showed arthritis at small (68.8%) and/or big (51.3%) joints, skeletal involvement (19%), enthesitis (13.2%). The number of tender joints improved from a mean of 8.6 (CI 95% 7.1/10.2) to 4.7 (3.1/6.3) at week 16, number of swollen joints from 3.4 (2.6/4.2) to 1.4 (0.9/1.9). The patient reported global disease activity (0–100) decreased from 55.1 to 38.6 at week 16. Further improvements were documented for enthesitis, PASA, EAP, RA, and pain. Efficacy of the therapy with Ustekinumab after 16 weeks was assessed as “very good” by 32.3% and as “good” by 44.8% of the treating physicians and by 34% and 40.2%, respectively, of the patients. In total, 60 adverse events were reported, of which four were serious. All in all safety of therapy with Ustekinumab after 16 weeks was assessed as “very good” by 51% and as “good” by 49% by the treating physicians, and by 55% and 37%, respectively, of the patients.

Conclusions: The non-interventional study SUSTAIN showed relevant improvements with elevated treatment satisfaction and good safety in patients with active psoriatic arthritis after 16 weeks under real world condition.


AB0764 MALIGNANCY AND SERIOUS INFECTIONS AMONG PSORIATIC ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL DRUGS IN A REGIONAL REGISTRY IN THE NORTHWEST OF SPAIN

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Background: Biological treatments have provided new opportunities for disease control for patients with psoriatic arthritis. However, it is important to evaluate their safety, since they expose them to an increased risk of developing malignant and serious infections.

Objectives: To examine the rate of solid tumors and serious infections among patients diagnosed with psoriatic arthritis (PsA) treated with biological drugs (BD) in 2011–2015.

Methods: We included all PsA patients (CASPAR criteria) under treatment with BD followed in our regional registry (reference population 2.055.000) between January 2011 and December 2015. In order to capture the incidence of new malignancy we excluded patients with a prior history of malignancy. Medical records were fulfilled for patients and were recorded solid tumors diagnosed (date of diagnosis and histology information) and all serious infections (requiring hospitalization or intravenous antibiotics) in this time period. Incidence rates (IRs) were calculated per 1000 Person-year (py). We used for this analysis sex, age, disease duration, current BD with or without current CMDR associated. Continuous variables were reported as mean ± standard deviation (SD). Categorical variables were reported as percentages and frequencies. Differences were considered statistically significant if p<0.05 (two-tailed).

Results: Among 604 patients 329 (54.5%) of whom were men, with a mean age of 53.3±12.6 years and a time since the diagnosis of PsA of 12.4±8.7 years. There were 14 cancers diagnosed during treatment (2.3%), with an IR of 0.48 cases per 1000 patient-years. Patients who at this time had a higher age had a higher IR, 63.4±10.0 years vs 53.1±12.6, than those who did not develop disease (p=0.010). Etaercept was the most used (42%) and no differences were observed among BDs (p=0.214) or between naïve and non-naïve to BD (p=0.384). Current CMDR associated (56.2%) did not differences in tumors (p=0.429). Prostate tumor was the most frequent (21.4%). There were 42 had serious infection (6.2%), with an IR of 13.9 cases per 1000 patient-years, and was more common in men (4.7% vs 8.8%, p=0.049). Severe infections were more frequent in patients non-naïve to BD (10.4% vs 5.4%, p=0.026). Pneumonia (28.6%), varicella-zoster virus infection (16.6%), osteosarcoma (14.3%) were more frequent. Latent tuberculosis infection was positive in 133 patients (22.0%) and 3 developed tuberculosis.

Conclusions: Patients older than 60 years with psoriatic arthritis treated with BDs had a higher incidence of tumor development. Most of patients were men and prostate tumor was the most frequent. Pneumonia was the most frequent serious infection and non-naïve to BD patients had a higher IR of serious infections.

References:

Acknowledgements: The authors are grateful for the support of the members of the Galician Society of Rheumatology (SOGARE).
Abstract AB0765 — Table 1. Core components by DAPSA states with secukinumab or placebo at Wk 16

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>300mg/150mg</th>
<th>PBO</th>
<th>300mg/150mg</th>
<th>PBO</th>
<th>300mg/150mg</th>
<th>PBO</th>
<th>300mg/150mg</th>
<th>PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>SJC (66)</td>
<td>0.4±0.7/0.2±0.4</td>
<td>1±0.1</td>
<td>0.2±0.4/0.3±0.5</td>
<td>0.5±1.0</td>
<td>0.6±0.5/0.6±0.5</td>
<td>0.6±0.6</td>
<td>0.7±0.7/0.4±0.4</td>
<td>0.6±0.6</td>
</tr>
<tr>
<td>TJC (68)</td>
<td>1.7±3.4/1.6±1.6</td>
<td>1.6±2.0</td>
<td>2.5±1.9/1.8±2.2</td>
<td>2.3±2.7</td>
<td>2.3±1.6/2.1±1.2</td>
<td>2.3±1.8</td>
<td>2.3±3.2/3.1±3.3</td>
<td>2.6±1.8</td>
</tr>
<tr>
<td>PGS (cm)</td>
<td>4.5±3.8/4.9±3.0</td>
<td>4.9±3.4</td>
<td>6.0±4.7/2.0±2.8</td>
<td>7.5±4.1</td>
<td>3.8±3.3/3.9±1.9</td>
<td>3.9±1.8</td>
<td>4.1±2.0/3.1±1.8</td>
<td>4.5±1.8</td>
</tr>
<tr>
<td>PP (cm)</td>
<td>9.1±1.7/9.1±1.7</td>
<td>9.1±1.7</td>
<td>1.6±2.0/1.6±2.0</td>
<td>2.6±1.5</td>
<td>2.6±1.5/2.6±1.5</td>
<td>2.6±1.5</td>
<td>2.6±1.5/2.6±1.5</td>
<td>2.6±1.5</td>
</tr>
</tbody>
</table>

* n=14 (300mg), 10 (150mg) and 4 (PBO); ** n=27 (300mg), 34 (150mg) and 12 (PBO); *** n=26 (300mg), 24 (150mg) and 22 (PBO); **** n=30 (300mg), 32 (150mg) and 49 (PBO).

Objectives: To explore the relationship between DAPSA states and function, health-related quality of life and PROs, and the individual DAPSA components in the different states in pts treated with secukinumab through 104 wks using pooled post-hoc analysis.

Methods: FUTURE 2 study design has been reported. DAPSA was derived as sum of five core components: tender joint and swollen joint counts (TJC 68, SJC 66), pt global assessment (PiGA) and pain (PP) assessed by a 10cm VAS, and PROs DAPSA states were determined by remission - REM: <4, MDA: ≤14, LDA: >14 and ≤28, high disease activity (HDA): >28. Means±SD of each core component of DAPSA were analysed at Wks 16, 24, 52 and 104 using observed data. The relationship between HAQ-DI, SF-36 PCS and MCS, PsAQoL, DLQI and FACIT - Fatigue with DAPSA states was assessed in the pooled treatment arms at each time point using a mixed-effect model for repeated measures (MMRM) analyses.

Results: Baseline characteristics were similar across treatment groups. DAPSA scores at baseline (mean±SD) were 42±17.4, 46±21.4 and 44±25.3 in the secukinumab 300mg, 150mg and placebo groups, respectively. Mean scores of each component by DAPSA states at Wk 16 were shown in table and were sustained through Wk 104. Significant differences were observed among secukinumab treated pts between REM vs. HDA and LDA vs. HDA states for PRO scores through Wk104 (Figure).

Conclusions: In pts treated with secukinumab 300 or 150mg, the five individual components related to DAPSA REM were <1 in contrast with other disease states and were sustained through Wk 104. DAPSA REM was associated with significantly greater improvement in physical function, health-related quality of life and fatigue indicating that it is an important target to be achieved and sustained in PsA pts.

References:


AB0766 SECUKINUMAB PROVIDES SUSTAINED REMISSION AND LOW DISEASE ACTIVITY RELATED TO DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA): 2 YEAR RESULTS FROM THE FUTURE 2 STUDY


Introduction: Secukinumab, a fully human anti-interleukin-17A monoclonal antibody, significantly improved American College of Rheumatology responses vs. placebo at Week (Wk) 24 that were sustained through Wk 104 in active PsA patients (pts) in the FUTURE 2 study1. This post-hoc exploratory analysis assessed DAPSA states through Wk 104.

Methods: In total, 397 active PsA pts were randomised to subcutaneous (s.c) secukinumab (300, 150 or 75mg) or placebo at baseline and Wks 1, 2, 3 and 4, and every 4 wks (q4w) thereafter. Placebo pts were re-randomised to secukinumab 300 or 150mg s.c q4w from Wk 16 or 24, depending on Wk 16 clinical response. DAPSA was derived as the sum of five variables: tender joint and swollen joint counts (TJC 68 and SJC 66); pt global assessment and pain assessed on a 10cm visual analogue scale; and C-reactive protein levels (mg/dl) with validated cut-off to indicate remission (REM) or low disease activity (LDA).

Objectives: To explore the relationship between DAPSA states and function, health-related quality of life and fatigue indicating that it is an important target to be achieved and sustained in PsA pts.

Results: Baseline demographics and clinical characteristics were similar across treatment groups and previously reported. DAPSA score at baseline (mean [SD]) was 42.0 (17.4), 46.8 (24.3) and 44.9 (25.3) in the secukinumab 300mg, 150mg and placebo groups, respectively. In the overall population, at Wk 16, REM was achieved in 14/97 (14.4%) with secukinumab 300mg and 10/100 (10%) with secukinumab 150mg vs. placebo 4/87 (4.6%); LDA in 27/97 (27.8%) and 34/100 (34%) vs. 12/87 (13.8%), respectively. REM or LDA were sustained through Wk 104 with secukinumab 300 and 150mg (55/84 [65.5%; REM + LDA] and 41/77 [53.2%; REM + LDA], respectively). The proportion of pts achieving each DAPSA state at Wks 16 and 104 by anti-TNF status (anti–TNF-naïve vs. inadequate response/intolerance to these agents [anti–TNF-IR]) and time since first PsA diagnosis (<2 vs. >2 years) using observed data. Only data for secukinumab 300 and 150mg (approved doses) are reported.

Conclusions: In pts treated with secukinumab 300 or 150mg, the five individual components related to DAPSA REM were <1 in contrast with other disease states and were sustained through Wk 104. DAPSA REM was associated with significantly greater improvement in physical function, health-related quality of life and fatigue indicating that it is an important target to be achieved and sustained in PsA pts.
IL-17-22-23 PATHWAYS IN PSORIATIC ARTHRITIS AND PSORIASIS

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Background: Psoriatic arthritis (PsA) is an immune-mediated chronic inflammatory rheumatoLOGY-associated with psoriasis. T helper 17 pathway has been shown to play an important role in PsA.

Objectives: In this study, we aimed to investigate concentrations of TH17 pathway cytokines such as IL-17, IL-22 and IL-23 in psoriasis (PsO) with/and without structural bone damage and psoriatic arthritis (PsA), and their relationship with disease activity and clinical findings.

Methods: A total number of 74 patients, 24 patients with PsA (mean age 57.5±11.37; 13 women, 11 men) and 25 patients with PsO and structural bone damage (mean age 49±13.92; 11 women, 14 men) and 25 patients with PsO and no structural bone damage (mean age 41±16.77; 7 women, 18 men), were recruited from the Department Internal Medicine 3 of the University of Erlangen-Nuremberg. Both PsO and PsA patients were evaluated according to the CASPAR criteria.

Results: Demographic and disease specific variables were recorded. Bone architecture of the metacarpal heads I and II were assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT, XtremeCT, Scanco, Switzerland). Disease activity was assessed with Disease Activity Score (DAS28). Psoriatic skin and nail disease activity were measured by the PASI.

Results: The ages of the patients in the three groups were similar. IL-17A concentrations were significantly different between the groups (p<0.001). However, we found there was no difference between PsA and PsO groups. Serum levels of IL-17A were significantly correlated to patient pain of VAS (r=0.318, p=0.06), VAS patient global assessment (r=0.272, p=0.021), DAS28 (r=0.394, p=0.001) and PASI (r=0.519, p=0.000) in PsO and PsA. PASI score were also positively correlated with IL23 (r=0.286, p=0.015) and S100A8 (r=0.288, p=0.011).

Conclusions: IL-17A seems to play an important role in development of PsA and bone damage in PsO. This role should be elucidated by further and larger clinical studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6768

AB0767 IL-17-22-23 PATHWAYS IN PSORIATIC ARTHRITIS AND PSORIASIS

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Background: Psoriatic arthritis (PsA) is an immune-mediated chronic inflammatory rheumatoLOGY-associated with psoriasis. T helper 17 pathway has been shown to play an important role in PsA.

Objectives: In this study, we aimed to investigate concentrations of TH17 pathway cytokines such as IL-17, IL-22 and IL-23 in psoriasis (PsO) with/and without structural bone damage and psoriatic arthritis (PsA), and their relationship with disease activity and clinical findings.

Methods: A total number of 74 patients, 24 patients with PsA (mean age 57.5±11.37; 13 women, 11 men) and 25 patients with PsO and structural bone damage (mean age 49±13.92; 11 women, 14 men) and 25 patients with PsO and no structural bone damage (mean age 41±16.77; 7 women, 18 men), were recruited from the Department Internal Medicine 3 of the University of Erlangen-Nuremberg. Both PsO and PsA patients were evaluated according to the CASPAR criteria.

Results: Demographic and disease specific variables were recorded. Bone architecture of the metacarpal heads I and II were assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT, XtremeCT, Scanco, Switzerland). Disease activity was assessed with Disease Activity Score (DAS28). Psoriatic skin and nail disease activity were measured by the PASI.

Results: The ages of the patients in the three groups were similar. IL-17A concentrations were significantly different between the groups (p<0.001). However, we found there was no difference between PsA and PsO groups. Serum levels of IL-17A were significantly correlated to patient pain of VAS (r=0.318, p=0.06), VAS patient global assessment (r=0.272, p=0.021), DAS28 (r=0.394, p=0.001) and PASI (r=0.519, p=0.000) in PsO and PsA. PASI score were also positively correlated with IL23 (r=0.286, p=0.015) and S100A8 (r=0.288, p=0.011).

Conclusions: IL-17A seems to play an important role in development of PsA and bone damage in PsO. This role should be elucidated by further and larger clinical studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1898

AB0768 SONOGRAPHIC SIGNS OF ENTHESITIS IN ESTABLISHED PSORIATIC ARTHRITIS AND HEALTHY VOLUNTEERS

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Background: Previous research in our group showed that sonographic signs of enthesitis are present in early and established PsA, but in young healthy volunteers as well. The Madrid Sonographic Enthesitis Index (MASEI) was only able to differentiate between patients and healthy volunteers after excluding knee and ankle joints.

Methods: A total number of 84 established PsA patients and 25 healthy volunteers aged 35–55 years were enrolled. Both PsO and PsA patients were evaluated according to the Classification Criteria for Psoriatic Arthritis (CASPAR) for the diagnosis of psoriatic arthritis (PsA), not all patients with PsA are seronegative. Measurement of anti-cyclic citrullinated peptides (ACPAs) is a useful key test for rheumatoid arthritis and PsA; however, the prevalence of ACPA in patients with PsA is unclear.

Objectives: We analyzed the clinical features of RF- or ACPA-seropositive patients with PsA in comparison with seronegative patients with PsA using the ISLAND registry (UMIN00002492).

Methods: One hundred patients with psoriasis referred from dermatologists for assessment of synovitis or enthesitis from July 2015 to August 2016 were enrolled. PsA was diagnosed by CASPAR, and synovitis or enthesitis was confirmed by ultrasound assessment. Factors compared between seropositive and seronegative patients included age, sex, smoking, use of disease-modifying antirheumatic drugs, prevalence of enthesopathy, eye symptoms, duration between skin onset and musculoskeletal onset, psoriasis area severity index, composite psoriatic disease activity (CPDAI), psoriatic arthritis screening and evaluation (PASE), disease activity score-28 (DAS-28), and laboratory data.

Results: In total, 52 patients had PsA and 48 patients had psoriasis without any musculoskeletal manifestations. Significant differences were observed in the age at onset of psoriasis (37.4 vs. 47.9 years, respectively; p<0.01) and several clinical parameters (CPDAI: 14.60 vs. 4.55, respectively; p<0.01; PASE: 50.8 vs. 32.0, respectively; p<0.01; DAS28 <3.7 vs. > 3.7, respectively; p<0.009). ACPA positivity was observed in 15.9% of patients with PsA and in 0.0% of patients with psoriasis (p<0.04). Among 44 of the 52 patients with PsA whose ACPA data were available, the duration from skin onset to joint onset was shorter in the 7 ACPA-positive patients (43±32.8 months) than in the 37 ACPA-negative patients (147±115.6 months), although the difference was not statistically significant (p=0.30). There were no statistically significant differences in the PASE, DAS-28, C-reactive protein concentration, or matrix metalloproteinase-3 concentration. The differences between RF positive and negative patients were not also statistically significant.

Table 1

<table>
<thead>
<tr>
<th>ACAP Positive (n=7)</th>
<th>ACAP Negative (n=37)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA3E</td>
<td>45 ±16.1</td>
<td>51 ±113.4</td>
</tr>
<tr>
<td>BIP positivity</td>
<td>28.6</td>
<td>40.5</td>
</tr>
<tr>
<td>DAS28 ESR</td>
<td>4.2±0.9</td>
<td>3.7±1.6</td>
</tr>
<tr>
<td>DAS28 CRP</td>
<td>0.77</td>
<td>0.8±1.7</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>0.56 [0.20–2.39]</td>
<td>0.48 [0.00–16.05]</td>
</tr>
<tr>
<td>MNP-3 (mg/ml)</td>
<td>133 [4.2–184.2]</td>
<td>69.1 [13.5–245.1]</td>
</tr>
<tr>
<td>Duration (skin/SpA) (mo)</td>
<td>54.3±15.2</td>
<td>147.6±15.9</td>
</tr>
</tbody>
</table>

All data are presented as mean ± standard deviation or median [range] unless otherwise indicated.

Conclusions: Among the patients with PsA in this series, ACPA positivity occurred in 15.9% and RF positivity occurred in 12.8%. Seropositive patients with PsA tended to have a shorter duration between skin onset and joint onset compared with RF-negative patients, although the prevalence of ACPA in patients with PsA is unclear.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6768
(median 12 (IQR 7.25–17) vs. 7.5 (5–9), P < 0.001), while the original MASEI did not differ significantly (Table 1). Confluent PD over a larger area was only seen in 8% of the established PsA patients. Structural damage on ultrasound was more pronounced in the patients compared to the healthy volunteers. Number of PD locations and PD score did not distinguish the two groups.

Table 1. Participant characteristics and sonoarthritic enthesitis scores

<table>
<thead>
<tr>
<th></th>
<th>PsA patients (n=84)</th>
<th>Healthy Volunteers (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>45 (54)</td>
<td>12 (48)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>59 (10)</td>
<td>51 (10)</td>
</tr>
<tr>
<td>Disease duration, median years (IQR)</td>
<td>8.0 (4-12.3)</td>
<td>4.0 (2.5–6.5)</td>
</tr>
<tr>
<td>LEI, median (IQR)</td>
<td>0.5 (0-2)</td>
<td>0 (0-0)**</td>
</tr>
<tr>
<td>Ultrasound</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MASEI, median (IQR)</td>
<td>15 (11–22)</td>
<td>13 (9–18)**</td>
</tr>
<tr>
<td>Modified MASEI, median (IQR)</td>
<td>12 (7.25–17)</td>
<td>7.5 (5–9)**</td>
</tr>
<tr>
<td>structural components</td>
<td>7 (3–10)</td>
<td>3 (1–6)**</td>
</tr>
<tr>
<td>inflammatory components</td>
<td>6 (3.5–8.5)</td>
<td>3.5 (2.5–5.5)</td>
</tr>
<tr>
<td>Power Doppler</td>
<td>in any enthesitis, n (%)</td>
<td>74 (88)</td>
</tr>
<tr>
<td>score, 3, (%)</td>
<td>7 (8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>locations, median (IQR)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>if positive, median (IQR)</td>
<td>1.5 (2.15–1.75)</td>
<td>1.5 (2.15–1.75)</td>
</tr>
</tbody>
</table>

PsA: Psoriatic Arthritis; SD: standard deviation, IQR: interquartile range; LEI: Leeds Enthesitis Index; MASEI: Madrid Sonoarthritic Enthesitis Score; modified MASEI: MASEI with new PD scoring method (1: one spot of PD, 1.5: some spots of PD, 2: confluent signal, 3: severe signal) and without knee entheses thickness. Structural components: erosions, calcifications, structure. Inflammatory components: bursitis, thickness and PD signal. PD: Power Doppler. *P < 0.05,** P < 0.01 (Wilcoxon rank sum test).

Conclusions: Inflammatory and structural changes of the enthesis measured with ultrasound are common in both unselected PsA patients and healthy volunteers, but more pronounced in established PsA patients.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3431

AB0770

CHANGE OF PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID12) QUESTIONNAIRE RELATED TO CHANGE IN DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS

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Background: The Psoriatic Arthritis Impact of Disease 12-item questionnaire (PSAID12) has been developed to measure impact of Psoriatic Arthritis (PsA) for purposes of monitoring and clinical management. Although validated in patients with longstanding disease, data on validity and sensitivity to change in early PsA is lacking.

Objectives: We aim to relate change in disease activity to change in PsAID12 score in early PsA and evaluate which PsAID domains are more likely to change.

Methods: Patients with a new diagnosis of PsA were included in the Dutch southwest Early Psoriatic Arthritis cohort (DEPAR). For this analysis, patients that have PsAID12 (range 0–10) and Composite Psoriatic Disease Activity Index (CPDAI) (range 0–15) data at two consecutive visits (i.e. 3 months apart) within the first year were included. In case multiple periods per patients were available, the first time period was chosen. The change in PsAID is compared to the change in disease activity over this period, measured with the CPDAI using Spearman’s correlation coefficient. Change in score on individual domains of the PsAID was analysed in subgroups of patients that perceived improvement in health and those that perceived worsening. The SF-36 question on self-perceived change in health was used to determine these subgroups.

Results: 143 unique patients had at least one period with two PsAID and CPDAI measures (67 from baseline-3 months, 25 6–9 months and 25 9–12 months). Mean age was 51 (SD 13.7) and 70 (49%) were male. The initial median PsAID was 3.35 (IQR 1.4–5.1) and the subsequent score was 2.25 (0.95–4.8 with a mean delta of 0.52 (P < 0.01). Median first CPDAI score was 4 (2–7) and 3 (1–5) for the second with a mean delta of 0.45 (P < 0.05). The difference in CPDAI score was significantly but moderately correlated with the difference in CPDAI (Spearman’s rho 0.267, P=0.0013). 58 patients (41%) report a better health status compared to 3 months ago. Figure 1 shows that patients with self-perceived improvement of health have the highest improvement in pain and only domains of skin problems and embarrassment/shame did not improve significantly. Patients reporting worsening of health (n=29) only have significantly lower scores in fatigue, discomfort and social domains.

Conclusions: Improvement in CPDAI disease activity is significantly but moderately associated with improvement in PsAID score, with the biggest improvement in the pain domain in patients with a self-reported improvement of health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3817

AB0771

SAFETY AND EFFICACY OF APREMILAST THROUGH 104 WEEKS IN PATIENTS WITH MODERATE TO SEVERE PSORIASIS WHO CONTINUE ON APREMILAST OR SWITCH FROM ETANERCEPT TREATMENT IN THE LIBERATE STUDY

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Background: Many patients (pts) with chronic plaque psoriasis exhibit nail and scalp involvement that can markedly affect quality of life and be difficult to treat.

Objectives: The phase 3b LIBERATE (Evaluation in a Placebo-Controlled Study of Oral Apremilast and Etanercept in Plaque Psoriasis) study (NCT01690299) evaluated the efficacy and safety of apremilast or etanercept vs. placebo in biologic-naive pts with moderate to severe plaque psoriasis. Efficacy assessments included effects on preexisting nail and scalp disease and skin lesions.

Methods: In this double-blind, double-dummy study, pts were randomized (1:1:1) to placebo (PBO), apremilast 30 mg BID (APR), or etanercept 50 mg QW (ETN) through Week 16; thereafter, all pts switched to or continued APR (PBO/APR, ETN/APR, APR/APRR) through Week 104. The primary end point was achievement of a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI) score (PASI-75) at Week 16 with APR vs. PBO; the secondary end point was PASI-75 achievement at Week 16 with ETN vs. PBO. Physician assessments were also conducted for overall disease activity (static Physician’s Global Assessment [sPGA]; scalp disease area and severity Physician Global Assessment [ScPGA], limited to patients with score ≥3 at baseline, indicating moderate to very severe scalp disease); and nail disease (Nail Psoriasis Severity Index [NAPSI], limited to patients with active disease [NAPSI ≥1] in the target nail at baseline). Responses were assessed at Week 104 using the last-observation-carried-forward (LOCF) methodology.

Results: The APR extension phase (Weeks 16 to 104) included 226 pts (PBO/APR n=73; APR/APR n=74; ETN/APR n=79). At Week 16, PASI-75 scores were significantly better for both APR and ETN; long-term treatment with APR maintained both PASI-75 and sPGA ≥3 or 1 response levels (Table). Improvements were seen in nail and scalp disease at Week 16, and responses continued to improve with APR treatment over 104 weeks and in pts who switched from ETN to APR (Table). ScPGA 0 or 1 was achieved by 50.0% to 59.2% of pts across treatment arms, and mean percent improvement from baseline PASI NAPSI score ranged from −48.6% to −51.1% (Table); the proportion of pts achieving NAPSI-50 response ranged from 48.6% to 65.2%. Adverse events (AEs) occurring in ≥5% of pts during Weeks 0 to 16 were diarrhea, nausea, nasopharyngitis, upper respiratory tract infection, and headache; long-term assessment by exposure-adjusted incidence rates [EIR] 100 pt-yrs showed no increase with longer-term APR exposure. No increase in EIR/100 pt-yrs of serious AEs occurred during the APR extension phase (3.45 to 5.49, across groups) vs. Weeks 0 to 16 (PBO 0.0; ETN 7.91; APR 12.57). Changes in laboratory parameters were infrequent and transient; EIR/100 pt-yrs remained low across groups through 104 weeks.

Conclusions: APR demonstrated efficacy through Week 104 in pts who continued APR and pts who switched from PBO or ETN to APR at Week 16. The AE profile remained consistent with prolonged APR exposure, and no new safety or tolerability issues were observed through Week 104 in pts with moderate to severe plaque psoriasis.
AB0772 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENT IN FUNCTION, QUALITY OF LIFE AND FATIGUE OVER 2 YEARS IN PATIENTS WHO ACHIEVED LOW DISEASE ACTIVITY RELATED TO PSORIATIC ARTHRITIS DISEASE ACTIVITY SCORE (PASDAS)

L.C. Coates1,2, T.K. Kvien3, P. Nash4, L. Gossec5, V. Strand6, L. Pricop7, L. Rasouliyan8, K. Ding9, S. Jugl9, C. Gaillez9 on behalf of the FUTURE 2 study group.

1University of Leeds; 2Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; 3Diakonhjemmet Hospital, Oslo, Norway; 4University of Queensland, Brisbane, Australia; 5UPMC Universitè Paris 06, Paris, France; 6University of Medicine, Palo Alto; 7Novartis Pharmaceuticals Corporation, East Hanover, United States; 8RTI Health Solutions, Barcelona, Spain; 9Novartis Pharma AG, Basel, Switzerland

Background: PASDAS is a composite index measuring disease activity in psoriatic arthropits (PsA), well correlated with HAQ and health related quality of life.

Objectives: To report the impact of secukinumab on individual core components of PASDAS and its relationship with function, quality of life and fatigue of PsA patients achieved PASDAS low disease activity (LDA) vs. high disease activity (HDA) through Week 104 using post-hoc analysis from FUTURE 2 trial.

Methods: 297 pts with active PsA were randomised to s.c. secukinumab (300, 150, or 75mg) or placebo in FUTURE 2 study. PASDAS is derived from physician’s global VAS, pts global VAS, SF-36 PCS, tender and swollen joints (TJC68 and SJC66), Leeds enthesitis count, dactylitis count and CRP level and has cut-points for HDA (≥3.2) and remission (REM ≤1.9). PASDAS was assessed at Wks 16, 52 and 104 and reported as observed using non-mutually exclusive categories at group level. Additionally, the SF-36 PCS, SF-36 MCS, HAQ-DI, FACIT-Fatigue, PsAQoL, and DLQI were assessed by PASDAS LDA and HDA at Wks 16, 52 and 104 using MMRM analyses.

Results: PASDAS component among pts reaching LDA and HDA at Wk 16 for each treatment group are shown in table and were similar at Wk 104. Secukinumab treated pts achieving PASDAS LDA had significantly greater improvements in function, physical and mental health quality of life and fatigue compared to HDA through Wk 104 (Figures).

Conclusions: In pts treated with secukinumab, the most improved individual components with PASDAS LDA were related to dactylitis, enthesitis, SF36-PCS, Physician global VAS and SJC at Wk 16 and Wk 104. PASDAS LDA was associated with better improvement in function, quality of life and fatigue than HDA confirming the importance to reach stringent target in a PsA pts with PsA associated with better improvement in function, quality of life and fatigue than

References:


Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Celgene, Pfizer, UC, MSD, Sun Pharma, Novartis, Lilly, L. Kvien Consultant for: bbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epiris, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: bbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epiris, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, P. Nash Grant/research support from: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, Consultant for: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, Speakers bureau: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, L. Gossec Grant/research support from: Abbvie, BMS, Cellgene, Janssen, Novartis, MSD, Roche and UCB, V. Strand Consultant for: Abbvie, Amgen, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, and UCB, L. Pricop Shareholder of: Novartis, Employee of: Novartis, L. Rasouliyan Consultant for: Novartis through employment at RTI Health Solutions, Employee of: RTI Health Solutions, K. Ding Shareholder of: Novartis, Employee of: Novartis, S. Jugl Employee of: Novartis, C. Galiez
**AB0773** EFFECTIVENESS OF GOLIMUMAB IN TNF-INHIBITOR PREVALENCE, CLINICAL AND RADIOGRAPHIC UNDERESTIMATED AXIAL AND ENTHESIAL INVOLVEMENT IN


1 Državni Univerzitet Novi Pazar, Departman za biomedicinske nauke, Novi Pazar; 2 Ambulatorio Reumatologia, Ospedale di Mesagne, Mesagne, Italy; 3 Državni Univerzitet Novi Pazar, Departman za biomedicinske nauke, Novi Pazar; 4 Institute Niska Banja, Nis, Serbia

**Background:** In real-life world settings, failure of a first TNF-inhibitor (TNFi) put rheumatologists against a crossroad to choose a further TNFi or a biologic drug with a different mechanism of action. 

**Objectives:** Aim of this study was to assess effectiveness of golimumab (GOL) as second line drug after failure of a first TNFi as treatment of patients affected with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or axial-spondyloarthritis (AxSpA).

**Methods:** GOAREL is a prospective cohort of patients starting GOL in community-based care rheumatology centers in Apulia (south Italy) since 2013. Of 494, we selected 368 patients (RA n.73, PsA n.168, and AxSpA n.127) commencing GOL as first ever biological (n.206, 55%) or second treatment (n.161, 44%) after inadequate response to a first TNFi (adalimumab (ADA, n.51), etanercept (ETA, n.81), or infliximab (IFX, n.29). Three patients failing certolizumab were excluded. Primary endpoint was to compare the drug retention rate of biological naïve and TNFi inadequate responders (TNFi-IR) patients on treatment with GOL. In addition, drug retention of second line GOL patients according to the fires TNFi was assessed. Drug survival was estimated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs) of 2-years drug discontinuation adjusted for demographics, type of disease, disease characteristics, body mass index, co-therapy with glucocorticoids or methotrexate, and prior TNFi were computed by backward selection Cox-regression model.

**Results:** 2-year drug survival on GOL of naïve and TNFi-IR patients was not significantly different (Figure 1). Mean survival time was 20.0 months (95% CI 18.9–21.0) for naïve and 20.4 months (95% CI 19.3–21.6) for TNFi-IR patients. Likewise, drug retention rates on GOL of TNFi-IR patients subdivided by previous TNFi was not significantly different and similar to naïve patients (Figure 1). Mean survival time was 19.0 months (95% CI 16.7–21.4) for prior-ADA, 20.5 months (95% CI 19.9–22.1) for prior-ETA, and 22.0 months (95% CI 19.6–24.3) for prior-IFX. Multiple Cox-regression model showed gender female as the only independent factor positively associated to the risk of GOL discontinuation (HR 2.5, 95% CI 1.5–4.2, p 0.0001).

**Conclusions:** In real-life setting effectiveness of GOL seems to be similar in naïve or TNFi-IR patients with RA, PsA, and AxSpa. Furthermore, clinical outcomes were not influenced by the previous TNFi.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3610

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**AB0777** UNDERESTIMATED AXIAL AND ENTHESIAL INVOLVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS IN A RUSSIAN RHEUMATOLOGICAL DAILY PRACTICE: COMPARED WITH RHEUMATOLOGICAL PRACTICE

M. Chamurtseva, E. Loginoa, T. Kostateva, Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

**Background:** Psoriatic arthritis (PsA) is frequently underdiagnosed by dermatologists due to its heterogeneous clinical manifestations such as peripheral arthritis, dactylitis, spondylitis and enthesitis. For the correct early diagnosis, choice of treatment and for better outcomes proper evaluation of all symptoms is required. 

**Objectives:** To compare the definition of the main clinical symptoms of PsA by dermatologists and rheumatologists in daily clinical practice.

**Methods:** 103 pts (male-47/female-56) with different forms of plaque psoriasis (PsO), mean age 44±13.69 years (yrs.), mean psoriasis duration 10.7±10.2 yrs., mean PASI 5.05±1.23 were included. In rheumatological clinic, all pts completed a PEST questionnaire and underwent clinical evaluation by a dermatologists in order to identify the main clinical symptoms of PsA such as peripheral arthritis, dactylitis, spondylitis and enthesitis. Later all pts were subsequently evaluated by dermatologists to confirm/exclude the diagnosis of PsA based on CASPAR criteria and underwent standard clinical examination to identify the same symptoms - peripheral arthritis, dactylitis, spondylitis (based on inflammatory back pain (IBP) ASAS criteria) and enthesitis (based on Leeds Enthesial Index (LEI) plus Plantar Fascia (PF)), Mtm%, t-test were performed. All p<0.05 were considered to indicate statistical significance. 

**Results:** 61 out of 103 pts with PsO (59.2%) had PsA based on rheumatological evaluation and CASPSSR criteria. Dermatologists diagnosed peripheral arthritis in significantly less cases compared to rheumatologists: in 15 (24.6%) and in 35 (57.4%) out of 61 pts (p<0.001) accordingly. No significant difference was seen in clinical evaluation of dactylitis by dermatologists or rheumatologists - in 37 (60.7%) and in 40 (65.6%) out of 61 pts accordingly (p=0.32). Heel pain was noted by dermatologists in 32 out of 61 pts (52.5%) according to PEST questionnaire. Dermatologists could not find enthesis according to LEI. Rheumatological examination based on LEI scale identified lateral epicondyles in 11 out of 61 pts (18%), enthesis of medial femoral condyles in 8 out of 61 pts (13.1%), enthesis of Achilles tendon insertions – in 25 out of 61 pts (41%). Enthesitis of PF were observed in 15 out of 61 pts (24.6%). Dermatologists noted back pain using PEST questionnaire in 30 out of 61 pts (49.2%). IBP based on ASAS criteria was not detected by a dermatologists in any case. In these 30 pts having back pain IBP was diagnosed by a rheumatologists in 21 (70%) cases; and in the rest 9 out of 30 pts (30%) mechanical back pain was observed. On the basis of clinical examination tendinitis was not noted by dermatologists, while rheumatologists found hand tendinitis in 13 out of 61 pts (21.3%).

**Conclusions:** Peripheral arthritis, axial and enthesis involvement were underestimated by dermatologists using PEST screening questionnaire, because it does not cover these symptoms in detail. ASAS criteria for IBP and standard enthesitis assessment should be implemented into Russian rheumatological clinical practice. To improve early PsA diagnosis in rheumatological practice, interdisciplinary educational training programmes and collaboration with rheumatologists are needed.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2771
THE EFFECT OF PREGNANCY ON DISEASE ACTIVITY OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis often affects patients at a childbearing age. The relationship between pregnancy and psoriatic arthritis, in terms of pregnancy outcomes and its effect on disease activity, has not been well studied

Objectives: To evaluate the effect of pregnancy on disease activity in psoriatic arthritis.

Methods: A retrospective review of files of female patients followed at Psoriatic arthritis clinic at the Tel Aviv Medical center was performed, patients with at least 1 pregnancy during follow up and one visit during or soon after pregnancy were included. A review of files was performed which included the follow-up: age, disease duration, pattern of PsA, disease activity before and during and after pregnancy, record of treatment, including IA injections. Postpartum period was defined as up to 1 year after pregnancy. PsA activity was defined as follow: no disease activity (no active synovitis), mild disease (up to 1 joint involved), moderate to severe disease (more than 2 joints involved). The follow-up during and after pregnancy was classified as: improvement, worsening or stable.

Results: 25 PsA women and 35 pregnancies were identified. 33 resulted in live healthy babies. One pregnancy was interrupted on week 23, so partial follow up was available. The mean age at pregnancy was 32.5 years. Table 1 summarizes statistical disease activity before, throughout pregnancy and during the postpartum period in the whole group. No significant change in disease activity was noticed throughout pregnancy while significant proportion of patients flared at postpartum. Before 21 pregnancies patients were treated with biologic agents. In 15, biologic treatment was discontinued close to pregnancy or during flared at postpartum. Before 21 pregnancies patients were treated with biologic agents. In 10, biologic treatment was discontinued close to pregnancy or during flared at postpartum. Before 21 pregnancies patients were treated with biologic agents. In 10, biologic treatment was discontinued close to pregnancy or during flared at postpartum.

Conclusions: Patients with PsA definitively flare after pregnancy. Our results suggest that stopping treatment with biologic agents before pregnancy is associated with flare during pregnancy and the postpartum period. It seems that in terms of PsA disease activity, it may be recommended to continue treatment with biologic agents throughout pregnancy.

Disclosure of Interest: None declared


CHARACTERISTICS OF AMYLOID A DEPOSITION IN PSORIATIC ARTHRITIS AND IN RHEUMATOID ARTHRITIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 RHEUMATOID AND 12 PSORIATIC ARTHRITIS PATIENTS

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Background: The aim of this study was to determine the prevalence and extent of amyloid A deposition on different tissue structures in various organs of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients.

Methods: AAs was detected in 34 (21.1%) females; 29, average age: 64.3 years, range: 63–32, onset of RA: 48.6, average disease duration: 14.8 years) of 161 RA, and in 2 (16%) female: 2 average age: 57.5 years, range: 63–52, onset of PsA: 47.5, average disease duration: 11.0 years) of 12 PsA patients.

RA and PsA were diagnosed clinically according to the criteria of the American College of Rheumatology (ACR) [1,2].

Amyloid deposits on different tissue structures [arteriolar, small artery, medium size artery, venule, small vein, medium size vein, interstitial collagen fiber, reticulin fiber] were evaluated, using these "global assessment" by the patient (PaGl) and by the physician (PhGl). The agreement and interplay between PaGl and PhGl are not well clarified in patients with PsA, however.

Disclosures: None declared

DOI: 10.1136/annrheumdis-2017-eular.1221

PATIENT AND PHYSICIAN GLOBAL ASSESSMENTS ARE POORLY CONNECTED IN INDIVIDUAL PATIENTS WITH PSORIATIC ARTHRITIS AND ONLY POORLY EXPLAINED BY OTHER CLINICAL MARKERS OF DISEASE ACTIVITY

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Background: Assessment of disease activity is important in the evaluation and monitoring of patients with psoriatic arthritis (PsA) in clinical care and research. As there is no single "gold standard" variable for assessment of disease activity several markers of disease activity are used, among these "global assessment" by the patient (PaGl) and by the physician (PhGl). The agreement and interplay between PaGl and PhGl are not well clarified in patients with PsA, however.

Objectives: The objective of the study was to examine associations on the group level and agreements on the individual patient level between PaGl and PhGl as scored on visual analogue scales (VAS) in the daily clinic by patients with active PsA and their rheumatologists.

Methods: Traditional disease activity data on 76 PaA patients with active disease planned to initiate biological treatment were extracted from the Danish DANBIO registry. Data comprised swollen joint count (SJC), tender joint count (TJC), CRP, patient and physician global assessment (PaGl and PhGl) and pain (VAS), HAQ-DI and DAS28-CRP (4v). Parametric statistics was used. The predictability of PaGl and PhGl, respectively, by all other disease markers mentioned and by age and sex was examined using stepwise multiple regression analysis. Agreement between the VAS scores was expressed as the bias (mean difference between intra-individual scores) and the 95% lower and upper limits of agreement (lLoA;ULoA) according to the Bland-Altman method.

Results: The prevalence and extent of amyloid A deposits on different tissue structures were compared by Student (Welch) t-probe.

Conclusions: The difference between average prevalence (£0.388) and average amount (£0.444) of amyloid A deposits in structures and PsA patients was not significant.

Disclosure of Interest: None declared

vs. PSo, PaSo was in general scored considerably higher than PSo. The two scores were poorly correlated not only on the individual level but also on group level with no systematic differences between the scores. PaSo was best predicted by pain, and PSo by SCJ reflecting patients and physicians diverging attitudes to the importance of the different disease manifestations. The findings highlight the challenge of understanding and dealing with discrepancies between assessments and attitudes by physicians and patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4092

<table>
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<tr>
<th>AB0779</th>
<th>CLINICAL MANIFESTATIONS AND PARAMETERS AFFECTING THERAPEUTIC RESPONSE IN A COHORT OF 411 PSORIATIC ARTHRITIS PATIENTS</th>
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<tr>
<td>M.P. Migkos, T.-E. Memi, T.E. Markatseli, A.A. Drosos, P.V. Voulgaris, University of Ioannina, Ioannina, Greece</td>
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Background: Psoriatic arthritis (PsA) has various clinical manifestations. The therapeutic response of patients may be affected by epidemiological parameters such as body mass index (BMI), disease duration, sex and the choice of therapy. Objectives: To illustrate clinical manifestations of psoriatic arthritis to assess the impact of epidemiological features and treatment choice on therapeutic response.

Methods: We retrospectively studied 411 patients diagnosed with PsA and we recorded the clinical manifestations of the disease. Data of 254 out of 411 patients were analyzed to examine the possible effect of BMI, disease activity, sex and treatment choice on therapeutic response. Patients were followed up at predefined time points (baseline, 12 weeks, 24 weeks, 48 and 240 weeks after initiation of treatment). The therapy response was assessed using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), disease activity score-28 (DAS) - C-Reactive Protein (CRP), DAS28-erythrocyte sedimentation rate (ESR) and Health Assessment Questionnaire (HAQ). Patients were categorized in three groups: patients treated with biological synthetic disease modifying anti-rheumatic drugs (DMARDs) (anti-tumor necrosis factor alpha (TNFα) agents), patients treated with synthetic DMARDs and combined therapy (biological and synthetic DMARDs).

Results: The interval between psoriasis and PsA in women is shorter (<p=0.041). PsA presented predominantly as asymmetric oligoarthritis (41.6%), followed by symmetric polyarthritis (24.5%). Arthritis of distal phalangeal joints was established in 3.14%, while 4.37% shown only enthesitis or dactylitis. Axial involvement was recorded in 26.27%. Twenty-eight patients had only axial disease and 60% had peripheral joint involvement. 23/411 patients (5.60%) had eye involvement, 8/411 (1.95%) and 6/411 (1.46%) had involvement of the urogenital and gastrointestinal system, respectively. Eleven patients had pulmonary fibrosis. In the subgroup analysis of 254 patients, disease duration was positively correlated in all time points (<p=0.005) with all disease activity scores. Statistical significant difference with respect to gender was observed for DAS28-CRP (3.93–2.96, 3.54–2.64 p<0.001) and DAS28-ESR (3.37–2.82 p=0.001, 3.06–2.26 p=0.023) at 12 and 24 wks respectively. More specifically women showed higher disease activity than males the first 6 months after treatment. BMI was not significantly correlated with the disease activity. Treatment with biological DMARD showed a statistically significant difference in all disease activity scores early in the disease course (<p=0.05) in comparison with those receiving conventional DMARD. After the first 12 wks all disease activity scores were rather stable with no differences between the treatment groups.

Conclusions: PsA manifests predominantly as asymmetric oligoarthritis. Extraarticular manifestations are less frequent. Higher disease duration was associated with higher disease activity. Women early on disease course had higher DAS-28 scores. Treatment with biological DMARD showed better response in PsA patients compared with synthetic early in the disease course. However, after the first 12 wks there were no significant differences in treatment response with respect to treatment choice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4784

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<th>AB0780</th>
<th>SECUKINUMAB SUSTAINS INDIVIDUAL CLINICAL RESPONSES OVER TIME IN PATIENTS WITH PSORIATIC ARTHRITIS: 2-YEAR RESULTS FROM A PHASE 3 TRIAL, FUTURE 2</th>
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<td>P. Emery1, I.B. McInnes2, P.J. Mease3, M. Schiff4, L. Trircp5, S. Shen5, Z. Wang5, C. Gaille6 on behalf of the FUTURE 2 study group. 1University of Leeds, Leeds; 2University of Glasgow, Glasgow, United Kingdom; 3Swedish Medical Centre and University of Washington, Seattle; 4University of Colorado, Denver; 5Novartis Pharmaceuticals Corporation, East Hanover, United States; 6Novartis Pharma AG, Basel, Switzerland</td>
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Background: Achieving sustained clinical response to biologics is part of treat-to-target recommendations in psoriatic arthritis (PsA) and is aimed at optimising treatment goals.1

Objectives: To evaluate patient (pt)-level secukinumab data and report the likelihood of improving, sustaining or worsening of American College of Rheumatology (ACR) response and disease status (disease activity score 28 based on C-reactive protein [DAS28-CRP]) from Week (Wk) 24 to 104 in pts with active PsA from the FUTURE 2 trial.2,3

Methods: The findings of the FUTURE 2 trial through Wk 104 have been previously reported.3 Post-hoc shift analyses were performed on ACR response between Wks 24 and 104 for subgroups of secukinumab-treated pts, based on their higher response rate at an earlier time point in 1 out of 4 categories (ACR non-responders [NR], ACR20, 50 or 70) by evaluating whether the response improved, sustained or worsened at a later time point using exclusive categories and as observed analyses. Similar shift analysis on DAS28-CRP derived criteria were performed in 4 exclusive categories extrapolated from rheumatoid arthritis: high, moderate, low disease activity (HDA, MDA, LDA) or remission (REM) only.4

Results: In total, 86/100 (86%) and 76/100 (76%) pts in the secukinumab 300 and 150mg groups, respectively, completed the 104-wk treatment. Of which, 73/70 and 81/75 pts in secukinumab 300/150mg were eligible for ACR and DAS28-CRP shift analysis, respectively, from Wk 24 to 104. Baseline demographics and clinical characteristics were balanced across the two dose groups.2,3 Most secukinumab-treated pts who achieved at least an ACR20, 50 or 70 response and Psoriasis Area and Severity Index (PASI) 75 or 90 response at Wk 24, improved or sustained their response at Wk 104 (Figure, data not shown for PASI response). Similarly, a majority of pts who were in the MDA, LDA or REM category at Wk 24 sustained or improved their disease status related to DAS28-CRP score at Wk 104 (Figure).

Figure: Shift analysis in ACR and DAS28-CRP responses from Week 24 to 104

Conclusions: In this post-hoc analysis, a majority of secukinumab-treated pts who achieved at least ACR20 and PASI 75 response or at least MDA at Wk 24 sustained or improved their ACR and PASI responses or sustained or reduced their disease status at Wk 104. Numerically higher sustained response and LDA or REM rate was observed for secukinumab 300mg, thereby extending the sustainability of response and lowering the disease activity that has been previously reported at group level.2,3

References:

Disclosure of Interest: P. Emery Consultant for: AbbVie, BMS, Merck, Novartis, Roche, UCB, I. B. McInnes Consultant for: Novartis, Amgen, Janssen, BMS, Pfizer, UCB, Abbvie, Celgene, Lilly, P. Mease Grant/research support from: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Covagen, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Biogen Idec, BMS, Crescendo, Janssen, Lilly, Pfizer, UCB, M. Schiff Consultant for: AbbVie, BMS, Lilly, J&J, Speakers bureau: AbbVie, L. Pricop Shareholder of: Novartis, Employee of: Novartis, S. Shen Employee of: Novartis, Z. Wang Employee of: Novartis, C. Gaillez Shareholder of: Novartis, BMS, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.1228
AB0781 PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS: RESULTS OF A FRENCH SURVEY

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Background: Early detection of psoriatic arthritis (PsA) in patients with skin psoriasis (Pso) is critical to reduce the risk of joint damage, disability, and comorbidities. However, PsA is mostly underdiagnosed in patients with Pso. Objectives: first to compare characteristics of patients with Pso without PsA with those of patients with Pso and PsA, then to compare patients with PsA and potential but undiagnosed PsA (puPsA) to the other patients.

Methods: 817 patients completed an online questionnaire published by the French Psoriasis Patients Association, including multiple-choice questions regarding in particular past and current symptoms. For analysis, a first comparison was performed between patients with Pso without known PsA and patients with PsA and PuPsA, then between patients with symptoms suggestive of PsA (puPsA group), i.e., patients with past or current joint or back pain accompanied by waking up at night and/or morning stiffness, with PsA patients on the one hand, and with patients without known PsA and without symptoms suggestive of puPsA, on the other hand.

Results: 746 patients reported having Pso of which 192 (25.7%) had also PsA. Among the 554 patients without known PsA, 190 (34.3%) had symptoms suggestive of PsA, 101 (18.2%) had rheumatologic symptoms without suggestive of PsA, and 263 (47.5%) had no rheumatologic symptoms. The comparison, in multivariate analysis, between patients with Pso and PsA and patients with Pso without known PsA showed significant differences (p<0.05): Pso and PsA patients had more often current bone or joint pain at any time (OR=7.8), joint pain during the day (OR = 2.45), stiff back or joints on waking (OR=1.77), painful and swollen fingers and toes (OR=3.15), past joint pain during the day (OR=3.05), and drug in tablet form (OR=2.07), biotherapy alone (OR=0.45) or with DMARDs (OR=16.06); conversely they had less often guttate psoriasis (OR=0.54). Results of the multivariate analysis comparing patients with puPsA to the other patients are shown in Tables 1 and 2 (comparison with patients with Pso and PuPsA in Table 1; comparison with patients with Pso without known PsA in Table 2).

Table 1. Multivariate analysis, patients with puPsA and Pso compared with patients with Pso and PsA

<table>
<thead>
<tr>
<th>Covariates (p&lt;0.05 for all OR)</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Current spine pain</td>
<td>OR=1.65 [1.23; 2.18]</td>
</tr>
<tr>
<td>Current bone or joint pain</td>
<td>OR=0.25 [0.15; 0.44]</td>
</tr>
<tr>
<td>Current joint pain during the day</td>
<td>OR=0.49 [0.29; 0.84]</td>
</tr>
<tr>
<td>Current back pain</td>
<td>OR=2.55 [1.2; 2.9]</td>
</tr>
<tr>
<td>Current painful and swollen fingers and toes</td>
<td>OR=0.29 [0.17; 0.51]</td>
</tr>
<tr>
<td>Past joint pain during the day</td>
<td>OR=0.39 [0.19; 0.79]</td>
</tr>
<tr>
<td>Biotherapy/Neither biotherapy nor DMARD</td>
<td>OR=0.28 [0.12; 0.67]</td>
</tr>
<tr>
<td>Biotherapy + DMARD/Neither biotherapy nor DMARD</td>
<td>OR=0.15 [0.04; 0.55]</td>
</tr>
</tbody>
</table>

Table 2. Multivariate analysis, patients with Pso without known PsA compared with patients with Pso and PsA

<table>
<thead>
<tr>
<th>Covariates (p&lt;0.05 for all OR)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current spine pain</td>
<td>OR=1.53 [1.2; 2.28]</td>
</tr>
<tr>
<td>Current fatigue</td>
<td>OR=2.53 [1.72; 3.72]</td>
</tr>
<tr>
<td>Other current symptoms</td>
<td>OR=0.33 [0.18; 0.60]</td>
</tr>
<tr>
<td>Hydration</td>
<td>OR=1.48 [1.01; 2.18]</td>
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</table>

Conclusions: That survey on Pso patients showed that a fourth of them also had PsA, but more importantly that about another fourth had puPsA, highlighting the underdiagnosis of PsA. It suggests that presence of fatigue and nail changes might raise suspicion of PsA in Pso patients.

Disclosure of Interest: P. Claudepierre Grant/research support from: AbbVie, MSD, Roche, Pfizer, Consultant for: AbbVie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche, UCB, P. Richebe: None declared, S. Benkhalifa: None declared, D. Sid Mohand: None declared, B. Charles: None declared, Y. Braults: None declared, M. Lahaia: None declared, M. Lahta: Consultant for: investigator or speaker for AbbVie, MSD, Celgene, Janssen, Novartis, Pfizer, Roche, Takeda, UCB, Lilly, Leo Pharma, Galderma, Astellas, Pierre Fabre, Dermatology.

DOI: 10.1136/annrheumdis-2017-eular.2397

AB0782 PSORIATIC ARTHRITIS EARLY ULTRASONOGRAPHIC CHANGES IN PATIENTS WITH PSORIASIS AND NAIL PSORIASIS: A COMPARATIVE STUDY WITH SUBJECTS WITHOUT PSORIASIS

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Background: Psoriatic Arthritis (PsA) has a prevalence of 30% amongst Psoriasis (Ps) patients. However in patients with ungual Ps the prevalence has been reported in up to 68% of cases. In musculoskeletal ultrasound (MSUS) studies the lesion most frequently reported is enthesis followed by synovitis in early PsA patients.

Objectives: To determine the presence of psoriatic arthritis early ultrasonographic changes in patients with psoriasis, nail psoriasis, and subjects without psoriasis.

Methods: Analytic, comparative, prospective and transversal study, in which patients with psoriasis, nail psoriasis, and subjects without psoriasis paired by age, were recruited. Each group underwent a skin and joint checkup, which included demographic data, comorbidities, psoriasis severity and joint signs and symptoms. The ultrasonographic evaluation consisted in a gray scale detection and classification according to severity scales, of synovitis, enthesis, synovial effusion and bone erosions in the distal interphalangeal joints of both hands.

Results: A total of 16 patients, 8 with psoriasis and 8 with nail psoriasis, as well as 9 subjects without psoriasis, were recruited. The psoriasis group included mostly men (87.5%), unlike the subjects without psoriasis (44.4%) and the nail psoriasis group (37.5%) (p=0.09). The mean age for the study population was 55.16 ± 8.09 years. There was no statistical significance between groups (p=0.430). The greatest prevalence of comorbidities was found in both groups with psoriasis. The mean time of disease duration in the nail psoriasis group was 20.12 ± 14.54 years, vs 13.37 ± 14.45 years in the psoriasis group (p=0.247). Synovitis was found in 100% of patients in the psoriasis group, vs 37.5% in the nail psoriasis group, and 62.5% in the subjects without psoriasis group (p=0.028). No enthesitis was observed in any group.

Conclusions: Synovitis was more frequent than enthesis in our population as an ultrasonographic finding of psoriatic arthritis. No association was found between other variables with synovitis, such as age, sex, disease duration and comorbidities.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5552

AB0783 THE RELATIONSHIP BETWEEN THE DEGREE OF SKIN INVOLVEMENT AND JOINT ACTIVITY IN PATIENTS WITH PSA: EXPERIENCE FROM THE CORRONA REGISTRY


Objectives: To characterize the relationship between skin severity and joint activity in patients with comorbid PsA and PsO at enrollment.

Methods: Data from the U.S. Corrona PsA/spondyloarthritis (PsA/SpA) registry were obtained from the period 3/21/2013–9/30/2016. Inclusion criteria included a diagnosis of PsA, a history of PsO, and age greater than 18 years. PsA patients were evaluated for skin severity as defined by Body Surface Area (BSA) and joint activity as defined by the level of clinical disease activity index (CDAI). Patient characteristics, including current and prior PsA medication use, were obtained during the enrollment visit. We evaluated the relationship between skin severity (BSA) and joint activity (CDAI) with multi-variable linear regression.

Results: 1,542 patients met inclusion criteria: 52.9% were women with mean (SD) age 53.7 (13.2) years, with median 9.0 years PsA disease duration, and 71 (4.6%) with fibromyalgia. 266 (18%) patients were on DMARD therapy, 430 (29%)
on csDMARDs only. 616 (42%) were on first line biologic/targeted synthetic (ts)DMARD therapy, and 172 (12%) were on second line biologic/tsDMARD therapy. The relationship between skin severity and joint activity was statistically significant ($p<0.0001$) with a correlation of $0.183$. Results were similar when adjusting separately for treatment and for duration of PsA and PsO. Greater age, female gender, higher dactylitis count, not achievement of MDA, higher HAQ, and patient reported pain and fatigue affected the relationship.

**Conclusions:** The relationship between skin severity and joint activity is statistically significant and varies by age, gender, MDA, HAQ, and patient reported pain and fatigue. This suggests degree of skin involvement is important to take into account when evaluating PsA patients.

**References:**


**Acknowledgements:** Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, AstraZeneca, BMS, Celgene, Crescendo, Lilly, Merck, Pfizer, Sun, UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer, UCB, C. Etzel Consultant for: Merk, Employee of: Corrona, LLC; J. Lisse Shareholder of: Eli Lilly and Company, Consultant for: AbbVie, Amgen, BMS, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer, UCB, E. Lespessailles 6, G. Schett 7, M. Paris8, L. Teng9, J. Wollenhaupt9. 6Medical Center and University of Washington School of Medicine, Seattle, United States; 2Toronto Western Research Institute, Toronto, Canada; 3Hospital Clínico Universitario, Santiago, Spain; 4Monash University, CabriniHealth, Melbourne, Australia; 5University of California, San Diego, School of Medicine, La Jolla, United States; 6University of Orléans, Orléans, France; 7University of Erlangen-Nuremberg, Erlangen, Germany; 8Celgene Corporation, Summit, New Jersey; 9Schön Klinik Hamburg Elbek, Hamburg, Germany.

**Background:** Dactylitis and enthesitis are common disease manifestations encountered in nearly 10–30% of patients with psoriatic arthritis (PsA). Previous clinical trial data suggests that anti-tumor necrosis factor (aTNF) is effective in controlling dactylitis and enthesitis among PsA patients, however there are limited data in real world studies.

**Objectives:** To evaluate the effectiveness of aTNFs on dactylitis and enthesitis in patients with PsA enrolled in Corrona, a large US observational cohort of patients with PsA and spondyloarthritis.

**Methods:** Adult PsA patients who initiated or were currently on an aTNF at recruitment (definition) between 3/2013–9/2016 and had a 12 month follow-up visit were included. Dactylitis was defined as a non-zero total dactylitis score on a scale 0–20 and enthesitis was defined by a non-zero score on the SPARRC enthesitis index, 0–16. The primary outcome was change in dactylitis and enthesitis scores at 12 months from baseline. Descriptive analysis of patient characteristics at baseline was examined and change in outcomes was evaluated using t-tests.

**Results:** There were 28 patients with dactylitis and 77 patients with enthesitis who met the inclusion criteria. Patients with dactylitis and enthesitis had a mean (SD): age of 49.2 (11.5) years, body mass index of 30.8 (6.6) and 31.4 (7.6), disease duration of 9.3 (9.1) and 8.1 (7.7) years, and 28.6% and 45.5% were on methotrexate combination therapy respectively. Patients had a mean clinical disease activity index of 15.1 in both groups, 40.0% and 17.1% were in minimal disease activity, mean (SD): body surface area was 4.4 (4.4) and 5.2 (2.6) and mean APACHE II score was 31.1 (28.5) and 43.3 (27.5) on a visual analogue scale (VAS) of 0–100, and more than 80% and 90% of patients had some morning stiffness in the dactylitis and enthesitis groups, respectively. At 12 months from baseline, there were significant improvements in both dactylitis and enthesitis scores in patients with PsA treated with aTNF (Table).

**Table:** Primary outcomes in PsA patients on aTNF at 12 months from baseline

<table>
<thead>
<tr>
<th>Dactylitis Count</th>
<th>At enrollment</th>
<th>At 12 month</th>
<th>Change in score (enrollment – 12 month visit)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>m28</td>
<td>52.2 (20.3)</td>
<td>8.1 (11.5)</td>
<td>-44.1 (13.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>n27</td>
<td>7.3 (2.9)</td>
<td>1.8 (2.3)</td>
<td>-5.5 (1.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** In this clinical registry, aTNF therapy significantly improved both dactylitis and enthesitis at 12 months. Further evaluation of secondary outcomes and larger studies with comparator cohorts will further validate the effectiveness of aTNFs in improving the outcomes in PsA patients.

**Acknowledgements:** This study is sponsored by Corrona, LLC. The Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer, UCB, C. Etzel Employee of: AbbVie, Inc; K. Douglas Shareholder of: AbbVie, Inc; Employee of: AbbVie, Inc; D. Hua Shareholder of: Corrona, LLC; H. Litman Employee of: Corrona, LLC, C. Karki Employee of: Corrona, LLC, J. Griffith Shareholder of: AbbVie, Inc; Employee of: AbbVie, Inc; DOI: 10.1136/annrheumdis-2017-eular.1532

**AB0785**

**CONSISTENT SAFETY PROFILE WITH UP TO 4 YEARS OF APREMILAST TREATMENT: ANALYSIS OF DATA FROM 1493 PATIENTS WITH PSORIATIC ARTHRITIS IN 3 LARGE, PHASE III, LONG-TERM STUDIES**


**Background:** Apremilast (APR), an oral phosphodiesterase 4 inhibitor, regulates immune activity in psoriatic arthritis (PsA) patients. Safety data were pooled from the phase 3 PALACE 1, 2, and 3 studies.

**Objectives:** Evaluate the long-term safety of APR treatment for up to 4 years in patients with active PsA despite prior conventional DMARDs and/or biologics.

**Methods:** Patients were randomized at baseline (1:1:1 to placebo, APR) to 30 mg bid (APR30), or 40 mg bid (APR40). PBO patients were re-randomized to take into account when evaluating PsA patients.

**Conclusions:** aTNF therapy significantly improved both dactylitis and enthesitis at 12 months. Further evaluation of secondary outcomes and larger studies with comparator cohorts will further validate the effectiveness of aTNFs in improving the outcomes in PsA patients.
to APR30 or APR20 at Week 16 (early escape) or Week 24. Double-blind APR treatment continued to Week 52; patients could continue APR during an open-label, long-term treatment phase for up to 5 years. Visits in years 2, 3, and 4 were scheduled at 13-week intervals. Safety was assessed at each visit throughout the study, and results are summarized here by exposure.

At least one PROM of 1494 patients were randomly selected and reviewed: 1 dose of study medication (PBO: n=495; APR30: n=497; APR20: n=501). At the 4-year data cut, the numbers of patients receiving APR30 and APR20 in each exposure period were 1441 in Weeks 0 to ≤52, 1028 in Weeks >52 to ≤104, 865 in Weeks >104 to ≤156, and 767 in Weeks >156 to ≤208. During the 0- to ≤52-week APR-exposure period, adverse events (AEs) occurring in >5% of APR30-exposed patients were diarrhea, nausea, headache, upper respiratory tract infection, and nasopharyngitis (Table). Most diarrhea and nausea AEs were reported within the first 2 weeks of treatment and usually resolved within 4 weeks; the frequency of gastroenterological AEs was higher with longer APR30 exposure. The frequency of other common AEs either decreased or remained stable with prolonged exposure (Table). Most AEs were mild/moderate in severity. During Weeks >156 to ≤208 of APR exposure, the discontinuation rate due to AEs was 1.7% with APR30, and the rate of serious AEs (SAEs) was 7.0%, consistent with earlier periods; most SAEs occurred in 1 patient each case. Rates were very low for major cardiac events, malignant neoplasms, and serious opportunistic infections, comparable to the first year of treatment. Rates of depression remained very low in Weeks >156 to ≤208. Marked laboratory abnormalities were infrequent, and most returned to baseline with continued treatment.

Conclusions: APR30 demonstrated a favorable safety profile and was well tolerated for up to 208 weeks, marked by the lack of accumulation of immunosuppression or need for specific laboratory monitoring. The incidence of AEs remained stable or decreased with long-term exposure to APR30.

Disclosure of Interest: P. Højgaard Speakers bureau: Received speaking fees once from Celgene and UCB not related to the current work. L. Klokker: None declared, A.-M. Orba: None declared, K. Holmsted: None declared, E. Bartels: None declared, Y. Leung: None declared, N. Goel Employee of: QuintilesIMS, M. de Wit: None declared, D. Gladman: None declared, P. Mease: None declared, L. Dreyer: None declared, L. Kristensen: None declared, O. FitzGerald: None declared, W. Tillett: None declared, L. Gossese: None declared, P. Hellwell: None declared, V. Strand: None declared, A. Ogde: None declared, D. Terwee: None declared, R. Christensen: None declared

DOI: 10.1136/annrheumdis-2017-eular.3840

AB0786 SYSTEMATIC REVIEW OF MEASUREMENT PROPERTIES OF PATIENT REPORTED OUTCOME MEASURES IN PSORIATIC ARTHRITIS: A GRAPPA-OMERACT INITIATIVE

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Background: An updated psoriatic arthritis (PsA) core domain set (COS) for randomized controlled trials (RCTs) was endorsed at the Outcome Measures in Rheumatology (OMERACT) meeting in 2016 and reflects the patient and physician perspectives [1].

Objectives: To synthesise the evidence on measurement properties of Patient Reported Outcome Measures (PROMs) in PsA in order to contribute to the development of a PsA core outcome measurement set (COMS) for RCTs according to the OMERACT Filter 2.0 Framework.

Methods: A systematic literature search was performed in EMBASE, MEDLINE and PsycINFO to identify studies published in English on PROM measurement properties in PsA. Two independent reviewers rated the quality of studies according to CONSORT-based Standards for the selection of health Measurement Instruments. [3] Extracted data on measurement properties and performed a qualitative evidence synthesis.

Results: Of 4703 identified references, 162 were read in full-text and 44 included in the systematic review (SR). Thirty-nine instruments, consisting of one or more scales, were analysed. PROMs measuring core set domains with at least fair quality evidence for good validity and reliability (and without evidence for inadequate measurement properties) were: Stockerau Activity Score for PsA (German) for the Musculoskeletal Disease Activity domain; the Psoriatic Symptom Inventory for Skin Disease Activity; the 36-Item Short Form Health Survey Physical Function scale and to a lesser extent the Health Assessment Questionnaire Disability Index and Bath Ankylosing Spondylitis Functional Index for Physical Function; the Psoriatic Arthritis Quality of Life Questionnaire, the Psoriatic Arthritis Impact of Disease questionnaire and VITACORA-19 (Spanish) for Health related Quality of Life/Life Impact; the Functional Assessment of Chronic Illness Therapy-Fatigue Scale for Fatigue, and the Social Role Participation Questionnaire for Participation. Evidence for content validity was lacking for most of these PROMs.

Conclusions: At least one PROM with some evidence for good validity and reliability was available for five out of eight inner circle domains of the PsA COS. Lack of content validity evidence constitutes a critical barrier for application to the PsA COS per the OMERACT Filter 2.0 Instrument Selection Algorithm [2]. This SR serves as a guide for additional research to increase knowledge of PROM measurement properties in PsA followed by stakeholder consensus for developing a PsA COMS.

PROSPERO: CRD42163032546

References:

AB0787 STUDY OF SERUM SCLEROSTIN LEVELS IN ASSOCIATION WITH ENTHESIAL ULTRASONOGRAPHY IN EGYPTIAN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) is characterized by focal bone erosions and new bone formation, suggesting an uncoupling of osteoblast–osteoclast homeostasis [1]. Serum sclerostin is a protein inhibitor of wnt signalling pathway of bone formation implicated in the suppression of bone repair in inflammatory arthritis. The role of sclerostin in osteoimmunology and inflammatory arthritis is still controversial [2].

Objectives: This study aimed at measuring serum sclerostin in psoriatic arthritis men and to correlate its levels with disease activity scores, ultrasonographic findings and bone mineral density in those patients.

Methods: This study included 30 male patients diagnosed with Psoriatic arthritis (PsA), 15 healthy age and sex matched volunteers as control group. Patients disease activity index measured. Clinical assessment by Leed’s enthesis Index (LEI) [3], Spinal manifestations scored according to Bath Ankylosing Spondylitis Activity Index [4]. Serum sclerostin measured using enzyme linked immunosorbent assay. Ultrasonography of enthesis at Leeds enthesis sites [5] and dual energy x-ray absorbiometry (DEXA) at the lumbar spine.

Results: The study included 30 PsA male patients with a mean age of 43.3±8.33 mean, body mass index (BMI) of 26.87±2.63 and 15 healthy age and sex matched

Figure 1. Ultrasonograpic longitudinal scan of the tendoachilles showing hypoechogenic area of edema & power Doppler signal at insertion.
controls with a mean age of 42.12±7.22 mean BMI of 25.87±3.51 with an
unsignificant difference between the two groups.
Serum sclerostin level significantly higher in PsA patients compared to controls
with a mean of (0.64 and 0.37ng/ml) respectively, positive significant correlation
with patients’ age, disease activity scores, ultrasonographic findings of inflam-
mation and damage at the enthesis as well as negative correlation with
activity of adjacent bone. Thus, a positive though non-significant correlation detected between
serum sclerostin and Leoids clinical enthesis index (LEI) and CRP.

Conclusions: sclerostin plays important role in pathogenesis of psoriatic arthritis and
associated with bone damage either systemic or localized. Further studies for the effect of treatment on serum sclerostin, ultrasonographic and bone mineral
density findings is recommended

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1317

AB0789 THE PSORIATIC ARTHRITIS PATIENT’S JOURNEY: SPECIAL EMPHASIS ON DIAGNOSIS AND TREATMENT DELAYS

Background: A delay in diagnosis and treatment of Psoriatic Arthritis (PsA) is associated with increased disability and damage in the long term. There is currently scarce data available about diagnosis delay, referrals delays, and time to first treatment in patients with PsA in developing countries.

Objectives: To describe the journey of patients with psoriatic arthritis, with special emphasis on diagnosis and treatment delays.

Methods: All patients with PsA registered in the Rheumatology Unit data base (between 2000–2016), with complete data, were included. Electronic medical records were manually revised, and the following data were obtained: date of first visit to a Dermatologist due to Psoriasis (PsO) symptoms, date of PsO diagnosis, date and type of first musculoskeletal symptom, specialty of physician seen at first visit for musculoskeletal symptoms, date of PsA diagnosis, date and reason for prescription of first Disease Modifying anti-Rheumatic Drug (DMARD). Predictive outcome variable was mean lag time between first musculoskeletal symptom and diagnosis of PsA. Other variables calculated were: mean lag time between first musculoskeletal symptom and first physician encounter because of those symptoms, mean lag time to first DMARD and mean lag time between PsO diagnosis and PsA diagnosis. Variables associated with a delay in PsA diagnosis (more than one year delay) were analyzed in multivariable analysis (logistic regression).

Results: 93 patients were included, mean age 60.8 years (SD: 15.3), 61% males. Mean age at time of PsA diagnosis was 52 years (SD: 14.8). The most common musculoskeletal symptom was arthralgia (46%), followed by arthritis (37%), enthesitis (6%), low back pain (6%), and dactylitis (4%). Mean lag time between first musculoskeletal symptoms and visit to a physician because of those symptoms was 16.8 months (SD: 44.4) (median: 1.92 (IQR: 0.35–11.6). In Only 33% of the cases the first specialist seen was a Rheumatologist. Mean lag time between first musculoskeletal symptom and diagnosis of PsA was 19.2 (SD: 28.8) months (Median: 7.2 (IQR: 2.4–21.6 months). In 90 patients (97%), the diagnosis of PsO preceded the diagnosis of PsA, a mean time of 15.1 years (SD: 14.4). 83 patients (89%) received traditional DMARDS, 82% because of diagnosis, more symptoms, with a mean lag time between PsA diagnosis and initiation of DMARDS of 11.4 months (SD: 31.2) (Median: 0.48 (IQR: 0–4.3) months). Forty-three patients (46.2%) had a delay on PsA diagnosis equal or greater than 1 year.

Conclusions: Mean time between symptoms’ onset and PsA diagnosis was relatively short. However, a delay greater that one year was observed in almost half of patients. As none of the variables studied was associated with a delay equal or greater than 1 year in PsA diagnosis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2231

AB0790 HYPERURICEMIA IN PSORIATIC ARTHRITIS: PREVALENCE AND ASSOCIATED FACTORS
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Background: Hyperuricemia is frequent in psoriatic arthritis (PsA) and it seems to be related to metabolic syndrome rather than to extensive psoriatic skin disease [1].
**AB0791 HIGH PREVALENCE OF METABOLIC DISORDERS AND OBESITY IN PSORIATIC ARTHRITIS COMPARED TO PSORIASIS ALLONE: A RETROSPECTIVE DERMATOLOGICAL CLINIC-BASED STUDY**

N. Batkaeva, T. Kortosova, E. Batkaev. Department of dermatology, RUODN University, Y.A. Nasonov research Institute of Rheumatology, Moscow, Russian Federation.

**Background:** An association between increased adiposity, obesity (ObS), and psoriasis has emerged. In addition to obesity, patients with psoriasis are more likely to have metabolic syndrome.

**Objectives:** To evaluate the prevalence of endocrine diseases, nutritional and metabolic disorder (ENMD) comorbidity in patients (pts) with PsA and Psoriasis (PsO) patients without arthritis in the dermatological hospital cohort.

**Methods:** 889 pts (Male-516/Female-329) with moderate-to-severe plaque PsO, mean age 50.4±17.6 years, mean PsO duration 21.5±14.7 were included. PsO pts with Endocrine, nutritional and metabolic diseases (E00-E90) (ENMD), including Disorders of thyroid gland (E00-E07), Obesity and other hyperalimentation (E65-E68), Diabetes mellitus (E10-E14) (DM) were identified in the hospital Database reporting and coding by International Statistical Classification of Disease and Related Health Problems (ICD-10) between 2010 - 2015 years. Mzm, t-test, χ² (%), were calculated. All p<0.05 were considered to indicate statistical significance.

**Results:** 302 out of 889 pts (33.9%) had PsA and 587 out of 889 pts (66.1%) had PsO alone. PsA pts were older than PsO pts – 55.3±15.7 and 50.4±17.6 (p<0.001). 155 out of 889 pts (17.4%) had ENMD. In PsA pts ENMD were found in significantly more cases than in PsO pts – in 76 out of 302 pts (25.2%) and in 79 out of 587 pts (13.5%) accordingly (χ²=18.986, df=2, p<0.0001). In PsA pts ENMD coding as E00-E07 were found in significantly more cases than in PsO pts – in 25 out of 302 pts (8.3%) and in 23 out of 587 pts (3.9%) accordingly (χ²=7.421, df=2, p=0.00645). Obs coding as E65-E88 were found in significantly more cases in PsA pts compared to PsO pts - in 54 out of 302 pts (17.9%) and in 64 out of 587 pts (10.9%) accordingly (χ²=8.4354, df=2, p=0.00368).

**Conclusions:** ENMD comorbidities are common for PsA and PsO without arthritis pts. Obs and disorders of thyroid gland were found in significantly more cases in PsA pts compared to PsO pts. Obesity and PsA are an unhealthy combination. Obesity may represent an additive cardio-metabolic risk factor in PsA subjects. High frequency of ENMD in PsA than PsO could be due to share inflammation pathways with insulin resistance and age. Patients with more severe psoriasis are at higher odds of endocrine, nutritional and metabolic diseases compared with those with mild psoriasis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5744

**AB0792 CURRENT STATUS AND UNMET NEEDS IN THE MANAGEMENT OF PSORIATIC ARTHRITIS WITH CONVENTIONAL SYNTHETIC AND BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS: TAIWANESE NATIONWIDE PHYSICIANS’ PERSPECTIVES**

T.-H. Li1, C.-C. Lai2, C.-Y.Tsai2. Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Chiayi Branch, Taichung Veteran General Hospital, Chiayi City; Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taipei Veteran General Hospital, Taipei City, Taiwan.

**Background:** Psoriatic arthritis (PsA) contributes to enormous burden of disease and thus early correct diagnosis and adequate therapeutic management are essential for physicians in practice; however, there have been several studies highlighting the inadequate diagnosis and suboptimal therapies for PsA worldwide and physicians generally report difficulties in managing psoriasis.

**Objectives:** To analyze the real-world clinical practice of PsA in Taiwan, and assess physicians’ adopted methods and difficulties of diagnosis, therapeutic consideration and strategy, in addition to rationales for biologic agents and unmet needs.

**Methods:** A nationwide cross-sectional observational study in Taiwan was conducted by means of the face-to-face in depth interviews with the 80 physicians, composed of 50 rheumatologists and 30 dermatologists, from November 2014 to January 2015.

**Results:** The major adopted diagnostic examinations for PsA are arthritis performance, psoriasis and nail dystrophy, roentgenological studies, personal and family history; however, more dermatologists rely on RF for initial diagnosis (p<0.05). The difficulties for diagnosis, considerations on therapeutic management and current prescription were reported and displayed some interdisciplinary difference. Rationales for biological agent selection were investigated and physicians generally favored etanercept in terms of milder symptoms or more conservative treatment. The main unmet needs for current biologic therapies for PsA included the aspects of better efficacy, safety, sustainability and oral administration.

**Conclusions:** The nationwide study is the first survey for real-world clinical practice of PsA in Asia and provides detailed messages about the diagnostic difficulties and therapeutic consideration, especially rationally and unmet needs on current biologic therapies, which may offer possible directions for new drug development. We also made interdisciplinary comparison, hence in order to improve comprehensive care.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1360

**AB0793 EFFICACY OF IVEKIZUMAB IMPROVING SF-36 SCORES IN BIOLOGICAL DAMAR-NAIVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 3 STUDY (SPIRIT-P1)**

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**Background:** In a phase 3 randomized controlled trial (RCT), ixekizumab (IXE), a high affinity mAb that selectively targets interleukin-17A, significantly improved signs and symptoms of psoriatic arthritis (PsA) and health status vs placebo (PBO)1.

**Objectives:** To evaluate the efficacy of IXE improving patient (pt)-reported health status, assessed by Short Form Survey (SF-36) physical and mental component summary (PCS and MCS) and domain scores.

**Methods:** In phase 3 RCT (SPIRIT-P1; NCT01695239), DMBARD-naive pts with active PsA (N=417) randomly received IXE 80 mg either once every 4 weeks (Q4W) or 2 Wks (Q2W) after a 160 mg starting dose, or 40 mg adalimumab (ADA) Q2W, or PBO. Health status was assessed by SF-36 at baseline, Wk 12, and Wk 24. Treatment comparisons were by mixed model for repeated measures for continuous data and logistic regression for categorical data. Missing values were imputed by nonresponder imputation.

**Results:** Baseline SF-36 scores were similar across treatment groups. At Wk 24, significant improvements were observed with ADA and IXEQ2W for PCS, and 5/8 domains (PF, RP, BP, GH, and RE), and with IXEQ4W for PCS and 6/8 domains (except VT and MH) (Figure) (post hoc for individual domains). In pts with baseline scores < A/G norms, significant improvements vs PBO were observed with ADA and IXEQ4W for PCS, MCS, and 5/8 domain scores (PF, RP, pf=0.001).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2969
EFFECT OF TOFACITINIB ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM TWO PHASE 3 STUDIES

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Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for active psoriatic arthritis (PsA). The safety and efficacy of tofacitinib (5 mg twice daily), administered orally in addition to conventional synthetic disease-modifying antirheumatic drug and/or phototherapy, in patients with active PsA has been investigated in two Phase 3 randomised controlled trials (RCTs: OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]).

Objectives: To evaluate patient-reported outcomes (PROs) in patients (pts) with active PsA enrolled in OPAL Broaden (N=392) and OPAL Beyond (N=384). OPAL Beyond pts had an inadequate response (IR) to one previous synthetic disease-modifying antirheumatic drug and were naïve to tumour necrosis factor inhibitors (TNF) whilst OPAL Beyond pts had an IR to one TNF.

Methods: Pts were randomised to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, placebo (PBO)→ tofacitinib 5 mg BID, PBO→ tofacitinib 10 mg BID and, in OPAL Broaden, also to adalimumab 40 mg subcutaneously every 2 weeks (active comparator). Pts receiving PBO advanced to either tofacitinib 5 mg BID or 10 mg BID at month 3 (M3) in both RCTs. Least squares mean changes from baseline in PtGA and Arthritis Pain (VAS) were compared to PBO at M3 (p<0.05). SF-36 normative values were similar between tofacitinib and adalimumab.

Results: Pts with active PsA in OPAL Broaden and OPAL Beyond RCTs receiving tofacitinib 5 mg and 10 mg BID reported improved PROs compared with PBO (Table 1). Greater improvements in PtGA and Arthritis Pain were observed earlier as Week 2 through M3 with both tofacitinib doses compared with PBO in both studies (p<0.05). Greater improvements were also reported in SF-36 Physical Component Summary, Dermatology Life Quality Index (DLQI) and Ankylosing Spondylitis Quality of Life (ASQOL) questionnaires. Nominal p values are reported without adjustment for multiple comparisons.

Conclusions: Pts with active PsA enrolled in OPAL Broaden (N=392) and OPAL Beyond (N=384) had greater improvements in PROs with tofacitinib compared with PBO.

Table 1. Percentage of patients with SF-36 scores ≥ normative values at week 24 (n) among the patients reporting SF-36 scores > normative values at baseline (N) (nonresponder imputation)

<table>
<thead>
<tr>
<th>SF-36 Scores, n/N (%)</th>
<th>PBO</th>
<th>ADA</th>
<th>IXE</th>
<th>IXEQ2W</th>
<th>IXEQ4W</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Component Summary</td>
<td>4/101 (4.0)</td>
<td>20/93 (21.5)</td>
<td>12/98 (12.2)</td>
<td>19/95 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Mental Component Summary</td>
<td>10/53 (19.2)</td>
<td>21/52 (40.4)</td>
<td>21/58 (36.2)</td>
<td>21/55 (38.2)</td>
<td></td>
</tr>
<tr>
<td>Physical Functioning Domain</td>
<td>5/94 (5.3)</td>
<td>22/91 (24.2)</td>
<td>14/97 (14.4)</td>
<td>19/97 (21.8)</td>
<td></td>
</tr>
<tr>
<td>Role Physical Domain</td>
<td>5/98 (5.1)</td>
<td>19/91 (20.9)</td>
<td>12/93 (12.7)</td>
<td>18/96 (22.1)</td>
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<tr>
<td>Bodily Pain Domain</td>
<td>12/95 (12.6)</td>
<td>28/87 (32.2)</td>
<td>27/96 (28.1)</td>
<td>28/93 (30.1)</td>
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<tr>
<td>General Health Domain</td>
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<td>14/88 (15.9)</td>
<td>16/92 (17.4)</td>
<td>21/93 (23.1)</td>
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<tr>
<td>Vitality Domain</td>
<td>11/73 (15.1)</td>
<td>22/66 (33.3)</td>
<td>21/68 (30.9)</td>
<td>28/68 (41.2)</td>
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<tr>
<td>Social Functioning Domain</td>
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<td>21/68 (31.3)</td>
<td>28/68 (41.2)</td>
<td>27/64 (42.2)</td>
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<tr>
<td>Mental Component Summary</td>
<td>7/54 (13.0)</td>
<td>17/59 (28.8)</td>
<td>23/64 (36.5)</td>
<td>26/64 (40.6)</td>
<td></td>
</tr>
<tr>
<td>Physical Component Summary</td>
<td>5/98 (5.1)</td>
<td>19/91 (20.9)</td>
<td>16/93 (17.2)</td>
<td>19/86 (22.1)</td>
<td></td>
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</table>

Discussion of Interest: V. Strand Consultant for: Eli Lilly and Company, Abbvie, Amgen, BMS, Boehringer Ingelheim, Celtrion, Corrona, EMDSerono, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Sandzol, Sanofi, UCB, A. Gottlieb Grant/research support from: Centocor (Janssen), Amgen, Abbott (Abbvie), Novartis, Celgene, Pfizer, Lilly, Levia, Merck, Xenoprot, Dermira, Baxalta, Consultant for: Amgen Inc.; Astellas, Akros, Centocor (Janssen), Inc.; Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbott Labs, (Abbvie), TEEVA, Eli Lilly, Ulcer, Novo Nordisk, Novartis, Dermisorp Ltd., Incyte, Pfizer, Canfield, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Bioterapies for Life, Glaxo Smith Kline, Xenoport, Catabasis, Meiji Seika Pharma Co., Ltd, Takeda, Mitsubishi,Tanabe Pharma Development America, Inc, Genentech, Baxalta, Kineta One, KPI Therapeutics, Crescendo Bioscience, Aclaris, Amlios, Reddy Labs, T. Kiven Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celtrion, Eli Lilly, Epixus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandzol and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celtrion, Eli Lilly, Epixus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandzol and UCB, A. Naegeli Employee of: Eli Lilly and Company, C.-Y. Lin Employee of: Eli Lilly and Company, J. Birt Employee of: Eli Lilly and Company.

Conclusions: Pts with active PsA receiving tofacitinib reported greater improve-
Osteoarthritis and comorbidity: association between mental features and cytokine levels

E. Trifonova, O. Sazonova, E. Zonova. Novosibirsk State Medical University, Novosibirsk, Russian Federation

Background: Studies of mental health in patients with osteoarthritis (OA) are topical at the present time. This applies especially to OA patients with such comorbidity as obesity, metabolic syndrome (MS) and type 2 diabetes mellitus (T2DM). Psychological features, quality of life (QoL) and depression degree also can be linked with immunopathogenesis of OA with obesity, MS, T2DM.

Objectives: To explore the mental health in knee OA patients with obesity, MS and T2DM and to estimate association between psychological and immunological features.

Methods: Patients (n=128) with bilateral knee OA according to ACR criteria were divided into four groups. Group 1 (n=17) had obesity, group 2 (n=17) had MS, group 3 (n=56) had T2DM and group 4 (n=38) had only knee OA without concomitant diseases. Patients with OA and obesity were characterized by low values of mental health (SF-MH) (median (Me) 52; interquartile range (IQR) 25–52.3; p=0.02). Serum cytokines levels were not different by groups knee OA patients with comorbidity and group knee OA patients without comorbidities. During comparative analysis, we found many statistically significant differences in PROs compared with PBO at M3 that were maintained throughout both RCTs.

Acknowledgements: To be presented at AAD 2017 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by S. Morgan of CMG and was funded by Pfizer Inc.


DOI: 10.1136/annrheumdis-2017-eular.8986

The predictive role of interleukine 6 and 10 in impairment of mental health in patients with knee osteoarthritis and uncontrolled type 2 diabetes mellitus

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Background: The influence of different interleukins on development and progression of osteoarthritis (OA) has been proved. However, there is lack of data on relationship between mental health and immunological features in OA patient with type 2 diabetes mellitus (T2DM).

Objectives: To estimate the relationship between mental health and the proinflammatory serum cytokine levels in patients with knee OA and T2DM depending on glycemic control.

Methods: A study was performed on 45 persons who had bilateral knee OA according to the ACR criteria and T2DM. Then patients were divided into two groups according to the compensation degree T2DM taking into account glycemic control. Group 1 (n=26) and Group 2 (n=19) had controlled T2DM. Group 2 (n=19) had uncontrolled T2DM. All patients were comparable by age, sex and duration of OA. Serum cytokine levels (IL-1β, IL-6, IL-10, IL-18, NO, and adipokines (adiponectin, leptin) using ELISA were measured. Blood glucose level was also estimated. The parameters of QoL, mental health, depression degree and coping strategies to overcome pain were measured by short form 36 (SF-36); Knee injury and Osteoarthritis Outcome Score –(KOOS) and with patient health questionnaire-9 (PHQ-9), Coping Strategy Questionnaire (CSQ). We used U-Mann-Whitney test to detect differences between selected groups. Correlation was assessed using Spearman correlation coefficient (rs).

Results: Patients with OA and uncontrolled T2DM had significant low values of role limitations due to emotional problems (SF-RE) (median (Me) 38; interquartile range (IQR) 25–52.5; p=0.02). Serum cytokines levels were not different between studied groups. Correlation analysis identified the relationships between parameters of mental health and serum cytokine levels in OA patients with uncontrolled T2DM. Certain data are presented (Table).

Conclusions: It follows from these results mental and immunological parameters of OA patients with uncontrolled T2DM can be linked. Such interleukins as IL-6 and IL-10 may play a role of potential biomarkers of mental impairment in this category of patients. This data should be verified by larger studies and may allow in future to develop programs of treatment and rehabilitation of OA patients with uncontrolled T2DM within personalized medicine.

References:
LONG TERM PROSPECTIVE MULTICENTER RANDOMIZED PLACEBO-CONTROLLED STUDY OF HYALURONIC ACID IN SMALL JOINTS OSTEOARTHRITIS (SJOA)

E. Tsytsova, E. Nasonov, M. Kramarenko, A. Ivanyuk, A. Foteeva, O. Polikarpova

Objectives: To investigate the efficacy and tolerability of amtolmetin guacil (AMG; Niselat®, Dr. Reddy’s Laboratories Ltd, India) versus previous therapy with nonsteroidal anti-inflammatory drugs (NSAID) in patients with knee osteoarthritis (OA) in terms of pain and functional activity. Methods: The open-label observational study included 220 patients aged 30–65 years who suffered from knee OA and intense pain during NSAID intake and had symptoms of dyspepsia in the absence of contraindications to the use of AMG. Among the comorbidities that occurred in 68% of the patients, there was a preponderance of hypertension (42%), lower extremity varicose veins (6.4%), and diabetes mellitus (6%). Treatment efficacy was evaluated using three domains of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) including pain, physical function, and patient’s global assessment.

Results: AMG had a marked analgesic effect confirmed by 40% or more pain reduction at 72.5% of the patients. The high analgesic effect of AMG was confirmed by a statistically significant (p<0.001) reduction in the WOMAC index (pain and stiffness) and by an increase in functional activity. There was a significant decrease in painless and painful signs of dyspepsia, as well as positive changes in the measures “overall assessment of dyspepsia severity” (p<0.001) and “satisfaction with treatment”. Overall assessment of AMG tolerability was only positive: excellent (33%), good (56%), and satisfactory (11%). There were no serious adverse events (AE). AE were graded as moderate and mild in 8 and 82% of cases, respectively. AE were recorded in 7.7% of the patients.

Conclusions: The findings suggest that AMG offers good prospects for knee OA treatment.

Disclosure of Interest: None declared

AB0799

DECREASED RATIO OF TIMP1/MMP-9 IS ASSOCIATED WITH HIGHER PAIN SENSITIVITY IN A SUBSET OF OSTEOARTHRITIC PATIENTS WITH LOW MECHANISTIC TARGET OF RAPAMICIN GENE EXPRESSION IN THE PERIPHERAL BLOOD

E. V. Tchetina, G. Jones, F. Cicuttini et al.

Objectives: To confirm that a lower ratio of TIMP1/MMP-9 is associated with increased pain perception in osteoarthritis patients. Methods: A total of 855 patients suffering from knee osteoarthritis were evaluated and divided into two groups based on the ratio of TIMP1/MMP-9. Results: The patients with the lowest ratio of TIMP1/MMP-9 had a significantly higher pain perception during movements and a higher percentage of patients with high pain sensitivity (p<0.001).

Conclusions: The results suggest that a lower ratio of TIMP1/MMP-9 is associated with increased pain perception in knee osteoarthritis patients.

Disclosure of Interest: None declared

AB0800

KNEE OSTEOARTHRITIS PATIENTS’ USE OF AND COMPLIANCE TO AN ORTHOTIC INTERVENTIONS

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Background: Knee osteoarthritis (KOA) is the most common form of arthritis with an estimated lifetime prevalence of 44.7% (1). The use of orthotic devices (knee braces, insoles, wedged shoes) is a generally accepted conservative therapy for KOA patients (2). However, it is suggested that their effectiveness is detrimentally affected by poor patient compliance due to discomfort while wearing these devices (3).

Objectives: The aim of this study is to objectively establish the compliance to an orthotic intervention using a thermal sensor (TS) and comparing it to patients’ self-reported wear time.

Methods: Ten medial KOA patients (mean±SD age 57.6±13.4 years, BMI 27.3±3.2 kg/m²), clinically diagnosed according to the ACR Guidelines, were recruited for this study. A small, light-weight TS with the size of an average lithium battery (0.5°C resolution) was placed in a newly developed ankle-foot-orthosis (AFO) that patients were asked to wear as often as possible during a period of six weeks. The TS measured the temperature every 5 minutes for 4 weeks. Patients rated the comfort of the orthosis during the first visit using a scale from 1 to 5 (1 being the most comfortable).

Results: The patients reported during these six weeks how many hours per day they had worn the orthosis and rated which amount of pain they felt each day (from 0=no pain to 10=most painful). To determine the patients’ compliance, the AFO wear time, derived from the TS, was compared to the wear time per day recorded in the patients’ diaries. The threshold to differentiate the wear
and non-wear times was set at 25°C. Timeframes during which the temperature rose above 25°C were classified as wear time. A Wilcoxon signed-rank test was performed between the different wear times and Spearman’s correlations between pain, comfort and wear time were determined.

**Results:** On average, patients wore the device for 143±80 h according to the form they filled out, whereas the TS measured only 83±36 h, leading to an overestimation of 72%. Patients reported an average pain level of 3±1.4 during the six weeks period and the AFO’s comfort was rated with 1.9±0.3. Statistical differences were found between the wear time reported by the patients and the wear time derived from the TS (p=0.005). Additionally, a significant correlation between the AFO comfort and the wear time derived from the TS was found (r = −0.81; p=0.001). No significant correlation was found between pain and wear time.

**Conclusions:** As can be expected, patients who found the AFO more comfortable were the ones who wore the orthosis for longer periods. The wear time recorded by the TS was significantly lower compared to the self-reports. This might be due to a social desire bias, overestimating the amount of hours of wearing the AFO as we asked the patients to wear it as often as possible. Secondly, patients might have trouble to accurately recall the amount of wear hours, thereby inducing an overestimation of wear time. As the reliability of self-reported measures seems to be questionable, such data should be interpreted with care.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1415

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**AB0802**

**EFFECTS OF DIETARY MAGNESIUM SUPPLEMENTATION AND INTRA-ARTICULAR MgSO4 INJECTION ON EXPERIMENTAL OSTEOARTHRITIS AND POTENTIAL MOLECULAR MECHANISMS BY MRNA AND lncRNA EXPRESSION PROFILES SCREENING**

G. Lei1, C. Zeng1, H. Li1, J. Wei2, T. Yang1, B. Wise3, X. Ding1, Y. Zhang1, Y. Yang1, Z. Deng1, J. Li1, Y. Cui1. 1Department of Orthopaedics; 2Health Management Center, Xiangya Hospital of Central South University, Changsha, Hunan Province, China; 3Department of Internal Medicine and Department of Orthopaedics, University of California, Davis School of Medicine, Sacramento, CA, Division of Rheumatology, Department of Internal Medicine, Rush University Medical Center, Chicago, IL, United States; 4International Medical Center, Xiangya Hospital, Central South University, Changsha, Hunan Province, China

**Background:** Epidemiological studies of ours and other groups have reported an inverse association between dietary and serum Mg with knee radiographic osteoarthritis (OA) [1–4].

**Objectives:** To investigate the effects of dietary magnesium supplementation and intra-articular MgSO4 on the development of experimental rat osteoarthritis, and explore the underlying potential molecular mechanisms by mRNA and IncRNA expression profiles screening.

**Methods:** Rat osteoarthritis model was induced by surgery. Articular cartilage damage was evaluated by modified Mankin score system after intervention of dietary magnesium supplementation or intra-articular MgSO4 injection. Microarray was performed to reveal alteration of expression profiles of mRNA and IncRNA after intervention of MgSO4 on human osteoarthritis chondrocytes. Bioinformatics analyses including gene ontology analysis, pathway analysis, target gene predictions and network analysis were used.

**Results:** Comparing with normal diet, dietary Mg supplementation showed significantly ameliorated cartilage damage at the medial femoral condyle, lateral tibial plateau and medial tibial plateau (P<0.05), and approaching significance at the lateral femoral condyle (P=0.06). All four locations exhibited mitigated cartilage damage in the intra-articular MgSO4 group compared with intra-articular saline (P<0.05). 1767 IncRNAs and 2558 mRNAs were upregulated while 994 IncRNAs and 1512 mRNAs were downregulated in chondrocytes with intervention of 50mM MgSO4 compared with control group (fold change >2.0). The top 6 IncRNAs which showed the largest difference were ENST00000429530.1, ENST00000425914.2, ENST00000561231.1, ENST00000560962.1, ENST00000419881.1, ENST00000419881.2. Bioinformatics analyses indicated that the differentially expressed IncRNA target genes of chondrocyte after intervention of 50mM MgSO4 are enriched in negative regulation of phosphatidylinositol 3-kinase signaling.

**Conclusions:** Both dietary magnesium supplementation and intra-articular MgSO4 injection may exert cartilage protective effects by causing widespread changes in the profile of IncRNAs and mRNAs of chondrocytes.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4647

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**AB0803**

**DOES INTRA-ARTICULAR INJECTION OF PLATELET-RICH PLASMA PROVIDE CLINICALLY PREFERABLE OUTCOMES IN THE KNEE OSTEOARTHRITIS? A DOUBLE-BLIND, RANDOMIZED CONTROLLED PILOT STUDY**

J. Moghimi1,2, R. Ghorbani1, H. Beiki1. 1Social Determinants of Health Research Center; 2Department of Internal Medicine, Semnan university of medical sciences, Semnan, Iran, Islamic Republic of

**Background:** Knee osteoarthritis (OA) symptoms Improvements with platelet-
Background: This double-blind randomized controlled trial, 34 patients with knee OA grade 2 or 3, from March 2013 to February 2016 were selected. Participants were randomly assigned one knee as the case and other knee was considered as control to receive three injections of either PRP or placebo. The administering doctor, and the patients were blinded to group allocation. Outcomes included safety and recruitment data, 100 mm the EuroQol-visual analogue scales (EQ-VAS), the international knee documentation committee (IKDC), the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Tegner Activity Score (TAS) at six and three months.

Results: Twenty four (100%) participants met the inclusion criteria. No treatment-related major adverse events were reported. The PRP group demonstrated significant improvements at all follow up time points in the WOMAC (3 months: p=0.017; 6 months: p=0.029, ETA=0.601). For the PRP group, the 11.47 mm reduction in EQ-VAS at 6 months (p=0.040) and the 7.35 mm at 3 months (p=0.035) was statistically significant improvement from baseline. The PRP group also significantly improved IKDC (p=0.039, ETA =0.619) and TAS (p=0.028, ETA =0.641) at three months. The placebo group showed improvements on only the IKDC Function at 3 months (p=0.019, ETA =0.591). There were no significant between-group differences for any of the self-reported measures at either time-point.

Conclusions: The study provides proof-of-concept evidence about the safety and feasibility of intra-articular injections of PRP necessary to appraise a larger clinical trial knee OA. Our preliminary findings also suggest PRP improves self-reported symptom severity, sports activity, and function in daily living activities, however no between-group differences were found. PRP may provide an effective and safe novel treatment for knee OA.

Acknowledgements: This study was supported by Semnan University of Medical Sciences, Semnan, Iran.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1387

AB0804 SINGLE-NUCLEOTIDE POLYMORPHISM (SNP) RS143383 GROWTH AND DIFFERENTIATION FACTOR 5 (GDF5) IN KNEE OSTEOARTHRITIS IN EGYPTIAN POPULATION

M. Hassani 1, N.A. Mohamed 2, S.A. Mahran 1, 1 Rheumatology Department; 2Medical Biochemistry, Assuit University, assuit, Egypt

Background: Osteoarthritis (OA), is an age-related common polygenic disease characterized by the thinning and loss of the articular cartilage in synovial joints such as knees. The etiology and pathogenesis of OA is largely unknown, the single-nucleotide polymorphism (SNP) rs143383 (C/T) influencing OA susceptibility across a range of ethnic groups.

Objectives: The present study investigated to identify the association of polymorphism in GDF5 gene with osteoarthritis in Egyptian population.

Methods: This Cross sectional study of 100 male ≥40 years that fulfilled American College of Rheumatology (ACR) for Knee OA and 100 controls recruited from the outpatient clinic of Department of Rheumatology, Assuit university, Egypt. Clinical symptoms were assessed with WOMAC index and VAS for knee pain. The severity of disease was determined by radiological grades (Kellgren Lawren). Body Mass Index (BMI) was recorded. DNA isolation and genotype analysis the method of (Southam et al, 2007) was followed for determining the GDF5 gene (T/c; rs143383) polymorphism. Amplification was performed.

Results: There were weak but significant associations present between the GDF5 polymorphism and knee OA at the allele level (C vs. T: 0.85, 95% CI =0.79–0.93) and genotype level (CC vs. CT: 0.72; CT vs. TT: 0.81; CC/CT vs. TT: 0.83; CC vs. CT/TT: 0.78) in the overall population. A stronger significant association was observed for CC vs. CT/TT (p=0.03, P<0.001) in comparison with other models.

In males we identified a second polymorphism, located in the 3’-UTR of GDF5, that influenced allelic expression of the gene independent of rs143383.

Conclusions: GDF5 is an OA susceptibility gene with association between the GDF5 polymorphism and clinical symptoms of knee OA in Egyptian population.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6001

AB0805 PANLAR CONSENSUS, RECOMMENDATIONS FOR THE MANAGEMENT OF OSTEOARTHRITIS OF THE HAND, HIP AND KNEE. SHORT TITLE: PAN-AMERICAN LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (PANLAR) OSTEOARTHRITIS (OA) STUDY GROUP

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Background: This consensus derives from a previous study of Demographic and Clinical Characteristics by the PANLAR OA study group, reporting significant results in terms of handling these patients and in which it were evident the need of reaching an agreement in the management of hand, hip and knee OA in Latin America (2).

Objectives: The aim is to update the recommendations for the treatment of knee, hip and knee OA by agreeing on key propositions relating to the management of hand, hip and knee OA, identifying and critically appraising research evidence for the effectiveness of the treatments and by generating recommendations based on the available evidence and expert opinion.

Methods: Recommendations were developed by a group of 40 specialists made up of rheumatologists and members of other medical disciplines. A systematic review of articles, meta-analyses and guidelines for the management of hand, hip and knee OA published from 2008 and January 2014 was done. The level of evidence and strength of recommendation were classified according to the Jadad scale (3). The level of agreement was established through a Delphi technique.

Results: Both ‘strong’ and ‘conditional’ recommendations are given for management of hand, hip and knee OA and non-pharmacological, pharmacological and surgical modalities of treatment are presented according to the different levels of agreement.

Conclusions: These recommendations are based on the consensus of clinical experts from a wide range of disciplines considering the available evidence, while balancing the benefits and risks of non-pharmacological, pharmacological and surgical treatment modalities. It is hoped that these recommendations will be utilized by healthcare providers involved in the management of patients with hand, hip and knee OA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1273

AB0806 THE EFFECT OF REPETITIVE ACTIVE RANGE OF MOTION VERSUS CONTINUOUS PASSIVE MOTION ON EARLY FUNCTIONAL OUTCOMES AFTER PRIMARY TOTAL KNEE REPLACEMENT

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Background: Continuous passive motion (CPM) is a common procedure in total knee replacement (TKR), but its effectiveness is controversial at early stage after TKR. Some studies have claimed that CPM promoting rapid postoperative recovery and the range of motion (ROM), However, some studies have demonstrated that CPM have any benefit on ROM, length stay of hospital and postoperative recovery (1, 2). Some studies have demonstrated that CPM improves the range of motion (ROM), however there is not any study that compared the effect of repetitive active range of motion (AROM) vs. CPM on early functional outcomes after TKR.

Objectives: The aim of this study was to compare the effect of AROM vs. CPM on early functional outcomes after TKR.

Methods: The study group consisted of 71 patients, who underwent primary TKR because of arthrosis were consecutively allocated to a AROM group (n=40, with
Validity of the Quadriceps Angle Measurement in Patients with Varus Knee Osteoarthritis: Compare the Goniometric and Photogrammetry Method to Radiography Method

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Background: Various measurement methods have been defined to assess the alignment of the lower extremities. The Q-angle measurement is reported to be associated with knee injury and patellofemoral dysfunction. The Q-angle has been assessed using radiographic scans, goniometry and photogrammetry methods in supine and standing positions. The radiography method is accepted to be the most accurate and valid measurement technique in measurement the Q-angle. But as a result of being expensive and time-consuming, this invasive method is not mostly preferred in research and clinics. The goniometric measurement of the Q-angle is practical because it is simple, requires inexpensive equipment (only a goniometer), and can be applied in a short time. Photogrammetry measurement technique is also an advantageous method for reducing measurement errors caused by goniometers and reduction of investigator errors.

Objectives: The aim of the present study, was to compare the clinical assessment of the Q-angle (goniometric and photogrammetric measurement methods) to a radiological assessment using radiograph (criterion validity) in patients with varus knee osteoarthritis.

Methods: The study group consisted of 15 (median age 68.6±11.9 years) patients with unilateral and bilateral varus knee osteoarthritis. Q-angle measurements were assessed on both lower extremities with three different goniometric methods (goniometric measurement method in standing position with quadriceps muscle relaxed; goniometric measurement method in supine position with quadriceps muscle relaxed; and contracted) using a 360° universal goniometer. After the goniometric measurements, photographs were taken with quadriceps muscle relaxed in standing position. For radiographic assessment, we used patients’ lower extremity scanograms, which had been determined to obtain the Q-angle (radiographic assessment). The goniometric and photogrammetry measurements were statistically analyzed using paired t-test.

Results: There was a good correlation between the radiographic assessment and photogrammetric measurement (r=0.623, p<0.001). Also a good correlation was observed between radiographic assessment and goniometric measurement (in standing position with quadriceps muscle relaxed; in supine position with quadriceps muscle relaxed and contracted) (r=0.676, p=0.001, r=0.616, p=0.0005; r=0.676, p<0.001, respectively).

Conclusions: According to our result, the photogrammetric measurement and the goniometric measurement appear to be valid alternatives to the radiographic measurement for determining the Q-angle. These alternative measures might be used by clinicians and researchers to measure the Q-angle of patients with varus knee osteoarthrosis in orthopaedic clinics.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5851

Comparing the Effects of Physical Therapy and Non-steroidal Anti-inflammatory Treatment on Sleep Quality, Quality of Life and Clinical Status in Knee Osteoarthritis

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Objectives: We aimed to compare the effectiveness of physical therapy (PT) and non-steroidal anti-inflammatory drug (NSAID) therapy on sleep quality, quality of life and clinical status in patients with knee osteoarthritis (OA).

Methods: Demographic characteristics of the participants were recorded. MOS sleep scale, Nottingham Health Profile (NHP) and Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) were used to evaluate sleep quality, quality of life and clinical status of patients before and after the treatment. All patients were divided into two groups as PT (57 patients) and NSAID (43 groups). The patients in the drug group were administered oral ketoprofen (50 mg/daily), and the patients in the PT group were administered five times a week, total 15 seances hot-pack, ultrasound and transcutaneous electrical nerve stimulation therapy.

Results: Demographic characteristics, MOS sleep scale and NHP were similar at baseline in both groups (p>0.05). WOAMC pain, stiffness, and physical function scores before treatment were significantly poorer in the PT group than the NSAID group (p<0.05). There were statistically significant improvements on the MOS sleep scale (except snoring subscore, p=0.05, table 1), NHP (except social isolation, p=0.209) and WOMAC pain, stiffness, physical function and total scores of both groups after treatments (p<0.05). Improvement was also similar when both groups were compared after the treatment (p>0.05). After the two treatment, significantly side effect was not observed.

Conclusions: PT and NSAID therapy has good effectiveness on sleep quality, quality of life and clinical status in knee OA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3910

Fall Risk and Related Factors in Knee Osteoarthrosis

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Background: Balance, as a complex task, may be affected in knee osteoarthrosis (KO) and this may cause fall instability and fall risk.

Objectives: The aim of this study was to determine the fall risk in patients with KOA with an objective computerized technique and to evaluate the potential risk factors for falls in these patients.

Methods: Patients with KOA and controls were included in this cross-sectional study. Gender, age, and body mass index (BMI) were recorded. Pain was evaluated with a visual analog scale (VAS). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess the patients and the Falls Efficacy Scale International (FES-I) was used for the evaluation of fall efficacy. Knee radiographs were recorded with the Kellgren–Lawrence grading scale. Fall risk analysis was performed by using the Tetrax Interactive Balance System, which is a computerized posturography device.

Results: One hundred patients with KOA and 30 controls were included. The age, gender, and BMI scores were similar between the groups. FES-I scores were significantly higher than in the controls (p<0.000). Using a computerized system, significantly higher fall risk results (p<0.000) and significantly low, moderate, and high fall risk distribution were recorded in the cases than in the controls (p<0.000). Fall risk was significantly related to age, pain, and the WOMAC scores of the patients.
Conclusions: Using an objective computerized technique, our study demonstrated a higher fall risk in patients with KIA than in healthy individuals. This higher risk was shown even in the early radiographic phases of the disease related to age, pain, and dysfunction. An understanding of factors on postural control seems to be critical in successful fall prevention in these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3072

AB0810 CORRELATION BETWEEN KNEE EXTENSOR MUSCLE STRENGTH AND GAIT ENDURANCE AFTER TOTAL KNEE ARTHROPLASTY

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Objectives: This study was undertaken to identify the relationship of objective physical performance and gait endurance after 1 month after total knee arthroplasty.

Methods: One-hundred ninety-five patients (32 males and 163 females; average age 72.6±6.1 years) who underwent a primary total knee arthroplasty (TKA). Patients completed 6-minute walk test (6MWT) to assess gait endurance. Additional physical performance test including timed up and go (TUG) test, timed Stair Climbing Test (SCT), instrumental gait analysis for spatio-temporal parameters, and isometric knee flexor and extensor strength of the surgical and nonsurgical knees 1 month after TKA were measured. To evaluate self-reported physical function, self-reported disease-specific physical performance measured by using the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) and self-reported quality of life measured by using EuroQOL five dimensions (EQ-SD) questionnaire. Visual analog scale (VAS) of post-operative knee pain was recorded each patient.

Results: In the bivariate analyses, the postoperative gait endurance had a significant positive correlation with the postoperative gait speed (r=0.48, p<0.001), cadence (r=0.40, p<0.001), stride length (r=0.58, p<0.001), postoperative peak torque (PT) extensor of non-surgical knee (r=0.49, p<0.001), postoperative peak torque (PT) flexor of non-surgical knee (r=0.34, p<0.001), EQSD (r=0.33, p<0.001) and a significant negative correlation with TUG (r=-0.46, p<0.001), SCT-ascent (r=-0.63, p<0.001), SCT-descent (r=-0.68, p<0.001), WOMAC pain score (r=-0.29, p<0.001), WOMAC stiffness score (r=-0.35, p<0.001), WOMAC function score (r=-0.43, p<0.001).

In the linear regression analyses, the postoperative Visual analog scale VAS (β=0.41, p<0.0001), peak torque (PT) extensor of surgical knee (β=0.56, p<0.001) and peak torque (PT) extensor of non-surgical knee (β=0.77, p<0.001) were factors predictive of the postoperative 6MWT.

AB0811 HYALURONIC ACID INTRA-ARTICULAR INJECTION VERSUS ORAL ATORVASTATIN IN THE TREATMENT OF KNEE OSTEOARTHRITIS

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Background: Osteoarthritis is a degenerative joint disorder of articular cartilage and is the most common type of arthritis in the elderly. Some studies have suggested that Hyaluronic acid and atorvastatin may have a role in the treatment of osteoarthritis.

Objectives: The purpose of the present study was to investigate and compare the potential effects of Hyaluronic acid and Atorvastatin on the symptoms of knee osteoarthritis.

Methods: We conducted a randomized, controlled trial in patients with knee osteoarthritis. Eligible patients were those who met the ACR criteria of primary knee osteoarthritis, radiologically ascertained grade I or II of knee osteoarthritis on the Kellgren-Lawrence scale, had a pain score (maximum 100) and age 50–70 years. Patients were not eligible if they had secondary osteoarthritis, systemic disease like diabetes, history of inflammatory arthritis, severe knee deformity (varus or valgus >50 degree), history of coagulopathy, severe cardiovascular disease, and active infections. Patients were enrolled from outpatient clinic of Imam Reza Hospital, Mashhad, Iran. We divided them randomly into two groups; Group 1 (n=35) received intra-articular Hyaluronic acid each week for three weeks, and group 2 (n=35) received oral atorvastatin 40 mg/day orally for six months. Symptoms were assessed by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline and every month up to 6 months.

Results: Twenty eight patients (40%) were male and 42 patients (60%) were female. There was not a significant difference between 2 groups regarding sex (P=0.626). Mean age of patients was 57.9±1.1 years. Groups mean age did not differ significantly (P=0.710). The pain and function scores were significantly decreased only in the Hyaluronic acid group in the second month (P<0.001). There was not any significant improvement in any group in the next months (figure 1).

Conclusions: Intra articular Hyaluronic acid improved the pain and function of patients with knee osteoarthritis in the second months after injection. Atorvastatin did not have any effect on the knee osteoarthritis symptoms during 6 months.

References:

Disclosure of Interest: None declared


AB0812 DIFFERENTIATED APPROACH TO THE TREATMENT OF OSTEOARTHRITIS WITH COMORBIDITIES


Background: A significant prevalence of osteoarthritis (OA), the most disability joint disease in the world, which is important in the search for the new treatment. Analysis of modern therapy of OA was the reason for research efficacy of NSAIDs and SYSADOA on biochemical, inflammatory and immunological signs in the treatment of OA.

Objectives: Differentiated approach to the treatment of OA depending of presence of hyperuricemia.

Methods: 176 patients (144 women, 32 men) was examined, aged (59.7±10.86 years with confirmed radiographic OA according to Kellgren and Lawrence scale. Division into groups was performed depending on treatment. For 14 days group 1 (n=30) received nimesulide 100 mg twice daily, and group 2 (n=30) - meloxicam after surgery. It may be possible to predict with good accuracy for postoperative gait speed. In addition, these results could be of importance in determining effective rehabilitation strategies focusing on resistance training for improvement of gait speed early after TKA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2042
PROPOSAL FOR THE CONSTITUTION IMPLEMENTATION AND MEDICAL SHIFT OF THE TIBIAL ARTICULAR SURFACE SHOULD BE TAKEN INTO ACCOUNT FOR ONE FACTOR OF MEDIAL OSTEARTHRITIS OF THE KNEE

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Background: Varus knee is one factor of medial osteoarthritis of the knee. According to the concept of the constitutional varus\(^1\), the bone growth disturbance at the growth plate in the medial proximal metaphysis of the tibia results in proximal tibia vara. In this situation, the tibia is bent at the proximal metaphysis and the tibial surface (TAS) may be shifted medially. The medial shift of the TAS will increase the mechanical loading in the medial side of the knee. The medial shift of TAS will also influence the value of the Hip-knee-ankle (HKA) angle because the tibial plafond that is the end point of the mechanical axis (MA) of the tibia will shift medially. The purpose of this study was to assess the extent of the medial shift of TAS in knees with medial osteoarthritis, and to assess the effect of this medial shift of TAS on the value of HKA angle.

Objectives: The purpose of this study was to assess the extent of the medial shift of TAS in knees with medial osteoarthritis, and to assess the effect of this medial shift of TAS on the value of HKA angle.

Methods: This study consists of 116 knees with medial osteoarthritis. The mean age was 75.3 years old. The mean standing femorotibial angle (FTA: lateral angle between femoral and tibial anatomical axes) was 183.6°. The anatomical axis (AA) was the central line of the femoral and the tibial shaft. On the anteroposterior view radiograph of the tibia, AA, MA and tibial plateau tangent were drawn. MA is the line between the center of the tibial spine notch and the center of the tibial plafond. Two angle parameters and two distance parameters were measured.

Results: Those angle between AA and MA (Angle AA-MA) (the value was positive when MA located medial to AA), angle between the tibial plateau tangent and the line perpendicular to AA (Angle plateau) were calculated. The distance between AA and the tibial spines notch on the tibial plateau (Distance AA-MA) (the value was positive when Point M located medial to AA), and the length of MA were calculated.

Conclusion: The knee angle underestimated varus deformity, the more the tibial articular surface shifted medially. The maximum Distance AA-MA was 16.1mm. In this case, HKA angle underestimated varus deformity up to 3°.

Distance AA-MA (mm)

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\(^{1}\)中华医学。
References:

Acknowledgements: none.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4521

AB0815 PREVALENCE OF DORSAL AND LUMBAR VERTEBRAL OSTEOARTHRITIS IN WOMEN OVER 50 YEARS OF AGE EVALUATED USING THE LANE RADIOGRAPHIC SCORE IN FIVE LATIN-AMERICAN COUNTRIES

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Background: Osteoarthritis is the most common musculoskeletal disease worldwide. Spinal osteoarthritis (OA) is a frequent cause of back pain and disability in patients over 60. The frequency of radiographically-evident dorsal and lumbar OA in Latin America is unknown.

Objectives: To determine the prevalence of dorsal and lumbar vertebral OA in a database-driven random sample of women 50 years of age and older from the Latin-American Vertebral Osteoporosis Study (LAVOS) in 5 LA countries (México, Brazil, Argentina, Colombia and Puerto Rico).

Methods: Lumbar and Dorsal X-rays were performed by a standardized protocol and analyzed independently by two trained radiologists and a general practitioner using the Lane score to establish diagnosis and degree of vertebral OA severity. Inter and intra observer agreement was determined to be k = 0.6.

Conclusion: As OA severity increases, so does the prevalence of OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-election.4521

AB0817 IMPROVING CARE FOR PATIENTS WITH OSTEOARTHRITIS IN FIVE EUROPEAN COUNTRIES: THE JIGSAW-E PATIENT PANEL

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Background: Patient and Public Involvement and Engagement (PPIE) is a key component of JIGSAW-E.

Methods: A two-day international workshop established the JIGSAW-E Patient Panel to act as the voice of patients and the public in the project and to co-develop clear information and resources for patients. Panel members meet regularly with the project teams in each of the five countries.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-electr.4644

AB0816 COMPREHENSIVE ANALYSIS OF A NEW CHEMICAL COMPOUND FOR THE TREATMENT OF OSTEOARTHRITIS BY A PROTEOOMIC APPROACH IN HUMAN CHONDROCYTES

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Background: Selective cyclooxygenase (COX)-2 inhibitors were developed to prevent NSAID-gastro-intestinal adverse effects. VA692, a new hydroxyethyl selective COX-2 inhibitor, showed anti-inflammatory, anti-necroitive and chondroprotective properties. Proteomics is being applied for the study of drug mode of action, toxicity and to identify new drug targets.

Objectives: The aim of this study was to analyze the anti-inflammatory effect of VA692, in comparison with celecoxib. By iTRAQ methodology, we quantitatively analyzed the different expressed profiles in T/C-28a2 cell line treated with the studied drugs in presence of IL-1β.

Methods: Human T/C-28a2 chondrocytes cell line were generated by Goldring group. Human articular cartilage was obtained from femoral heads of five OA patients. Cells were incubated with VA692 and celecoxib (1, 0.5 and 0.05 μM) in presence of Interleukin (IL)-1β (5ng/ml) for 48h. The expression of inflammatory cytokines and anti-oxidative enzymes was evaluated by quantitative qRT-PCR, PGE2 release by ELISA, and apoptosis and ROS production by flow cytometry. T/C-28a2 cell line was also processed to carry out western blot tests and finally employed for the iTRAQ analysis. Statistical analysis was performed by ANOVA and Bonferroni multiple comparison tests.

Results: IL-1β-stimulated chondrocytes showed a significant increase (p < 0.001) of COX-2, IL-1β, IL-6, IL-8, superoxide dismutase (SOD)-2 and catalase (CAT) expression, as well as IL-1β-induced overexpression, as well as IL-1β-induced overexpression. The tested drugs significantly counteracted the effect of IL-1β, with a better modulation by VA692 1μM in T/C-28a2 cell line (p < 0.01 for COX-2, IL-1β, IL-8, CAT; p < 0.001 for IL-6, SOD-2). Regarding apoptosis and ROS production, the new drug was able to significantly reduce (p < 0.05) their increase induced by IL-1β (p < 0.05). Proteomic analysis led to identification of 797 proteins in T/C28a2 cell line, 123 of which were significantly modulated by VA692 in presence of IL-1β (p < 0.001), and 34 by IL-1β alone (p < 0.05). 22 proteins were commonly modulated in both groups, thus indicating that 101 proteins were regulated by VA692 in a specific manner. Among the proteins down-regulated by VA692, some with structural function were detected as responsible for the counteraction cell death (the shock proteins) and glycolytic enzymes. Proteins involved in calcium metabolism and in ribosome biogenesis resulted up-regulated instead, as well as SOD-2 as confirmed by western blot analysis.

Conclusions: Our data demonstrated the anti-inflammatory effect of VA692, suggesting also its anti-apoptotic and anti-oxidant role. The proteomic profile showed that VA692 induced not only an anti-inflammatory effect in chondrocytes but, interestingly, this compound also seemed to regulate their anabolic response.

Disclosure of Interest: None declared

References:

DOI: 10.1136/annrheumdis-2017-eular.3612

AB0818 IMPROVING CARE FOR PATIENTS WITH OSTEOARTHRITIS IN FIVE EUROPEAN COUNTRIES: THE JIGSAW-E PATIENT PANEL

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Background: EULAR guidelines for osteoarthritis (OA) endorse high quality care and support to self-manage with core recommended treatments such as exercise, weight loss and the provision of written information and education. An EU-funded project, Joint Implementation of Guidelines for oSteoArthritis in Western Europe (JIGSAW-E), aims to improve the management of OA across five European countries (UK, Netherlands, Norway, Denmark, Portugal) by implementing an intervention to enhance the OA consultation. Coordinated, cross-border Patient and Public Involvement and Engagement (PPIE), working in active partnership with the project team, is an essential component of JIGSAW-E.

Objectives: To describe the PPIE in the JIGSAW-E project.

Methods: A two-day international workshop established the JIGSAW-E Patient Panel to act as the voice of patients and the public in the project and to co-develop clear information and resources for patients. Panel members meet regularly with the project teams in each country. The Patient Panel is coordinated and supported by dedicated PPIE teams in the UK and Netherlands.

Results: The JIGSAW-E Patient Panel consists of Patient Champions and patient representatives from newly established or existing patient groups in each of the five countries. The Patient Champions form a core group of seven patient representatives who work closely with the Patient Panel and the JIGSAW-E team. PPIE activities have included:

- On 3 Patient Champions sit on the JIGSAW-E project steering committee.
- In the Netherlands, Patient Panel members substantially contributed to the translation and cultural adaptation of a guidebook for patients with OA. This process will continue as JIGSAW-E is rolled out in each of the five countries.
- Patient Panel members in the UK have helped refine an OA Quality Indicator questionnaire for use in JIGSAW-E.

A glossary of terms has been developed to support the involvement of Patient Panel members throughout the project.

Conclusions: Effective and meaningful PPIE is a central component to delivery and success of raising awareness and implementing the OA management
recommendations on a national level. The Patient Panel represents a step forward in international collaboration of PPIE within implementation projects. The Patient Panel is producing culturally appropriate and relevant information and resources for patients in five European countries. Future activities may include the development of patient stories to support increased adoption of JIGSAW-E, providing the patient perspective during training of health care professionals, and the digitisation of patient resources into Smartphone or tablet Apps.

References:
[1] https://goo.gl/a4xYUV.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2711

AB0819 PERSONALIZED ARTICULATING JOINT DISTRACTION FOR TREATMENT OF TIBIOFEMORAL OSTEOARTHRITIS: CLINICAL FEASIBILITY
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Background: Osteoarthritis (OA) patients encounter progressive pain and functional disabilities, including joint stiffness, due to degeneration of the joint tissues. For knee OA, the most prevalent form, available treatment strategies are limited in number and focus primarily on minimizing the functional disability, inflammation, and pain in a conservative manner since still no unambiguously proven effective disease modifying approaches are available. Progress in the development of joint sparing procedures however, has demonstrated the regenerative capacity of the osteoarthritic joint and with that the delay for conventional last resort therapy such as total knee arthroplasty (TKA). Knee Joint Distraction (K JD) is a joint preserving procedure that can postpone knee arthroplasty in case of knee osteoarthritis for over 5 years [1]. Distraction is applied with an external fixator for 6–8 weeks.

Objectives: To reduce the burden on patients during treatment originating from a restriction in joint flexion during KJD, we evaluated an articulating frame. A personalized articulating KJD-device was developed, biomechanically tested, and technical feasibility was evaluated in cadaveric legs. Reproduction of joint specific motion was demonstrated and articulating KJD was concluded to be technically feasible. In this study, clinical feasibility was tested in 3 patients.

Methods: Patients received rigid knee joint distraction treatment in general practice. After 2–4 weeks, the frame was removed in the outpatient clinic and the joint was flexed in a continuous passive motion (CPM) device until 30° flexion was reached, or motion became painful. Subsequently, the articulating frame was attached to the bone pins (figure 1), followed by computerized personalization of the hinge from a non-invasive motion measurement. After assembling the custom parts, weight-bearing and non-weight-bearing radiographs were taken at 0, 15, and 30° flexion for joint space width measurements. Finally, the articulating device was replaced by the rigid frame and treatment was continued according to clinical practice.

Results: For none of the three patients, the articulating distractor could be personalized. In the first patient, 15° flexion was achieved on the CPM, but pin positions did not allow for positioning of the frame. In the other patients, 8° and 15° flexion was measured, which was too little motion for the custom software to generate personalized hinge parts. Pain at the pin sites during motion was reported by all patients.

Figure 1. The articulating frame assembled to the bone pins and bone pin clamps as used for rigid joint distraction in clinical practice, and previous to measurement of joint-specific motion and customization of joint specific hinge parts.

Conclusions: Despite confirmation of joint-specific articulating distraction on cadaveric legs, clinical feasibility could not be demonstrated, mainly due to painful motion of soft tissues along the bone pins.

References:

Disclosure of Interest: None declared

AB0819 IS INCREASING THE TREND OF PRIMARY TOTAL HIP ARTHROPLASTIES FOR THE PATIENTS WITH OSTEOARTHRITIS, BUT DECREASING THE RATE OF WOMEN IN SUPER-AGING AREA OF JAPAN IN LAST TWELVE YEARS?
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Background: Elderly people over 65 year-old have increased year by year in many countries [1]. Because their rate was from 19.5% at 2004 to 26.8% at 2015 in Japan and 50.8% at 2015 in our super-aging area, the numbers of total joint arthroplasties have increased too [2]. In fact, the numbers of total hip arthroplasty predicted increasing from six hundred fifty-six thousand cases at 2010 to one million three hundred seventy-six thousand cases at 2020 in USA [3]. The rate of total joint arthroplasty, including primary total hip arthroplasty, may reflect trends in management and health outcomes of elderly people with osteoarthritis (OA) in our super-aging area of Japan [4].

Objectives: The aim of this study was to analyze the trend of primary total hip arthroplasties for the patients with OA in our institutes in the last twelve years.

Methods: We surveyed the number and rate of orthopaedic surgeries and primary total hip arthroplasties in our two institutes from 2004 to 2015.

Results: We had 19,862 cases of orthopaedic surgeries, including 3,782 primary total hip arthroplasties in the last twelve years. They have increased year by year (r=0.92, p<0.05, Fig. 1). Mean age was 64.5 old-year (62.4–66.8) in last twelve years, had become older year by year (r=0.78, p<0.05, Fig. 1). Mean age was 64.5 old-year (62.4–66.8) in last twelve years, and related to total numbers of orthopaedic surgeries in our super-aging area of Japan [4]. Mean rate of female was 87% (85–91) in last twelve years, had gradually decreased year by year (r=-0.68, p<0.05), 91% at 2004 vs 85% at 2015.

Conclusions: The rate of total joint arthroplasties including primary total hip arthroplasty increased year by year, and related to total numbers of orthopaedic surgeries in our super-aging area of Japan. Mean age at receiving primary total hip arthroplasty was older annually but mean rate of women had gradually decreased year by year. Although majority of OA hip consist of female which have secondary dysplastic acetabulum in our country, it might increase gradually the patients of man with OA hip in super-aging time in Japan.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2181
Osteoporosis

AB0820  FREQUENCY OF OSTEOPOROSIS AND ASSOCIATED RISK FACTORS IN MEXICAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The risk of osteoporosis in patients with rheumatoid arthritis (RA) is of particular interest as it can be associated with genetic and environmental factors. The frequency of generalized osteoporosis in different studies is variable.

Objectives: The aim of the study was to investigate the frequency of osteoporosis as well as to describe the risk factors in RA population.

Methods: Retrospective study, including patients with RA who had at least 2 densitometries in their follow up. We collected demographic characteristics, use of glucocorticoids (GC), other medications and antibody profile. Variables were compared between groups with or without osteoporosis. The frequency of osteoporosis was calculated according to the T-score and logistic regression was performed to explore the association of osteoporosis and relevant variables. Statistical analysis was performed using R software version 3.2.1. Baseline characteristics were compared between groups of patients (osteoporosis in the lumbar spine, femoral neck and hip) defined according to the T-score results. We used x2 or Fisher test for categorical variables as appropriate and Wilcoxon test for continuous variables. A logistic regression model was used to explore the relationship between osteoporosis and variables that could contribute as risk factors.

Results: One hundred and five patients were included, 96.2% were women, RA evolution of 7 (ICR 8) years. The frequency of osteoporosis was: lumbar spine 55.2%, hip 12%, and femoral neck 25.7%. Patients with lumbar spine osteoporosis had higher age (62 vs 58 years, p=0.13), lower weight (57 vs 63.8 kg, p=0.00004) and higher FRAX scores (26.5 vs 11.5, p=0.004; 8.5 vs 2.4, p=0.02). The associated risk factors were: weight (OR 1.09, 95% IC 1.03–1.15, p=0.001), GC use (OR 4.36, 95% IC 1.00–18.89, p=0.049), menopause (OR 22.78, 95% IC 2.73–190.12, p=0.003). There was no association with disease activity.

Conclusions: High rates of osteoporosis were found in patients with RA and the risk factors in RA population.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6567

AB0822  CLINICAL FEATURES AND PREDICTIVE FACTORS OF ORAL BISPHOSPHONATE-RELATED OSTEONECROSIS OF THE JAW: AN ANALYSIS OF 8 CASES IN A SINGLE INSTITUTION

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Background: Oral bisphosphonates (BPs) have been increasingly prescribed for the treatment of and prophylaxis for osteoporosis over the past decade. More than 190 million prescriptions for oral BPs have been dispensed worldwide, and, thus, the number of patients that develop oral BP-related osteonecrosis of the jaw (BRONJ) is expected to increase in the future. Although previous studies have investigated oral BRONJ, predictive factors have not yet been identified [1].

Objectives: The aim of the present study was to clarify the clinical features and predictive factors of oral BRONJ.

Methods: We included 8 patients who had taken oral BPs and were diagnosed with BRONJ at Mitsui Memorial Hospital (Tokyo, Japan) between 2011 and 2016. The following details were collected for each patient from a review of medical charts: sex, age, type of BP used, duration of BP administration, co-morbidities, laboratory values at presentation including hemoglobin, albumin, and serum creatinine values, clinical stage of the lesion, site affected, and pathological findings. Laboratory values of patients with BRONJ were compared with those of 242 patients (as a control group) who were prescribed BPs in October 2016 at our hospital. The Mann-Whitney U-test and chi-squared test were used for statistical comparisons between the oral BRONJ and control groups. Risk factors for BRONJ were assessed using multivariate analyses with a logistic regression analysis. All analyses were performed using SPSS ver. 21.

Results: The mean age and female ratio in the oral BRONJ and control groups were 64 years and 80%, and 71±12.7 years and 66.1%, respectively (p=0.26, p=0.61). The mean interval between the initiation of BP therapy and a confirmed diagnosis was 45.9±35.5 months. Seven patients had lesions in the mandibular bones and alveolus and were used in six cases. Oral BPs were administered to three patients with rheumatoid arthritis or multiple sclerosis, all of whom were given a maintenance dose of corticosteroids. The remaining three out of 5 oral BP users developed BRONJ after dental extraction. Regarding laboratory results, serum albumin values were significantly lower in the oral BRONJ group than in the control group (3.7±0.3 g/dl and 4.2±0.4 g/dl, respectively, p<0.01). Serum hemoglobin levels were slightly lower in the oral BRONJ group than in the control group (11.3±1.3 g/dl and 12.4±1.7 g/dl, respectively, p<0.06). A multiple logistic regression analysis identified serum albumin levels as the only significant predictive factor for oral BRONJ (OR=0.14; 95% CI 0.03–0.71, p<0.05). A pathological examination was available in six patients, with Actinomyces being identified as the causative agent in five of them.

Conclusions: Oral BRONJ mainly developed in patients with long-term corticosteroid use for an underlying illness or those who underwent dental extraction, and hypoaalbuminemia was the only laboratory marker identified as a predictive factor for BRONJ.
EVALUATION OF OSTEOPOROSIS AND FRACTURES IN PATIENTS WITH DIABETES MELLITUS TYPE 2: RESULTS OF A 5-YEAR FOLLOW-UP

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Background: The treatment of Osteoporosis is difficult to monitor and so usually incomplete resulting in inadequate response.

Objectives: To evaluate the minimum period of treatment required with Bisphosphonates and Parathyroid hormone in order to see a significant change in serial Bone Mineral Density analysis (BMD).

Methods: Low BMD patients were subjected to yearly infusion of Zoledronic Acid 5mg (ZA) verses daily Subcutaneous injections of Teriparatide 20 μg (PTH). A single center pixel beam body densitometer was used to measure serial BMD at baseline and yearly. Average BMD measures from the Spine L2, L3 and L4 (BS) and Total Hip (BH) were evaluated. The percentage change in the mean BS and BH readings was calculated to look for the least significant change (LSC) in the density scores.

Results: Significant change of 4.65% was seen (LSC=2.6%)2 in the Spine in the PTH group after one year of treatment while it took two years in the ZA group for a 2.77% change. There was no significant change (LSC=0.6%) in both groups in the BH. A p<0.05 was considered statistically significant. The finding is summarized in Table 1.

Table 1

Study group of 100 patients

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>N</th>
<th>Gender</th>
<th>Age range</th>
<th>BS*</th>
<th>BH**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>Female</td>
<td>Years</td>
<td>After 1 yr</td>
<td>After 2 yrs</td>
<td>After 1 yr</td>
</tr>
<tr>
<td>ZA - Zoledronic Acid</td>
<td>50</td>
<td>12</td>
<td>38</td>
<td>42-79</td>
<td>2.19</td>
</tr>
<tr>
<td>PTH - Teriparatide</td>
<td>50</td>
<td>10</td>
<td>40</td>
<td>40-75</td>
<td>4.651</td>
</tr>
<tr>
<td>BS - Least Significant Change for single DXA machine</td>
<td>2.50%</td>
<td>3.60%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BS - BMD Spine; BH - BMD Total Hip; LSC - Least Significant Change

Conclusions: Significant result of treatment with PTH requires a period of one year of therapy while with ZA it needs two years. The LSC in BMD is seen in the Spine and not in the Total Hip BMD.

References:
[2] Shepherd JA1, Lu Y. A generalized least significant change for individuals measured on different DXA systems.
AB0827

COMPARISON OF THE CAPABILITY OF RADIAL BONE MINERAL DENSITY AND CALCEANAL QUANTITATIVE ULTRASOUND VARIABLES IN THE IDENTIFICATION OF MEN WITH OSTEOPOROSIS

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Background: Bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) is considered the gold standard for the management of osteoporosis. Recently, quantitative ultrasound (QUS), which is easy to use, inexpensive, portable, does not use ionizing radiation, and has also been shown to provide information about bone quality and to predict fracture risk, has gained growing interest in this area.

Objectives: The aim of this study was to compare the capability of one-third radius (33% radius) DXA BMD measurements and calcaneal QUS (cQUS) variables for identifying axial osteoporosis as measured by DXA in men.

Methods: Axial BMD measurements at the lumbar spine and at the hip (femoral neck and total hip), 1/3 radius BMD of the non-dominant forearm were made using DXA and cQUS variables at both sides as measured twice were obtained in 179 men aged between 24 and 85 years. Osteoporosis was defined based on the WHO criteria in men aged 50 and over, a man having been considered as osteoporotic in the presence of a T-score <−2.5 in any of the axial regions measured.

For defining axial osteoporosis or BMD below the expected range for age, Z-scores were used which were younger than the age of 50 years. Receiver operating characteristic (ROC) analysis was used to assess the osteoporosis identification capability of measurements.

Results: The areas under ROC curves (AUCs) for 1/3 radius BMD, its T-score, the lowest means (as calculated as the mean of the two calcaneal QUS measurements for each heel) of quantitative ultrasound index (QUI), QUI T-score, broadband ultrasound attenuation (BUA), speed of sound (SOS), and estimated heel BMD (eBMD) for identifying axial osteoporosis or BMD below the expected range were found as 0.755, 0.767, 0.760, 0.717, 0.768, and 0.764 (p < 0.001 for all), respectively.

Conclusions: In conclusion, AUCs pointed to similar for QUI, QUI T-score, and eBMD or even better for (SOS) osteoporosis discriminative capability of cQUS variables in comparison to radial DXA BMD variables. These findings may have implications that cQUS variables, particularly SOS, may be used for the identification of osteoporosis in men whose axial BMD cannot be measured by DXA due to certain circumstances as well as in circumstances where DXA is not available.

References:

Disclosure of Interest: None declared


AB0828

MAJOR RISK FACTORS OF OSTEOPOROSIS IN RA FEMALE PATIENTS WITH NORMAL MENSTRUAL CYCLE

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Background: Only postmenopausal women were in the researcher’s focus in the majority of publications on osteoporosis (OP) risk factors (RF) in RA female patients (pts). Meanwhile the data on OP RF in menstruating women presented in the rare available papers are not consistent.

Objectives: To identify the major OP RF in RA female pts with normal menstrual cycle.

Methods: 51 RA pts (based on ACR criteria) female pts with normal menstrual cycle aged 20 to 51 years (mean age 41±1.7 years) were examined. The following info was included in each individual pts’ files: anthropometric parameters, social and demographic data, case history, clinical examination and lab findings, traditional OP RF, pts’ joint status, comorbidity status, pain intensity assessments and VAS evaluation of pts’ general health status. Axial bone mineral density (BMD) was measured with DXA scan using Z-score calculator. Based on the OP status all pts were divided into 2 groups:pts with OP – 16 (31.4%), and pts without OP – 35 (68.6%).

Results: Comparative analyses of the groups showed that: OP pts were younger (31±10 vs 42±8.5 years, p=0.02), Disease duration was comparable in both groups. Clinical manifestations of inflammation activity (mean DAS 28 score and hsCRP) were statistically significantly more pronounced in the OP group vs the pts without OP (4.9±1.1 vs 4.19±1.06, p=0.049; 27.8 (10.8–45.5) vs 7.4 (1.4–27.7) mg/L, p=0.02, respectively). High DAS 28 (50 vs 20-6%, RR=2.43, 95% CI 1.07–5.53, p<0.03) scores were more often documented in the OP pts. Pronounced feet and hand bone destruction based on the radiographic findings was documented in the majority of pts in both groups, although in the OP pts the joint space narrowing counts (97 (62.5–121) vs 73.5 (53–87), p=0.02) and the total Sharp score (98 (64.5–183) vs 89.0 (63–112), p=0.03) were statistically significantly lower in the OP pts. The mean of the following major OP RF in the RA female pts were more pronounced: bone loss (83.1 vs 37.1%, RR=2.19, 95% CI 1.34–3.57, p=0.004), as well as GCs -pulse therapy (56.3 vs 25.7%, RR=2.18, 95% CI 1.08–4.45, p=0.04), had higher GCs cumulative dose (18.8 (8.1–30.7) vs 6.4 (0.8–14.1), p<0.01), higher GC daily dose at the time of examination (8.8 (6.3–10) vs 5 (3.8–6.3)mg/day, p=0.01) and higher average daily dose in the previous year (8.8 (5–10) vs 3.8 (2.5–6.3)mg/day, p=0.01) versus the pts without OP. Analysis of traditional RF (low body weight/BMI, long immobilization periods, smoking, family history of OP and others) showed no difference between the two groups. Discriminant analysis revealed the following major OP RF in the RA female pts were more pronounced: RA activity (based on the Das 28 score) and GCs dose at the time of examination (given GCs therapy lasts ≥3 months). Meanwhile the patient’s body weight and age at the onset of RA were identified as protective factors for BMD. Based on the abovementioned risk and protective factors and the derived coefficients the authors designed a formula allowing to predict of OP in female RA pts before menopause with high accuracy (area under the ROC-curve=0.833). The model accuracy is 85.1%.

Conclusions: RA activity and GCs dose (GCs therapy duration ≥3 months) were identified as the major OP RF in young RA female pts before menopause, thus adequate and timely therapy aimed at obtaining RA control and achieving remission should be considered as key OP prevention strategy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2312

AB0829

BONE METABOLISM IN LIVER TRANSPLANT PATIENTS TWO-YEAR STUDY. INFUENCE OF MEDICAL INTERVENTION PRIOR TO SURGERY AND ANTIRESORPTIVE TREATMENT

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Background: Osteoporosis is a frequent complication in patients with chronic liver diseases, mainly in advanced stages or with evidence of cholestasis. During the first few months after liver transplant (LT) it seems that there is an accelerated bone mass loss and greater fracture risk.

Objectives: To study the antiresorptive treatment effect in bone metabolism in patients undergoing LT and to evaluate whether medical intervention prior to LT decreases the risk of osteoporosis.

Methods: We recruited patients from the LT Protocol of Osteoporotic Risk Assessement. The patients were evaluated 3–4 months before surgery, shortly after transplant (month 0) and 6–12–18–24 months after surgery. Data of bone metabolism biomarkers, densitometric values and antiresorptive treatment was collected. Biostatistical analysis with R (3.3.2.) was performed.

Results: We selected 163 LT patients of which 86 completed 24 months follow-up. From the total cohort, 77.8% were men and the mean age at transplantation 54.5±9.4 years old. 92.6% of patients were supplemented with vitamin D after surgery and 19.6% initiated antiresorptive treatment. We observed that 25-OH Vitamin D, PTH, beta-CTX and P1NP levels were corrected through the follow-up. T-score during the first year of follow-up decreased slightly and at 24 months the tendency was towards increase. This pattern was stronger in lumbar spine (t-score -1.48±1.34 after surgery and -1.28±1.06 at 24 months). Statistical analysis showed that antiresorptive treatment significantly influence lumbar and hip densitometric values (P<0.001 and P<0.001 respectively) as well as P1NP levels (P<0.003 and P<0.012 respectively). Moreover, obesity (P<0.004), as well as beta-CTX (P<0.029) and 25-OH Vitamin D (P<0.024) standardization improved hip densitometric values. Finally, LT patients evaluated before surgery showed better lumbar densitometric values than those evaluated after the transplant (P<0.007).
Conclusions: We observed 25-OH/vitamin D levels and bone metabolism biomarkers correlation during the first two years after LT. Medical intervention prior to LT as well as antiresorptive treatment seem to play a decisive role in bone mineral density improvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5855

AB0830 BONE MINERAL DENSITY IN MULTIPLE MYELOMA: 39 CASES

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Background: In multiple myeloma (MM), osteolysis affects more than 80% of patients. This leads to bone pain, pathological fractures and hypercalcemia. These lesions result from the hyperactivation of osteoclast activity and decreased osteoblasts one. The real impact of this osteolysis on bone mineral density remains largely understudied. To the best of our knowledge the impact of MM on bone mineralization was studied worldwide only for 6 times where our study is the second biggest one.

Objectives: The aim of the study was to evaluate bone mineralization in the patients with multiple myeloma according to the criteria of diagnostic (IMWG: International Myeloma Working Group 2014, during a period of 5 years (2011–2016).

Methods: This is a transverse and descriptive study. The bone mineral density was measured by dual-energy X-ray absorptiometry with Lunar Prodigy in spine (L2-L4) and femoral neck.

Results: Thirty-nine patients were collected. The average age was 63±10 years [50 years, 86 years] upon them 26 men and 13 women. The sex-ratio is equal to 2. 18 patients were smoking (35%), 9 of them had diabetes and only 2 were alcoholic (6%). The Body Mass Index (BMI) average was 29 kg/m². Only one case was underweight (3%). The reason of seeking health carewas poor general state in 14 cases (49%), bone pain in 22 cases (78%), 5 cases among them of generalized bone pain (23%) and 12 cases of rachialgia (4.5%) and only 4 cases of pathological fracture in stage II. The distribution of patients into staging proceeding according to the Durie and Salmon Classification was as follows: 25 cases (84%) in stage III, 3 cases (10%) in stage II, 2 cases (7%) in stage I, and 27 cases (90%) Type A and 3 cases (10%) type B. The average of the monosonal score was 34/G [2.5G, 88G]. The heavy chains antibodies were IgG type in 19 cases (84%), IgA type in 7 cases (24%), IgM type in only one case (4%) and IgD type in only one case (4%). The light chains were kappa type in 19 cases (84%) and Lambda type in 11 cases (37%). The ISS score was equal to 1 in 6 cases (23%), equal to 2 in 13 cases (44%) and equal to 3 in 8 cases (30%). The average bone mass in the spine was 0.99/±.254/cm² [0.63/cm²; 1.89/cm²] and in the femoral neck 0.86/±.254g/cm² [0.63/cm²; 1.89/cm²]. The average of the Z-score in the spine was -0.76/±1.89 [4.4; 5.7] and in the femur -0.42/±0.962 [2.8; 1.4]. The mean T-score in the spine was -1.62/±2.025 [-4.9; 5.6] and in the level of the femur -1.57/±1.178 [-3.7; 1]. There was a decrease of bone mineral density noticed in 15 patients (39%) in at least one place (T-score more than 2.5 SD below normal of young healthy persons. Seventeen patients (58%) were candidates for autogenous bone graft. They had induction chemotherapy (Dexamethasone-thalidomide). Others were treated by MPT protocol (Prednisone-Thalidomide-Dexamethasone) in 8 cases (28%), CDT protocol (Cyclophosphamide-Thalidomide-Dexamethasone) in one case (4%) and MP protocol (Melphalan -Prednisone) for the remaining (10%).

Conclusions: BMD analysis suggests that MM is associated with systemic bone disease with progressive loss of bone mass at both the spinal and lumbar levels. In order to better study the impact of multiple myeloma and chemotherapy on bone densitometry, a densitometry control about 5 years is favorable.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6754

AB0831 FRAX SCORE: AN INTERESTING WAY FOR GASTROENTEROLOGISTS TO ASSESS FRACTURE RISK IN PATIENTS WITH LONG-TERM PROTON PUMP INHIBITORS

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Background: Proton pump inhibitors (PPI) are widespread nowadays. Recent concerns have emerged about possible bone complications of long-term use of PPIs, such as low bone mineral density (BMD) and an increased risk of fractures. Proton pump inhibitors (PPI) are effective in many indications. Nevertheless, some serious adverse effects associated with prolonged exposure, including a fracture risk, have occurred. This could be explained by two main mechanisms: decreased absorption of calcium secondary to decreased gastric acidity and inhibition of proton pump of osteoclasts reducing bone resorption.

Methods: We studied 52 patients. Those who have been taking PPI for at least one year. In all patients, we specified the indication and duration of PPI. We then looked for the main personal or family risk factors for osteoporosis. Bone mineral density (BMD) was performed in all patients and Frax score was calculated for those older than 40 years.

Objectives: The aim of our study was to evaluate the usefulness in our practice of this score in patients under long-term PPI.

Results: We included 52 patients. The mean age was 49.5 years old. The male-female ratio M/F was 0.48. At least three risk factors were found in more than 50% of the population. The calculated daily calcium intake was insufficient in 94% of the patients. The mean duration of PPIs intake was 45 months. The most frequent indication was gastro esophageal reflux disease (76%). The PPI prescription was appropriate in 94% of the cases. The prevalence of osteopenia and osteoporosis was respectively 52% and 19%. The predictive factors of low BMD were an age ≥50 years old (p<0.03), the menopause (p<0.0001), a calcium intake ≤550 mg/day (p<0.003), and a PPI use duration ≥30 months (p<0.006). The multivariate study could not be undertaken because of co linearity of the factors.

Conclusions: The long term PPI use is associated to the risk of bone complications, especially among patients at risk for osteoporosis. It seems reasonable to be more vigilant in prescribing PPIs and use lowest effective dose for patients with appropriate indications, and to screen these complications if necessary.

Disclosure of Interest: None declared


AB0833 BONE MINERAL DENSITY IN TUNISIAN PATIENTS WITH AUTOIMMUNE HEPATITIS

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Background: Bone loss in autoimmune hepatitis (AIH) is scanty and conflicting. The pathogenic mechanisms are not completely elucidated.

Objectives: This study aimed to assess the prevalence and risk factors for bone loss in patients with AIH.

Methods: Bone mineral density (BMD) using X-ray absorptiometry at both lumbar spine and femoral neck sites was measured in patients with AIH. Were excluded patients with diseases disturbing the bone density. Osteopenia was considered if T-score < -1.5 DS and osteoporosis if T-score < -2.5 DS.
Results: Twenty eight patients were enrolled in the study. They were 19 women (sex-ratio M/F=0.6), with a mean age of 54 years [extremes: 13 - 73 years]. Most patients had type 1 AIH (89.2%). Seventeen patients were diagnosed at stage of cirrhosis (60.7%). Associated auto-immune manifestations were observed in 42.8% of cases. Overlap syndrome with primary biliary cirrhosis was noted in 20.7% of cases. A total of 27.9% of patients were on steroid treatment and 24.26% of patients were on steroid treatment for more than 6 months. BMD was low in 9 patients (32%) as follow: osteopenia in 6 cases and osteoporosis in 3 cases. There was a correlation between bone loss and use of steroid treatment but it wasn’t statistically significant (p=0.07).

Conclusions: In our series, the prevalence of bone loss in AIH is high (45%). This data suggest that bone status should be assessed routinely in patients with AIH, especially in those on steroid treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6442

AB0834 RISK FACTORS FOR DECREASED BONE MINERAL DENSITY IN INFLAMMATORY BOWEL DISEASE IN A TUNISIAN COHORT

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Background: Patients with inflammatory bowel disease (IBD) are at risk for metabolic bone disease. Many studies have identified various risk factors but most of them have involved western patients.

Objectives: The aim of this study was to investigate the prevalence and the risk factors for metabolic bone disease in Tunisian IBD patients.

Methods: Retrospective study including patients with IBD admitted in our department between January 2011 and December 2015. Demographic and clinical characteristics of patients were analysed. Bone mineral density of the femoral neck, total femur and lumbar spine was quantified by dual-energy X-ray absorptiometry.

Results: Among 82 patients followed for IBD (70.7% with Crohn’s disease; 29.3% with Ulcerative colitis), a bone densitometry was performed in 56% of cases (n=46). 16 patients have osteopenia and 7 had osteoporosis, as assessed by T-score. Variance analysis showed that Crohn’s disease in particular ileal disease, high steroid dose and the presence of extra-intestinal manifestations were significantly associated with a low bone mineral density (all p<0.05). In the other hand, IBD duration since diagnosis, sex, tabagism were not associated with bone loss.

In multivariate regression analysis, risk factors for decreased bone mineral density were IBD duration since diagnosis, high steroid dose, ileal crohn’s disease and extra-intestinal manifestations.

Conclusions: In our Tunisian cohort of IBD patients, Crohn’s disease, high steroid dose and extra-intestinal manifestations were associated with increased risk for metabolic bone disease. High risk patients should be identified and appropriate therapies should be started early to improve long term quality of life.

 Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5301

AB0835 DENOSUMAB AS A FIRST CHOICE DRUG FOR GLUCOCORTICOID INDUCED OSTEOPOROSIS TREATMENT INSTEAD OF BISPHOSPHONATE

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Background: Glucocorticoid induced osteoporosis (GIO) is serious problem for raising risk of bone fragile fracture. In general, first choice drug for GIO is bisphosphonate (BPH), however, denosumab (dMAB), a monoclonal antibody of receptor activator of nuclear factor kappa-B ligand, is closed up as an alternative selection for GIO recently.

Objectives: The aim of this study is to evaluate effectiveness of dMAB in bone mineral density (BMD) for GIO treatment compared to BPH.

Methods: In this study, all patients who had been glucocorticoid steroid (GCs) have been administered for more than three months, who met indication criteria for GIO what was determined by the Japanese Society for Bone and Mineral Research in 2014, that is matrix calculated in adding points of past fracture history, age, dosage of GCs, and BMD value (1), were enrolled. Before March 2013, data was lacking, so patients who have been administrated GCs after April 2013 were picked up. Patients BMD at GCs administration, at 6 months after initial treatment, if drug was changed, also at 6 months after second treatment, for minimum lumbar spine (LS), femoral neck (FN), and greater trochanter (GT) were measured with dual-energy X-ray absorptiometry (DEXA). Patients were classified by drug for initial treatment and second drug if administrated. Patients age, initial, average, and total dose of GCs, term length of administration, and BMD and its gain for each chance were compared with Mann-Whitney U-test and Student’s paired T-test.

Results: 149 patients in whom 48 with no drug administrated (N), 24 for BPH naive and continued (BB), 22 for BPH naive and changed to dMAB (BD), 21 for dMAB naive and continued (DD), 34 for dMAB naive and changed to BPH (DB) were counted. In these, sex distribution was 26 for men and 123 for women. Underlying disease for administration of GCs were rheumatoid arthritis for 114, polymyalgia rheumatica for 12, idiopathic thrombocytopenic purpura for 9, systemic lupus erythematosus for 6, and others for 8. For groups, age at baseline, initial, average, and total dose, and term length of administration of GCs demonstrated no significant difference between any pairs of the groups. BMD at baseline for Group N demonstrated significant greater per-cent of young adult mean (%YAM) than Group DD (p<0.01) in all parts, yet greater than the other groups but not statistically significant. In Group N, BMD had significantly decreased from the baseline to 6 months later in all parts (p<0.01). In the other groups, BMD had shown gain at 6 months after drug administration in all part, however, in Group DB showed mean %YAM loss for GT after first and second drug administration compared to Group BD had shown %YAM loss after first but gain after second drug for FN (Table 1).

Conclusions: From these results, dMAB is effective role in raising BMD for GIO as a initial drug, and a second drug even after inadequate response to BPH. dMAB could be possible to be chosen as a first choice drug for GIO treatment.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3106

AB0836 PERFORMANCE OF QUANTITATIVE ULTRASOUND AND SIX OSTEOPOOROSIS RISK INDEXES IN MENOPAUSAL WOMEN: VALIDATION AND COMPARATIVE EVALUATION STUDY


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Background: A number of questionnaire-based systems and the use of portable quantitative ultrasound scanners (QUS) have been devised in an attempt to produce a cost-effective method of screening for osteoporosis.

Objectives: to assess the sensitivity and specificity of different techniques and their ability to act as screening tools in relation to dual energy X-ray absorptiometry (DXA).

Methods: 295 white menopausal women aged over 60 were enrolled. Each subject completed a standardized questionnaire which permits the measure of six osteoporosis indexes and had bone mineral density (BMD) measured using QUS and DXA. Sensitivity and specificity of the different techniques in relation to DXA were plotted as receiver-operator characteristic (ROC) curves at DXA T-score total hip ≤ -2.5 (osteoporosis).

Results: BUA sensitivity and specificity values were respectively 76.8% and 51.2% at the total hip. The optimal cut-off T-score for QUS was -2 at the total hip. The osteoporosis self-assessment tool (OST) provided consistently the highest AUC (0.80) among the clinical tools and had the best sensitivity and specificity balance (90.2% vs.44.5%). OST negative likelihood ratio was 0.22.

Conclusions: OST (based only on the weight and the age) performed slightly better than QUS and other risk questionnaires in predicting low BMD at the total hip.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1449

AB0837 BONE METABOLISM AND OSTEOPOROSIS RISK FACTORS ANALYSIS IN SPINAL CORD INJURY PATIENTS AT TWELVE MONTHS FOLLOW UP

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Background: The spinal cord injury associated with the immobilization of the
patient leads to a decrease in bone mass. The bone loss greater is observed in the 6 months after the spinal cord injury, and stabilizing between 12–16 months after the same. The incidence of fractures oscillates between 1.5% and 6%.

**Objectives:** To assess bone metabolism and bone fracture incidence in SCI patients.

**Methods:** Prospective study of SCI patients from the Spinal Cord Injury Unit of La Fe Hospital. In all cases densitometry, x-ray image, bone metabolism biomarkers and clinical evaluation have been performed according protocol. Statistical techniques was carried out using R software 3.2.3, using mixed linear regression models.

**Results:** We studied 40 patients with SCI, 54% of them men and 46% women, with a mean age of 59.5 years (57.3–63.5). The 58% of patients showed thoracic injuries, 48.6% paraparesis and 46.7% presented level C in Asia scale. The baseline study was performed in 100% of patients (n=40), 65% in month 6 (n=26), 30% in month 12, and in 25.5% in month 18 (n=9). The 32.4% of patients received supplementation with calcium and vitamin D at month 0, 66.7% at month 6 and 100% at month 12.

In month 6, the 11.1% was treated with antiresorptive drugs. An increase in vitamin D values can be observed in the population with follow-up (values of 16.82 in month 0 to 39.33 in month 12), justified by the supplementation, and there is an increase in Calcium and a decrease in phosphorus values.

There was also a decrease in PTH levels in month 12 (32.3) compared to month 0 (34.08), as well as a decrease in bctx levels. Probably related to the increase of vitamin D intake.

Despite a decrease in the densitometric parameters at month 6, a slight recovery was observed in bone mineral density at month 12. No bone fractures were seen during Follow-up in none of the patients.

Results from biochemical markers and densitometry are showed in the table below.

### Table: Biochemical Markers and Densitometry during Follow-up

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Month 0</th>
<th>Month 6</th>
<th>Month 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>9.04 (0.47)</td>
<td>9.57 (0.36)**</td>
<td>9.39 (0.34)**</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.83 (0.62)</td>
<td>3.42 (0.24)**</td>
<td>3.4 (19.94)**</td>
</tr>
<tr>
<td>25 OH Vitamin D</td>
<td>16.82 (10.4)</td>
<td>37.27 (15.5)**</td>
<td>39.33 (19.94)**</td>
</tr>
<tr>
<td>PTH</td>
<td>34.08 (21.74)</td>
<td>36.16 (19.46)</td>
<td>32.3 (12.6)</td>
</tr>
<tr>
<td>BCTX</td>
<td>0.94 (0.46)</td>
<td>0.62 (0.87)**</td>
<td>0.34 (0.21)**</td>
</tr>
<tr>
<td>Lumbar spine tscore</td>
<td>-0.24 (1.58)</td>
<td>-0.25 (1.11)</td>
<td>-0.3 (1.27)</td>
</tr>
<tr>
<td>Femoral neck tscore</td>
<td>-0.73 (1.34)</td>
<td>-1.35 (1.03)**</td>
<td>-1.26 (1.25)**</td>
</tr>
<tr>
<td>Hip bone tscore</td>
<td>-0.74 (1.25)</td>
<td>-1.56 (1.29)**</td>
<td>-1.52 (1.4)**</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001.

### Conclusions:
A high percentage of our patients with spinal cord injury has a vitamin D deficiency. In addition, the lower values are associated with cases where the mobility limitation is higher. As patients increase vitamin D values, a decrease in the bctx and PTH parameters is observed.

No fractures were detected during follow-up.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5487

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**EB0838**

**EPIDEMIOLOGY AND ANALYSIS OF FALLS IN PATIENTS DURING BALNEOTHERAPY IN DANUBIUS HEALTH SPA PIESTANY**

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**Background:** Patients falls in hospitals are frequent and undesirable complications that may lead to negative outcomes such as injuries, prolonged hospitalization and legal liability.

**Objectives:** To investigate the incidence and characteristics of patients hospitalized in the Health Spa Piestany.

**Methods:** Prospective analysis of falls in the group of in-patients of health spa during a year since 01.01.2015 to 31.12.2015.

**Results:** Overall there were hospitalized in the health spa 25 774 in-patients. The mean age of patients was 64,02±13,16 years. There were women - 15 301, mean age (63.81±11.57) years and men 10 473, with mean age (64.43±9.22) years. Falls were confirmed in 131 patients (women 94, mean age 68.55±12.02 years and men 37 males, mean age 70.39±7.82 years. Fractures have been confirmed in 19 patients, all of them non-vertebral. The ankle distortion were in 11 patients and lacerated wounds in 10 patients. There were collapse status in 8 and commotoe cerebri in 1 patient. Spa therapy had to be discontinued only in 5 from 131 patients due to falls. The annual incidence of falls reached 5,08 cases/1000 patients.

### Table 1. Patients characteristics at baseline

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs) median, (1st Quartile- 3rd Quartile)</td>
<td>65, (58–67)</td>
<td>51-65</td>
</tr>
<tr>
<td>&gt;65</td>
<td>48</td>
<td>35%</td>
</tr>
<tr>
<td>Female</td>
<td>76</td>
<td>55%</td>
</tr>
<tr>
<td>UAE</td>
<td>121</td>
<td>87%</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>72</td>
<td>52%</td>
</tr>
<tr>
<td>Received 4 Denosumab doses or more</td>
<td>86</td>
<td>62%</td>
</tr>
<tr>
<td>DXA scan at DHA at Baseline</td>
<td>136</td>
<td>98%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>12</td>
<td>9%</td>
</tr>
<tr>
<td>Fractures</td>
<td>12</td>
<td>9%</td>
</tr>
</tbody>
</table>

**Conclusions:** Denosumab was effective and safe in our patients. Long-term follow up is required to verify these findings in our population.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5278

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**AB0839**

**THE EFFICACY AND SAFETY OF DENOSUMAB LOCAL EXPERIENCE**

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**Background:** Denosumab was introduce to the United Arab Emirates Market in 2013. Given the limited experience in using Denosumab in the region we have explored it efficacy and safety in daily practice.

**Objectives:** To assess the efficacy and safety of Denosumab in our practice.

**Methods:** Inclusion criteria: All patients received Denosumab in a dose of 60mg every six months. Underwent DEXA scan in Dubai Health Authority. Exclusion from analysis: Other Doses of Denosumab, who received less than 3 doses, and those with no follow up DXA scan. Outcome measures: 1) Efficacy: Proposed Criteria for Assessing Clinical Response [1,2], a) “inadequate”: incident fracture and significant BMD decrease. b) “possible inadequate”: incident fracture or Significant BMD decrease. c) “appropriate”: no fracture and stability or increase in BMD. 2) Safety: Reviewing the medical records and conduct patients interview for occurrence of the following adverse events. Statistical analysis: Descriptive statistical analysis, Graphpad Prism 6 was used.

**Results:** 143 patient identified. Out 139 patients 86 were eligible for analysis (See table 1). At baseline 39% had normal vitamin D level, 57% had insufficiency and 4% had deficiency. 20 of 86 did not undergo repeated DXA scan. 9% had osteoporia and 91% had osteoporosis before initiating Denosumab in comparison 8% had normal bone mineral density, 45% had osteopenia and 47% post four injections of Denosumab. Table 2 summarize the comparison between the responders and non-responders. There was a significant positive correlation in the increase in bone mineral density among the responders at the femoral neck and the lumbar spine. (r=0.56, 95% confidence interval: 0.31–0.74, P-value <0.0001)

**Table 2. Comparison between the appropriate Response group “Responders” and inadequate response group “Non-responders”**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Odds Ratio</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>52</td>
<td>14</td>
<td>0.0001</td>
<td>0.05–0.2</td>
</tr>
<tr>
<td>Rhamnoic Diseases</td>
<td>6</td>
<td>36</td>
<td>0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Fracture</td>
<td>0</td>
<td>3</td>
<td>0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-treatment fractures</td>
<td>9</td>
<td>1</td>
<td>9.5</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Conclusions:** Denosumab was effective and safe in our patients. Long-term follow up is required to verify these findings in our population.

**References:**

AB0840 LOCAL FRACTURE LIASON SERVICE (FLS): PRELIMINARY RESULTS

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Background: Hip fracture has great impact on morbi-mortality, but a large percentage of patients do not receive treatment.

Objectives: To know the characteristics of patients with hip fracture and its evolution in the first 6 months.

Methods: A prospective, 6-month follow-up study of patients over 60 years old admitted for hip fracture, evaluated in a local FLS. At 3 months after discharge, patients are evaluated for: epidemiological data, fracture income (days of admission, prior and discharge of osteoporosis (OP) drugs, general biochemistry and vitamin D), OP records and possible diseases or osteoporizing drugs, lumbar spine and hip Bone densitometry (BMD) lateral dorsal and lumbar spine radiology and the treatment was decided. The electronic history before and after the fracture were reviewed.

Results: Of 152 patients >60 years old, admitted in 2016 due hip fracture, 77 (51%) were during the first 6 months. However, radiology or BMD data were not available for 30 (39%) patients, 16 (21%) for death and 14 (18%) for loss of follow-up. Mean BMI was 26.02±6.2. The mean age of menopause was 49±5 years. 1% of the patients received corticosteroids and 2% of patients an osteoporosis disease (COPD) was found. Mean time of admission was 7.57±2.51 days. In 3% of the patients, before the fracture were receiving OP treatment, which continued to discharge. The mean level of calcium, phosphorous and alkaline phosphatase was normal. However, the mean level of 25OH vitamin D was 13.55±8.63 nm (range: 12 to 25 ng/ml).

In 11 of the 27 (41%) patients, in whom radiology was available, the presence of vertebral fracture was demonstrated. The mean T-score for lumbar BMD was 1.8±1.65 DE (32%; the result was normal, 36% osteopenia, 32% OP), femoral neck 2.5±0.77 DE (27%; osteopenia, 77% OP) and in total hip: 2.5±0.86 DE (56%; osteopenia and 44% OP). In 100% of patients evaluated in Rheumatology, initiated treatment for OP: zolodronate: 40%; alendronate: 20%, denosumab: 25%; PTH: 15%.

Conclusions: In patients with hip fracture: 1) Mortality is high (21%), in the first 6 months after fracture, 2) The prevalence of vertebral fracture is 40%. 3) It is accompanied by very low blood levels of vitamin D. 4) In a high percentage the result of BMD is normal or osteopenia. 5) A minimum number of patients receive specific treatment for osteoporosis after fracture. 6) Evaluation in a FLS, ensures the evaluation and treatment of patients.

Acknowledgements: The study was supported by a research grant from the Asociación para la Investigación en Reumatología de la Marina Baixa (AIREMB).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4234

AB0841 MEDICAL AND SOCIAL CONSEQUENCES IN HIP FRACTURES DEPENDING ON THE METHOD OF TREATMENT

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Background: medical and social significance of osteoporosis is determined by its consequences - fractures of the vertebrae and the bones of the peripheral skeleton. Osteoporosis is one of the high rates of mortality and disability among older adults.

Purpose: to follow basic health and social consequences among the surviving patients with hip fractures aged 50 years or older at 6, 24 months.

Objectives: The study included 432 patients (328 women and 104 men) with hip fracture and accompanying osteoporosis. The study assessed the risk factors and the impact of treatment on the consequences of osteoporosis fractures.

Methods: Surgical treatment was performed in 171 (40.04%) patients, conservative - 34 (7.8%) (p<0.0001). After 24 months from the time of the fracture using surgical treatment, restoration of function was observed in 72 (57.6%) and 32 (27.35%) patients who received surgical and conservative treatment, respectively (χ2=4.62, p=0.031).

Conclusions: the obtained during this study data suggest that the immediate and long-term consequences in patients with a fracture of the proximal femur depends on the method of treatment. Surgical treatment is the method of choice for the treatment of patients with this type of fracture.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5716

AB0842 SARCOPEania AND OSTEOPOROSIS IN PATiENTS WITH RHEUMATOID ARTHRiTHiS

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Background: Musculoskeletal disorders in RA are characterized by lesions of the peripheral joints, the development of local and systemic osteoporosis (OP), as well as a decrease in muscle mass and strength, which are currently being considered within the framework associated with chronic diseases syndrome and are accompanied by cachexia and sarcopenia.

Objectives: To determine the prevalence and the relationship between sarcopenia and OP in patients with RA.

Methods: 156 RA patients were examined, of whom 83 postmenopausal women (mean age 61.7 years) and 73 males (mean age, 59 years). The control group consisted of 35 healthy subjects matched for age and sex. Exclusion criteria were: other rheumatic and endocrine diseases, severe somatic diseases, cancers, etc. The states of bone mineral density (BMD) at the lumbar spine (L-1-L-4) and femoral bone were assessed by dual-energy X-ray absorptiometry (DXA).

Results: Most RA patients (83% women and 83% men) were decreased in BMD of osteoporosis (OP) level. BMD were negatively correlated with radiographic stage of RA, the DAS 28 and HAQ. IPC also revealed significant correlations with laboratory parameters such as creatinine, total protein, albumin, rheumatoid factor, and 1,25 (OH) D. Investigation of body composition showed a statistically significant reduction ITM RA patients compared to the control group, with no differences between the groups for fat mass. Sarcopenia had 25% of women and 55% men with RA, whereas the control groups, 8.7% and 0%, respectively. The majority of patients of both sexes sarcopenia observed on the background of the normal range of body fat index. Status of TM in patients with RA was statistically significant (p<0.05) associated with femoral BMD and lumbar spine (r=0.3), BMI (r=0.5), force compression (r=0.4) RA radiographic stage (r=0.4), indicators of total protein (r=0.5).

Conclusions: Patients with RA, together with OP/sarcopenia have a significant reduction in muscle (lean) mass. Sarcopenia in patients with RA was observed in the majority of men (55%) and 25% of women, significantly more than the control groups. Implementation of the DRA with the program “whole body” will allow to identify not only bone, but also muscle loss in RA patients, which will help to intensify targeted therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3165

AB0843 RELATIONSHIP BETWEEN THE HISTOLOGICAL CLASSIFICATION OF MARSH AND THE AFFECTATION OF THE BONE METABOLISM IN PATIENTS WITH A RECENT DIAGNOSIS OF CELIAC DISEASE

L. López 1, M. Larrea 2, A. Erra 1. 1Rheumatology; 2Gastroenterology, Hospital San Rafael, Barcelona, Spain

Background: Celiac disease is a chronic autoimmune pathology that affects people with genetic predisposition, caused by a permanent intolerance to gluten. Its prevalence has been estimated at around 1% but about 30% of patients are diagnosed after age 60. Its diagnosis is made through clinical data, serological markers, study of duodenal biopsy (BD) and response to the gluten-free diet. The histological study (Marsh classification) remains the gold standard to the diagnosis and allows classification of the disease in 4 types: grade I (less histological lesion) of Marsh and the bone metabolism in patients with a recent diagnosis of celiac disease.

Objectives: To evaluate if there is a relation between the histological classification of Marsh and the bone metabolism in patients with a recent diagnosis of celiac disease.

Methods: Prospective study, which included all patients with a recent diagnosis of celiac disease by the Digestive Service during the period 2014–2016. This diagnosis was made through a clinical, serological (anti-transglutaminase IgA, anti-endomysium IgA), histological BD and genetic study (HLA DG2 and HLA DQB). All patients underwent a study of phospho–calcium metabolism including: calcium, phosphatemia, vitamin D, PTH, alkaline phosphatases, 24-hour calciuria and a densitometric study (BMD). We present the inclusion data of these patients.
Results: 15 patients were included: 11 women and 4 men, with a mean age of 42.2 years (SD±16). The genetic study was performed in 12 patients: 75% were positive for HLA DQ2 and 25% for HLA DQB. The determination of antibodies was positive in 12 patients (73%) and negative in 3 (18%). These 3 were positive for the genetic study (2 HLA DQ2 and 1 HLA DQB). The study of BD showed: type I in 4 patients; Type IIa in 2 patients; Type IIb in 6 patients; Type IIIC in 3 patients. BMD showed normal values in 33%, osteopenia in 47% and osteoporosis (OP) in 20% of patients. Thus, 67% had an alteration in BMD at the time of diagnosis. 100% had a Vit D deficit, with a mean value of 14.3 ng/mL (range 4.15–26.8). 75% of them had values below 20 ng/mL (40% less than 10 ng/mL). 40% had secondary hyperparathyroidism (SHP), 83% of which had an alteration in BMD (67% osteopenia and 16% OP). The BD of the patients with SHP and alteration of the BMD showed a histological pattern type Marsh III. No patient presented an alteration in the values of calcemia, phosphataemia or calcuria.

The relationship between the degree of alteration in BMD and the Marsh classification (table) was studied. 72% of patients with a Marsh III had an alteration in BMD (3 OP and 5 osteopenia vs 3 normal).

<table>
<thead>
<tr>
<th>DMO</th>
<th>Marsh I</th>
<th>Marsh IIa</th>
<th>Marsh IIb</th>
<th>Marsh IIIC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Normal</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

Conclusions: Most patients with celiac disease have an alteration in BMD. In our study, all patients with celiac disease had a Vit D deficiency with no alteration of calcemia or calcuria. Only in patients with SHP, there is a correlation between alterations in BMD and a higher degree of Marsh. Most patients with a histological Marsh III have abnormalities in BMD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3114

AB0845 FALSIS: RISK AND PREVENTION IN PRIVATE RHEUMATOLOGY PRACTICE

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1Private Rheumatology Practice, la Garenne-Colombes; 2Private Rheumatology Practice, Antony; 3Private Rheumatology Practice, Colombes; 4Private Rheumatology Practice, Bois-Coulombes, France.

Background: Menopausal and osteoporotic women have a higher risk of fractures when falling. Fall prevention is important when taking care of those women.

Objectives: After identifying fall risk factors, defining the % of fractured fallers and the part of osteoporotic women in this population, we want to evaluate the relevance of balance tests and to favor prevention measures for those patients.

Methods: 110 patients, 60 years and older (including 24 controls), having fallen within a year, have seen 28 private practice rheumatologists in the larger Paris area and were subject of our multicentre retrospective study.

Results: Fallers mean age was 75 years. 37% of the fallers within a year fractured after falling. Among them, 95% were post-menopausal fractures versus 64% when including the control group. After dexamethasone was given to all groups except the blank group to induce osteoporosis, the rats in different groups were treated with saline, MDP, or different doses of

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5114

AB0846 TECHNETIUM-99 CONJUGATED WITH METHYLENE DIPHOSPHONATE AMELIORATES GLUCOCORTICOID INDUCED OSTEOPOROSIS IN RATS

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Background: 99Tc-MDP has been used in Chinese RA patients for over 15 years and many more studies have focused on this agent in RA. However, the previous studies limited in its effect on the effects of anti-inflammation. As a special form of bisphosphonate, the anti-osteoporotic effect of 99Tc-MDP is unclear.

Objectives: To systematically investigate the effect of technetium-99 conjugated with methylene diphosphonate (99Tc-MDP), an anti-inflammatory drug effective in treating rheumatoid arthritis (RA), on cortical and cancellous bones in glucocorticoid-induced osteoporotic (GIO) rats, as well as comparing the effect of

Methods: Forty-eight Sprague-Dawley rats were randomly divided into six groups: blank, negative control, high dose, medium dose, low dose, and positive control groups. After dexamethasone was given to all groups except the blank group to induce osteoporosis, the rats in different groups were treated with saline, MDP, or different doses of

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5140

AB0847 OSTEOPOROSIS AND ATHEROSCLEROSIS - ALTERNATIVE OR COEXISTENCE

L. Lagvilava. Rheumatology, Clinic "Consilium Medulla", Tbilisi, Georgia

Background: The majority of scientific research data promote the idea that OP and Atherosclerosis are inter-connected via OPG system. Scientists have speculation that OPG is the molecular bond between artery hardening and bone resorption. Thus the mechanism explained above makes obvious the co-existence of two: Artery hardening and Osteoporosis.

Objectives: There are number of ongoing Clinical trials on Denosumab therapy in preventing diagnosis of Osteoporosis and Atherosclerosis. The increase of Bone mineral density is associated with less intensive hardening of arteries. This fact inspired us to study bone mass in patients with cardiovascular events and atherosclerosis.

Methods: 1675 men, age range 38–78 years, mean age 59±4.3 Disease duration 6.4±1.75 with the diagnosis of Atherosclerosis (revealed on coronaryography, assessed lipid profile). At the moment of research Stable Angina Pectoris (Stable Angina) found in 20% (335); unstable angina non-ST elevation in 48% (804); - Myocardial Infarction 32% (536) Bone Mass was assessed by DXA Absorbtimetry technique (Hologic 1000) and T and Z Scores (WHO 1994). As a control group 680 healthy Georgian men 40–70 age range were assessed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5240

AB0848 OSTEOPOROSIS AND Atherosclerosis - ALTERNATIVE OR COEXISTENCE

L. Lagvilava. Rheumatology, Clinic "Consilium Medulla", Tbilisi, Georgia

Background: The majority of scientific research data promote the idea that OP and Atherosclerosis are inter-connected via OPG system. Scientists have speculation that OPG is the molecular bond between artery hardening and bone resorption. Thus the mechanism explained above makes obvious the co-existence of two: Artery hardening and Osteoporosis.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5240
deteriorated than cortical 3. Correlation between T Score values and clinical forms of Atherosclerosis were not observed 4. The best understanding of interrelations of bone mineral density (BMD) is the main diagnostic tool in osteoporosis, and it is the most effective and accurate measurement for identifying and monitoring the disease. However, several studies have been conducted with the object of detecting whether these skeletal changes in the mandible are specific to the osteoporotic stage.

Objectives: The purpose of this study was to determine whether the mandibular indices on panoramic radiographs are useful for identifying women with osteoporosis or osteopenia (low BMD).

Methods: Tunisian women aged from 30 to 60 years, who consulted the Rheumatology department of Fattouma Bourguiba university hospital in 2017. The mean BMD using the dual-energy X-ray absorptiometry (DEXA), were recruited to participate in this case-control study. Among the 60 women selected, 30 were diagnosed with osteoporosis or osteopenia (T-score < -1; cases) and 30 with normal T-score (T-score > -1; controls). The mandibular cortical index (MCI) and the panoramic mandibular index (PMI) were measured from digital panoramic radiographs in the right and left mandibles and the mean was calculated for each subject. The M, PMI and M/M ratio values were evaluated using the Z test, and the MCI was evaluated using the Chi2 test.

Results: The mean age of patients with osteoporosis/osteopenia was 58.61±8.11 and 56.07±9.72 in the control group. The mean bone mineral density (BMD) in vertebral site was 0.856±0.090g/cm² and 1.216±0.185g/cm² in control group. In femoral site, it was 0.877±0.221g/cm² and 1.061±0.142g/cm² respectively. The mean T-score in vertebral site was -2.38±0.185D in osteoporosis/osteopenia group and 0.64±1.58DS in control group. In femoral site, it was -1.57±0.97DS and 0.21±1.16 respectively. The analysis of the panoramic radiography showed that in the osteoporosis/osteopenia group: the mean value of M was 3.56±0.89, the mean PMI was 0.255±0.06 and the mean M/M ratio was 0.71±0.14; concerning the MCI: 46.7% were classified C2 stage and only 16.6% were classified C1 stage. This study showed that the M and the PMI were significantly smaller in the group with osteoporosis/osteopenia. However, the M/M ratio was not significantly different. Therefore, the MCI was significantly more affected in the osteoporosis/osteopenia group.

Conclusions: In our study, we proved that the M, PMI and M/M values were affected in women with osteoporosis/osteopenia, compared with normal patients. Therefore, these indices could be used as an ancillary method in the diagnosis of osteoporosis in women.

References:
4] M. Brahem 1, M. Gugirm 1, M. Khemiss 2, I. Chababni 2, E. Chebil 3, M. Yones 4, T. Ben Aliya 2, M. Ben Khelifa 2, I. Bejia 1, M. Touzi 1, S. Zrour 1, N. Bergaoui 1, 1Rheumatology; 2Stomatology; 3Fattouma Bourguiba Hospital Monastir, Monastir; 4Maxilla-Facial; 1Rheumatology, Tamer Star Mahdia, mahdia, Tunisia

AB0849
ASSOCIATION BETWEEN PERIODONTITIS AND OSTEOPOROSIS

M. Brahem 1, M. Gugirm 1, M. Khemiss 2, I. Chababni 2, E. Chebil 3, M. Yones 4, T. Ben Aliya 2, M. Ben Khelifa 2, I. Bejia 1, M. Touzi 1, S. Zrour 1, N. Bergaoui 1, 1Rheumatology; 2Stomatology; 3Fattouma Bourguiba Hospital Monastir, Monastir; 4Maxilla-Facial; 1Rheumatology, Tamer Star Mahdia, mahdia, Tunisia

Background: Both periodontitis and osteoporosis have similar sign of bone resorption and have multifactorial etiological factors, although the mediator factors or mechanism may be different. How to prevent and treat these two bone-loss diseases is always an important issue in public health. However, the relationship of them is still uncertain.

Objectives: The aim of our study is to evaluate the relationship between periodontitis and osteoporosis.

Methods: Tunisian women aged from 30 to 60 years, who consulted the Rheumatology department of Fattouma Bourguiba university hospital between February to December 2017. The measure the bone mineral density (BMD) using the dual-energy X-ray absorptiometry (DEXA), were recruited to participate in this case-control study. Among the 60 women selected, 30 were diagnosed with osteoporosis or osteopenia (T-score < -1; cases) and 30 with normal T-score (T-score > -1; controls). The oral examination was done by a dentist in the stomatology department in the same hospital.

Results: The mean age of patients with osteoporosis/osteopenia was 58.61±8.11
[51–56 and 57-72 in the control group.]The mean bone mineral density (BMD)in vertebral region was 0.856±0.095g/cm² and 1.216±0.185g/cm² in control group. In femoral site, it was 0.877±0.221g/cm² and 1.061±0.142g/cm² respectively. The mean T-score in vertebral site was -2.387±0.814 DS in osteoporosis/ osteopenia group and 0.643±1.587 DS in control group. In femoral site, it was -1.577±1.670 and 0.513±1.162 respectively.

The study showed an excessive tooth mobility in 60% and 36.7% of controls without a significant difference, a gingival recession in 50% and 30% of controls, the presence of periodontal pockets in 23.3% and 16.7% of controls without a significant difference, a plaque index ≥2 in 53.3% of osteoporosis/osteopenia patients and 63.3% of controls and a non rectilinear trajectory of mouth opening in 13.3% and 3.3% of controls.

Conclusions: Our study showed that patients with osteoporosis or osteopenia have a poor oral hygiene, but without significant difference with control group. However, patients who were diagnosed as osteoporotic must pay more attention to their periodontal health. Good oral hygiene maintenance might be a crucial factor for preventing the deterioration of osteoporosis progressing.

References:
[1] Yi-Fang Huang et al. The Impact of Oral Hygiene Maintenance on the Association Between Periodontitis and Osteoporosis; Medicine; Volume 95, Number 6, February 2016.

Discussion of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5184

Table 1. Rationale for Zoledronate Commencement

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<tr>
<th>Rationale</th>
<th>Number</th>
<th>%</th>
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<tr>
<td>Intolerance</td>
<td>24</td>
<td>38</td>
</tr>
<tr>
<td>GI Contradication</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>Inefficacy</td>
<td>24</td>
<td>38</td>
</tr>
<tr>
<td>Other Contradication</td>
<td>4</td>
<td>7</td>
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</tbody>
</table>

Table 2. Side Effects of Zoledronate

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bony Pain</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Flu-Like Symptoms</td>
<td>5</td>
<td>46</td>
</tr>
<tr>
<td>Aches</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Acid-Reflux</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Rash</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>18</td>
</tr>
</tbody>
</table>

Conclusions: The majority of our patients had improvements or stability in bone mineral density T-scores with only 20% experiencing side effects. Our results show that the vast majority of our patients are treated with zoledronate in concordance with guidelines. Nonetheless we can make improvements in recording FRAX scores and monitoring vitamin D levels. This has been highlighted to the multidisciplinary osteoporosis team and changes have been instigated. We plan to reaudit in due course.

References:

AB0852 INCREASED INFECTION RATE WITH CONCOMITANT RANK LIGAND INHIBITOR DENOSUMAB AND BIOLOGIC THERAPIES FOR RHEUMATIC DISEASES: REALITY OR ILLUSION?

EXPERIENCE WITH 40 PATIENTS OVER 66 MONTHS AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

P.S. Chhibbar, G. Ehresmann. Rheumatology, University of Southern California, Los Angeles, United States

Background: Patients with autoimmune diseases are at increased risk of early onset osteoporosis due to multiple reasons including prolonged exposure to corticosteroids and the disease process itself in RA patients. Same patients are more likely to be on TNF inhibitors or other biologics, which causes them to be at an increased risk of infections. Denosumab, an anti-RANK ligand inhibitor, itself a biologic, used to treat osteoporosis, is associated with increased infection risk as Receptor activator of nuclear factor kappa B ligand (RANKL) is also expressed on activated T and B lymphocytes (1). It is unknown if there is an added risk of infections when TNF inhibitors/biologic agents and denosumab are used concomitantly.

Objective: To determine if denosumab and biologics are associated with increased infection risk.

Methods: Data was collected and analyzed on 40 patients in the rheumatology clinic who had been on denosumab and TNF inhibitor/ other biologic for 66 months at the Keck Medical Center of USC.

AB0851 ZOLEDRONATE AUDIT – ARE WE MEETING EUROPEAN GUIDELINES?

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Background: Zoledronate is recommended by European guidelines for the treatment of osteoporosis particularly where first-line oral drugs are ineffective or contraindicated. EULAR’s guidelines are complemented by UK organisations including the National Institute of Health and Care Excellence (NICE), National Osteoporosis Guidelines Group (NOGG), British Society of Rheumatology (BSR) and the National Osteoporosis Society (NOS).

Objectives: The aim of our audit was to ascertain whether our use of zoledronate was compliant with current guidelines and review the real life experience.

Methods: We performed a retrospective audit of fifty patients who were commenced on zoledronate for the treatment of osteoporosis during 2012–2016 in our Trust. Data gathered included the reasons for commencement, whether patients had appropriate monitoring and the effect it had on DXA and FRAX scores.

Results: The age ranged from 44–88 years; 67% were between 60–80 years with 80% females. Vertebral fracture fragility were the most common type of fracture (42%), Zoledronate was commenced primarily because of either intolerance or inefficacy to oral anti-osteoporotic treatment (Table 1). It was commenced as first line in 20% because of contraindications to oral drugs. Almost 70% of our patients received zoledronate for two or three years. There was an improvement by 43% and 38% in the DXA T-score for the spine and hip respectively. Stable T-scores were recorded for the spine and hip in 49% and 54% respectively, whereas 8% deteriorated. Three patients sustained a fragility fracture and a further 11 experienced side effects (Table 2); five patients consequently stopped treatment. Only 3% had recorded FRAX scores pre- or post-zoledronate treatment. All of our patients had their calcium and renal function measured before each zoledronate infusion whilst over 80% had their vitamin D checked. All of our patients had dental checks prior to treatment. Following post-treatment DXA scans 46% continued zoledronate and 16% were on a drug-free holiday. A third were switched to denosumab due to ineffectiveness, side effects or contraindications.
Denosumab has become a useful parental therapy for the treatment of postmenopausal women with osteoporosis. The annual BMD of the lumbar spine showed a 9.11% increase, while also positive changes were noted in the proximal femur as a 1.89% increase. The BMD changes were 11% (L: Lumbar spine) and 1.1% (F: Femur) for the T-scores >-4.0, 6.3% (L) and 0.9% (F) for the T-scores -3.0~ -4.0, and 3.8% (L) and 0.5% (F) for the T-scores >=-3.0 respectively. This study suggests that Ibandronate (Bonviva®) treatment in postmenopausal women with osteopenia or osteoporosis is effective in terms of improving BMD.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1036

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**AB0853**

**DENOSUMAB: CLINICAL PERSPECTIVE AND DRUG SURVIVAL IN A SECONDARY CARE SET UP IN UK**


**Rheumatology, Queen's Hospital, Burton on Trent, United Kingdom**

**Background:** Denosumab has become a useful parental therapy for the treatment of osteoporosis. FREEDOM extension study has shown safety and effectiveness of denosumab beyond 8 years. Real life data on the efficacy and safety of denosumab is lacking. There are no studies looking at the drug survival in postmenopausal women with osteoporosis population either. Observational data from clinical practice can provide unique clinical perspective for novel therapies like denosumab.

**Objectives:**
1. To look at the baseline characters of patients receiving denosumab in a secondary care unit in UK.
2. To study the drug survival rate, analyse the reasons for discontinuation of therapy.
3. To assess fractures during the course of denosumab therapy.

**Methods:** We looked at the case records retrospectively of all the patients receiving denosumab therapy from 01/01/2011 to 31/12/2016. A database to record baseline characters, indications and previous fracture was prepared. Renal function, calcium, alkaline phosphatase (ALP), vitamin D levels at baseline and renal function, calcium and ALP levels for each injection visit were noted. Vitamin D status was assessed at least once a year. Reasons to stop therapy were recorded.

**Results:** 237 patients were offered the treatment. One patient declined the treatment at the beginning. 5 (2.1%) patients had fracture on treatment. 2 had a hip fracture and one of them had a previous fracture (humerus). Other fracture sites were ankle, humerus and metatarsal. None of them had any further fractures during the follow up period. 61 patients discontinued therapy during the course of treatment over 3 years. 8 (4.2%) had infections, 7 (3.6%) due to declining eGFR and 9 (4.7%) were lost to follow up. 1 patient had jaw necrosis after the first injection. 1 developed hepatitis after the first injection which resolved on withdrawal of therapy. 6 (3.1%) patients withdrew consent for therapy. 19 (8%) patients died causes unrelated to denosumab therapy. 23 (9.7%) patients moved away. Treatment was stopped due to other side effects in 3 patients (2 had rash and 1 headache). There were no reports on hypersensitivity, hypercalcemia.

**Conclusions:**
1. Majority patients were elderly and female. Majority were high risk and had received osteoporosis treatments previously.
2. Denosumab therapy was well tolerated and nearly 2/3rd were still receiving therapy at 3 years. Treatment was withdrawn due to an adverse event in only 14 (6%) patients.
3. Fracture rate was very low and there were no repeat or multiple fractures.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5290

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**AB0854**

**THE BMD CHANGE AFTER IBANDRONATE (BONVIVA®) TREATMENT IN OSTEOPENIC POSTMENOPAUSAL WOMEN**

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Orthopaedic Surgery, Dongguk University International Hospital, Seoul, Korea, Republic Of

**Background:** Ibandronate (Bonviva®) is effective in the treatment of postmenopausal women with osteoporosis. But, there were few data about Ibandronate (Bonviva®) treatment in Korea. We evaluated the effect of Ibandronate (Bonviva®) therapy on bone mass and compared the effectiveness on bone mineral density (BMD) in 1-year treatment group.

**Objectives:** The aim of the study is to assess the effect of 1-year treatment with Ibandronate (Bonviva®) on bone mineral density (BMD) in postmenopausal women with osteopenia or osteoporosis.

**Methods:** The BMD was assessed in 118 postmenopausal women with osteopenia or osteoporosis from March 2007 to January 2011. 42 patients who treated with 2.5 mg per day of Ibandronate (Bonviva®) were enrolled to study. BMD of lumbar spine (L2-L4) and femur was assessed by dual energy absorptiometry at baseline, 12 months after treatment.

**Results:**
- The annual BMD of the lumbar spine showed a 9.11% increase, while also positive changes were noted in the proximal femur as a 1.89% increase. The BMD changes were 11% (L: Lumbar spine) and 1.1% (F: Femur) for the T-scores > -4.0, 6.3% (L) and 0.9% (F) for the T-scores -3.0~ -4.0, and 3.8% (L) and 0.5% (F) for the T-scores > -3.0 respectively.
- The 10-year risk of a major osteoporotic fracture was 20% in those with BMD measurements (P=0.001, P=0.002) respectively among male patients with BMD measurements (n=74).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1036

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**AB0855**

**THE DISPARITIES BETWEEN FRACUTURE RISK ASSESSMENT (FRAX) WITH BMD AND WITHOUT BMD IN KOREAN PATIENTS WITH ANKYLOSING SPONDYLITIS- MULTICENTER TRIAL**


1 Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Inha University, INCHEON; 2 Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Chung-Ang University, Seoul; 3 Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Ajou University, Suwon; 4 Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Ulsan University, Gangneung Asan Hospital, Gangneung; 5 Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Keimyung University, Daegu, Korea, Republic Of

**Objectives:** The aims of this study are to determine the proportion of patients with ankylosing spondylitis (AS) at high risk for major osteoporotic and hip fractures of Fracture risk assessment (FRAX) in Korean and to determine if a care gap exists for high risk.

**Methods:** This study is a multicenter study including 163 AS patients in 5. All of the AS patients fulfilled the modified New York criteria. The classification of osteoporosis according to each AS Criteria was based on T-score < -2.5. The FRAX criteria for high risk of osteoporotic fracture, which is 10-year probability of ≥20% for major osteoporotic fracture or ≥3% for hip fracture, were calculated by the FRAX tool including the bone mineral density (BMD) values. We assessed various demographic factors, clinical and laboratory findings of AS, and medication use for AS and osteoporosis, and then evaluated the risk factors for osteoporotic fracture.

**Results:** The mean age of AS patients was 44.3 years, and 42 patients were female (25.2%) with 23 postmenopausal women 56.1%. Osteoporotic fracture was detected in 16 (9.8%) male and 14 (6.5%) female AS patients. Among the patients >65 years of age, 2 (12.5%) and 8 (50%) were at high risk for a major osteoporotic fracture (10-year probability >20%) and hip fracture (>3%), respectively. Among patients with BMD measurements (n=106), the 10-year risk of a major osteoporotic fracture was 36.5% in those without BMD measurements. (P=0.001, P=0.002) respectively among male patients with BMD measurements (n=74). There is no statistic difference of the 10-year risk of a major osteoporotic fracture

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1036

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**Table AB0853 – Table 1. Baseline characters**

<table>
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<tr>
<th>Total no of patients</th>
<th>Gender</th>
<th>Fracture F/M (mean/ range)</th>
<th>Age (in years)</th>
<th>eGFR mean (range)</th>
<th>Prior fracture F/M (mean/ range)</th>
<th>Baseline bone density (data for 99 patients)</th>
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<tr>
<td>326</td>
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<td>210 (65%)/ 216 (61%)</td>
<td>76 (65–95)</td>
<td>37.9 (17.7–90)</td>
<td>93 (39.4%)</td>
<td>Osteoporosis 61 (61.6%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>7 (3%)</td>
<td>Vertebral 37 (39.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>65 (27.4%)</td>
<td>Wrist 12 (13%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>65 (27.4%)</td>
<td>Hip 8 (9.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22 (8.8%)</td>
<td>Normal 8 (8.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9 (3.8%)</td>
<td>Multiple 4 (4.3%)</td>
<td></td>
</tr>
</tbody>
</table>
and hip fracture between those calculated with BMD and those without BMD measurements (P = 0.05) respectively among female patients (n=32).

Conclusions: A substantial gap exists between FRAX with BMD and without BMD in Korean patients with AS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5575

AB0856 T-SCORE OF THE SPINE AS PREDICTOR OF THE FEMORAL NECK FRACTURE

S.D. Jandric
Department for FRM, Faculty of Medicine, University of Barjala, Banja Luka, Republic of Srpska, Bosnia and Herzegovina

Background: Osteoporosis is defined as a progressive, systemic skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. There are numerous hip fracture risks. Bone mineral density (BMD) and T-score measured by dual-energy X-ray absorptiometry (DXA) are the main determinants of the clinical evaluation of hip fracture risk. World Health Organization classification defined osteoporosis as T-score below -2.5 SD.

Objectives: The aim of this study was to estimate differences in DXA measurements (BMD and T-score of the spine) and potential predictors of the femoral neck fracture in the patients with osteoporosis.

Methods: This study included 181 patients with osteoporosis (165 female and 16 male), average age of the 65, 6±5.8 years (range of 44.1 to 87.3 years). Eighty one patients had fracture of the femoral neck. All patients in this group were managed operatively by hip arthroplasty, after clinical and radiological diagnostic procedures. DXA measurement was performed on Advanced Prodigy Lunar densitometer. Reference for these patients was postoperatively. BMD of the femoral neck was measured on the no operated side. Age, sex, height, weight, BMI, BMD and T-score of the spine at the level of L1-L4, BMD of the right and left femoral neck were estimated. The control group included 100 patients with osteoporosis (93 female and 7 male), average age of the 65.1±8.5 years. Student’s t-test and Logistic regression were used for statistical analysis. Dependent variable was presence of the fracture of the femoral neck and independent variables were age, sex, height, weight, BMI, BMD and T-score of the spine and BMD of the femoral neck.

Results: Results of our study showed statistically significant difference between T-score of the spine (t=-2.973, p<0.001) as well as between BMD of the spine (t=-12.376, p<0.001) of patients with and without fracture of the femoral neck. T-score of the spine was significant predictor of fracture of the femoral neck (p<0.01) when controlled by age, sex, height, weight, BMI, BMD and T-score of the spine of the right and left femoral neck were estimated. The control group included 100 patients with osteoporosis (93 female and 7 male), average age of the 65.1±8.5 years. Student’s t-test and Logistic regression were used for statistical analysis. Dependent variable was presence of the fracture of the femoral neck and independent variables were age, sex, height, weight, BMI, BMD and T-score of the spine and BMD of the femoral neck.

Conclusions: T-score and BMD of the spine were statistically significantly lower in patients with fracture of the femoral neck than in patients with osteoporosis without fracture. T-score of the lumbar spine was significant predictor of fracture of the femoral neck in patients with osteoporosis. Probability of femur neck fractures increased with the decrease of T-score of lumbar spine in patients with osteoporosis. These results can help in predicting femur neck fractures.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2768

AB0857 PROBLEMS OF DIAGNOSTICS AND PROPHYLAXIS OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN REAL CLINICAL PRACTICE

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Background: Oral glucocorticoids (GC) are used in different medicine fields and appear as risk factors of glucocorticoid-induced osteoporosis (GIO).

Objectives: The aim is to estimate the frequency of use of prophylaxis of OP, use drugs that are approved for GC and also an awareness of GIO of patients with prolonged intake of GC.

Methods: 50 patients (10 men and 40 women), taking GC, took part in research. 30 patients (60%) were from rheumatology department, 5 patients (10%) from pulmonology department, 5 patients (10%) from gastroenterology department and 10 patients (20%) from nephrology department of Republic Clinical Hospital. Mean age of patients - 48.84±14.03 years (from 26 to 73). The following signs were estimated: clinical data, osteoporosis risk factors, instrumental tests (X-ray, densitometry). FRAX assessment of fracture risk was performed, the Questions A and B about osteoporosis risk factors were estimated.

Results: The duration of intake GC – 5,9±3.4; 5.8 years. Minimal dose of GC per day (if receiving prednisone) – 7.5 mg; maximal dose – 60 mg. 10-year risk of major osteoporotic fractures by FRAX, adjusted according to GC dose - 18.1±11.01, 32 patients (64%) were given recommendations for changing lifestyle and diet for GIO prophylaxis, 40 patients (80%) - recommendations for intake of calcium and vitamin D medications, but only 31 patients (62%) followed recommendations and started the intake of calcium medications. From the said number of patients only 14 patients (45.2%) used appropriate daily dose of calcium and vitamin D.

Discussions: Drugs that are approved for GIO were have to be prescribed for 18 patients, but only 6 patients (33.3%) underwent treatment, principally bisphosphonates. Only half of them underwent densitometry after starting the therapy. 72.2% patients with GIO used calcium and 30.7% were taking appropriate daily dose of calcium and vitamin D. 70% rheumatologic patients knew about GIO and in 90% cases calcium and vitamin D drugs were recommended. Only 50% of patients from non-rheumatologic departments knew about GIO and in 65% cases calcium and vitamin D drugs were recommended.

Conclusions: Clinical recommendations in real clinical practice are rarely applied. Glucocorticoids constitute a significant risk factor of GIO. 50% patients recommend pharmacological prophylaxis. Only half of patients received osteoporosis therapy, only half of them underwent densitometry. Patients are insufficiently informed about necessity of changing lifestyle and diet for GIO prophylaxis. Education for patients taking GC and training for rheumatologic and non-rheumatologic specialties are necessary.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6867

AB0858 ASSOCIATION OF BONE MINERAL DENSITY WITH DEVELOPMENT OF HEART FAILURE IN DIABETIC PATIENTS

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1Endocrinology, Gomel State Medical University, Gomel; 2Endocrinology, Belarusian State Medical University, Minsk; 3Functional Diagnostics; 4Endocrinology, The Republican Research Center for Radiation Medicine and Human Ecology, Gomel, Belarus

Background: Diabetes mellitus has shown to be a significant risk factor for the development and prognosis of heart failure (HF) and associated with an increased risk of fractures [1]. Osteoporosis and heart failure are generally considered two distinct diseases, but recent evidence suggests a link between both diseases.

Objectives: The aim of the study was to investigate the association of bone mineral density with the risk of developing heart failure in diabetic patients.

Methods: 85 patients both sexes with type 2 diabetes aged 58.69±9.07 years were studied. Besides standard laboratory parameters, the echocardiographic and BMD measurements were performed. Estimated glomerular filtration rate was measured.

Results: Among diabetic subjects, 8 patients (9.4%) had osteoporosis, 21 (24.8%) had osteopenia and 56 (65.8%) had a normal BMD. Increased serum NT-proBNP (p<0.001) and decreased left ventricular ejection fraction (EF) (p<0.03) were significantly correlated with low T-score L1-L4 cutoff points between groups (normal, osteopenia, and osteoporosis). Multivariable stepwise linear regression analysis of the significant variables revealed that NT-proBNP, EF were independent predictors of lumbar BMD among female patients with diabetes mellitus. After adjusting for age, gender, and related comorbidities, the osteoporosis group was associated with a significantly higher risk of coronary artery disease in women with diabetes. However, no association between BMD and HF was found in men.

Conclusions: Osteoporosis and bone mineral density may independently increase the risk of heart failure in women with diabetes mellitus. Our data suggested that early detection of abnormal BMD should warrant for early search of undetected HF in diabetic women. A further study is needed to elucidate the effects of BMD on cardiac function in diabetic patients.

References:

Acknowledgements: We acknowledged the help from the Republican Research Center for Radiation Medicine and Human Ecology for the technical assistance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3887

AB0859 CAN ZOLENDRONIC ACID USE LEAD TO IMPAIR RENAL FUNCTION IN OSTEOPOROSIS PATIENTS?

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Background: Bisphosphonates are recommended in patients with osteoporosis patients, clinical concerns had been considered in kidney safety.

Objectives: This study investigated the safety of bisphosphonate effects on renal function in patients with magnetic resonance imaging (MRI)-proven acute osteoporotic vertebral fractures after vertebroplasty.

Methods: This retrospective study was conducted in osteoporotic patients with acute vertebral fractures treated with vertebroplasty between January 2001 and December 2005. Their gender, age, body mass index (BMI, kg/m²), co-morbidity were recorded, as well as their use of zolendronic acid. Those with increase in creatinine was defined as progression of renal function. Logistic regression was used to adjust the variables.

Results: There were 989 patients (783 females; mean age, 74.08±9.26 years).
Results: Activity and BTMs besides baseline data of every 6 months were utilized for analysis with respect to data of RA disease activity [DAS28-CRP, SDAI, CRP, MMP-3] and bone turnover markers (BTMs) and various data (baseline patients' characteristics, parameters of RA disease). The correlation coefficient was calculated between %increase of BMD at 24 months were measured at baseline and every 6 months until 24 months. Spearman's rank correlation coefficient which were correlated with %increase of LSBMD at 23 months were %increase of LSBMD at 6 months (0.61), baseline P1NP (0.33) and time averaged %decrease of TRACP-5b (0.30). Parameters (correlation coefficient) which were correlated with %increase of THBMD at 24 months were %increase of LSBMD at 6 months (0.42), %increase of THBMD at 6 months (0.69), baseline P1NP (0.36), time averaged %decrease of P1NP (0.37), baseline TRACP-5b (0.29) and time averaged %decrease of TRACP-5b (0.29). Although denosumab (DMB) at 24 months was not correlated with disease activity of RA, taCRP was significantly correlated with taP1NP (0.57) and taTRACP-5b (0.45).

Conclusions: DMB was effective in RA-OP. Early response of BMD, baseline values of BTMs and response of BTMs were suggested to be the predictors of the efficacy of DMB in RA-OP. Inflammation of RA was correlated with not BMD but BTMs.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3938

Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

## AB0861 EXPRESSION CONTROL BY METHYLATION OF THE TLR1, TLR2, TLR4, IL1B, ALPK1 SLC2A9 AND SLC22A12 GENES IN MONOCYTES OF PATIENTS WITH GOUT

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Background: The gout is an inflammatory multifactorial disorder where the diet, age, sex, absorption regulation of uric acid in kidney and genetic, contribute to the onset of the disease. The balance of uric acid concentration not only depends on metabolism of purines but also on the clearance of uric acid, in which many proteins participate in the reabsorption and transport of urate. Is unknown if the peripheral blood leukocyte cells can change their expression and regulation mechanism of the urate transporters by the presence of uric acid in these patients. The asymptomatic patients with a higher mean of uric acid expression and methylation analysis are designed specific primers which can analyze the gene expression and methyltion pattern of the TLR2, TLR4, SLC2A9, SLC22A12, SLC22A3 and ABCG2 in neutrophils and peripheral blood monocytes from patients with gout and controls

Methods: The isolation of peripheral blood monocytes and monocytes cells was performed by negative immunomagnetic selection (MACSpress kit, EUA). By flow cytometry were analyzed the previously separate cell populations, mononuclear (MN), polymorphonuclear (PMN) cells and neutrophils (N) (CD15, CD16, CD14). The DNA and RNA extraction was realized with a without columns kit and with trizol technique. Taq DNA polymerase, DNA polymerase (Taq DNA) and dNTPs were added to the reaction. The DNA standard samples were extracted with a without columns kit and with trizol technique. The DNA standard samples were extracted with a without columns kit and with trizol technique. The DNA standard samples were extracted with a without columns kit and with trizol technique. The DNA standard samples were extracted with a without columns kit and with trizol technique.

Results: The difference between asymptomatic gout patients (n=12) and controls (n=12), in the biochemical parameters (Table 1), in the higher levels of uric acid and triglycerides that the patient presents. Actually, we’ve already evaluated the genetic expression of TLR1, TLR2, TLR4 and IL1b in mononuclear cells of 5 asymptomatic gout patients and 5 controls (Pilot 1). Interestingly, IL1b is UP-regulated in sample group by a mean factor of 16.350 and TLR2 is UP-regulated in sample group in comparison to control group by a mean factor of 3.686.

Table 1. Characteristics of patients and controls

<table>
<thead>
<tr>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants (n)</td>
<td>12</td>
</tr>
<tr>
<td>Age (years)</td>
<td>40.75</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.27</td>
</tr>
<tr>
<td>SM (%n)</td>
<td>8.33</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>58.33</td>
</tr>
<tr>
<td>Urates (mg/dL)</td>
<td>8.13</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>84.83</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>196.33</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>276.67</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.02</td>
</tr>
</tbody>
</table>

Conclusions: The asymptomatic patients with a higher mean of uric acid (8mg/dL) and triglycerides (145.60 mg/dL) had a higher expression of IL1b and TLR2 compared to controls.
THE SENSITIVITY OF THE DOUBLE CONTOUR SIGN IN HAND JOINTS WOULD BE BETTER BY THE DORSAL SURFACE EXAMINATION

A.M. Mahdi 1,2, H. Rkain 1, M. Erraoui 1, R. Watfeh 3, S. Aktaou 3, L. Tahiri 1,

OBJECTIVES:
To compare the prevalence of ultrasonographic gout specific sign double contour between the dorsal and palmar surfaces of the hand joints.

METHODS: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B and Doppler modes. 560 articular sites were studied at their dorsal and palmar surfaces. We compared the prevalence of the hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) between the dorsal and palmar surfaces at each site studied.

RESULTS: The mean age at onset was 54.7±12.6 years, and the median diagnosis duration was 0 (0.3) years.

The results of the US examination are summarized in Table 1

Table 1. comparison of double contour prevalence between the dorsal and palmar surfaces of wrist, MCP, PIP and DIP joints in the studied population

<table>
<thead>
<tr>
<th>Joints (N=400)</th>
<th>Dorsal surface (%)</th>
<th>Palmar surface (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist joints (N=120)</td>
<td>12.6</td>
<td>7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Radiocarpal (N=30)</td>
<td>20</td>
<td>6.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Ulnocarpal (N=30)</td>
<td>13.3</td>
<td>6.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Scaphotrapezial (N=30)</td>
<td>3.3</td>
<td>13.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Trapezio ligament (N=30)</td>
<td>13.3</td>
<td>3.3</td>
<td>0.1</td>
</tr>
<tr>
<td>MCP (N=150)</td>
<td>8</td>
<td>6.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCP 1 (N=30)</td>
<td>3.3</td>
<td>10</td>
<td>0.1</td>
</tr>
<tr>
<td>MCP 2 (N=30)</td>
<td>13.3</td>
<td>6.7</td>
<td>0.014</td>
</tr>
<tr>
<td>MCP 3 (N=30)</td>
<td>6.7</td>
<td>6.7</td>
<td>0.002</td>
</tr>
<tr>
<td>MCP 4 (N=30)</td>
<td>6.7</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCP 5 (N=30)</td>
<td>10</td>
<td>10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PIP (N=150)</td>
<td>4</td>
<td>7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IP (N=30)</td>
<td>3.3</td>
<td>10</td>
<td>0.1</td>
</tr>
<tr>
<td>PIP 2 (N=30)</td>
<td>6.7</td>
<td>3.3</td>
<td>0.9</td>
</tr>
<tr>
<td>PIP 3 (N=30)</td>
<td>6.7</td>
<td>13.3</td>
<td>0.01</td>
</tr>
<tr>
<td>PIP 4 (N=30)</td>
<td>3.3</td>
<td>10</td>
<td>0.1</td>
</tr>
<tr>
<td>PIP 5 (N=30)</td>
<td>0</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DIP (N=120)</td>
<td>0.8</td>
<td>3.3</td>
<td>0.033</td>
</tr>
<tr>
<td>DIP 2 (N=30)</td>
<td>0</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DIP 3 (N=30)</td>
<td>0</td>
<td>0</td>
<td>0.002</td>
</tr>
<tr>
<td>DIP 4 (N=30)</td>
<td>0</td>
<td>3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DIP 5 (N=30)</td>
<td>0</td>
<td>6.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: These preliminary results suggest that the popliteus groove could be regarded as a sentinel area for detecting MSU crystals. These findings lead to further investigations aimed at identifying the factors and associated with MSU crystals deposition at popliteus groove level.

REFERENCES:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4462
than 6 month) was examined by clinical, laboratory, X-ray and ultrasonography. After investigation the following diagnoses were made: Gout in 32 patients, Osteoarthritis in 28 patients, Rheumatoid arthritis in 28 patients, Psoriatic arthritis in 16 patients. Ultrasound investigation of affected joints was performed in all subjects by linear probe 18 MHz. Urate crystal deposits were seen on the surface of the hyaline cartilage as a hyperechoic thin line or dots on the cartilage, wich sometimes imitate double contour of bones [2, 3]. Sensitivity and specificity of ultrasound sign were compared with subcutaneous tophi, bone cysts (X-Ray sign) and hyperuricemia.

Results: The urate crystal deposits in gyaline cartilage of at least one of affected joints were revealed in 28 of 32 (87.5%) patients with Gout, in 3 of 28 (10.7%) patients with Osteoarthritis and 1 of 16 (6.3%) patients with Psoriatic arthritis. Comparative data of sensitivity and specificity of crystal deposits, bone cysts, subcutaneous tophi and hyperuricemia are represented in table below. Table 1. Sensitivity and specificity of different diagnostic markers in yearly stage of gout

<table>
<thead>
<tr>
<th>Diagnostic marker</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperechoic linear urate deposits in gyaline cartilage</td>
<td>87.5</td>
<td>94.4</td>
</tr>
<tr>
<td>Bone cysts</td>
<td>21.7</td>
<td>86.8</td>
</tr>
<tr>
<td>Subcutaneous tophi</td>
<td>25.0</td>
<td>98.6</td>
</tr>
<tr>
<td>Uric acid level from 360 mkmol/l to 480 mkmol/l</td>
<td>46.9</td>
<td>86.1</td>
</tr>
<tr>
<td>Uric acid level more than 480 mkmol/l</td>
<td>34.4</td>
<td>97.2</td>
</tr>
</tbody>
</table>

Conclusions: Ultrasound detection of urate crystal deposits in gyaline cartilage in patients with gout in yearly stage has a high sensitivity and comparable level of specificity with other diagnostic markers of Gout.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1292

AB0865

SERUM URATE AND ITS ASSOCIATION WITH RACE IN YOUNG ADULTS: BASELINE ANALYSIS FROM A RANDOMIZED CLINICAL TRIAL

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Background: Increased levels of serum urate (sUA) have been reported in association with hypertension, chronic kidney disease and obesity. All these conditions are over-represented in US African Americans, who also have greater environmental risk factors for hyperuricemia development including elevated fructose intake. Our group has previously reported that young African Americans have lower sUA concentrations than Caucasians after adjustment for clinical and demographic factors.

Objectives: To determine whether there is a differential association between sUA and race in young adults.

Methods: We examined baseline data on consecutively enrolled individuals (age 18 – 40 years) in an interventional study aimed at lower blood pressure (BP) through the administration of urate-lowering therapy. African Americans were over-represented in the sample by study design. Inclusion criteria included a sUA of ≥5.0 mg/dL for men or ≥4.0 mg/dL for women. After means comparisons between races, we performed multivariable adjustments for age, gender, BP, and body mass index (BMI) a multiple linear regression model. Data reported are mean ±standard deviation.

Results: 86 participants recruited from Birmingham, AL were included in the analysis. Participants had a mean age of 28.5±6.9 years, 36% were female, 41% were African Americans (AAs), and the mean BMI was 29.2±6.8 kg/m². The mean sUA was 5.9±1.2 mg/dL (n=77, range: 3.9 to 8.5 mg/dL). We found a significantly lower sUA for African Americans compared to persons of other races (5.4±1.2 mg/dL vs 6.2±1.1 mg/dL, p=0.005). After multivariable analysis the difference in sUA between AAs and other races was attenuated to non-significance (p=0.03) due to the effects of BMI and gender. As expected, the association between sUA and gender was significant (Table).

Conclusions: In this cross-sectional analysis of young adults, AAs had lower sUA concentrations than other races. However, this difference is explained by the effect of gender differences in sUA and BMI. A potential limitation is that participants were enrolled after they met a sUA threshold so not all the ranges of sUA in a normal population are represented in this analysis. Larger studies will be needed to fully address this question.

References:

Acknowledgements: National Institute of Arthritis and Musculoskeletal and Skin Diseases P50AR060772, K24AR052361 (to KGS).

Disclosure of Interest: M. Saddekni: None declared, A. Gafio Grant/research support from: Amgen, AstraZeneca, Consultant for: Cymabay, Ardea, Employee of: US Government, P. Foster: None declared, S. Biggers: None declared, E. Rahn: None declared, P. Li: None declared, K. Saag Grant/research support from: AstraZeneca, Crealta, Takeda, Consultant for: Ardea/AstraZeneca, Crealta, Takeda

DOI: 10.1136/annrheumdis-2017-eular.5390

AB0866

EVALUATION OF THE ACHIEVEMENT OF A THERAPEUTIC TARGET OF ≤6 MG/DL IN ALGERIAN PATIENTS TREATED FOR GOUT

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Background: Gout is one of the most prevalent rheumatic conditions in the developing world, due of the aging of the population and the modifications in the life style. The 2014 EULAR recommendations for the management of gout have defined the therapeutic target of 60 mg/L for gouty patients (recommendation 8). The aim of the study was to assess the adherence of Algerian patients with gout to these recommendations.

Methods: We have retrospectively analyzed patients files aged 18 and more, followed in a rheumatology setting for gout, in 4 centers in Algeria. Demographic, clinical and lab data were collected. We have excluded files with missing data. Were noted the used therapeutics and serum uric acid in every patient through time. Tolerance was noted.

Results: We have analyzed 145 complete files: 98 men (68%), with a mean age of 65.4±11.4 years. All patients except two had rheumatic manifestations, which joints and what findings should be assessed for diagnosing gout? Ann Rheum Dis. 2014;73(10):1522–1528.

Tolerance was noted.

Conclusions: In rheumatology settings in Algeria, more than 93% of gouty patients received allopurinol, with an excellent tolerance. However, it seems that dosage is insufficient, with only 58% of patients achieving the EULAR recommendation 8. More efforts have to be provided to optimize this therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4031
AB0867
PEGLOTICASE RE-TREATMENT AFTER A GAP IN THERAPY: DATA FROM TWO PHASE III TRIALS AND AN OPEN-LABEL EXTENSION STUDY
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Background: Pegloticase is a PEGylated recombinant uricase approved in the US for treating adult patients with chronic refractory gout. As a biologic medication, pegloticase is administered intravenously every 2 weeks. It is currently not known whether a gap in the standard biweekly regimen can be tolerated or will be associated with a loss of efficacy. During the pivotal trial testing of pegloticase, some patients experienced a delay before participation in the randomized control trial (RCT) after the open-label extension (OLE) that followed. Analysis of the clinical impact of this gap was carried out to understand whether therapeutic benefit would be affected.

Objectives: The objective of this analysis was to determine, among pegloticase responders, the effect of a 28 or more day gap between doses of pegloticase on the subsequent urate lowering response and frequency of infusion reactions.

Methods: These analyses utilized results from two RCTs of pegloticase and a 2-year OLE. In the RCTs, 36 of 85 patients, who were dose with pegloticase every two weeks, were classified as responders (persistent urate lowering during intensive monitoring at 3 and 6 months of the RCT), and went on to enroll in the OLE and receive additional doses of pegloticase. Of these 36 patients, 14 had a gap between pegloticase doses of more than 28 days.

Results: Among the 14 patients with a gap of more than 28 days between doses of pegloticase therapy the length of the gap ranged from 34 to 167 days (mean = 72.5 days, median = 59.5 days). Of these 14 patients, 8 received pegloticase on an every-4-week dosing schedule in the OLE and remained on every 2-week dosing. Ten of the 14 patients maintained their serum urate level <6mg/dl in the OLE. Five of 6 that remained on every 2 week dosing and 5 of 8 that went to every 4 week dosing continued to have se rum urate <6mg/dl. (see table 1). By logistic regression analysis, the length of the gap had no significant effect on the subsequent urate lowering effect of pegloticase. Of the fourteen patients with a gap in pegloticase therapy, 2 (14%) had infusion reactions during a total of 632 infusions in the OLE yielding a re-treatment IR rate of 0.32%.

Conclusions: The majority of patients in this limited dataset who were previously responders to pegloticase dosed every 2 weeks continued to maintain a serum urate lowering response to pegloticase after a gap in therapy. Infusion reactions during re-treatment occurred in 2 patients with a re-treatment infusion reaction rate of 0.32%.

References:

Disclosure of Interest: None declared

AB0868
IS IT APPROPRIATE TO DISCONTINUE COLCHICINE THERAPY IN GOUT PATIENTS IN REMISSION?
Y. Özdem’Inan 1, N. Alpay Kanıtez 2, S. Çelik 2, S. Yılmaz Öner 2, C. Bes 2, 1Bakırköy Dr Sadi Konuk Training and Research Hospital, Istanbul, Turkey; 2Rheumatology, Bakırköy Dr Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Background: Colchicine can reduce the risk of recurrent attacks and it is an appropriate first-line gout attack prophylaxis therapy. There is limited data in the literature about duration of colchicine treatment in patients with gout disease.

Objectives: In this study, we aimed to investigate the frequency of gout attacks between patients with colchicine treatment and patients who are colchicine terminated.

Methods: 54 gout patients under colchicine treatment were enrolled to the study. The subjects were divided into 2 groups. Group 1 (n=19) was consisted of patients whom colchicine therapy was terminated because of remission for three months; group 2 (n=35) was consisted of patients on colchicine treatment. Groups were compared according to the existing of new gout attacks after the 3rd month. Baseline and the third months of the uric acid levels were also analyzed in each group.

Results: The body mass indexes, the disease intervals, the number of the attacks, and the duration of the attacks were not significantly different (p > 0.05 for all) (Table 1). Compared to the group 2, the newly gout attacks were not found to be different in group 1 for 3 months (p > 0.05) (Table 1). The uric acid levels were significantly decreased both in two groups (p < 0.05) (Table 2).

Table 1. Demographical and clinical characteristics of patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>3rd month</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, F/M</td>
<td>0/19</td>
<td>12/23</td>
<td>0.450</td>
</tr>
<tr>
<td>Age, years</td>
<td>53.36±14.06</td>
<td>62.11±12.72</td>
<td>0.024</td>
</tr>
<tr>
<td>BMI</td>
<td>28.22±3.57</td>
<td>30.29±5.63</td>
<td>0.008</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>7.40±1.30</td>
<td>8.21±1.92</td>
<td>0.108</td>
</tr>
<tr>
<td>Disease age, months</td>
<td>111.63±72.70</td>
<td>53.48±59.75</td>
<td>0.170</td>
</tr>
<tr>
<td>Number of the attacks, one year</td>
<td>2.68±0.35</td>
<td>3.37±1.75</td>
<td>0.413</td>
</tr>
<tr>
<td>Duration of the attacks, days</td>
<td>16.73±16.32</td>
<td>10.91±14.50</td>
<td>0.202</td>
</tr>
<tr>
<td>Newly attacks in 3 months</td>
<td>5/14</td>
<td>7/28</td>
<td>0.734</td>
</tr>
</tbody>
</table>

Conclusions: The colchicine is the mainstay treatment for gout disease. It not only prevents the attacks of the gouts also prevents the development of uric acid nephropathy and tocolgize the secondary gout attacks. This study showed that, in gout patients in remission, termination of the colchicine treatment does not affect the development of the new attacks as shown similar attacks were also observed in non-terminated patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1423

AB0869
STRESS FRACTURES, A RETROSPECTIVE STUDY OF 325 FRACTURES IN 227 PATIENTS IN RHEUMATOLOGY PRACTICE BETWEEN 2000 AND 2015
C. Nourisson, J.-J. Dubost, B. Pereira, A. Tournade, S. Maloche-Guimand, M. Soubrier. CHU Clermont Ferrand, Clermont-Ferrand, France

Background: Stress fractures are common in both young and active patients (fatigue fracture) as well as in elderly osteoporotic patients (insufficiency fractures).

Objectives: The aim of this study was to describe characteristics of stress fractures treated in rheumatology at the Clermont-Ferrand University Hospital, to compare them according to their anatomic location (pelvis, lower limb or feet/ankle) and their diaphyseal or metaphyseal/epiphyseal location.

Results: Between 01/01/2000 and 12/31/2015, 325 fractures were identified in 227 patients divided in 176 women (including 116 postmenopausal women) and 51 men. Population average age was 65.2 years (15–99 years), 142 (43.7%) fractures occurred at pelvis, 93 (28.6%) at lower limbs and 87 (26.8%) at feet and ankles. The fracture was spontaneous in 63.6% of cases. History of pain was recorded in 92.3% with more frequently (90.3%) mechanical pain. Diagnostic delay was on average 70 days. In 51 patients (22.5%) an orthopedic factor could have promoted stress fracture.

Conclusions: 94 patients (23.8%) had a history of chronic inflammatory rheumatism, 28 (12.3%) of cancer, and 20 (8.8%) had chronic renal failure. Among the possible iatrogenic factors, 51 patients (23.4%) received oral corticosteroid therapy, 20 (9.2%) methotrexate, 59 (27%) proton pump inhibitor and 17 (7.8%) serotonin reuptake inhibitor. 49 patients (22.5%) already had vitamin-calcium supplementation, 37 (17%) received biphosphonate therapy. 56.6% were osteoporotic and 29.5% were osteopenic.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1424

Table 1. Continued responder proportions and infiltration rate reactions by OLE dosing group

<table>
<thead>
<tr>
<th>Dosing Group</th>
<th>Total</th>
<th>Continued Responders</th>
<th>Percentage</th>
<th>Infiltration Reaction Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined</td>
<td>14</td>
<td>10</td>
<td>71%</td>
<td>0.32</td>
</tr>
<tr>
<td>Every 2 weeks</td>
<td>6</td>
<td>5</td>
<td>83%</td>
<td>0.30</td>
</tr>
<tr>
<td>Every 4 weeks</td>
<td>8</td>
<td>5</td>
<td>62.5%</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Table 2. Before and after treatment comparisons of the uric acid levels

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of the attacks, one year</td>
<td>7.40±1.30</td>
<td>8.21±1.92</td>
<td>&lt;0.008</td>
</tr>
<tr>
<td>Duration of the attacks, days</td>
<td>16.73±16.32</td>
<td>10.91±14.50</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Newly attacks in 3 months</td>
<td>5/14</td>
<td>7/28</td>
<td>0.734</td>
</tr>
</tbody>
</table>
AB0870

METABOLIC AND CARDIOVASCULAR GOUT ARE THE MOST FREQUENT CLINICAL VARIANTS OF THE DEBUTING GOUT

E. Mikhnevich 1, T. Pavlovich 1, E. Mytnik 2
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Background: Gout is phenotypically and genotypically heterogeneous. In most cases, renal mechanism plays an important role in the development of gout. At the same time, gout, as a rule, occurs on the basis of pre-existing comorbid pathology.

Objectives: To determine clinic-pathogenic variants of gout depending on a leading comorbid pathology at the gout debut.

Methods: We included 604 patients with confirmed gout from our Center database. During 2010–2016, comorbidities were registered before the gout onset, at its appearance, during and at the last examination. Metabolic syndrome (MS) was defined as follows: DM, obesity, dyslipidemia. CVD included CHD, atrial fibrillation, CHF and stroke. Patients after organ transplantation and with terminal renal failure observed in specialized centers were not recruited.

Results: In 67.1% (n=405) of patients, the gout developed on the basis of pre-existing MS, thus, this variant may be called a metabolic gout (MG) and considered as a component of MS. The patients with MS were younger, the mean age of symptoms onset was 42 (35–48) years. At the first gout attack, all patients had BMI 25 kg/m², 8.2% (n=33) had pre-existing HTN, and in 14.3% (n=58) of cases the diagnosis of HTN was firstly made. No one patient had diabetes mellitus (DM). Regular frequent or regular alcohol intake alcohol intake together with other MS factors were favoring gout attack in all patients. At the last examination, only 38.1% (n=230) of patients had MS without any CVD, the mean age was 50 (45–55) years; 98.7% (n=227) had BMI 25 kg/m²; 73.9% (n=170) presented with HTN; 59.1% (n=136) showed dyslipidemia; 6.5% (n=15) had DM. In 8.3% (n=19) of patients, changing the lifestyle and normalizing the weight resulted not only in decreased hyperuricemia but lowers attack rate or even their total disappearance during a 5 year follow-up. The second variant of gout onset developing in patients with pre-existing CVD, can be called a CV gout or cardioenovascular (CRV) gout. This type of gout was revealed in 28.5% (n=172) of patients, the age at the debut of gout was 60 (55–64) years (p<0.001). 97.7% (n=163) had HTN (χ²=30.1, p<0.001) and 27.3% (n=47) – DM (χ²=32.65, p<0.001), both features were more common in CV gout. 85.5% (n=147) had BMI 25 kg/m² (F=0.066, p<0.001). Regular alcohol intake was considerably lower – 33.7% (n=58) (χ²=16.7, p<0.001), but medication use was higher – diuretics in 14.5% (n=25) (χ²=21.77, p<0.001) and low-dose aspirin in 37.2% (n=64) of patients (F=0.24, p<0.001). At the last examination, the mean age of patients was 63 (59–69 years) (p<0.001), chronic GFR 60 ml/min was observed in 47.7% (n=82) of patients (F=0.34, p<0.001).

Conclusions: In our opinion, there are two main clinic-pathogenetic variants of debuting gout – metabolic and cardiovascular, the both with different conditions of occurrence, progression and prognosis. In clinical practice, it is reasonable to differentiate these variants, that is determined by the need to simplify complex multimodal diagnostic and therapeutic approach to the patients with gout.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3524

AB0871

NSAIDS AND LIVER FUNCTION IN PATIENTS WITH GOUTY ARTHRITIS

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) have been associated with hepatotoxicity. Drug-induced liver injury (DILI) in patients under NSAIDs therapy is more frequently presented by hepatocellular damage with elevated serum alanine aminotransferase (ALT) levels (1).

Methods: 376 patients with GA registered in our database were included in our retrospective study. Males made 92.8% (n=349). Mean age was 57 (50–62) years; mean duration of gout – 7 (3–10) years. NSAIDs were prescribed to the patients in 24 (18–32) U/l after treatment (p<0.001). The second variant of gout onset developing in patients with pre-existing CVD, can be called a CV gout or cardioenovascular (CRV) gout. This type of gout was revealed in 28.5% (n=172) of patients, the age at the debut of gout was 60 (55–64) years (p<0.001). 97.7% (n=163) had HTN (χ²=30.1, p<0.001) and 27.3% (n=47) – DM (χ²=32.65, p<0.001), both features were more common in CV gout. 85.5% (n=147) had BMI 25 kg/m² (F=0.066, p<0.001). Regular alcohol intake was considerably lower – 33.7% (n=58) (χ²=16.7, p<0.001), but medication use was higher – diuretics in 14.5% (n=25) (χ²=21.77, p<0.001) and low-dose aspirin in 37.2% (n=64) of patients (F=0.24, p<0.001). At the last examination, the mean age of patients was 63 (59–69 years) (p<0.001), chronic GFR 60 ml/min was observed in 47.7% (n=82) of patients (F=0.34, p<0.001).

Conclusions: In our opinion, there are two main clinic-pathogenetic variants of debuting gout – metabolic and cardiovascular, the both with different conditions of occurrence, progression and prognosis. In clinical practice, it is reasonable to differentiate these variants, that is determined by the need to simplify complex multimodal diagnostic and therapeutic approach to the patients with gout.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3524

AB0872

DIAGNOSTIC EFFICIENCY OF DETERMINING THE PURINE METABOLISM ENZYMES ACTIVITY IN THE DIFFERENTIATION OF GOUT


Background: Serum uric acid (UA) level is the most important risk factor for gout. At the same time many people with the gout do not suffer from the hyperuricemia, and UA level can return to normal during gout exacerbation.

Objectives: to improve the diagnostics of gout.

Methods: 53 gout patients were the target group. The mixed control group was consisted of 150 rheumatoid arthritis patients, 95 osteoarthritis patients, 55 ankylosing spondylitis patients. The diseases were diagnosed in accordance with the international standards. Adenine deaminase, Adenosine deaminase (ADA), AMP-deaminase (AMPADA), Guanine deaminase, Guanosine deaminase, Guanosine phosphorylase, 5-nucleotidase, Xanthin dehydrogenase (XDH), Xanthin Oxidase, Purine nucleoside phosphorylase activities were determined in blood serum with subsequent evaluation of sensitivity (Se), specificity (Sp), likelihood ratio of positive (LRP) and, likelihood ratio of negative (LRN) result, predictive value of positive and negative results.

Results: The AMPDA and ADA activities were defined as a screening marker to diagnose of the gout from a joint syndrome another genesis. Threshold AMPDA activity 1.67 IU was characterized with the predictive value of negative results (without taking into account the prevalence) near 100%, Se 98%, Sp 62.45%. Cutoff value (CV) of ADA activity (9.57 IU) was characterized with LRN 0.104, Se 92.45%, Sp 72.65%, the sum (Se+Sp) 165.10%, which was maximum not only for this test but also for all the studied enzymes. The predictive value of negative results (without taking into account the prevalence) was 98.20%. The clinically significant CV of positive result for the ADA activity definition was identified also: LRP was 6.93 (Se 22.64%, Sp 86.73%) for the range of 12.58 IU and above. This fact allows the use of this test not only for the screening, but also, in some cases, for the verification of gout with significant pretest probability of this disease. Two CV were selected for the XDG activity: 7.49 μM/1·min (Se 47.17%, Sp 97%), 13.9 μM/1·min (Se 99.25%, Sp 99.58%). The result of XDG activity determining in the range of 7.49 - 8.39 μM/1·min is an important argument in favor of the gout presence, but this may be useful for differential diagnosis only at high pretest probability of the gout.

Conclusions: Determination of the ADA activity was gave way to AMPDA activity determination at the gout screening and to XDG activity determination at gout verification. However, the ADA multi-functionality, evidenced clinically significant presence of the second CV (positive results) and a small proportion of the cases, which covered a "grey area" between CV (27.48%), provided the ability to use this marker as a backup in the absence of diagnostically relevant AMPADA and XDG activities.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3542
AB0873
CHARACTERISTICS OF ADHERENCE, PERSISTENCE AND THERAPEUTIC ALLIANCE IN PATIENTS WITH GOUT
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Background: Adherence is the extent to which the patient takes their medications and follow the directions prescribed by their doctor. It has two components: compliance (the degree or extent of conformity to the recommendations about daily-day treatment by the provider with respect to the timing, dosage, and frequency) and persistence (the duration of time from initiation to discontinuation of therapy). The therapeutic alliance is the patient physician relationship that allows the patient to participate actively in their treatment. The reported adherence varies from 43 to 70% in patients with chronic diseases. In gout, the adherence varies from 10 to 46%.
Objectives: To evaluate the characteristics of adhesion in patients with gout.
Methods: Patients with gout from the GRESGO cohort were included. Sociodemographic, clinical, and treatment data were collected and the HAC-DI, EuroQol-5d and a specific questionnaire of adherence and therapeutic alliance were applied.
Results: The study included 238 patients (97.1% male), with a mean age of 47.7±12.7 years, educational level 9.2±4.2 years. The adherence index (prescribed doses/doses taken) was 86%. Only 28.6% never stopped treatment. 41% took the doses at the correct time. Most frequent causes of suspensions were lack of supply (37%) and forgetfulness (30%). Only 5% buy all of their medications. 10% follow the lifestyle changes. 46.6% do not take the medication when they disagree with their doctor.
Conclusions: Despite having a good adherence index there are discrepancies with the qualitative answers, since more than 70% did not have good persistence and more than 90% did not comply with the schedule.
Disclosure of Interest: None declared

AB0874
CHARACTERISTICS OF GOUT IN CAMEROON, CENTRAL AFRICA: A HOSPITAL-BASED STUDY
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Background: Few data are available on the characteristics of gout in sub-Saharan Africa (1). Objectives: We performed this study with the aim to present the clinical, laboratory and imaging characteristics of gout at the time of diagnosis in Cameroon. The results obtained will be compared with data from the Western literature.
Methods: We performed a cross-sectional study among the 10,186 out patients seen at the Rheumatology unit of Douala General Hospital, Cameroon, between 2004 and 2014. We included patients with gout diagnosis (ACR criteria 1977). The main socio-demographic and clinical data on gout at the time of diagnosis were collected.
Results: A p=0.05 level was significant.
Results: We included 511 patients (5.02%) including 415 men and 96 women. The mean age was 55.9±10.8 years. Joint pain (n=508, 99.4%), joint effusion (n=198, 38.7%) and fever (n=20, 3.9%) were the most frequent complaints. Joint stiffness and/or tenderness Tophi location

<table>
<thead>
<tr>
<th>Joint stiffness/or tenderness</th>
<th>n (%)</th>
<th>Tophi location</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee</td>
<td>300 (62.6)</td>
<td>Elbow</td>
<td>72 (66.0)</td>
</tr>
<tr>
<td>Ankle</td>
<td>187 (39.0)</td>
<td>MTP1</td>
<td>20 (18.3)</td>
</tr>
<tr>
<td>Wrist</td>
<td>128 (26.7)</td>
<td>Wrist</td>
<td>10 (9.2)</td>
</tr>
<tr>
<td>Elbow</td>
<td>81 (16.9)</td>
<td>PIP</td>
<td>9 (8.2)</td>
</tr>
<tr>
<td>PIP</td>
<td>52 (11.7)</td>
<td>Foot</td>
<td>9 (8.2)</td>
</tr>
<tr>
<td>MCP</td>
<td>35 (11.7)</td>
<td>IDP</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Foot</td>
<td>50 (10.4)</td>
<td>Ankle</td>
<td>4 (3.6)</td>
</tr>
<tr>
<td>Shoulder</td>
<td>45 (9.8%)</td>
<td>Knee</td>
<td>8 (7.3)</td>
</tr>
<tr>
<td>Others MTP</td>
<td>30 (6.3)</td>
<td>MCP</td>
<td>15 (3.1)</td>
</tr>
<tr>
<td></td>
<td>24 (5.0)</td>
<td>Others MTP</td>
<td>6 (5.5)</td>
</tr>
<tr>
<td></td>
<td>15 (3.1)</td>
<td>MCP</td>
<td>5 (4.6)</td>
</tr>
<tr>
<td></td>
<td>30 (6.3)</td>
<td>Achille tendon</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td></td>
<td>30 (6.3)</td>
<td>Imprecises location</td>
<td>18 (16.5)</td>
</tr>
</tbody>
</table>

Comorbidities were present in 344 patients (67.3%), hypertension (n=208, 40.7%), obesity (n=151, 29.5%), osteoarthritis (n=111, 21.7%), osteogastroduodenal complaints (n=74, 14.5%), diabetes (n=52, 10.2%), and chronic kidney diseases (n=42, 8.2%). Associated factors (p<0.05) in the occurrence of gout were obesity, alcohol intake, diuretics intake, and menopause (in women). Conclusions: Gout has the same clinical, laboratory and imaging characteristics in Cameroon than in Western countries. The main difference comes from the place of the knee as the main joint involved by gouty arthritis at the time of diagnosis in our study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6990

AB0875
DO WE CONTROL GOUT IN PRIMARY CARE FOLLOWING EULAR RECOMMENDATIONS?
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Background: Inadequate control of hyperuricemia in gout patients can lead to more arthritis, activity limitations and higher gout-related treatment costs. General Practitioners can use well tolerated urate-lowering drugs, but some patients are inadequately controlled. European League against Rheumatism (EULAR) has published new guidelines1 in 2016 with similar serum Uric Acid (sUA) goals.
Objectives: To evaluate sUA control in patients diagnosed with gout who were attended in primary care and to compare them to EULAR 2016 guidelines1.
Methods: Retrospective analysis, carried out in 2 primary care health centres (8 family doctors) in Spain. We selected patients that have consulted in the last year diagnosed with gout at any time. Demographic variables, gout-related drugs and last sUA level were collected. Adequate control was defined as sUA level <6 mg/dL.
Results: We analyzed 231 patients diagnosed with gout, mean 70.1±10.1 years old (CI95% 63.3–76.7), 199 (81.8%) were men. The mean sUA was 6.55 mg/dL (CI63.36–7.69 mg/dL). 39% were adequately controlled according to EULAR (sUA <6 mg/dL) and clearly inadequate (>7mg/dL) in 35.5%. 10% had Really bad control (sUA >9 mg/dL). There was no difference between control in male 6.58 mg/dL (IC95%, 6.33–6.83 mg/dL) and female 6.40 mg/dL (CI95%, 5.73–7.07). Control improves in elder people: <60 years 7.01 mg/dL (CI63.65–7.42) vs. >70 years 6.30 mg/dL (CI95%, 6.00–6.60). The only 14 patients receiving febuxostat achieved similar control using allopurinol (6.5 versus 6.7 mg/dL).
Conclusions: The degree of control of sUA in primary care patients in our area is mostly optimal and acceptable, but it can be optimized in more than half of the cases. In a few patients the control is lousy. The worst-controlled patients were the youngest.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6981

AB0876
OSTEOMALACIA: MODALITIES OF PRESENTATION AND ETIOLOGY OF 20 CASES
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Background: Osteomalacia is a defect of mineralization of the protein framework of the skeleton.
Objectives: We try through our series to determine the presentation modalities and the various causes of this fragile benign osteopathy.
Methods: It is a descriptive retrospective study of cases collected in our rheumatology department between 2001 and 2016, concerning patients with osteomalacia.
Results: Twenty patients were collected: 13 women and 7 men with an average age of 53±19 years [22 years, 80 years]. The mean duration of the disease is 45 months [5–172]. The findings were: bone pain in 55% of cases, pelvic pain in 45% of cases, a waddling gait in 5 cases (25%), fractures with low energy in 20% of cases. Functional impairment of the lower limbs in 35% of cases and a biological discovery in 2 cases (10%). Hypocalcemia, phosphorus deficiency and hypocalcioria were found in 14 cases, ie 70%. Alkaline phosphatases were elevated in 12 cases, with a variable rate of 2 to 7 times normal. The PTH, performed in 17 cases, was elevated in 53% of the cases. In our series, all
patients had hypovitaminosis D. In addition, an associated iron deficiency anemia was detected in 50% of the cases, biological stigma of digestive malabsorption in 40% of the cases and renal insufficiency in 15% of the cases. Standard radiographs showed diffuse demineralization in 90% of cases, Looser-Milkman streaks in 40% of cases and fractures in 30% of cases. Bone scintigraphy among 8 patients revealed diffuse hyperfixation in 4 cases (50%), localized hyperfixation in 3 cases (37%) and non conclusive images in only one case (12.5%). Bone densitometry performed in 5 patients showed secondary osteoporosis in 80% of cases. The diagnosis of osteomalacia was retained in 2 cases, celiac disease in 5 cases, renal insufficiency in 1 case, phosphate diabetes in 3 cases including Fracture due to hyperparathyroid and hyperphosphatemia in one case and tubular involvement as part of ankylosing spondylitis in one case. Etiology was a neoplastic cause in 4 cases including multiple myeloma. All the patients had a vitamin-calcium treatment (calcium intake between 500mg and 2g per day with an average of 2.5 gpd, phosphate in 2 cases and other vitamin C in 1 case and tubular involvement as part of the tumor was the reason behind a clinical-biological improvement in the case of thyroid tumors. The outcome was favorable in the short term for all cases.

Conclusions: Osteomalacia is a generalized benign osteopathy, essentially linked to a deficiency in vitamin D often unrecognized. The diagnosis is simple and the treatment is easy, but the ignorance of the etiological forms can be responsible for an unfavorable evolution.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6986
16), mean body mass index was 33 kg/m² (SD, 10), 73% were male; 67% were
white Americans, 25% were African Americans and 7% other/mixed race/ethnicity.
Participants took a median of 35 minutes to complete study assessment.
Almost half of the participants were taking medications for the treatment of gout:
allopurinol, 42%; leflunomide, 1%; probenecid, 0%; colchicine, 29%. Forty-five
percent participants were taking none of these medications. 41% smoked ever,
27% were using a special diet and participants had alcohol use an average of
2 days in the last week. Average number of gout flares were four in the last
year. Dietary assessments showed that average daily intakes were as follows:
calories, 2005; carbohydrate, 221 gm; fiber, 19 gm; caffeine, 197 ml.
The HEI2010 score of 64 was comparable to what was observed with NHANES
for people in the average age range of this study.

Conclusions: Patients recruited in an Internet gout study, successfully responded to
assessments, and had patient characteristics similar to gout populations described previously.
The dietary assessments in this provide may provide a unique insight to design interventions to improve diet to improve gout outcomes.

References:
[1] Singh JA, Bharat A, Edwards NL. An internet survey of common treat-

ACKNOWLEDGEMENTS: This work was supported by a grant from UAB COERE
and UAB TRC centers.


AB0880 PHARMACODYNAMIC EFFECTS AND SAFETY OF VERINURAD (RDEA3170) IN COMBINATION WITH ALLOPURINOL VERSUS ALLOPURINOL ALONE IN ADULTS WITH GOUT: A PHASE 2A, OPEN-LABEL STUDY

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Background: Verinurad (RDEA3170) is a high-affinity, selective URAT1 inhibitor in
development for the treatment of gout and asymptomatic hyperuricemia.

Objectives: This Phase 2a, randomized, open-label, multicenter study investigat-
gated the multiple-dose pharmacodynamics (PD), pharmacokinetics (PK), and
safety of oral verinurad in combination with allopurinol versus allopurinol alone in
adults with gout (NCT02498652).

Methods: Patients aged ≥18 and <75 years with gout and serum uric acid (sUA): >8 mg/dL were randomized to 1 of 2 cohorts to receive allopurinol (300 mg) in combination with verinurad (dose range 2.5 mg to 20 mg) and allopurinol 300 mg or 600 mg alone (each treatment period was 7 days). Medications were administered once daily ~30 min after breakfast (for allopurinol 300 mg b.i.d. group, the second allopurinol dose was in the evening). Colchicine 0.6 mg for gout flare prophylaxis was initiated at approximately Day -14 (start of urate-lowering therapy [ULT]) washout) or Day -7 if not on ULT. Serial blood and urine samples were measured on Days -1, 1, 7, 14, 21, 28, and 35 for PD and PK endpoints. Safety assessments included adverse events (AEs) and laboratory, electrocardiogram, and vital sign parameters.

Results: Forty-one patients were randomized (n=20–21 per cohort). Serum PD data pooled across cohorts demonstrated maximal % decrease in sUA from baseline (Emax) at 6–10 h after verinurad and allopurinol combination treatment. Addition of verinurad (2.5 mg to 20 mg) to allopurinol decreased sUA in dose-dependent manner (Figure). Greater sUA reductions were observed for dose combinations of verinurad: ≥5 mg with allopurinol 300 mg versus allopurinol 600 mg alone, while allopurinol 600 mg once daily was equivalent to allopurinol 300 b.i.d.

Conclusions: Verinurad coadministration with allopurinol dose-dependently decreased sUA. All dose combinations of verinurad and allopurinol in this study were generally well tolerated with no serious AEs or renal-related events during combination treatment.


AB0881 ASSESSMENT OF SUDOMOTOR FUNCTION IN PATIENT WITH GOUT

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Background: Sodinomotor function is an anti-invasive device measures sweat gland dysfunction using electrochemical skin conductance (ESC) of hands and feet and is useful for assessing peripheral small fiber nerve function. Little is known about the dysfunction of peripheral small fiber nerve in patients with gout.

Objectives: To evaluate the prevalence and characteristics of small fiber neuropathy (SFN) in patients with gout compared with a healthy control group and to identify factors associated with SFN in gout.

Methods: 80 male patients with well symptom controlled gout (age: 58±12) and 80 healthy controls were enrolled. Each patient was required to fast over 8 hours before blood samples. Serum fasting glucose, fasting insulin, uric acid, serum 25-(OH) D, lipid profiles, Creatinine (Cr) and r-GTP were measured. Body mass index (BMI) and Homeostatic model assessment insulin resistance (HOMA IR) were calculated. Patients already diagnosed with hypertension and diabetes were excluded.

Results: The mean feet and hands ESC were significantly lower in the gout group than the control group. Mean Hands ESC was irrelevant to age, BMI, fasting glucose and insulin, HOMA-IR, vtt D, uric acid, Cr, and lipids. However, mean feet ESC showed significant correlation with fasting glucose (r=-0.7, p<0.01) and HOMA-IR (r=-0.5, p=0.03).

Conclusions: Sudomotor function was significantly lower in patients with gout than the control group. Mean feet ESC was correlated with fasting glucose and insulin resistance in patients with gout. These results suggest that dysfunction of SFN in gout patients is associated with insulin resistance and impaired fasting glucose.

Disclosure of Interest: None declared.


AB0882 EFFICACY OF INTRALESIONAL SODIUM THIOSULFATE IN DISABLING TUMORAL CALCINOSIS: ABOUT TWO CASES

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Background: Tumoral Calcinos is (TC) is a difficult-to-treat complication that can occur during the course of several diseases such as dermatomyositis or genetic hyperphosphatemia. It is a painful and disabling condition that can give rise to local complications including joint mobility reduction, cutaneous ulceration and superinfection. Until now, many treatments have been used with inconsistent efficacy.

Objectives: Intravenous sodium thiosulfate gives promising results in calciphylaxis and ectopic calcifications, and intra-lesional injections could be effective for tumoral calcinosis.
Results: The mean age at onset was 54.7±12.6 years, and the median diagnosis duration was 0 (0.3) years.

Conclusions: Intra-lesional injection of STS seems to be a promising treatment for TC. More studies are needed to confirm these results, and to understand the mechanisms implicated in the calcinosis resorption.

Disclosure of Interest: None declared

AB0884 PREVALENCE OF ULTRASONOGRAPHIC GOUT SPECIFIC SIGNS OF HAND AND FINGERS JOINTS

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Methods: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. 540 articular sites were studied at their dorsal surface. The ultrasound has objectified the presence of two signs: hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) and the tophaceous deposits at the joint cavity.

Results: The mean age at onset was 54.7±12.6 years, and the median diagnosis duration was 0 (0.3) years.

The results of the US examination are summarized in Table 1.

Table 1. Prevalence comparison of DC and tophaceous deposits between dorsal and planar surfaces at MTP joints

<table>
<thead>
<tr>
<th>Joints (N=150)</th>
<th>Double contour (%)</th>
<th>Tophaceous deposits (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dorsal surface</td>
<td>Plantar surface</td>
</tr>
<tr>
<td>MTP 1 (N=30)</td>
<td>33.3</td>
<td>10</td>
</tr>
<tr>
<td>MTP 2 (N=30)</td>
<td>13.3</td>
<td>0</td>
</tr>
<tr>
<td>MTP 3 (N=30)</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>MTP 4 (N=30)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MTP 5 (N=30)</td>
<td>3.3</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Our study suggests that globally, DC predilect significantly in dorsal than in planar surfaces of MTP joints. These results should be verified on a larger population.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3773

AB0883 THE SENSITIVITY OF GOUT SPECIFIC ULTRASOUND SIGNS AT THE METATARSOPHALANGEAL JOINTS WOULD BE BETTER BY THE DORSAL SURFACE EXAMINATION

M.A. Mahdi1, H. Rkain1, M. Erraoui1, R. Watfeh2, S. Aktaou1, L. Tahiri1, R. Bahiri1, F. Allali1, N. Hajjaj-Hassouni1, Rheumatology; 2Faculty of Medicine and Pharmacy, University Mohamed V, Rabat, Morocco

Objectives: To compare the prevalence of ultrasonographic gout specific signs at the dorsal and plantar surfaces of the metatarsophalangeal joints (MTP).

Methods: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. 150 articular sites were studied at their dorsal and plantar surfaces. The ultrasound has objectified the presence of two signs: hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) and the tophaceous deposits at the joint cavity. We compared the prevalence of the two signs between the dorsal and palmar surfaces at each site studied.

Results: The mean age at onset was 54.7±12.6 years, and the median diagnosis duration was 0 (0.3) years.

Conclusions: This study showed a predilection for the gout specific ultrasound signs (DC and tophaceous deposits) of the wrist and MCP joints. The contribution of musculoskeletal ultrasound seems to be very interesting to objectively the presence of gout specific signs in the hand and fingers joints.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3877


Conclusions: This study showed a predilection for the gout specific ultrasound signs (DC and tophaceous deposits) in the tarsometatarsal and metatarsophalangeal joints, especially in the first MTP. The contribution of musculoskeletal ultrasound seems to be very interesting to objectify the presence of gout specific signs of the foot joints.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2468

AB0886 PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF VERINURAD (RDEA3170), A SELECTIVE URIC ACID REABSORPTION INHIBITOR, IN HEALTHY ADULT MALE SUBJECTS

M. Gillen1, Z. Shen2, J.N. Miner3, 1AstraZeneca, Gathersburg, MD; 2Ardea Biosciences, Inc., San Diego, CA, United States

Background: Verinurad (RDEA3170) is a selective uric acid reabsorption inhibitor in clinical development for the treatment of gout and asymptomatic hyperuricemia.

Objectives: The aim of this study was to evaluate the pharmacokinetics, pharmacodynamics, and tolerability of verinurad following single and multiple doses in healthy adult males.

Methods: This was a Phase 1, randomized, double-blind, placebo-controlled, single- and multiple-ascending dose study. Panels of 8 male subjects (6 active, 2 placebo) received single oral doses of verinurad or placebo in either a fasted state or under the conditions of at least one concentration-time (tmax) was approximately 1.25–2.0 hours post-dose under fasted conditions. A

Results: A total of 81 adult males aged 18–54 years enrolled and completed the study. Following single oral doses of verinurad, absorption was rapid and exposure (maximum plasma concentration [Cmax] and area under the plasma concentration-time curve [AUC]) increased in a dose-proportional manner up to the maximum dose tested; Cmax was achieved at 0.5–0.75 hours post-dose in the fasted state, and was slightly delayed to 1.25 hours post-dose in the fed state. Food appeared to decrease AUC by about 23% and Cmax by about 50%. Following multiple daily doses, there was modest accumulation of verinurad. Urinary excretion is a minor elimination pathway for unchanged verinurad. Reductions in body weight. Mean reductions in serum uric acid following once-daily multiple doses, there was modest accumulation of verinurad. Cmax and AUC were 38% and 23% higher, respectively, in Japanese versus non-Asian subjects, largely due to the difference in body weight. Mean reductions in serum uric acid following once-daily multiple dosing of verinurad 10 mg were 62% and 58% at maximum reduction and 46% and 44% at 24 hours post-dose in Japanese and non-Asian subjects, respectively.

Verinurad was well tolerated at all doses. One Japanese subject discontinued verinurad due to an AE of urticaria that resolved after 11 days. No serious AEs, Grade 3 or 4 AEs, or clinically significant laboratory or ECG abnormalities were noted.

Conclusions: Verinurad significantly lowered serum uric acid and was well tolerated in both healthy Japanese and non-Asian males, despite small differences in plasma pharmacokinetics. These data support further evaluation of once-daily verinurad as a treatment for hyperuricemia with or without gout in the Japanese population.

Acknowledgements: The authors thank Caroline Lee and Zannong Shen of Ardea Biosciences, Inc., for critical review of the abstract.


AB0888 TENOFOVIR INDUCED OSTEOMALACIA: A PROFILE BASED ON THREE PATIENTS WITH LOW PHOSPHORUS AND NORMAL LEVELS OF VITAMIN D AND PARATHYROID HORMONE

M. Levy, Desert Oasis Healthcare, Palm Springs, California, United States

Background: Tenofovir can induce proximal renal tubular changes that result in vitamin D deficiency2, Less commonly, osteomalacia related to hypophosphatemia3 can occur and has been documented with bone biopsy4. The clinical details of 28 reported cases of tenofovir induced osteomalacia, some of whom had vitamin D deficiency and secondary hyperparathyroidism, was recently summarized3. To describe the clinical presentation and course of three HIV patients with tenofovir induced hypophosphatemic osteomalacia and compare to cases previously reported.

Methods: The clinical, laboratory, and radiologic features of three HIV patients referred for evaluation of pain and osteopathy were reviewed.

Results: All three patients were male, had diffuse pain, suffered multiple clinical fractures, and were on combination long and short acting opioids at the time of presentation. Two were in wheelchairs and two had neuropathy. All patients had hypogonadism and proteinuria and case 1 had glycosuria. All patients had normal serum albumin, vitamin D, vitamin A, and parathormone levels. Urinary protein electrophoresis, magnesium, CBC, calcium, CPK, sedimentation rate. TSH. Case 1 had fractures of the hip, sacrum, and humerus; case 2 hip and ribs; and case 3 ribs, pelvis and knee. The technetium bone scan showed a similar pattern of increased uptake in multiple ribs, calcaneus, metatarsal bones, knees, and

Acknowledgements: The authors thank Caroline Lee of Ardea Biosciences, Inc., for critical review of the abstract.
Factors contributing to length of inpatient hospital stay for patients with acute gout arthropathy at the Northern Hospital: An observational study

M. Mian, M. N. Hossain, M. Omair, D. Liew, C. E. Owen, A. M. Foote, R. R. C. Buchanan

Background: Gout is a common inflammatory arthropathy with a reported prevalence ranging from 1.7% to 4% within Australia – one of the highest in the world, second only to New Zealand. Epidemiological studies have established that its prevalence has increased steadily over recent years, with the impact of the disease on the rise.

Gout has been reported to be associated with a wide range of patient presentations, accounting for 2-3% of all hospital admissions each year. The acute medical presentation to hospital with a large corresponding economic burden.4

Conclusions: To review our experience regarding SLE patients who developed gout, and to perform a literature review of reported cases to date.

Methods: Retrospective review of patients with SLE and crystal-proven gout in our Rheumatology Unit, a tertiary care center. We recorded clinical and laboratory variables related to both diseases. Then, we performed a bibliographic review in Pubmed (1965 – 2016) to identify reported cases of coexistence of both diagnoses.

Results: Out 189 SLE patients seen in our Unit, we have identified two cases with crystal-proven gout: 1) A 68 years-old woman with SLE and nephritis diagnosed 30 years ago, who developed polyarthritis affecting her hands; 2) A 47 years-old man with lupus for 22 years with nephritis and renal failure, who developed acute arthritis involving right knee and ankle. In both cases, urate crystals were demonstrated at synovial fluid. The table shows the results of the literature review together with our two cases. To date, 36 cases with coexistent SLE and gout have been reported. Median age at time of gout diagnosis was 43.5 years (IQR: 75 32.5–52.0), being 26 females (72%). SLEA levels were found notably high (median 13.5mg/dL), and tophi, a marker of gouty severity, were demonstrated in almost half of cases (44.4%). The majority of patients (91%) were on glucocorticoids at time of gout diagnosis. According to common factors leading to hyperuricemia, lupus-related renal damage (8%) and use of diuretics (83%) predominated in the series.

References:


Disclosure of Interest: None declared


AB0889

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References:


Disclosure of Interest: None declared


AB0889

Systemic Lupus Erythematosus and Gout: Really an Unusual Association?

N. Quíll, M. Andrés

Background: Patients with systemic lupus erythematosus (SLE) often suffer from cardiovascular comorbidity such as hypertension, dyslipidemia or coronary heart disease. However, the association with gout – an independent cardiovascular risk factor – is considered unusual - it is not reported in the EULAR textbook (1), and might not be taken into account when acute arthritis occurs in SLE patients, also due to the predominance of women in this disease.

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References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5929

AB0889

Systemic Lupus Erythematosus and Gout: Really an Unusual Association?

N. Quíll, M. Andrés

Background: Patients with systemic lupus erythematosus (SLE) often suffer from cardiovascular comorbidity such as hypertension, dyslipidemia or coronary heart disease. However, the association with gout – an independent cardiovascular risk factor – is considered unusual - it is not reported in the EULAR textbook (1), and might not be taken into account when acute arthritis occurs in SLE patients, also due to the predominance of women in this disease.

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References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5929
HIGH FREQUENCIES OF CVD RISK FACTORS, OBESITY, METABOLIC SYNDROME, AND VITAMIN DEFICIENCIES IN A DANISH COHORT OF GOUT PATIENTS

O. Slot, Copenhagen Center for Arthritis Research, Rheumatology, Copenhagen University Hospital Rigshospitalet Glostrup, Glostrup, Denmark

Background: Gout is associated with increased risk of Cardio-Vascular Disease and death.

Objectives: To measure the frequencies of a number of potentially modifiable and death.

Results: 88 males (62.1±13.6 years) and 12 females (74.1±6.9 years) were included. See Table for results.

Comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous CVD (n=36/100)</td>
<td>36%</td>
</tr>
<tr>
<td>Hypertension (BT&gt;140/90 mmHg)</td>
<td>80%</td>
</tr>
<tr>
<td>Hypertension without antihypertensive treatment (n=22/100)</td>
<td>22%</td>
</tr>
<tr>
<td>Diabetes (n=28/100)</td>
<td>28%</td>
</tr>
<tr>
<td>Nephropathy (eGFR&lt;60 ml/min)</td>
<td>29%</td>
</tr>
<tr>
<td>One or more comorbidities</td>
<td>86%</td>
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</tbody>
</table>

Comorbidity risk factors

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<th>Risk Factor</th>
<th>Prevalence</th>
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</thead>
<tbody>
<tr>
<td>BMI, mean±SD (n=95)</td>
<td>29.6±5.3</td>
</tr>
<tr>
<td>BMI ≥30 (n=44/95)</td>
<td>46%</td>
</tr>
<tr>
<td>Metabolic Syndrome (n=68/95)</td>
<td>72%</td>
</tr>
<tr>
<td>P-High Density Lipoprotein</td>
<td>32%</td>
</tr>
<tr>
<td>P-Low Density Lipoprotein</td>
<td>43%</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>50%</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>40%</td>
</tr>
<tr>
<td>Cobalamin</td>
<td>24%</td>
</tr>
<tr>
<td>Folate</td>
<td>16%</td>
</tr>
<tr>
<td>25 (OH) vitamin D3</td>
<td>48%</td>
</tr>
<tr>
<td>25 (OH) vitamin D2</td>
<td>19%</td>
</tr>
</tbody>
</table>

Conclusions: Nephropathy, obesity, and dyslipidemia are known to correlate to hyperuricemia and gout. Reciprocally hyperuricemia and gout may lead to development of comorbidities, i.e. hypertension, CVD, and nephropathy. Almost half the patients in this study were obese emphasizing the correlation between hyperuricemia and gout and obesity. Weight reduction is beneficial for control of hyperuricemia and gout, and is an important lifestyle factor that may be addressed in the treatment of hyperuricemia.

Disease-related knowledge of gout

Awareness of the cause of gout attack, flare prevention induced by ULT, tendency to have chronic arthritis, and relationship with adverse to UA lowering treatment.

Conclusion: There are significant sustained clinical benefits with long-term pegloticase treatment in patients with chronic refractory gout achieving a UA lowering effect during the initial 3 months of therapy. Significant decreases in TJC, SJC, and pain were noted along with significant improvements in PGA suppression of gout flares, and resolution of tophi. In most patients, maximal benefit was noted after 6–12 months of pegloticase therapy, with many patients meeting newly proposed criteria for gout remission.

References:


RELATIONSHIP WITH ADHERENCE TO URATE-LOWERING THERAPY IN EAST CHINA

R. Yin1, T. Fu1, Q. Zhang1, L. Zhang1, L. Li2, Z. Gu1, Department of Rheumatology, Affiliated Hospital of Nantong University; 2School of Nursing, Nantong University, Nantong, China

Background: Gout is a chronic rheumatic disease caused by deposition of monosodium urate crystals in and around the joint, with a reported prevalence of 1.1% in mainland China and 6.24% in Taiwan, making it the most common form of inflammatory arthritis. With the disease progression, gout can cause permanent joint destruction, bone erosion, and organ damage. Urate-lowering therapy (ULT) is necessary to lower and maintain serum urate (sUA) levels at a therapeutic target of <360 μmol/L, as it is associated with fewer gout flares, reduction of tophus size, and deprecation of urate crystal stores in synovial tissues, making gout the only chronic arthritis that can be “cured.” Disease related knowledge of gout patients should be assessed before attempting to improve health education. To date, except one study from south China, all other published papers about gout knowledge and medication adherence are from other countries. To our knowledge, there is no survey from east China.

Objectives: The current study aimed to investigate knowledge related to gout and its risk factors, and the relationship with adherence to urate-lowering therapy in patients with gout in east China.

Methods: A cross-sectional study of 229 gout patients recruited from the Affiliated Hospital of Nantong University between April 2015 and November 2016 was conducted with two questionnaire, Gout Knowledge Questionnaire (GKQ) and Compliance Questionnaire on Rheumatoid (CQR). Chi-square analysis, t-test, rank sum test, as well as logistic regression analysis were used to analyze data. Results: 215 patients (94.28%) in east China had knowledge of gout, and 9.1% (13/143) adhered to ULT. Age, employment, income, alcohol use, family history, acute flares in preceding 1 year, and colchicine use were associated with awareness of gout-related knowledge, and age, income, alcohol use, and colchicine use were the predictors. Among patients with ULT, patients adherent to ULT tended to have chronic arthritis, knowledge of gout attacks, and adherence to ULT. Awareness of the cause of gout attack, flare prevention induced by ULT and comorbidity were correlated with medication adherence, and the cause of gout attack as well as flare prevention induced by ULT were predictors of adherence to ULT in gout patients in east China.
Conclusions: In this study, 78.5% of patients in east China didn’t have gout-related knowledge. Patients’ knowledge on gout is a significant independent determinant of adherence to ULT.

Acknowledgements: This study was supported by grants from the Cultivative Distinguished Young Scholars Project of Nantong University (2nd); the 2015 Graduate Innovation Project of Nantong University (YX150705); and College graduate research and innovation of Jiangsu Province (KYZZ15-0353).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3071

AB0894 TREATMENT ADHERENCE TO URATE-LOWERING THERAPY IN CHINESE GOUT PATIENTS

R. Yin 1, H. Cao 1, F. Fu 1, Q. Zhang 1, L. Zhang 1, L. Li 2, Z. Gu 1 1Department of Rheumatology, Affiliated Hospital of Nantong University; 2School of Nursing, Nantong University, Nantong, China

Background: Gout, which is characterised by deposition of monosodium urate monohydrate (MSU) in synovial fluid and other tissues, is the most common form of inflammatory arthritis in man and older women. In addition to recurrent acute arthritis, subcutaneous tophi and chronic painful arthritis, gout also affects morbidity and premature mortality. Previous studies have reported that effective ULT can decrease sUA levels enough to prevent further crystal formation, dissolve existing urate crystals and eliminate the causative agent, thus reducing the frequency of acute gout attacks and preventing urate nephropathy, uric acid nephrolithiasis, and the deposition of tophi: a common cause of progressive joint damage, deformity and functional impairment, making gout the only chronic arthritis that can be “cured”. However, gout patients’ adherence rate to ULT is low, ranging from 10 to 46%. Emerging data suggest that poor adherence to long-term ULT use may be an important contributor to the suboptimal outcomes seen in gout and nonadherence may be worse in gout than in any other chronic disease. This suggests that there is a strong need to make a further study on drug adherence and its risk factors.

Objectives: Non-adherence in gout patients using urate-lowering therapy (ULT) may lead to joint destruction and permanent disability. Purpose of this cross-section survey was to explore Chinese gout patients’ adherence rates and investigate potential risk factors for medication non-adherence.

Methods: A total of 129 gout patients were recruited from the Affiliated Hospital of Nantong University from August 2015 to September 2016. Patients were asked to complete a standardized self-report questionnaires (Compliance Questionnaire on Rheumatology, Treatment Satisfaction Questionnaire for Medication version II, Health Assessment Questionnaire, Confidence in gout treatment questionnaire, Gout Knowledge Questionnaire, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, and 36-Item Short Form Health Survey). Data was analyzed by independent sample t-test, rank sum test, chi-square analysis as well as logistic regression modeling.

Results: Based on CQ9, 9.6% of gout patients were adherent to ULT. Adherence was associated with HAQ, GKQ, treatment satisfaction for medication, confidence in gout treatment and MCS. Other demographic, clinical and psychological characteristics were not related to adherence. Logistic regression models identified HAQ, GKQ and MCS as predictors of medication non-adherence.

Conclusions: In the current study, 90.4% of gout patients didn’t adhere to their ULT prescription. HAQ, GKQ, treatment satisfaction for medication, confidence in gout treatment and MCS were relevant to medication adherence, and HAQ, GKQ and MCS were independent predictors of medication non-adherence in patients with gout. These findings could help medical personnel develop useful interventions to improve gout patients’ medication adherence and quality of life.

Acknowledgements: This study was supported by grants from the Cultivative Distinguished Young Scholars Project of Nantong University (2nd); the 2015 Graduate Innovation Project of Nantong University (YX150705); and College graduate research and innovation of Jiangsu Province (KYZZ15-0353).

Disclosure of Interest: None declared


AB0895 OSTEOPOROISIS RISK FACTORS IN PATIENTS WITH CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION DISEASE (CPPD)

S. Vladimirov, M. Eliseev, O. Zheylabina, A. Smirnov, S. Glukhova. V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Osteoporosis (OP) risk factors (RF) in CPPD patients are not sufficiently studied, although some of these RFs may be more prevalent in CPPD pts than in general population [1].

Objectives: To identify the input of individual RFs into OP development in pts with CPPD.

Methods: 64 patients with CPPD (35 males and 29 females), but without OP were included into open prospective study. CPPD was confirmed based on McCarty criteria (detection of calcium pyrophosphate crystals in the synovial fluid using polarized microscopy and detection of chondrocalcinosis based on joint radiography or US examination). 40 pts of those had acute and/or chronic arthritis, and 24 pts had osteoarthrits with CPP crystal depositions. Mean age was 57.6±10.2 years, mean follow up – 4.85±0.96 years. Bone mass density (BMD) was measured by dual energy X-ray absorptiometry (DXA) at the forearm, lumbar spine and total hip was performed in all pts at baseline. OP was diagnosed by BMD (T-criterion < -2.5). The following OP risk factors were evaluated in this study: sex; age ≤ 55 years for females and > 65 years for males, smoking, alcohol, fractures in past medical history, fractures in parents, BMI ≥20 kg/m², BMI ≥25 kg/m², serum levels of calcium, magnesium, vitamin D, hyperparathyroidism (HPT), chronic kidney disease (GFR < 60 mL/min), intake of diuretics and glucocorticosteroids (GCs), Erythrocyte sedimentation rate (ESR) > 20 mm/h, C-reactive protein (CRP) > 5.0 mg/L. Odds ratio (OR) (95% confidence interval, CI) was estimated for each risk factor and logistic regression analysis was performed. Statistical analysis was made using SPSS v. 11 package, p values of < 0.05 were considered statistically significant.

Results: OP was identified in 22 (34%) out of 64 pts with CPPD (13 males and 9 females) by the end of the study. The following factors were associated with OP: age ≥ 55 years in females (odds ratio (OR) 5.0, 95% CI: 1.021–24.49; p=0.047), age > 65 years in males (OR 3.9, 95% CI 1.3–11.5; p=0.014), HPT (OR 15.38, 95% CI 1.7–137.9; p=0.015), elevated ESR (OR 3.38, 95% CI 1.14–10.5; p = 0.028) and CRP (OR 6.42, 95% CI 2.05–20.05; p = 0.001) (Fig. 1).

Only hyperparathyroidism was identified by logistic regression analysis (sensitivity- 71%, specificity- 82%) as OP-associated risk factor (OR 14.24, 95% CI 1.05–194.05; p=0.046) (Table 1).

Table 1. Data from multiple logistic regression analysis

Study | OR | Lower | Upper | p
---|---|---|---|---
sex | 2.115 | 0.259 | 5.709 | 0.805
BMI >25 kg/m² | 1.483 | 0.325 | 6.774 | 0.611
Age >65 | 1.293 | 0.274 | 6.093 | 0.745
Diuretics intake | 2.777 | 0.189 | 40.817 | 0.457
HPT | 14.245 | 1.046 | 194.055 | 0.046
CKD | 1.025 | 0.082 | 12.876 | 0.985
lower vit.D3 | 0.553 | 0.116 | 2.173 | 0.357
Elevated ESR | 3.830 | 0.764 | 19.214 | 0.101
Elevated CRP | 3.855 | 0.608 | 24.44 | 0.152

Conclusions: Hyperparathyroidism is the key risk factor for OP in CPPD pts. Among other risk factors chronic inflammation (ESR and CRP levels) is of highest importance.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3575

AB0896 THE EFFECT OF SERUM URIC ACID LEVELS ON TOPHUS STATUS AND FLARES IN PATIENTS WITH GOUT: A SYSTEMATIC REVIEW

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Background: Gout is a chronic, progressive, inflammatory disease characterised by elevated serum uric acid (sUA) levels. sUA levels above its saturation point result in the deposition of monosodium urate crystals, which lead to gout flares and tophi (1). Multiple studies support the use of sUA levels as a marker for clinical improvements; hence the therapeutic goal is to lower sUA levels (<6.0 mg/dL) to improve the symptormorosity of gout and reduce the risk of associated comorbidities (2,3).

Objectives: To conduct a systematic review to identify studies reporting the effect of sUA levels on the incidence of gout flares and tophus status in adult patients with gout/hyperuricaemia, with a focus on publications reporting a correlation between the parameters.

Conclusions: Hypouricemia is the key risk factor for OP in CPPD pts.
Methods: Publications were identified by interrogating electronic databases: Medline & MEDLINE In-Process, EMBASE and the Cochrane Library (accessed 6 Sept 2016). Eligibility criteria included adult patients with a diagnosis of acute/chronic gout or hyperuricemia, with no restriction on publication date, study design or geography.

Results: In total, 69 studies met the pre-defined inclusion criteria and were reviewed; of these, 17 reported the relationship between sUA levels and flares (n=12) and/or tophus status (n=11). Two studies were multinational (North America), and 15 were single country [US (n=10); Spain (n=2); New Zealand (n=1); Germany (n=1); Japan (n=1)]. The majority of studies had a follow-up period of <1 year and 31% reporting 10 years' follow-up. All 12 studies evaluating flares reported that achieving sUA levels <6 mg/dL was associated with a decreased risk of gout flares, compared with sUA levels >6 mg/dL (p < 0.05 in 8 studies). All 11 studies evaluating tophus status reported that achieving sUA levels <6 mg/dL was associated with improvements in tophus status, compared with sUA levels >6 mg/dL (p < 0.05 in 4 studies). The remaining 42 studies reported the impact of urate lowering therapy on sUA levels and gout flares or tophus status, but not the correlation between the parameters. The qualitative results in these studies indicated that increases in sUA levels were associated with an increased risk of gout flares and worsening of tophus status.

Conclusions: Maintenance of sUA levels <6 mg/dL is associated with improvements in tophus resolution and flare reduction in adult patients with gout/hyperuricaemia. Whilst longer-term follow up studies (>5 years) are warranted, this review further supports that decreases in sUA levels are a marker for clinical improvements.

References:


AB0897 FUNCTIONAL DISABILITY AND HEALTH-RELATED QUALITY OF LIFE IN CHINESE PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

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Background: As the most common arthritis in adults, gout is a painful, inflammatory disease that may cause functional disability and decreased health-related quality of life (HRQoL). However, there are currently no known reported studies related to functional disability and HRQoL of gout patients from China.

Objectives: This cross-sectional study aims to investigate the effect of demographic variables, disease parameters, and psychological status on functional disability and HRQoL of Chinese gout patients.

Methods: A self-report survey was administered to 226 gout patients and 232 healthy individuals using the Short Form 36 health survey (SF-36) for HRQoL and the Health Assessment Questionnaire-Disability Index (HAQ-DI) for functional disability. Gout patients were asked to complete the 10 cm Visual Analog Scale (VAS) for total pain, the Patient Health Questionnaire (PHQ-9) for depression, and the Generalized Anxiety Disorder (GAD-7) questionnaire for anxiety. Blood samples were taken to examine the level of uric acid (UA). Independent samples t-tests, Chi square analyses, and logistic regression were used to analyze the data.

Results: Our results found that individuals with gout have poorer HRQoL and the mean functional disability score was 0.34 (SD 0.54), representing mild disability. SF-36 and almost all components of the SF-36 score were associated with place of residence, hypertension, DM, cardiovascular disease, disease duration, number of flares/last year, total pain, number of tophi, presence of tender joints, colchicine use, corticosteroids use, depression, and anxiety (p < 0.05). This variable was also significantly related to the HAQ-DI score (p < 0.05). Additionally, there were significant relationships among age, income/year, allopurinol use and HAQ-DI (p < 0.05). Stepwise multiple linear regression identified number of flares/last year, place of residence, depression and anxiety as the most significant predictors of functional disability. Disease status (total pain, number of flares/last year, presence of tender joints, cardiovascular disease, colchicine and corticosteroids use) and psychological disorders (depression and anxiety) were significantly accounted for poor HRQoL.

Conclusions: Chinese gout patients experienced mild disability and poor HRQoL. Disease status and psychological status were important risk factors linked to functional disability and HRQoL in Chinese gout population. These data suggest medical personnel should pay more attention to functional disability and HRQoL of gout patients and make suitable interventions to relieve their psychological disorders and finally to reduce their functional ability and improve their HRQoL.

Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).

AB0898 SLEEP QUALITY IS ASSOCIATED WITH ALCOHOL USE AND FUNCTIONAL CAPACITY IN CHINESE PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

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Background: Poor sleep quality is common in patients with chronic diseases and may lead to the decreased quality of life. The increasing prevalence of poor sleep in individuals with chronic medical conditions is associated with adverse demographic, clinical, and psychological characteristics. However, there are currently no known reported studies related to the sleep quality of gout patients.

Objectives: This study aims to evaluate the prevalence of poor sleep quality and investigate the contributors of poor sleep in Chinese gout patients.

Methods: A self-report survey was administered to 226 gout patients and 232 healthy individuals using the Pittsburgh Sleep Quality Index (PSQI) for sleep quality, the Patient Health Questionnaire (PHQ-9) for depression, and the Generalized Anxiety Disorder (GAD-7) questionnaire for anxiety. Gout patients completed the 10 cm Visual Analog Scale (VAS) for total pain, and the Health Assessment Questionnaire-Disability Index (HAQ-DI) for functional capacity. Blood samples were taken to examine the level of uric acid (UA). Independent samples t-tests, Chi square analyses, and logistic regression were used to analyze the data.

Results: Our results found that the prevalence of poor sleep (PSQI<5) was 55.3% and the mean global score of PSQI was 6.69 (SD 3.48) in patients, which were significantly higher than the controls (17.7% and 3.83 (SD 1.88), respectively). There were significant correlations among alcohol use, HAQ-DI, PHQ-9, GAD-7 and sleep quality in gout patients. Patients with yellow rice wine and wine use preferred to have better sleep quality. While, disease stage was associated with hypertension, total pain, number of tophi, presence of tender joints and swollen joints. Meanwhile, logistic regression models identified alcohol use and depression as predictors of poor sleep quality.

Conclusions: More than half of Chinese gout population suffered from poor sleep, which significantly higher than healthy individuals. These findings suggested medical personnel should pay more attention to the sleep quality of gout patients, especially those with depression. Additionally, it is beneficial for the patients with normal UA level to take moderate yellow rice wine and wine to improve their sleep quality.

Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6023

AB0899 DEPRESSION AND ANXIETY CORRELATE WITH DISEASE-RELATED CHARACTERISTICS AND QUALITY OF LIFE IN CHINESE PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

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Background: Depression and anxiety are common worldwide and may lead to disease aggravation and decreased health-related quality of life (HRQoL). The increasing prevalence of depression and anxiety in gout patients is associated with demographic and gout characteristics. However, there are currently no known reported studies related to the association between HRQoL and depression and anxiety in gout patients.

Objectives: This cross-sectional study aims to evaluate the prevalence of depression and anxiety and investigate the potential risk factors for depression and anxiety in Chinese gout patients.

Methods: A self-report survey was administered to 193 gout patients and 208 healthy individuals from September 2015 to September 2016. Patients were asked to complete a set of standardized self-report questionnaires [Visual Analog Scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder (GAD-7) questionnaire, Short Form 36 health survey (SF-36)]. Independent samples t-tests, χ2 analyses, and logistic regression were used to analyze the data.

Results: We found 15% of gout patients had depression, and 5.2% had anxiety, which were significantly higher than the healthy controls (1.4 and 1.0%, respectively). There were significant correlations among education, pain, disease duration, stage of gout, disability, number of tophi, presence of tender joints, HAQ-DI, and psychological status. Meanwhile, logistic regression analysis identified number of tophi, HAQ-DI, and MH scale as predictors of depression in gout patients. Education, GH, and VT domains were significantly accounted for anxiety.

Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3081
Conclusions: The prevalence of depressive and anxious symptoms among gout patients was higher than healthy individuals. Education, disability, tophi and HRQoL were important risk factors linked to this disorder in Chinese gout population. These findings suggested medical personnel should pay more attention to the psychological health of gout patients and make objective interventions to relieve their depression and anxiety, especially those with low education level, more than two tophi, severe disability, and poor HRQoL.

Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3082

**AB0900**

**SERUM URIC ACID LEVEL VARIATIONS DURING GOUT ATTACKS ARE LINKED NEITHER TO INFLAMMATION NOR TO URIC ACID FRACTIONAL EXCRETION: A PROSPECTIVE STUDY OF 35 PATIENTS**

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**Background:** Acute gout is usually associated with a decrease in serum uric acid (SUA) level but the mechanism responsible for this phenomenon remains unclear.

**Objectives:** We aimed to investigate relationships between changes in SUA level, urinary excretion of uric acid and biochemical markers during gout attack.

**Methods:** SUA, eGFR (estimated glomerular filtration rate), serum CRP level and urinary excretion of UA, expressed as fractional excretion of UA (FeUA), from 35 ULT (urate-lowering therapy)-free and diuretic-free gout patients were prospectively measured during acute gout attack (Tc) and intercritical (Tic) phase.

**Results:** In 11 patients, data were available after achievement of SUA target (Tt) (< 360 μmol/l) under ULT. Demographics data and waist circumference (WC) were collected. Data are expressed as mean ± SD.

**Results:** There were 32 men, mean age 57.9 years, mean body mass index 28.6 kg/m², and mean waist circumference 104 cm. Overall 17.1% had type 2 diabetes, 37.1% dyslipidemia, 54.3% hypertension, 34.4% obesity, 74.3% abdominal obesity and 51.4% chronic kidney disease (CKD, 31.4% CKD 2 and 20% CKD 3–5). Gout duration was 3.9±6.7 years, 28.6% of patients had tophus abdominal obesity and 51.4% chronic kidney disease (CKD, 31.4% CKD 2 and 10.1% CKD 3–5).

**Objectives:** The prevalence of depressive and anxious symptoms among gout patients was higher than healthy individuals. Education, disability, tophi and HRQoL were important risk factors linked to this disorder in Chinese gout population. These findings suggested medical personnel should pay more attention to the psychological health of gout patients and make objective interventions to relieve their depression and anxiety, especially those with low education level, more than two tophi, severe disability, and poor HRQoL.

**Acknowledgements:** This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4808

**AB0901**

**CLINICAL SIGNIFICANCE OF URATE DEPOSITION IN TENDON: A DUAL-ENERGY CT STUDY**

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**Background:** Dual-energy computed tomography (DECT) is an advanced imaging modality that shows the deposition of monosodium urate (MSU) crystal in tissue as a color signal. The MSU crystal deposit around the symptomatic joint is considered as positive finding, but the clinical significance of urate deposition around the tendon is still unclear.

**Objectives:** The aim of this study was to compare the clinical characteristics and DECT findings in people with MSU crystal deposition in the joints and people with urate deposition in the tendons.

**Methods:** DECT was performed in 71 patients who complained of recurrent painful swelling of the joints, and 35 of them showed MSU crystal deposition in the joints on DECT. Clinical manifestation and serum uric acid level data were collected.

**Results:** Most of the included patients were middle-aged (mean age 50 years, SD 15) and 67 patients (94%) were male. All patients who had MSU crystal deposition in joints on DECT had a history of typical gout attacks, and 29 patients (81%) had a history of gout attacks among patients with urate deposition only in tendons (p<0.01). The mean uric acid level of patients included in the study was as high as 7.5±2.2 mg/dL. In the highest uric acid level, the absolute value was higher in patients with urate deposition in joints, but there was no statistical significance. The correlation between the gout attack site and the urate deposit sites was 91% in patients with joint involvement, but only 6% in patients without joint involvement (p<0.001). There were 4 patients (11%) who showed gouty erosion without MSU crystal deposition in joints on DECT.

**Conclusions:** The MSU crystal deposition in the tendon was not correlated well with clinical features, suggesting that it is more likely to be associated with artifact or asymptomatic hyperuricemia. However, in some patients, MSU crystal deposition may be observed only in the tendon, even with gouty erosion. Therefore, careful interpretation of the DECT results is necessary.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6331

**Infection-related rheumatic diseases**

**AB0902**

**TUBERCULOSIS SCREENING IN PATIENTS RECEIVING BIOLOGIC THERAPY**


**Background:** The advent of biological treatments has greatly improved the management of chronic inflammatory diseases (CID). However, these biologics increase the risk of infection including the possible development of tuberculosis (TB). Screening of latent tuberculosis infection (LTBI) is therefore necessary prior to their initiation, especially in Tunisia, which is considered as a high-incidence area of TB.

**Objectives:** The aims of this study were to identify the prevalence of LTBI among patients candidate to initiate biologics, to analyze the tolerance of preventive therapy and to detect active TB or conversions of immunodiagnostic tests under biologics.

**Methods:** A retrospective study was conducted, over a period of 14 years (2002–2016). Patients with CID, candidate to initiate biological treatment, were included. The screening of LTBI was performed according to the national Tunisian guidelines. Clinical data, screening and follow-up information on biological therapy were assessed.

**Results:** A total of 76 patients were enrolled in the study, 32 men and 44 women with a mean age of 66 years [17–80]. Rheumatoid arthritis (RA) was the most common CID (44%). The diagnosis of LTBI was established in 16 cases (21%). Among them, 3 had a Tuberculin Skin Test (TST) more than 10mm associated with a positive Interferon Gamma Release Assay (IGRA), 11 had only a positive TST, and 2 had only a positive IGRA. One of them had a history of pulmonary TB but adequately treated. All patients with positive screening were considered for preventive treatment. Thirteen (81%) received an association of isoniazid-rifampicin for 3–6 months, and 3 (19%) received isoniazid for 6 months.

**Toxicity** was reported in 4 cases (25%): hepatotoxicity (n=1), dermatologic toxicity (n=1), fever (n=1) and stomachache (n=1). During the follow-up period, no case of reactivation has been reported among patients with LTBI. Out of the 60 patients with negative baseline screening, only 4 have been re-screened (6%) and none had conversions in immunodiagnostic tests. However, among patients who screened negative, one case of active pulmonary TB has been reported in a woman who had an ankylosing spondylitis (AS) and who was receiving infliximab (n=1). She had CAD/PH and TB exposure.

**Conclusions:** Our study showed that the Tunisian recommendations allowed detecting a LTBI in 21% of biologic therapy candidates. The initial screening and the prophylactic treatment improve the safety of these treatments. However, we noted a low rate of re-screening, as the Tunisian guidelines do not recommend
Laboratory FINDINGS in patients with Chikungunya fever in subacute/chronic phases

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Background: Chikungunya fever (CF) is an arbovirus with a high attack rate, affecting large proportion of the population in its outbreaks (85%-90% of infected are symptomatic). In general, it is recommended to carry out laboratory tests when patients reach subacute phase or show signs of severity at the beginning of the disease. There are few studies showing which laboratory results are relevant and their clinical applicability.

Objectives: To recognize the most frequent findings of laboratory tests in a cohort of patients with CF and chronic joint symptoms and to correlate laboratory results with clinical data.

Methods: Patients with diagnosis of CF (clinical and epidemiological criteria) were followed in a cohort study. Clinical data and laboratory tests were collected in a regular schedule in the first months of the disease.

Results: A total of 54 patients were enrolled during 10 months, persistent changes in some patients were recorded (table).

Table 1. Persistent laboratory findings in patients with Chikungunya Fever in subacute/chronic phases

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50% Decreased vitamin D (53.8%)</td>
<td>50%+</td>
<td>Decreased</td>
</tr>
<tr>
<td>40%−50% Increased CRP (43.3%)</td>
<td>40%−50%</td>
<td>Increased</td>
</tr>
<tr>
<td>30%−40% Decreased: HDL cholesterol (36.5%), eosinophil (37.3%)</td>
<td>30%−40%</td>
<td>Decreased:</td>
</tr>
<tr>
<td>20%−30% Increased: glucose (28.3%), GGT (27.4%), γ-glutamyl (24.6%)</td>
<td>20%−30%</td>
<td>Increased:</td>
</tr>
<tr>
<td>10%−20% Increased: triglycerides (17.6%), LDH (17.3%), ferritin (13.7%), ALT (13.2%), direct bilirubin (12.0%), u1 globulin (11.7%)</td>
<td>10%−20%</td>
<td>Increased:</td>
</tr>
<tr>
<td>5%−10% Hypercholesterolemia (8.0%) Increased: neutrophils (7.54%), LDL (5.88%), folic acid (5.76%), platelets (7.54%) Decreased: CPK (7.54%), albumin (5.88%), cholesterol (5.88%)</td>
<td>5%−10%</td>
<td>Increased:</td>
</tr>
</tbody>
</table>

CRP = C reactive protein, GGT = gamma glutamyl transferase, LDH = lactate dehydrogenase, ALT = alanine aminotransferase, CPK = creatine phosphokinase.

In the subacute phase, the ESR (erythrocyte sedimentation rate) correlated with number of swollen joints (r=0.45, p=0.03), VAS (visual analogue scale) of pain (r=0.72, p=0.0002), WAS patients’ general health (r=0.50, p=0.02), VAS by physician (r=0.45, p=0.03) and with HAQ (r=0.51, p=0.01). In subacute phase the VAS of morning stiffness correlated with CRP (r=0.46, p=0.02). In chronic phase, CRP correlated with VAS of pain (r=0.47, p=0.02) and there was a reversal in the correlations between ESR and WAS of general health of the patient (r=0.54, p=0.03), VAS of physician (r=0.52, p=0.02), swollen joints (r=0.46, p=0.03) and HAQ (r=0.56, p=0.01). ESR and SF-12 (mental component) were correlated (r=0.61, p=0.01).

Conclusions: Levels of ESR correlated with measures of pain and worsening of functional capacity in subacute phase. In chronic phase, there was reversal of this correlation, indicating that ESR does not reflect clinical worsening of patients at this stage. Further clinical studies are needed to better analyze other alterations.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5599
References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4687

AB0906 PYOGENIC SEPTIC ARTHRITIS: IS THERE A DIFFERENCE WHEN GERM IS NOT IDENTIFIED?

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Background: Pyogenic septic arthritis (PSA), defined by the presence of living microorganisms and a synovial fluid of purulent character, is a therapeutic emergency. Germ isolation is a primordial step in the diagnostic and therapeutic approach.

Objectives: The aim of this study was to study the differences between PSA with positive and negative bacteriology.

Methods: This is a retrospective study which included medical records of patients treated for PSA in a rheumatology department over seventeen years. The epidemiological and paraclinical data were recorded. We used the SPSS 11.5 for the statistical analysis to compare patients with (group 1) and without an isolated causative agent (group 2).

Results: We evaluated 49 patients with a diagnosis of PSA. They were 26 (53.1%) men and 23 (46.9%) women. The average age was 55±18.7 years (ranging from 15 to 95 years). Comorbidities were observed in 31 (63.3%) patients. The onset of symptoms was acute in 37 (75.5%) patients and progressive in 12 (24.5%) patients. The most common symptoms were joint pain and stiffness (100%) and functional impotence (87.8%). All patients were treated with double or triple antibiotics. Among the studied patients, 27 (55.1%) had negative culture results. Statistic analysis used to compare cases with an isolated pathogen to those cases without an isolated pathogen, noted female predominance in group 2 but there was no statistically significant difference (p=0.252). Patients in group 1 and group 2 had a comparable mean age (p=0.08). Patients in both groups had comparable risk factors for PSA (p=0.549). Acute onset was more common in group 2 (51.4% versus 48.6%) but without a significant difference (p=0.507). Biological inflammatory syndrome was more frequent in group 2 but with no statistically significant difference (p=0.235). The study of the appearance of the synovial fluid did not indicate a statistically significant difference between the two groups (p=0.125). The abnormalities of standard x-rays were similar in both groups (45.2% in group 1 versus 54.8% in group 2, (p=1)). The statistical study of all other variables didn’t show differences between the two groups.

Conclusions: PSA was not associated with major differences if the germ was or was not isolated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6187

AB0907 CONTRIBUTION OF IMAGING IN THE DIAGNOSIS OF INFECTIOUS SPONDYLODISCITIS

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Background: Infectious spondylodiscitis represents a diagnostic and therapeutic emergency. Imaging is fundamental in the management of the disease.

Objectives: The aim of this study is to analyze the contribution of imaging in the diagnosis of infectious spondylodiscitis.

Methods: This is a retrospective study which included medical records of patients treated for psoas abscess during the twelve past years [2006–2016]. Epidemiologic, clinical, and imaging data (Standard X ray, Computed tomography (CT), magnetic resonance imaging (MRI)) were recorded and analysed.

Results: Ninety patients were included in this study. The average age was 55 years [16–86] with an even distribution between males and females. Mean symptom duration was 4 months. The most frequently isolated pathogen was Mycobacterium tuberculosis (83.3%), followed by pyogenic germs (21.2%) and Brucella (15.5%). Standard X ray were pathological in 89% of cases: showed narrowing of intervertebral space (72.2%), endplate destruction (42.2%), erosions of vertebra (13.3%), opacity (12.2%), vertebral fracture (10%), paravertebral spinal (5.2%) and posterior arch lesion (2.2%). Standard radiographs were normal in 12 cases and in 1 case, spinal CT showed vertebral destruction with “mirror image”. Spinal MRI, performed in the remaining 11 cases, confirmed the diagnosis in all cases and showed paravertebral collections (n=3), epiduritis (n=3), psoas abscess (n=2), microabscess (n=1) and spinal compression (n=1). In case of posterior arch lesion and vertebral fracture, MRI confirmed the diagnosis by showing paravertebral collections.

Conclusions: Management of infectious spondylodiscitis has benefited from advancements in imaging allowing an early diagnosis and treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2770

AB0908 BIOLOGICAL AND RADIOGRAPHIC FINDINGS IMPACT ON GERM IDENTIFICATION DURING SEPTIC ARTHRITIS

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Background: Septic arthritis may cause damage and inflammation in short period of time. The germ determination must be the first objective to allow targeted treatment. Bacteriologic tests remain negative in 7–35% of cases of septic arthritis.

Objectives: The aim of this study was to determine the impact of biological and radiographic findings on germ identification during septic arthritis.

Methods: This was a retrospective study which included medical records of patients treated for septic arthritis during the last seventeen years. Epidemiologic, biologic, bacteriologic and therapeutic data were recorded and analysed. We made a comparison between patients who had a germ identified (Group 1) with whom who hadn’t (Group 2).

Results: Fifty nine patients with septic arthritis were included in this study. The average age of the patients was 54.6±19 years and a sex ratio (F/M) of 0.9. Causative agents were isolated in 27 patients (45.7%). Biological data showed leukocytosis in 25 (42.4%) patients. Mean leucocyte count was 10673±5003. Leukopenia was noted in 1 case. One patient had neutropenia. Lymphopenia was observed in 4 patients (6.7%). Two patients had hyperlymphocytosis. Anemia, mainly of the inflammatory type, was noted in 47 cases (79.6%). The mean Creative protein (CRP) was 150.±16106, and the mean erythrocyte sedimentation rate (ESR) was 104.9. Twenty three patients (38.9%) had other perturbations of the biological balance: cholesterol (n=1), cytolysis (n=4) and renal perturbation (n=1). Radiological signs suggestive of septic arthritis were observed in 40 cases (67.8%): articular pinching (28.8%), geodes and erosions (14%), total destruction of the joint (0.76%) or thickening 1 the soft parts at the beginning (11.8%). Ultrasound exam, performed in 22 cases, showed articular effusion (n=15), synovial thickening (n=8), a soft tissue collection (n=3), and periartricular erosion (n=2). CT, performed in 6 patients, was normal in all cases but 1. No abnormalities were noted: collection of soft parts (n=2), joint effusion (n=2), bone demineralization (n=1), bone erosion (n=1) and osteochondritis (n=1). MRI, performed in 2 patients, was pathologic in both cases and showed synovitis and cortical erosion with medullary edema. The comparison of the 2 groups according to germ identification showed that biological inflammatory syndrome was more frequent in group 2 (100% versus 96.8%) but without a statistically significant difference (p=0.346). Mean value of CRP and ESR were comparable in the two groups (p=0.65 and 0.19). The mean value of hemoglobin was comparable in the two groups (10.87 versus 9.64 g/dl) (p=0.566). It was similar about the blood count. Abnormalities of standard x-rays were similar in both groups (70.4% in group 1 versus 65.5% in group 2) (p=0.784). The most frequent radiological abnormality in the two groups was articular pinching (40.7% in group 1 and 46.8% in group 2).

Conclusions: In our study, the biological and radiological data had not shown any impact on the identification of the germ.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3835

AB0909 SEPTIC PSEUDARTHROSIS OF THE HUMERUS TREATMENT USING ORTHFIX EXTERNAL FIXATION

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Background: The septic pseudarthrosis of the humerus is a very difficult process that poses a twofold challenge: the infection eradication while trying to get consolidation.

Objectives: The aim of this study was to analyze the results of the treatment of septic pseudarthrosis of the humerus with Orthofix monolateral axial external fixator.

Methods: This is a retrospective study which included 17 medical records of patients treated for septic pseudarthrosis of the humerus during and stabilization by Orthofix over a period of 7 years.

Results: They were 13 women and 4 men with a mean age 44 years. The fracture site was most often at the distal half of the humerus. The initial treatment of the fracture was pinning or intramedullar nailing. Surgical management of pseudarthrosis was performed 3.5 months after the first surgical procedure. All cases had a bone debridement and stabilization with a monoplane Orthofix axial external fixator. Fifteen cases were performed bone graft. The mean period of stabilization was 7months. Patients were evaluated clinically and radiologically each month. At the mean of three years of follow-up, we obtain osseous consolidation for all patients in the average of seven months. All patients underwent rehabilitation of the shoulder and elbow after treatment. The functional result were excellent results for 42.9% of cases, good results for 35.3% and poor results in 21.7%. The Quick DASH score average was 28.5. The average of the elbow motion was 109 ° of flexion with an average of 30 ° of deficit in extension. The useful range of motion of the elbow was preserved in 14 patients. There was a shaft angulation under 20 ° in 3 cases and over 20 ° in 3 other cases. We noted
in four cases a bone shortening consolidations of 2 cm. We had a case of radial nerve neuroparesis which regressed spontaneously.

**Conclusions:** Orthosix is the method of choice for the treatment of the septic pseudarthrosis of the humerus.

> Associate eradication of the germ antibiotic and steroid intake sponges it allows to maintain the member. Furthermore, the monolateral axial fixator is tolerated well and allows movement of the shoulder and elbow throughout the period of treatment.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3852

**AB0910 INFECTION SPONDYLODISCITIS IN THE SANITARY AREA OF TORREALEGA BETWEEN 2000 AND 62 CASES**

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**Objectives:** To analyze the clinical characteristics, most frequent diagnostic methods and different treatments used in spondylodiscitis (SD) in our sanitary area.

**Methods:** Descriptive and retrospective study of patients with the diagnosis of infectious SD (clinical or microbiological) from 2000 to 2016. In each case we studied the presence of underlying diseases, an episode of infection in the previous 6 months, way of presentation, location, diagnostic methods, treatment and evolution, comparing among different etiologies.

**Results:** 62 patients were diagnosed of spondylodiscitis. 41 men (24–90 years: mean 71.7), 56 were pyogenic, 3 tuberculosis (TBC) SD, and 1 candida. The patients of TBC were younger (mean age, 45.5 ± 0.05). An underlying disease was observed in 51 patients, specially Diabetes Mellitus (DM) (31%) of SD. 4 patients were Rheumatoid Arthritis patients. A previous episode of bacteremia or a primary source of infection was identified in a 35% of the cases, obtaining a microbiological isolation in 135 (79.5%) SD (43 bacterial, 3 TBC and 1 Candida). The most frequent presentation symptoms were: lumbar pain (95.1%), fever (50%) and neurological deficit (18%). Leucocytosis was present in only a third (33.8%). In the 94% of SD caused by G+, hemocultures positive were obtained, in comparison to a 55% of SD caused by G (p = 0.016).

The most frequent presentation symptoms were: lumbar pain (95.1%), fever (50%) and neurological deficit (18%). Leucocytosis was present in only a third (33.8%). In the 94% of SD caused by G+, hemocultures positive were obtained, in comparison to a 55% of SD caused by G (p = 0.016).

**Conclusions:**

- The majority of the patients had pain in the presentation, but only half of them had associated fever.
- The most frequent location of SD was lumbar.
- We established a 8% of mortality rate in our sanitary area.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5891

**AB0912 ASSESSMENT OF CLINICAL AND RADIOLOGICAL PROGNOSTIC VARIABLES IN PATIENTS WITH SPONDYLODISCITIS**

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**Background:** Spondylodiscitis is an infectious disease of the intervertebral space, often caused by hematological spreading from a distance septic focus, especially Endocarditis. Because of its low incidence combined with an ambiguous symptoms, delay diagnosis and treatment of this condition, raising probability of an undiagnosed outcome.

**Objectives:** To identify poor prognosis variables in patients with Spondylodiscitis

**Methods:** Observational retrospective study with non-naive population. Patients from 2010 to 2016 was performed. Demographic information, clinical history, laboratory test and radiological data were compiled from the clinical history management software. Statistical analysis was performed with the software R (version 3.4.2).

**Results:** We included 55 patients, with a mean age of 63.47 (16.11) years old. Males predominated (69%). The average time with axial pain was 64.44 (80.63) days. Mean length of hospital stay was 64.44 (80.63) days and readmission rate was 32.7%. 20% of patients required further surgical procedures. Most of patients showed high CRP levels in the first 48 hours and an average value of 112.97 (83.64) mg/L. Underlying endocarditis proportion was 16.4% and in this patients hospital stay was significative higher; nevertheless, it was not correlated with worse prognosis. 50% of patients showed vertebral destruction on MRI; 14.8% cord compression and 20.4% of patients developed neurological complications (7 of them paraparesia). Furthermore, vertebral destruction was statistically correlated with epidural abscess (P = 0.026). Isolation and microbiological identification in blood cultures was possible in 83.6% of patients. Most frequent bacteria was Gram positive (50.09%), then Gram negative (18.2%), mycobacteria (10.3%) and fungi (3.6%).

**Conclusions:** Delay in diagnosis is an important issue in Spondylodiscitis patients. Higher complications rates are mainly in relation to greater vertebral destruction. Underlying infectious endocarditis was described in a small proportion of patients in contrast to other studies. Presence of epidural abscess was also correlated with vertebral destruction, for this reason, patients with this finding should be more carefully follow-up.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5891

The results of the laboratory and the clinical findings are given in table:

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F. Females, M. Male, AI: Aortic valve insufficiency, MI: Mitral valve insufficiency, MS: Mitral valve stenosis, TI: Tricuspid valve insufficiency.
AGREEMENT STUDY AND EXPERT CONSENSUS FOR THE CLINICAL PICTURE OF CHIKV INFECTION

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Background: World Health Organization suggested case definitions to suspect and diagnose chikungunya virus infection which are: possible case, probable case and confirmed case. Although useful, when applied in practice, its lack definition for specific joint involvement and absence of other systemic symptoms apart from fever, leads to a broad clinical spectrum which increases the need for laboratory tests.

Objectives: To establish agreement on clinical criteria of CHIKV infection based on clinical expertise of specialists from affected areas of Colombia and to develop a set of clinical criteria.

Methods: A group of specialists in rheumatology, epidemiology and bacteriology from different parts of Colombia with experience in diagnosis and treatment of CHIKV patients from the epidemic of 2014–2015 met to reach agreements on clinical characteristics of CHIKV infection. A series of questions were formulated and agreement in percentage was calculated on the following answers: totally agree, not in agree or disagree, disagree and totally disagree. Agreement was set when the sum to the answers totally agree and agree or disagree and totally disagree of was ≥50%. When agreement was not reached, the moderator performed a discussion with the opinions of the confronting members of the group and after that reformulated the question. This procedure was made until agreement was reached. With the results a set of clinical criteria was proposed.

Results: The agreement percentage to the formulated questions are depicted in table 1. Disagreement was achieved with mucosal involvement (100%), G/I involvement (88%), and arthralgia and arthritis in shoulders (63% and 100%) and elbows (100%).

Conclusions: Agreement was achieved in abrupt onset of symptoms, and the presence of fever, rash, myalgia, fatigue, and symmetrical arthritis or arthralgia of wrists, hands, knees, ankles and feet. A set of clinical criteria was proposed (figure 1).

Disclosure of Interest: None declared


CUTANEOUS LEISHMANIASIS IN PATIENTS TREATED WITH BIOLOGICAL THERAPY

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Background: Leishmaniasis is a chronic protozoon disease endemic in several areas of the world. In the Mediterranean basin cutaneous leishmaniasis is caused by Leishmania infantum and usually produces localized skin lesions. Biological therapy (BT) may increase the risk of reactivation or development of infections such as tuberculosis, mycoses and protozoan diseases. However, there is scarce literature on Leishmania infections in patients treated with anti-TNF drugs. We have diagnosed five cases of cutaneous leishmaniasis in patients treated with anti-TNF drugs in the last four years.

Objectives: To show the clinical characteristics and the evolution of cutaneous leishmaniasis in patients treated with BT at a tertiary level hospital.

Methods: We reviewed the clinical characteristics, previous treatments, the complementary tests used for the diagnosis, the main disease, the therapy used for the treatment of the infection, the clinical evolution and the reintroduction of the treatment.

Results: In the last four years we have diagnosed five cases of cutaneous leishmaniasis in patients treated with BT. Four of them were men and one a woman, the age range was 35 to 61 years old. In four of them the symptoms were only cutaneous, but one of them also had systemic impairment, basically hepatosplenomegaly. For the diagnosis skin biopsy, positive PCR for Leishmania DNA from skin samples, serology and response to treatment were all needed. Three cases were patients treated with adalimumab and two treated with infliximab. Three patients had Crohn's disease, one psoriatic arthritis and the other ankylosing spondylitis. The diagnostic delay was between 5 and 24 months. All patients were treated with EV liposomal amphotericin B, and two of them also received intralereal injections of meglumine antimoniate. In all cases resolution was achieved, and there have been no relapses to date after reintroduction of BT.

Conclusions: We have to consider cutaneous leishmaniasis in patients with BT who present compatible skin lesions, especially in endemic areas. It is important to be aware of this type of condition in order to make a fast and accurate diagnosis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4259
FREQUENT CONVERSION AND REVERSE CONVERSION OF TUBERCULIN SKIN TEST BUT NOT OF AN INTERFERON GAMMA RELEASE ASSAY (T-SPOT.TB) DURING LONG TERM BIOLOGIC TREATMENT OF RHEUMATIC PATIENTS

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Background: There are limited data regarding the value of tuberculin (TB) rescreening in rheumatic patients on biologic (bDMARD) therapies who had a negative baseline TB screening.

Objectives: To examine the rates of conversion and reverse conversion at repeated TB screening testing with 2 available assays (tuberculin skin testing-TST and an interferon gamma release assay-IGRA: T-SPOT.TB) in rheumatic patients with negative baseline screening during long term bDMARD treatment.

Methods: Rheumatic patients with negative baseline screening (TST and T-SPOT.TB) were re-screened one year after TNF inhibitor (TNFi) therapy (1st rescreening) and ~6 years later on bDMARDs (2nd rescreening). The rate of conversion and reverse conversions of the 2 assays were recorded. Only patients who did not receive isoniazid (INH) therapy between the 1st and 2nd rescreening were analyzed.

Results: Among 70 patients with negative TB baseline screening, 21 patients with 2 re-screenings were identified; one patient with TST conversion at the 1st rescreening who converted back to negative at the 2nd rescreening after INH treatment, was excluded from the study. 20 patients were finally included in the study (RA-7, PsA-6, AS-5, other diseases=2). 50% were women with a mean age of 57±12.4 years and mean disease duration at the last screening of 13.1±6.2 years. The mean interval between the 1st and 2nd rescreening was 68.6±13 months. At the last evaluation, 90% (18/20) were still on bDMARDs (TNFi=55%, non-TNFi=45%), 45% (9/20) on non-biologic DMARDs and only one patient (5%) on corticosteroids. None of the patients displayed conversion or reverse conversion with TST rescreening compared to 6 (30%) with TST at the 2 rescreenings (p=0.02). At the 1st rescreening, 4/20 (25%) had converted their TST to positive; at the 2nd rescreening, 2 reverted back to negative (1 patient with PsA on etanercept and 1 with RA on steroids, methotrexate and golimumab) while the other 2 remained TST positive (1 with PsA on etanercept and 1 with Still's disease exposed to etanercept, tocilizumab and canakinumab). Among the 16 patients who remained TST negative and T-SPOT.TB negative at the 1st rescreening, 2 (12.5%) became TST positive at the 2nd rescreening (12 mm and 7 mm, respectively). Both patients were on long term infliximab treatment without history of TB exposure. After thorough evaluation, no evidence of active TB infection was found in any of the 6 patients who converted TST either in the 1st or 2nd rescreening.

Conclusions: Among rheumatic patients with negative baseline TB screening, conversion or reverse conversions were much more frequent with TST compared to an IGR (T-SPOT.TB) at repeat testings during long term bDMARD therapy. These preliminary findings need to be taken into account while designing the appropriate repeat TB screening strategy for this group of patients.

Acknowledgements: Supported by research grants from the Special Account for Research Grants (S.A.R.G.), National and Kapodistrian University of Athens, Athens, Greece.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4582

WHIPPLE DISEASE: A RARE DISEASE DIFFICULT TO DIAGNOSE

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Background: Whipple disease is a very rare disease needing a long term treatment. The most frequent symptoms are recurrent arthralgia or arthritis, chronic diarrhoea, abdominal pain and weight loss.

Objectives: In this work, we have highlighted the main clinical features and diagnostic procedures that lead to the diagnosis and comment on the clinical response, treatment, and the factors of relapse.

Methods: Subjects were recruited from the Internal Medicine and Rheumatologic Departments of an University Hospital from November 1997 to January 2016. Overall, 12 subjects were finally diagnosed.

Results: Mean age was 54.3 years (age range: 30–81), with more male patients (58.3%). Almost all patients had articular symptoms and impaired general condition (91.7%); and a majority had digestive symptoms (75%). Regardless of the symptoms, the most efficient diagnostic tools were the PCR screening on the gastrointestinal biopsies and saliva (83.3% and 72.7% positive results, respectively). More than half of the patients relapsed (55.6%). The relapsing patients were older (63.2 (44–81)) and mostly male with a majority (60%) of digestive symptoms and a delayed diagnosis.

Conclusions: In current practice, it is very difficult to diagnose Whipple disease. In order to decrease the delay between the first symptoms and the diagnosis, effective tools such as saliva and stools PCR should be used since higher delays of diagnosis lead to a higher number of relapses.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6975
AB0918 REACTIVE ARTHRITIS POST VIRAL – AN UNUSUAL PRESENTATION IN AN EPIDEMIC IN NORTH INDIA
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Background: This study was performed at a Private hospital in New Delhi, India during the epidemic phase of Viral fever. The peak months of viral fever from mosquitoes (Aedes Aegypti) like Dengue and Malaria (Anopheles) has been from July to October, till the holy festival of Diwali arrives. Chikungunya came like a wave this time along with dengue and Malaria. The worst epidemic since the last 6 years. A disease common in South India, took North India by a storm. 15–20 deaths were also reported due to Chikungunya virus. Apart from Chikungunya (serology negative) there were a lot of other viruses causing arthritis. Our study deals with post viral arthritis, a new variant which has never been described before.

Objectives: 1. To study the pattern of arthritis after viral fever. Is it reactive or a new variant
2. To observe for the evolution of Acute viral arthritis into chronic arthritis
3. The management of Post viral arthritis

Methods: It is a retrospective study conducted at the end of the epidemic. The patients are being followed up for next 3 months to observe for resolution of symptoms, persistent arthritis or evolution into chronic form. 100 patients are being included which were examined and independently assessed by 3 different consultants.

Inclusion criteria: 1. All patients who presented with complaints of persistent joint pains and swelling preceded by fever (Average duration 4–8 weeks). 2. Documented synovitis (Oligoarticular and polyarticular)

Exclusion criteria: 1. Known case of Rheumatoid Arthritis, Connective tissue disease, Vasculitis and Spondyloarthopathy. 2. Arthralgia with no documented synovitis. 3. Patients on DMARDS previously.

Results: Detailed results are still under compilation as patients are under follow up (6 months) for further course.

No of patients: 100
Average Age: 47
Average Disease Duration: 6 weeks (after fever)
Average No of Joints involved: 3–4
Symmetry: All Asymmetrical (Large+ Small)
80% patients had asymmetrical joint involvement. Most common joints were: MCP followed by PIP and then the large joints: shoulders and ankles. It was associated with significant early morning stiffness (30 minutes) like other inflammatory arthritis. 60% had response to short course of NSAIDS and low dose steroids (Injection Depomedrol 80 mg intramuscular once a week) and recovered in 2 weeks, 30% had a prolonged course of 4–6 weeks, but did not need any further medications. 5% developed into Chronic arthritis (Further follow up pending)

Conclusions: Reactive arthritis is a known entity and it has typical involvement of the lower limbs, usually preceded by urinary tract infection or GI infection. Even with Viral arthritis, the presentation of joint pains and swelling is usually during the acute fever episode. The pattern described here was different. All the patients had fever at presentation which lasted for 3–5 days and 4–6 weeks later they developed synovitis. There was characteristic involvement of Small joints of the hands (PIP and MCPS) (different from reactive).We are still in process of collecting follow up data which will give us a clue on prognosis of this arthritis and future prospects. So, what do we label it as ... Reactive arthritis-a new variant or a post viral arthritis.

References:

Disclosure of Interest: None declared

AB0920 TUBERCULOSIS OSTEOARTHRITIS OF THE PUBIC SYMPHYSIS: REPORT OF TWO CASES
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Background: Infection of the symphysis pubis is a rare complication for less than 1% of cases of osteoarthritis. The predisposing causes reported are pelvic surgery, trauma and intravenous drug abuse. We report cases of osteoarthritis of the pubic symphysis due to mycobacterium tuberculosis which is extremely rare.

Results: The two patients were 47 and 75 year-old women. They were admitted because of three month’s history of progressive perineal pain and a hypogastric mass without fever in the first case, and bilateral inguinal pain with limited flexion and rotation of the right hip in the second one. Blood tests showed an elevated erythrocyte sedimentation rate (ESR) of 27 mm and 75 mm. The leucocytes rates were at 5580/mm³ and 6000/mm³. Plain X-ray revealed irregularity and widening of the symphysis pubis. Tuberculin skin test was positive in one case and negative in the other. Chest radiograph was normal. The bacteriological cultures for tubercule bacillus in sputum and urines negative. The typhic and brucellian serological diagnosis as well as blood cultures were negative. CT scan showed irregular destruction and erosion of the pubic bone with a soft tissue mass. A biopsy of the symphysis was performed. Histologic examination of the bone material revealed a granulomatous inflammation with caseous necrosis confirming the diagnosis of tuberculosis. Anti-tuberculous treatment was prescribed and led to recovery.

Conclusions: Tuberculosis is a major health problem in Mediterranean countries, including Tunisia. These two cases present a timely reminder that tuberculosis should always be considered as part of the differential diagnosis of treatment of tuberculosis osteoartthritis of the pubic symphysis. Radiological investigations with plain X-rays, CT, MRI and bone scan are helpful. Treatment of tuberculosis osteoarthritis of the pubic symphysis is based mainly on anti-tuberculous drugs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6940

AB0921 INFECTIOUS SPONDYLODICTYSIS: EPIDEMIOLOGICAL, CLINICAL, PARACLINICAL AND THERAPEUTIC ASPECTS
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Background: Spondylodictysis is an infection of a disc and the two adjacent vertebrae due to the introduction of a pyogenic, usually by the haematogenous route. It’s quite a rare disease accounting for 2–7% of all cases of septic osteoarthritides [1, 2].

Objectives: To study the clinical, microbiological, radiological, therapeutic and evolving of infectious spondylodictysis

Methods: A retrospective descriptive study conducted over years in the department of rheumatology, including all patients with infectious spondylodictysis. Clinical given were collected from paper patients records.

Results: We included 67 patients. There were 38 men and 29 women. The mean age was 55 years. The male to female ratio was 38:29. Risk factors of spondylodictysis were observed in 19 patients. The approximate time from onset of symptoms to diagnosis was from 3 to 365 days (median, 132 days). Back pain was the most common symptom. Spinal syndrome was found in all patients. The most frequent location of spondylodictysis was lumbar spine. Signs of spinal cord compression including paraplegia or paraparesis of the lower limbs were observed in 31 patients. Pachymeningitis was associated in 1
case. The paravertebral abscesses were associated to the disc involvement in 23 cases. Epiduritis was associated in 21 cases. Plain radiography, performed in the majority of cases (83 cases, 94%), demonstrated pathologic pictures in 56 (83.5%) patients. MRI, performed in 60 (89.5%) patients, disease was in all patients. Pathogens were isolated in 43 (64.1%) cases. Tuberculosis was the most common cause. The leading causative agents in non tuberculous spondylodiscitis were: Staphylococcus aureus (8 isolates, 11.9%), brucella (7 isolates, 10.4%), Escherichia coli (2 isolates, 2.9%) and streptococcus B (1 isolates, 1.4%). Two microorganisms combined (mycobacterium tuberculosis and a pyogenic) was found in one case. Medical treatment was adapted to the prescribed seed. Surgical treatment was performed in 6 patients. After therapy, 59 (98%) patients had regression of symptoms, two patients had a permanent neurological impairment (paraplegia), one patient had recurrence of infection and one patient was dead.

Conclusions: Infectious spondylodiscitis has been diagnosed with increasing frequency. It should be taken into consideration in differential diagnosis in patients with significant back pain and laboratory evidence of an acute inflammatory process, especially metastatic spinal disease or inflammatory spondylodiscitis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6916

AB0922 CLINICAL MANIFESTATIONS AND OUTCOMES OF ACUTE SEPTIC ARTHRITIS IN SONGKLANAGARIND HOSPITAL: A 10-YEAR RETROSPECTIVE STUDY

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Background: Septic arthritis is a rheumatologic emergency. Its delayed diagnosis and treatment cause joint morbidity and mortality. Cases involving antimicrobial-resistant bacteria have been reported.2,3

Objectives: To determine the clinical manifestations and outcomes of septic arthritis, find the factors associated with mortality, and discover the incidence of drug-resistant organisms in our institution

Methods: A retrospective study was performed. Septic arthritis was defined as the presence of acute inflammatory arthritis indicated by a positive synovial fluid or synovial tissue culture for bacteria. A total of 116 septic arthritis patients, who visited Songklanagarind Hospital from January 2005 to December 2014, were reviewed.

Results: The patient median age was 58 (IQR: 46, 72). Sixty-one patients (52%) were female. The median onset of symptoms and symptoms until diagnosis were 5 (IQR: 2, 7) and 6 (IQR: 3, 10) days, respectively. Eighty-eight cases (76.7%) had underlying diseases that might predispose to joint infection. Sixty-nine cases (59.5%) had pre-existing joint disease. Joint pain was the most common presenting symptom, and 58% of the cases had fever. The most common presentation was monoarthritis (87%), which was predominantly associated (78%) with knee joint involvement. The median synovial fluid leukocyte counts were 64,460 cells/L (IQR: 30,300; 129,000). Blood cultures were positive in 53 patients (49.1%). Synovial fluid cultures commonly had Streptococcus spp. growth (41%). Seven cases (7%) involved drug-resistant organisms. All of them were either diagnosed with septic arthritis during hospitalization or had a history of previous surgery. Twenty-five percent of the cases obtained the empirical antibiotic, ceftriaxone, and 86 patients (80%) underwent arthroscopy drainage. The mortality rate was 12%, and its associated factors were cancer, liver disease and advanced age.

Conclusions: Streptococcus spp. is an emerging cause of septic arthritis in Southern Thai patients. Physicians should be aware of this in patients presenting with fever and acute monoarthritis, particularly those with comorbidities and underlying joint diseases. The proper empirical antibiotic of choice is ceftriaxone.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4310

AB0924 THE ROLE OF SELF LIMITING BEHAVIOUR, DEPRESSION AND SLEEP IN THE SEVERITY OF FATIGUE IN PATIENTS WITH FIBROMYALGIA

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Background: Fatigue and sleep disturbances are prominent symptoms in Fibromyalgia (FM) and significantly affect the level of the patients’ impairment. Some studies reported a synergic interaction of depression and poor sleep quality associated with fatigue (e.g. [1]): while Marques et al. [2] showed a significant association of the fatigue severity with a limiting behaviour self-regulatory style of the patients, i.e. reducing daily activities and excessive resting.

Objectives: The purpose of this cross-sectional study was to analyse the predictors of severity of fatigue in Italian patients with FM.

Methods: Outpatients with a FM diagnosis who fulfilled both ACR/EULAR 1990 and 2010 criteria [3,4], after a medical visit at the Fibromyalgia center at Sapienza University Hospital “Umberto I”, were invited to participate in a study on their cognitions and behaviours where during one week a wrist actigraph (AMTI MotionLogger Watch). Actigraphic sleep parameters were averaged over six days. After 7 days the participants returned the actigraph and answered a structured interview conducted by a trained psychologist which included validated scales measuring depression (Brief Symptom Inventory [5]), perceived fatigue (Checklist of Individual Strength [6]), sleep habits (Sleep Disorder Questionnaire [7]) and behaviour regulation patterns (All-or-nothing and Limiting behaviour scales from Behavioural Responses to Illness Questionnaire [8]. In the previous month and during the study, pharmacological and non-pharmacological treatments were unchanged.

Results: Actigraphic monitoring and structured interview were completed by 39 female FM patients, with a mean age of 44.9 years (SD=8.55) and an illness mean duration of 6.5 years (SD=5.72). The majority of the patients reported insomnia complaints (80.5%) and 29 (74.4%) met the DSM criteria for chronic insomnia. Fatigue severity resulted as the best subjective measure of fatigue, and was positively and significantly correlated with self-management through limiting behaviour, and with Total Time in Bed (TTB) measured through actigraphy. The correlation between TTB and Total Time Slept (TTS) and depression were not significant. Hierarchical regression considering TTB, Depression and Limiting behaviour, showed that all these variables give a significant independent contribution to the prediction

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1737

Fibromyalgia

AB0925 MEETING THE FIBROMYALGIA CRITERIA HAS A NEGATIVE IMPACT ON TNF INHIBITORS EFFICACY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Fibromyalgia and spondyloarthritis can coexist and the overlap between the two diseases could have consequences on TNF inhibitors efficacy.

Objectives: To evaluate TNF inhibitors efficacy in patients with axial spondyloarthritis fulfilling or not fibromyalgia criteria.

Methods: Prospective observational bicentric study on 25 patients who met ASAS 2009 axial spondyloarthritis criteria. Fibromyalgia was defined by ACR 2010 fibromyalgia criteria or by a ≥5/6 score of the Fibromyalgia Rapid Screening Tool. Following items were recorded before and after a 6 months treatment with TNF inhibitors: Visual Analog Scale for pain and for patient global disease activity, values of ESR and CRP, number of tender joints. NASSE score, number of Yenus tender points. All patients filled a self-questionnaire with BASDAI, BASFI, FIRST and ACR 2010 fibromyalgia scale items using SSS and WPI. Criterion of judgment: an ASAS partial remission state was compared in patients with or without fibromyalgia.

Results: Of the 25 patients enrolled, 15 (60%) fulfilled ACR 2010 fibromyalgia criteria and 9 (36%) had a ≥5/6 FIRST score. The proportion of patients fulfilling an ASAS partial remission state was significantly lower in patients with fibromyalgia according to the ACR 2010 criteria (20% vs 70%, p=0.034) or to the FIRST score (0% vs 62.5%, p=0.002). These patients had more severe disease activity and physical function than the patients without fibromyalgia. In this study, some factors were related with absence of ASAS partial remission: female gender, prior TNF inhibitor failure, ACR 2010 fibromyalgia criteria positivity, to have more than 11 Yenus points and to have a ≥5/6 FIRST score.

Conclusions: Meeting the fibromyalgia criteria might have an impact on ASAS partial remission state and on efficacy of TNF inhibitors in patients with axial spondyloarthritis. The FIRST score was more specific to predict an absence of ASAS partial remission than the ACR 2010 fibromyalgia criteria. TNF inhibitors should be used with circumspection in case of FIRST score ≥5/6 in patients with axial spondyloarthritis.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4310
GENDER DIFFERENCE IN FIBROMYALGIA: COMPARISON BETWEEN MALE AND FEMALE PATIENTS FROM AN ITALIAN MONOCLINICAL COHORT

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Background: Fibromyalgia (FM) is one of the main causes of chronic widespread pain (CWP). It is characterized by CWP, which is the cardinal symptom, and the presence of more than 11 tender points (hyperalgesia). [1] Other symptoms such as fatigue, sleep disturbances, difficulties with memory and concentration, irritable bowel syndrome, headache, depression are frequent. Worldwide mean prevalence of FM is 2.7% with female/male ratio of 4:1. In Italy the prevalence is 3.7% with the same female/male ratio. [2]

Objectives: The aim of the study is to analyze clinical features of a cohort of male patients with CWP and to evaluate gender differences in patients diagnosed as FM.

Methods: The study population consisted of 101 consecutive male subjects referred to the Clinic for the Diagnosis and Therapy of Fibromyalgia, in the period between January 2007 and October 2016, matched with a control group of 101 females with CWP referred to the clinic in the same period. Complete clinical evaluation was performed in all patients.

Results: Ninety-seven male subjects (96%) were referred to the clinic for a history of musculoskeletal pain, among these 53% reported fatigue and 60% complained about sleep disorders. A stressful trigger (work or family problems, bereavement, infections) at the onset of pain was reported by 42% of patients. Fifty-two percent of patients reported mood changes. Physical examination showed hyperalgesia in 15% of the subjects and a mean tender points’ (TP) count was 4.6 (range 0–18). The diagnosis of FM was performed according to ACR 1990 criteria, since the enrollment included patients referred to the clinic before the publication of the latest ACR criteria [3, 4]. Only 18 male subjects (18%) fulfilled the classifying criteria. In the female group CWP was reported by 97%, fatigue by 65%, and sleep disorders by 72% of patients. Stressful events were reported by the 50% of female population. Mood changes were described by 54% of female subjects and were predominantly depressive. Physical examination revealed hyperalgesia in 48 subjects (47%) and the mean TP count was 11 (range 0–18). The diagnosis of FM was confirmed in 60% of subjects. Comparing the two cohorts of patients with FM, mean age at the time of the visit and mean age of onset of symptoms resulted significantly higher in females than in males (p=0.02 and p=0.04 respectively). There was no statistically significant difference in the number of TP, in fatigue, sleep and mood disorders and in the percentage of stressors considered as a trigger for the disease. Hyperalgesia was the only feature more common in females than in males (p=0.03).

Conclusions: The significant higher frequency of hyperalgesia in women suggests a different presentation of CPW, that is the cornerstone of FM, in the two sexes. Moreover, the prevalence of FM was higher in females than in males when 1990 ACR criteria were used. It can be assumed that further gender differences could be showed applying 2010 ACR criteria.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5762

AB0926 AUTONOMIC DYSFUNCTION IN FIBROMYALGIA MAY BE MEDIATED BY HYPERMOBILITY SYNDROME

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Background: Neuropsychiatric symptoms are common in Fibromyalgia (FMS). FMS is associated with dysautonomia, particularly orthostatic intolerance, in which there is a phenomenological overlap with anxiety. FMS and dysautonomia are both associated with joint hypermobility (JHS).

Objectives: To investigate whether signs and symptoms of dysautonomia in FMS are mediated by JHS.

Methods: Eighteen patients with FMS (all female; mean age 41.06 years) and 19 controls (14 female; mean age 46.62 years) were recruited. JHS was assessed by Brighton Criteria. Multi-systemic symptoms suggestive of dysautonomia were quantified using Autonomic Symptoms and Quality of Life Scale (ASQoLS). Neuropsychiatric symptoms were formally quantified including anxiety level (BAI), depressive symptom level (BDI), panic disorder symptom severity (PDSS) and dissociative experiences (DES). All participants underwent autonomic function testing (9 minute tilt table with heart rate (HR) recording).

Results: Statistical comparison between groups was performed using independent samples t test and chi squared as required, correlations were explored using pearson or spearman rho as appropriate. Formal mediation analysis was performed using the method of Baron and Kenny (1), which stipulates that a mediator variable must reduce the statistical relationship between the independent and dependent variable.

Conclusions: FMS patients had significant objective features of dysautonomia including higher baseline HR (p=0.01) and maximal HR during tilt (p=0.02) compared to controls and reported significantly higher autonomic symptom burden (p=0.001). Symptoms correlated with changes in physiology during autonomic challenges in patients (r=0.53, p=0.039), but not controls. Across the study anxiety score correlated with absolute change in pre-tilt and average HR during tilt (r=0.483, p=0.050) and symptoms of dysautonomia (r=0.813, p=0.001). Dysautonomia symptoms correlated with DES (r=0.793, p=0.001), PDSS (r=0.742, p=0.001), interoceptive sensibility (r=-0.627, p=0.007) and BDI (r=0.502, p=0.040). There was a significant association between JHS and FMS (p=0.001), but not generalized joint laxity. Across all participants, dysautonomia symptoms correlated with JHS (r=0.353, p=0.032) and JHS participants reported higher heart rates during autonomic challenge (p=0.002) and greater symptom burden (p=0.001). The significant relationship between autonomic symptoms and maximum HR during tilt was fully mediated by presence of JHS or FM (Figure 1). JHS partially mediated the relationship between FMS and increased anxiety scores and fully mediated the relationship between FMS and maximum HR during tilt (Figure 2).

References:

Acknowledgements: This work was supported by a MRC CRTF to JAE and supported by BSUH NHS Trust NIHR Clinical Research Facility.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5048
Background: Fibromyalgia (FMS) is a chronic health problem characterized by a wide range of physical and psychological symptoms. There are few high-quality instruments to evaluate the participation and social functioning of fibromyalgia patients. Farin et al. designed the Fibromyalgia Participation Questionnaire (FPQ) as an instrument for measuring the participation and social functioning of FMS patients. The original version of FPQ has been demonstrated to have acceptable internal consistency, reliability, and criterion validity.

Objectives: To test reliability and validity of Turkish version of Fibromyalgia Participation Questionnaire (FPQ-T).

Methods: One hundred and eighty-four female fibromyalgia syndrome patients were included in the study. All patients filled FPQ-Turkish (FPQ-T) questionnaire which was obtained by translation from German according to the guideline for the cross-cultural adaptation process. The patients filled the revised Fibromyalgia Impact Questionnaire (FIQ) and reevaluated FPQ-T two hours later. Internal consistency reliability of FPQ-T was assessed by calculating “if item deleted” using Cronbach alpha and “item-total correlation” coefficient for each item of the questionnaire. Consistency of scale scores and correlation of test-retest values were assessed. Test-retest values were compared using Wilcoxon test. Criterion validity was measured using FIQ scales by Spearman’s rho correlation coefficient.

Results: For internal reliability, Cronbach alpha coefficient was calculated as 0.957 for non-working and 0.958 for working patients. Cronbach alpha values of 0.939, 0.871, and 0.914 were obtained for daily, social, and work life, respectively. Correlation coefficients were 0.888 for daily life, 0.859 for social life, and overall 0.901 in non-working group versus 0.896 in working group. Comparison of scores obtained from test-retest measurements showed no significant difference except for Item-3. Correlation of symptom severity score (SSS) and FPQ-T were r=0.390 (p<0.001) for the non-working and working sub-groups, respectively. Construct validity evaluation showed significant correlation between SSS and FPQ-T.

Conclusions: The results of our study showed that FPQ-T is reliable and valid for assessing participation and social functioning in fibromyalgia patients in our society.

References:

Disclosure of Interest: None declared


RELIABILITY AND VALIDITY OF TURKISH VERSION OF FIBROMYALGIA PARTICIPATION QUESTIONNAIRE

A. Mutti, P. Sarzi-Puttini.

Aim of our work was to study the relationship between fatigue, being reported by over 75% of patients. However, the relationship between fatigue and disease duration (p<0.001), SSS score (r=-0.651, p<0.001), PSD score (r=-0.522, p<0.001), and with the total number of somatic symptoms (r=-0.594, p<0.000) (Fig. 1, right panel). Furthermore, for each of the 40 somatic symptoms suggested by 2010 criteria, the presence of the symptoms was associated with higher levels of fatigue (Fig 1, left panel).

Conclusions: The results of our study confirm that fatigue is a prominent feature of fibromyalgia. Higher levels of fatigue reflect higher levels of widespread pain, and a higher burden of somatic symptoms.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6534
CROSS-SECTIONAL ANALYSIS OF THE AUTONOMIC NERVOUS SYSTEM (HEART RATE VARIABILITY): CORRELATIONS WITH PSYCHOLOGICAL DIMENSIONS IN WOMEN WITH FIBROMIALGIA, RHumatoid ARTHRITIS AND HEALTHY WOMEN

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Background: Autonomic nervous system (ANS) dysfunction has been proposed to play a role in the pathophysiology and maintenance of rheumatic diseases, including fibromyalgia (FM) and rheumatoid arthritis (RA). Heart rate variability (HRV) analyses provide a quantitative marker of ANS activity. Some studies suggest an association between reduced HRV parameters and psychological dimensions, namely a negative emotional state. This led us to hypothesize an association between rheumatic diseases and higher sympathetic activity mediated by a negative emotional state.

Objectives: To establish correlates between HRV parameters with rheumatic disease groups and psychological dimensions.

Methods: Sixty women (FM, n=20; RA, n=20; healthy controls (Ct), n=20) completed a self-reported questionnaire addressing demographic characteristics, the Eysenck Personality Questionnaire, the Hospital Anxiety and Depression Scale, and the Beck Depression Inventory-II (BDI-II). HRV analysis was performed by photoplethysmography between 8:00 and 10:00am, after an overnight fast, in a sitting position, for 5 minutes. We obtained the time and frequency-domain indices of HRV, including SDNN (standard deviation of the NN intervals), RMSSD (root-mean square differences of successive R-R intervals), high frequency power (HF), low frequency power (LF) and very low frequency power (VLF). Statistical analyses were performed considering: A) Rheumatic disease groups (FM/RA/Ct), and B) Psychological scores (irrespective of disease group): higher versus lower tertile in the personality questionnaires and score above (depression) versus below 20, in BDI-II. Between-groups comparisons were performed with Kruskal-Wallis test and analysis of covariance (age was adjusted during analyses), as appropriate.

Results: Neuroticism, anxiety and depression scores were significantly higher in FM and RA patients compared with controls (p<0.05). However, no statistically significant difference was observed in HRV parameters between disease groups and psychological dimensions, except for depression. The values of HF power (parasympathetic activity) were lower in the high depression group compared to the low depression group (p<0.05). The ratio of LF/HF was higher among the depression group than the control group (p<0.05).

Conclusions: This study did not find significant differences in the HRV between the three rheumatic disease groups. The results confirm that depression is accompanied by dysfunction of the autonomic nervous system, specifically lower parasympathetic activity. These results suggest that psychological dimensions, namely depression, must be taken into account when evaluating the ANS and its impact in disease pathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5974

PREVALENCE OF TYPE D PERSONALITY IN TURKISH PATIENTS WITH FIBROMYALGIA SYNDROME

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Background: Type D personality is a distressed personality type involving two personality traits, namely negative affectivity and social inhibition, which are described as tendency to experience negative emotions and to inhibit self-expression in social relationships, respectively (1).

Methods: The present study investigated the prevalence of type D personality in Turkish patients with fibromyalgia (FM) and evaluated the association between type D personality and clinical parameters of FM. Although there is adequate number of studies focusing on the relation between FM and psychological conditions such as depression and anxiety; this topic has been rarely addressed in the literature.

Methods: A total of 100 patients with FM fulfilling 1990 American College of Rheumatology (ACR) diagnostic criteria and 50 healthy controls were included. Type D personality was assessed by Type D Scale-14 (DS-14). FM disease severity was determined by Fibromyalgia Impact Questionnaire (FIQ), functional status by Stanford Health Assessment Questionnaire (HAQ), and health-related quality of life (HRQoL) by Nottingham Health Profile (NHP). Severity of pain and fatigue were measured by Visual Analog Scale (VAS).

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5833

Table 1. Markers before and after treatment in all measurement parameters

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Treatment Mean ±SD (min-max)</th>
<th>After Treatment Mean ±SD (min-max)</th>
<th>z</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of tender points</td>
<td>12.0±1.24 (10–15)</td>
<td>7.31±2.26 (2–11)</td>
<td>-3.840</td>
<td>0.000**</td>
</tr>
<tr>
<td>VAS at night</td>
<td>6.8±1.30 (2–9)</td>
<td>0.51±0.64 (0–2)</td>
<td>-3.843</td>
<td>0.000**</td>
</tr>
<tr>
<td>VAS in activity</td>
<td>7.31±1.4 (4–9)</td>
<td>1.1±0.81 (0–2.2)</td>
<td>-3.850</td>
<td>0.000**</td>
</tr>
<tr>
<td>VAS in pain</td>
<td>6.42±1.46 (3–9)</td>
<td>0.49±0.81 (0–2.4)</td>
<td>-3.834</td>
<td>0.000**</td>
</tr>
<tr>
<td>Distance of Tragus-Wall (cm)</td>
<td>12.08±1.95 (9–17)</td>
<td>10.72±1.90 (8.20–15.60)</td>
<td>-3.529</td>
<td>0.000**</td>
</tr>
<tr>
<td>Distance of processus spinosus-Skapula (cm) (R)</td>
<td>10.65±3.03 (6.50–17)</td>
<td>10.26±1.76 (7–15)</td>
<td>-2.007</td>
<td>0.045*</td>
</tr>
<tr>
<td>Distance of processus spinosus-Skapula (cm) (L)</td>
<td>11.21±1.17 (17–17)</td>
<td>10.26±1.76 (7–15)</td>
<td>-2.842</td>
<td>0.044**</td>
</tr>
<tr>
<td>Trunk Lateral Flexion (°) (R)</td>
<td>36.47±3.35 (30–40)</td>
<td>37.03±3.39 (30–40)</td>
<td>-1.821</td>
<td>0.069</td>
</tr>
<tr>
<td>Trunk Lateral Flexion (°) (L)</td>
<td>35.47±3.41 (27–41)</td>
<td>36.68±3.28 (30–40)</td>
<td>-3.534</td>
<td>0.000**</td>
</tr>
<tr>
<td>Distance of hand-floor (cm)</td>
<td>6.86±0.84 (0–17)</td>
<td>5.18±3.92 (0–14)</td>
<td>-3.219</td>
<td>0.011**</td>
</tr>
<tr>
<td>FIQ</td>
<td>56.23±18.74 (19.79–85.58)</td>
<td>46.39±17.99 (19.59–67.98)</td>
<td>-3.724</td>
<td>0.000**</td>
</tr>
<tr>
<td>HAD-A</td>
<td>10.89±3.9 (5–19)</td>
<td>7.03±3.29 (0–9)</td>
<td>-3.632</td>
<td>0.000**</td>
</tr>
<tr>
<td>HAD-D</td>
<td>9.78±3.29 (2–15)</td>
<td>5.05±2.06 (0–9)</td>
<td>-3.849</td>
<td>0.000**</td>
</tr>
<tr>
<td>PSQI</td>
<td>10.52±3.40 (5–15)</td>
<td>3.63±2.47 (0–8)</td>
<td>-3.830</td>
<td>0.000**</td>
</tr>
</tbody>
</table>

Wilcoxon Test, *p<0.05; **p<0.001.VAS: Visual Analog Scale;FIQ: Fibromyalgia Impact Questionnaire; HAD-A: Hospital Anxiety and Depression Anxiety; HAD-D: Hospital Anxiety and Depression Depression; PSQI: Pittsburgh Quality of Sleep Questionnaire Index.
Back pain, mechanical musculoskeletal problems, local soft tissue disorders

**AB0933** PREDICTIVE MODEL FOR SHOULDER PAIN USING CLINICAL AND EPIDEMIOLOGICAL VARIABLES

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**Background:** Shoulder pain is a very common complaint with poor prognosis and high recurrence. To evaluate the shoulder pain, anamnesis and physical examination are used, but a diagnosis of certainty is difficult. Clinical history and specific exploration maneuvers tend to be poorly correlated with the underlying problem. There are few studies that assess the predictability of shoulder pathology using patient characteristics and exploration.

**Objective:** To assess if the combination of exploratory maneuvers and clinical data predicts the type of affection of the painful shoulder in a sensitive and specific way.

**Methods:** We conducted a prospective study with patients who attended to the Rheumatology Department of HUP la Fe by painful shoulder between February 2016 and January 2017, excluding those with known inflammatory diseases.

A rheumatologist performed the anamnesis and the selected exploratory maneuvers: Jobe and Gerber test and palpation of the acromioclavicular joint. A second rheumatologist, blind to physical examination and medical history, performed the shoulder ultrason sound scan. Biostatistical analysis was performed using software R version 3.3.2.

**Results:** 119 patients (66.4% women) with a mean age of 60±12.56 years and shoulder pain were collected. Time of pain evolution was 20.43±24.09 months and the right shoulder was the most affected one (71.4%). The association between the maneuvers of Jobe and the involvement of the supraspinatus (SE), as well as the Gerber maneuver with the affection of the subscapular were statistically significant. However the sensitivity and specificity of both maneuvers are very low, so that alone is not suitable to identify the affected tendon or the type of affection. Thus, a predictor model (nomogram) of the most common shoulder pathologies (subacromiodeltoid bursitis, tendinosis or SE tears) was developed using epidemiological and clinical examination variables.

**Conclusions:** Based on our results, the predictor model performed using epidemiological and clinical examination variables would be able to predict the most frequent pathologies of the shoulder. Imaging tests have a certain delay time, and by applying this predictor model, a diagnosis of presumption could be established in primary care, giving the opportunity to institute an early treatment.

In addition, patients could be referred more efficiently to the appropriate specialty (rheumatology, traumatology or rehabilitation), avoiding delays.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1547

**AB0934** TREATMENT OF LATERAL EPICONDYLITIS WITH ESWT: A SHAM-CONTROLLED DOUBLE BLINDED RANDOMISED STUDY

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**Background:** Lateral epicondylitis is a term describing the clinical condition that causes pain and sensitivity in musculotendinous adhesion sites of the wrist extensor muscles originating from the lateral epicondyle of the humerus, resulting in repetitive stresses due to overuse (1.2).

**Objectives:** The aim of this study was to investigate the efficiency of extracorporeal shockwave therapy (ESWT) in the treatment of lateral epicondylitis as randomized, non-blinded, controlled and randomized trial.

**Methods:** 47 patients (35 women, 12 men) with lateral epicondylitis were included in the study. The mean age of patients was 45.94±10.46 years. Patients were randomized into two groups: active ESWT (n=22) and sham ESWT (n=25). Patients were randomly allocated to receive 1 session per week for 3 weeks of either sham or active ESWT.

Patients were evaluated before the treatment, and at the end of the first week, first month and third month after the last treatment session with Patient-rated Tennis Elbow Evaluation Questionnaire (PRTEE), Visual Analogue Scale (VAS) for pain assessment and physical examination of lateral epicondyle of the elbow with special clinical tests.

**Results:** Compared with pretreatment values in ESWT group, significant improvement was observed in all parameters after treatment. At the first week after the therapy significant improvement was observed in sham group but at the first and third month after the therapy no significant difference was found. Comparison of ESWT and sham over 3 months after the treatment, significant improvements were observed in ESWT group in all parameters.

**Conclusions:** There was a significant decrease in pain and a significant improvement in function following ESWT. Although there was a reduction in pain and improvement in function with sham treatment as well, this difference was not as significant as in active group.

**References:**
3] Rheumatology Department, HUP la Fe; Biostatistics Unit, IlS la Fe; Medical School, UCV, Valencia, Spain

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.8508

**AB0935** THE ROLE OF EPIDURAL INJECTIONS IN PATIENTS WITH CHRONIC SCIATICA: A REVIEW BASED ON THE EVIDENCE OVER THE PAST 5 YEARS

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**Background:** Among various modalities applied in the management of painful conditions of the spine, epidural injections (EI) are one of the most commonly utilized interventions. EI can be administered in the lumbar spine by either caudal (CE) or interlaminar (IEL), or transforaminal (TEI) approaches and various steroids have been used in these injections(1,2). The purpose of EI is to provide analgesia for a varying duration, whilst making it easier for the patient to undergo a rehabilitation program during this time(1).

**Objectives:** The aim of this review is to evaluate the efficacy of the different types of EI in patients suffering from chronic sciatica, based on the evidence published over the past 5 years.

**Methods:** Relevant studies were retrieved by searching PubMed, Medicine, The Cochrane Library and UpToDate. Publications from 2012 to 2016 which specified the use of EI to treat chronic sciatica were considered, and all the studies selected were written in the English language only.

A total of 11 articles were gathered, of which 5 were excluded after analysis of their title and abstract. Of the 6 papers included in this study, 5 are systematic reviews and 1 is a meta-analysis of 10 randomized controlled trials. The outcomes measured were improvement in pain and functional status. TheNumeric Rating Scale (NRS) and Visual Analogue Scale (VAS) were the most commonly used baseline scales for pain evaluation. The Oswestry Disability Index (ODI) was the most used scale for the functional disability scoring system in the literature.
Results: 4 of the 6 papers included in this review reported improvements in pain ranging from 30 to 83% and in functional status ranging from 26 to 86% from the pre-injection state, with follow-up periods lasting up to 2 years after the EI. 2 of these 4 studies showed Level II evidence for EI for long-term efficacy in managing chronic sciatica, with no significant difference among CEI, IEI or TEI. The remaining 2 papers (out of the total 6) associated EI with immediate improvements in both pain and function, but found the benefits to be unsustained. 1 paper reported 1 serious adverse event in one of the trials analyzed and found the data on harms to be sparse on most trials. Another paper concluded that injecting local anesthetic alone might be preferable to injecting local anesthetic with steroid as omitting the steroid could lessen the risk of rare, but possibly fatal, complications.

Conclusions: Despite variability in the studies included and methods used for data synthesis, most of the articles included in this review showed positive results for both pain relief and improvement in function for EI. Although no studies found significant difference among CEI, IEI or TEI in terms of efficacy, each approach has its advantages and these should be taken into account when choosing the best approach for each patient. As supporting evidence, this review shows that EI with or without steroids are a fast, safe and clinically effective treatment method for patients with chronic sciatica.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2747

AB0936 FLEXIBILITY AND STRENGTH OF THE TRUNK IN CHRONIC LOW BACK PAIN TWO YEARS AFTER A FUNCTIONAL RESTORATION PROGRAM

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Background: Low-back pain affects significantly the flexibility and the muscular strength of the trunk. It was demonstrated in literature the positive effect of restoration programs in these parameters at short-term evaluation.

Objectives: Evaluate the flexibility and the muscular strength and endurance of the trunk two years after a functional restoration program

Methods: Prospective study on patients with low back pain evaluated before, at the end of the restoration program and two years later. We have evaluated the following parameters: trunk flexibility by use of the Schöber index and the finger–ground distance test (FGD), hamstring flexibility by measurement of the thigh-leg (TL) angle, back flexor and back extensor endurance, assessed with the Shirado test and the Sorenson test, respectively.

Results: Thirty patients were evaluated. Initially, the results reported decreased flexibility: 53% with FGD >15° cm; 37% with the thigh-leg (TL) angle >15° and decreased muscle endurance: Shirado 30.26±29.662s; Sorenson 26.3860±18.5208s. The short-term efficacy of the program showed significantly improvement in all parameters (p<0.01). However, this improvement decreased 2 years later but remained significant. This loss can be attributed to the fact that 70% of patients abandoned self-rehabilitation exercises.

Conclusions: The restoration program seems to have good effect in short and long term evaluations in the flexibility and muscular strength of the trunk.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4954

AB0937 DUPUYTREN'S CONTRACTURE: 15 YEARS OF EXPERIENCE WITH 36 CASES

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Background: Dupuytren's contracture is characterized by thickening and retraction of the palmar aponeurosis due to fibroblastic proliferation leading to progressive and irreducible fingers' flexion. Dupuytren's contracture appears to be a disease with poor clinical symptomatology and the therapeutic progress, in particular the needle aponeurotomy, continues to increase.

Objectives: We propose to describe the epidemiological, clinical and therapeutic characteristics- particularly the needle fasciotomy- of Dupuytren's contracture diagnosed and treated in our Rheumatology department.

Methods: This is a retrospective descriptive study that collected patients with Dupuytren's disease over a 15-year period from 2001 to 2016.

Results: Thirty-six patients were collected. The mean age was 63±10 years (46 years, 83 years, 83 years) and the sex ratio was 5. 34% of the patients were manual workers, of whom 42% were masons, 25% were farmers and 17% were carpenters. 8% of longshoremen and 8% of dressmakers. The personal history was diabetes in 63% of cases, of which 26% were unbalanced, hypertension in 31% of cases and hypercholesterolemia in 14% of cases. 6% of patients were epileptic. 23% of patients were ethyl and 13% were smokers. 6% had an associated Ledderhose disease. 9% of our patients had a family history of Dupuytren's disease. The mean time to diagnosis was 60 months (03 months to 180 months). The clinical examination noted an exclusive involvement of the left hand in 22% of cases, right hand in 12% of cases and bilateral involvement in 66% of cases. The fingers affected were: 59% the ring finger, 49% the little finger, 23% the middle finger, 12% the index and 5.5% the inch, in order of frequency of mention. The stages of Dupuytren's disease at their discovery were as follows: stage 4 (25%), stage 3 (34%), stage 2 (24%) and stage 1 (17%). Skin examination showed that 58% of the skin was inflicted and 42% of the skin was soft. From a therapeutic point of view, 86% of the patients benefited from a needle aponevrotomy with a good progression in 97% and a recurrence in 8% of the cases. In all stages combined, the average postoperative therapeutic gain was 0.83 stage at the Left hand and 1.43 stage at the right.

Conclusions: The Dupuytren's contracture is the object of a scientific subject whose wealth grows exponentially. These range from the paternity of his first description, to the place of the last therapeutic modalities.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6967

AB0939 CHANGE IN THE SURGICAL TREATMENT FOR CERVICAL SPINE DISORDERS RELATED TO RHEUMATOID ARTHRITIS DURING RECENT 15 DECADES

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Background: Since the appearance of biological DMARDs in Japan, disease control of rheumatoid arthritis has been ameliorated. Inflamed synovitis and destructive arthritis declined dramatically, which resulted in a decrease in the number of synovectomy and joint prosthesis gradually. On the other hand,
AB0940 EFFICACY AND SAFETY OF PLATELET RICH PLASMA PERI-NEURAL INJECTION IN TREATMENT OF DIABETIC NEUROPATHY: DOUBLE BLIND RANDOMIZED CONTROLLED TRIAL

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Background: Neuropathy is a common complication of diabetes mellitus (DM) not only leads to an impaired quality of life, but also to an increased morbidity and mortality. Autologous platelet-rich plasma is easy and cost-effective method. Platelet-derived angiogenesis factor capable of stimulating new capillary growth and revascularisation.

Objectives: evaluate the clinical efficacy and safety of perineural PRP injection in the treatment of diabetic neuropathy (DN) compared to tradition medical treatment.

Methods: Sixty patients were selected from Endocrinology unit Department of Internal Medicine, Assuit University Hospital, Egypt that type II diabetes mellitus neuropathy (DN) of at least 5 years duration of symptoms, regardless of age and gender double blindly divided into two groups, both groups had control blood glucose. Group I underwent PRP pre-neural injection under ultrasound guidance and group II underwent medical treatment. Baseline pain and nerve conduction study of upper and lower limb nerves and sural nerve conduction studies, F-wave nerve conduction study were determined at 3 months after the procedure. Primary outcome was the total effective rate. The total effective rate = (the number of patients with significant effect - the number of patients with effect)/total number of patients. A “significant effect” meant that limb pain, numbness, and fatigue were significantly reduced, nighttime sleep was improved, and NCV from electrophysiology increased >5 m/s or returned to normal. An “effect” meant that the symptoms mentioned above were relieved, and NCV compared with pre-treatment increased ~5 m/s. “Failure” meant that the symptoms did not improve, and there were no changes in NCV electromography.

Results: We recruited 60 diabetic patients (type II) with peripheral neuropathy with a mean age 35.27±12.86 years with disease duration of 7.42±3.51 years. Of these, 56% cases with upper limb neuropathy only while the rest 44% had sural nerve plus upper limb nerves neuropathy. Nerve conduction study showed axonal affection in only 26% and all had delayed distal latency and prolonged motor conduction velocities. generalized DN is found in 70% of total patients and 30% of had focal Entrapment of the nerve includes median neuropathy at the wrist 50%, ulnar neuropathy at the elbow 30% and peroneal neuropathy at the knee 20% and no patients had radiculoplexus neuropathy.

Conclusions: Autologous platelet-rich plasma is an easy and cost-effective method as a treatment of diabetic peripheral neuropathy.

Disclosure of Interest: None declared


AB0941 PATIENTS PROFILE AT ORTHOGERIATRIC UNIT: NEW MODEL OF CARE

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Background: Fractures in elderly patients its a prevalent problem. Older patients due their characteristics requires a specific care. The orthogeriatric Unit has been shown to be one of the most beneficial units. It is important to evaluate the model results.

Objectives: Evaluate the main variables of fractures patients treated at a orthogeriatric Unit and their complications

Methods: This is a partially concurrent prospective study, taking place in a large urban academic hospital GHdC in Belgium. The participants were 87 consecutive elderly people, admitted directly to a geriatric-based orthogeriatric ward.

Results: A total of 87 patients were included. The average age was 85.2±5.2 years, 20 male, 67 female. Most of them (n=44, 52%) were admitted for a hip fractures, 44% (n=38) were transferred from emergency department, ISAR score was 3.8±1.1, Preoperative stay was less than 24 h for 54% of our population, delirium incidence was 24%, Mini mental state examination was 20.6±6,4, the Cumulative Illness Rating Scale was 17±4.5, the mean number of medicine was 6.8±3.3, Activity of Daily Living 15 days after admission was 12.2±5.5. Delirium was the principal complication 55% (n=44). Mean hospital stay between admission and discharge/transfer to convalescence unit was 23.8±12.9. In-hospital mortality was 11% (n=10).

Conclusions: Fractures is a frequent and disabling pathology among geriatric fragile population, its treatment requires an interdisciplinary approach. This must be managed by the collaboration between geriatrician and orthopedist. We believe that the orthogeriatric Unit providing subspecialty and acute care will improve the general outcome of fragile geriatric patients.

References:

Acknowledgements: Geriatric multidisciplinary team working in GHdC Charleroi Belgium.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5845
**AB0943** SIGNIFICANCE OF MUSCLE VOLUME & FATTY DEGENERATION OF LUMBAR PARASPINAL MUSCLE IN SPINAL IMBALANCE

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**Background:** Spinal sagittal imbalance which is closely associated with low back pain is considered as a factor in a variety of spinal disorders.

**Objectives:** The present study was to determine the relationship between the sagittal imbalance and sarcopenia, especially cross sectional area (CSA) and fatty degeneration (FD) of muscle around the spine.

**Methods:** Overall, 165 patients were included in this study, classified by three groups according to the distance from sagittal vertical axis to posterior end of upper end plate of sacrum. 38 patients were classified as group 1 (distance ≥9cm), 50 and 53 patients as group 2 (distance 5–9cm) and group 3 (distance <5cm). For measurement of CSA and FI of paraspinal muscles, five transverse T1W images of S1-S5 were obtained from PACS and measured with Adobe Photoshop 7.0, by counting the number of pixels included in each selected muscle area. A variance analysis on average muscle surface area of those five images was done with SPSS 19.0 Windows version (SPSS Inc., Chicago, IL, USA).

**Results:** Of 37 responders, 15 (40.5%) did not show any flare (Table 2). Disease free survival on Et: Of 37 responders, 22 flared. No factors could predict flare in pts who recd tapering Et dose or after stopping Et. Some needed repeat cycles of Et/2nd BRM. Kaplan Meier curve of responders confirmed that no pt would be flare free at 63mths of follow up.

**Conclusions:** Et is safe to use & had no adverse events in 89%. Needed most for ERA. Effective in 84%. On using shortterm Et, 59% flared either on tapering/stopping. These pts responded to reinitiation of Et/BRM. Kaplan Meier curve of responders confirmed that no pt would be flare free at 63mths of follow up.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2228

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**Paediatric rheumatology**

**AB0944** USE,SAFETY AND EFFICACY OF ETANERCEPT IN JIA—A SINGLE CENTRE RETROSPECTIVE STUDY FROM NORTH INDIA

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**Background:** The treatment paradigm for Juvenile Idiopathic Arthritis (JIA) has changed in last decade:Early diagnosis,objective assessment & appropriate use of biologic response modifiers (BRMs) are common place.ETanercept (Et) is available in India for 15yrs. BRM use in developing world is fraught with the cost & safety concerns regarding TB, at our centre, full dose Et is used for 3–6 mths, followed by dose tapering as tolerated.

**Objectives:** 1. To determine use, safety & efficacy of Et in JIA. 2. To determine the factors that determine responders vs non responders. 3. To determine the factors that determine disease free survival on stopping Et

**Methods:** This study was done by 15thJune15 to 15thDec16 (18mths) at Sir GangaRam Hospital. Inclusion criteria: All JIA pts who took Et for min 12 wks & attended the outpatients during the study period. Outcome: All pts who achieved the Wallace criteria of inactive ds, clinical remission on (CRoM) or off medication within 4 months were termed as responders.

**Results:** Use: 46pts recd Et (29M,17F). Median (Md) age at JIA onset: 9.08yrs (1.16–16.5).Md delay to diagnosis: 4mths (0.5–60). Md age at initiation of Et: 11.6yrs (4.25–20.3). Indications: Partial response to Intraarticular steroids/bridging steroids & DMD-ARD-32; Started upfront for high dis burden: 14: Diagnoses: ERA30 (65%), Poly JIA (17%), OJIA 3 (7%), SOJIA 3 (7%) & UJIA 2 (4%). Safety: Screening: Mantoux <6, Quantiferon <2; anti tuberculosis therapy for latent TB: 8. Side effects: 41 (88%) had no adverse event. 5 pts – 1 each had enteric fever, varicella, uveitis, hemolysis, malaria. Follow up: Md duration of follow up=47.5 mths (2–147). Medications at last follow up: Et ongoing in 20 (43.5%), 12 on 2nd BRM, 12 off BRM & 2 lost to follow up. Status at last follow up: Of 37 responders - 8 currently active.

**Disclosures of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4228

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**AB0945** COHORT STUDY OF 112 PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS DURING TRANSITION FROM PEDIATRIC TO ADULT CARE

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**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory arthritis in children. The International League of Associations for Rheumatology 2001 (ILAR) classification includes 7 subgroups: systemic JIA, polyarticular JIA, oligoarticular JIA, enthesitis related arthritis (ERA), psoriatic arthritis and undifferentiated arthritis. Most paediatric inflammatory arthropides persist into adulthood. Therefore, a transition from paediatric to adult rheumatology is a necessary step. Transition is defined as an active process by which a young patient with a chronic disease develops skills and resources to gradually take control of their condition. The transition phase should be anticipated and structured because of the risk of failure in monitoring. However difference in classification criteria in paediatric and adult rheumatology can cause significant difficulty for adult rheumatologists.

**Objectives:** The aim of this study was to determine the characteristics of juvenile-onset arthritis seen during the transition period and to compare paediatric classification criteria to those of adults.

**Methods:** A retrospective bi-centre study was performed. Patients with JIA according to ILAR classification were included and had a consultation at transition. JIA classification criteria were compared to ACR/REULAR 2010 criteria

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4892
CALCINOSIS IN CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A SINGLE-CENTRE IN NORTH INDIA

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Background: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune inflammatory muscle disorder that can result in severe disability or death. Calcinosis is a unique and a poorly understood long-term complication of JDM (1). Calcinosis can present in various forms like nodular calcinosis, tumoral deposits, calcinosis universalis. We present here the images of calcinosis in children with JDM.

Methods: All children diagnosed to have JDM and registered in Pediatric Rheumatology Clinic at Post Graduate Institute of Medical Education and Research, Chandigarh, India, were evaluated for presence of calcinosis. Consent was taken from patients or caregivers.

Results: A total of 36 patients were evaluated. Twelve (33.33%) patients had calcinosis (Fig 1). Interestingly, 4 children had calcinosis at the time of diagnosis. In any of the two first appointments, 20 patients (24.7%) were active in the 2 first appointments N (%) 20 (24.69) 15 (28.30) 4 (40) Time of disease onset - Median (IQR) 10.3 (4.5–14.2) 6.5 (2.1–12.9) 0.02 (11.5–15.6)

Conclusions: Our study confirmed the articular destructive potential of polyarticular systemic JIA and an ocular risk in polyarticular JIA. Comparison of JIA criteria to adult rheumatism criteria showed that polyarticular JIA with positive rheumatoid factor fulfilled ACR/EULAR criteria for RA. However, oligoarticular JIA and polyarticular JIA without rheumatoid factor did not fulfill any adult rheumatism criteria and seem to be paediatric entities. Finally, most patients with ERA and psoriatic arthritis fulfilled the ASAS criteria for spondyloarthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6205

AB0948 INSUFFICIENT CALCIUM INTAKE IN PEDIATRIC POPULATION WITH RISK FACTORS FOR OSTEOPOROSIS

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Background: Compliance with daily calcium requirements in paediatric and young age is necessary to acquire peak bone mass, especially in populations that meet one or more risk factors for fractures.

Objectives: To study the characteristics of the pediatric population with at least one risk factor for developing low bone mass/osteoporosis and to measure their calcium intake.

Methods: Demographic and clinical data were prospectively collected from patients aged 2 to 20 years that met at least 1 risk factors for bone fragility, including: inflammatory diseases, treatment with Immunosuppressants and/or compliance with daily calcium requirements in paediatric and young age is necessary to acquire peak bone mass, especially in populations that meet one or more risk factors for fractures.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5185
corticosteroids, malabsorptive disorders, chronic systemic disorders such as nephropathies or hematologic diseases, etc. The patients or their legal tutors signed the Informed Consent in order to participate in the study. The average daily calcium intake was collected through the Spanish INDICAD 2001 study survey, together with a comprehensive anamnesis. If patients or their family reported taking food not included in the survey, its calcium content were consulted in the Spanish Food Composition Database published by the BEDCA Network of the Ministry of Health Science and Innovation.

Results: Data were collected from 50 patients, with a mean age of 9.2 years (2–20); 28 (56%) female, 86% Caucasian, 6% Arab, 2% Asian and 6% Latin. The most frequent factors of treatment were: Food intolerances/ malabsorption: 32%; nephropathies: 22%; JIA: 16%; vasculitis: 10%, other inflammatory diseases: 8%. 42% had received systemic corticosteroids at some point, and 16% were receiving corticosteroids at present. Average daily calcium intake was 718 mg/d. They were divided by age groups, attending to daily calcium needs per group. In Table 1 we can observe the Recommended Daily Amount (RDA) of calcium by the Spanish Association of Pediatrics and the consumption collected, by age group.

<table>
<thead>
<tr>
<th>Age group</th>
<th>% Age</th>
<th>RDA (mg/d)</th>
<th>Average intake (mg/d)±SD</th>
<th>Range: min-max (mg/d)</th>
<th>% That reaches RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-school (2–3 a)</td>
<td>14% 700</td>
<td>819±280</td>
<td>513–1346</td>
<td>57.1%</td>
<td></td>
</tr>
<tr>
<td>School (4–9 a)</td>
<td>32% 1000</td>
<td>702±420</td>
<td>254–1075</td>
<td>18.9%</td>
<td></td>
</tr>
<tr>
<td>Teenagers (10–17 a)</td>
<td>48% 1300</td>
<td>689±350</td>
<td>350–1925</td>
<td>8.3%</td>
<td></td>
</tr>
<tr>
<td>Young (18–20 a)</td>
<td>6% 1100</td>
<td>797±172</td>
<td>621–985</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

Only 3 children with low calcium intake were taking supplements. A decrease in calcium RDA adherence was observed with increasing age, statistically significant (p<0.005). There was also a lower calcium intake in the non-Caucasians compared to Caucasians statistically significant (p=0.044), which was not associated with age.

Conclusions: Calcium intake in the population under 21 years old with at least 1 risk factor for developing low bone mass/osteoporosis is lower than recommended. In addition, recommendations are based on the physiological needs of the healthy populations and it could be expected to be insufficient for those with chronic diseases. It should be noted that calcium intake in the groups with higher requirements (adolescents and young people) is lower, with a reduction in the proportion of patients who meet the compliance with the RDA as age increases. Studies with a larger population are needed to ratify these results together with serum calcidiol levels.

Disclosure of Interest: None declared


AB0949 THE ANNUAL COST OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The management of juvenile idiopathic arthritis (JIA) includes various methods including such as medication, hospitalization, rehabilitation.

Objectives: To determine how much juvenile idiopathic arthritis cost; the components of this cost; how new treatments, i.e. biologics, improve the disease course and hospital expenditures.

Methods: This study was conducted in Dokuz Eylul University, Pediatric Rheumatology Unit between March 2015-March 2016. One-hundred six JIA patients who had a follow-up period of at least 1 year according to International Edmonston 2001 criteria were included. This retrospective cost study evaluated the data of these patients and calculated the direct cost for the follow-up period. Clinical data was collected from patient files that were in department’s archive and cost data was gathered from Probel Hospital Information Management system. Patient data form covering sociodemographic and clinical information, patient drug form and annual medical cost form was filled out for each patient.

Results: 58.5% (n=62) of patients was female and 41.5% (n=44) was male. The mean age was 12.0±4.3 years. 34.0% (n=36) of patients was oligoarticular type, 7.3% (n=8) was polyarticular type, 22.6% (n=24) was enthesitis related arthritis (ERA), 8.5% (n=9) was psoriatic type and 6.6% (n=7) was systemic type. The cost of medication counted for 87.1% (453,244.94 TL) of total direct annual cost. The most total direct medical cost was highest for ERA (n=742.55±381 TL) while the annual cost was calculated as 10451 TL per person for biologic using patients, for the patients using non-biologic treatments it was determined as 1472 TL per person. 1 TL=0.32 € 1 TL=0.35 $

Conclusions: Medication is responsible for most of the total direct medical cost in patients with JIA. Our results showed concordance with previous studies on the subject. This situation could be attributed to biological agents that are being used in treatment in recent years. More prospective studies on the effectiveness of cost of treatment, with greater amount of patient and more homogenous subgroups are needed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5743

AB0950 PREDICTORS OF RESPONSE TO ETANERCEPT TREATMENT DEPENDING ON JUVENILE IDIOPATHIC ARTHRITIS CATEGORY

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Background: Anti-TNF biologics are highly effective and widely used in clinical practice for the treatment of JIA. However, some children lack of response with low reliable predictors of a good or poor response to treatment found [1–3]. As clinical picture patterns are significantly differ for 7 JIA subclasses, we propose to find predictors of response to therapy for each of JIA category.

Objectives: To identify clinical and laboratory parameters associated with response to etanercept treatment in 12 months in patients with different JIA categories.

Methods: Patients from four JIA categories (n=195) were divided to groups with excellent, intermediate and poor response after 12 month treatment with etanercept according to ACRPedi criteria, achieving inactive disease by Wallace criteria and JADAS-71 cut-off point. For each of JIA category univariate and multivariate logistic regression analysis was conducted to identify potential baseline factors associated with treatment response. Baseline factors included clinical, laboratory and anamnestic data.

Results: From total cohort 91/58/88.5 percent of patients achieved ACR30/50/70/90 in one year etanercept treatment: 45.5% patients were considered excellent responders, 30% - intermediate responders, and 24.5% - poor responders. Highest efficacy of therapy was shown in persistent oligoarticular patient, lowest – in enthesitis-related arthritis and polyarthritis patients. Potential baseline predictors of excellent and poor response which were significant are described in the table.

JIA category | Predictors of excellent response | Predictors of poor response |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Persistent oligoarticular</td>
<td>smaller amount of DMARD</td>
<td>–</td>
</tr>
<tr>
<td>Extended oligoarticular</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Enthesitis-related arthritis</td>
<td>shorter disease duration (DD)</td>
<td>– longer DD</td>
</tr>
<tr>
<td>RF-negative polyarticular</td>
<td>– smaller number of joints with limited range of motion (LOR)</td>
<td>– lower CRP level at the baseline</td>
</tr>
<tr>
<td></td>
<td>lower age at disease onset (ADD)</td>
<td>older ADD</td>
</tr>
</tbody>
</table>

Analysis showed that poor response in all JIA categories was mainly associated with demographic data (longer DD and older ADD). However, factors associated with excellent response significantly differed depending on JIA category (anamnestic factors, number of involved joints, laboratory factors, and demographic factors).

Conclusions: Response to etanercept therapy is strongly associated with JIA category. Shorter disease duration and lower number of DMARDs used before start of etanercept, lower number of joints with LOM, and lower C-reactive protein at baseline are predictors of better response to etanercept.

References:

Disclosure of Interest: E. Kashchenko Grant/research support from: Novartis, E. Alexeeva Grant/research support from: Roche, Abbott, Pfizer, Bristol-Myers Squibb, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Bristol-Myers Squibb, Medac, Novartis, Pfizer, T. Bzarova Grant/research support from: Roche, Pfizer, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, S. Valieva Grant/research support from: Roche, Bristol-Myers Squibb, Medac, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, K. Isayeva Grant/research support from: Roche, Novartis, M. Soloshenko: None declared, A. Karaseva: None declared

DOI: 10.1136/annrheumdis-2017-eular.3916

AB0951 FACTORS ASSOCIATED WITH RESPONSE TO ADALIMUMAB TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Tumor necrosis factor inhibitors are highly effective and safe in treatment of juvenile idiopathic arthritis (JIA). Nonetheless, to select the optimal therapy and to achieve maximum therapeutic effect it is necessary to consider the individual characteristics of the patient. Adalimumab (ADA) is widespread use for mild and severe polyarticular JIA especially in the presence of uveitis, but there is lack of data about clinical and laboratory predictors of response to ADA in different JIA categories.

Objectives: To identify clinical and laboratory parameters associated with
response to adalimumab treatment in 12 months in patients with different JIA category.

Methods: Analysis include patients with enthesis-related arthritis (ERA, n=56), RF-negative polyarthritis (pRF, n=50), extended oligoarthritis (extOligo, n=30), and polyarthritis (polyArth, n=62) with median age 10.5 (IQR 6–14) and median JADAS-71 19.5 (IQR 15–28). Patients were divided to response groups after 12 month treatment with ADA according to ACRpedi criteria, achieving inactive disease by Wallace criteria and JADAS-71 cut-off point as excellent, intermediate and poor responders. For each JIA category univariate and multivariate logistic regression analysis was conducted to identify potential baseline factors associated with treatment response. Baseline factors included clinical, laboratory and anamnestic data.

Results: ADA was shown to be effective in all groups with 90%/89%/82%/63% children with ACR30/50/70/90 during one year therapy. The most significant factors (p<0.05) associated with response to ADA treatment are presented in summarized table. Our findings demonstrated that different predictors corresponded with different JIA categories. Interestingly subjective scales of disease activity was shown to be strongly associated to therapy. At the same time VAS severity at baseline were inversely correlated with achievement of good response. Duration of morning stiffness correlated with excellent response in children with 2 different categories. However, for ERA patients shorter duration was associated with better response to treatment while vice versa for ExtOligo patients.

Conclusions: Predictors of response to ADA treatment differ in JIA categories. Low disease activity parameters (clinical and laboratory) at baseline not always predict good response to therapy.

Disclosure of Interest: E. Kashchenko Grant/research support from: Roche, Abbott, Pfizer; Bristol-Myers Squibb, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Bristol-Myers Squibb, Medac, Novartis, Pfizer, T. Bzavora Grant/research support from: Roche, Pfizer, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, T. Bzavora Grant/research support from: Roche, Bristol-Myers Squibb, Speakers bureau: Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Medac, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, K. Isaeva Grant/research support from: Roche, Novartis, M. Soloshenko: None declared, A. Karaseva: None declared

DOI: 10.1136/annrheumdis-2017-eular.3354

AB0953

ARTHRITIS FOLLOWING PARASITIC INFECTION IN THE DIFFERENTIAL DIAGNOSIS OF JUVENILE IDIOPATHIC ARTHRITIS

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Background: According to literature arthritis is a rare complication following parasitic infection. In the Italian pediatric population parasitic infection is mainly caused by Enterobius vermicularis; it is often asymptomatic but common symptoms can be anal nocturnal itching, insomnia, irritability, abdominal pain together with arthralgia.

Objectives: To describe cases of mono or poliarthritus due to parasitic infection in young patients followed at the Verona’s Pediatric Rheumatology Clinic from 2010 to 2016.

Methods: Medical records of 8 patients followed at the Pediatric Rheumatology were analyzed. The mean age of 8 patients was 8 (F:M 3.5). The following data were evaluated: anamnesis data, clinical symptoms (anal itching, irritability, arthralgia, abdominal pain and arthritis), Blood test and scotch tape test. All patients underwent joint ultrasound (US). Physical symptoms of joint’s involvement were evaluated in all children by an experienced rheumatologist.

Results: 6 patients had symmetrical poliarthritus, 2 patients had monoarthritus (knee and hand). Symptom’s complaint were systemic (12,5%), abdominal (25%), and general pruritus (25%). Blood test confirmed high inflammation indices (25%) and hyperesinophilia (12,5%).Serological tests and stool investigations allowed to diagnose the following infections: Enterobius vermicularis (6 cases) giardia lambiia (1 case); dientamoeba fragilis (1 case).Joint US evidenced synuvium hyperplasia in 75% of the cases and tenosynovitis in 50% of the cases.After appropriate antiparasit treatment complete articular and systemic symptomatic remission was observed (100% cases); also joint US control normalized 2 cases, after about 6 months, were re-evaluated for arthritus relapse and in both cases a parasitic reinfection was confirmed.

Conclusions: Analysis of this series of patients underlimes the following data: arthritis can be a manifestation of parasitic infection; treatment must be aimed against the parasite involved in order to achieve complete clinical and laboratory data remission; reinfection must always be considered in cases of relapse; differential diagnosis of this form of arthritis with other chronic polyarthritis is fundamental due to the risk of disseminated infection in case of immunosuppressive treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4876

AB0952

EXPERIENCE OF TOCILIZUMAB USE IN TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS IN CHELYABINSK REGIONAL CHILDREN HOSPITAL

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Background: Recently due to application of interleukin (IL)-6 inhibitors prognosis for systemic juvenile idiopathic arthritis (sJIA) has significantly improved. 526 children with JIA are under monitoring in Chelyabinsk region, 42 children have sJIA. Tocilizumab is the drug of choice for sJIA treatment. It is registered within the Russian Federation for use in children older than 2 years. In Chelyabinsk Regional Children Hospital tocilizumab has been used for 5 years.

Methods: 18 children (12 boys, 6 girls) aged from 2 to 17 (mean age 10.7 years) diagnosed with sJIA were under monitoring. Disease duration was from 6 months to 15 years (mean duration 6 years). JIA was diagnosed based on ILAR diagnostic criteria. SJIA was diagnosed in 16 children, severe polyarthritis was diagnosed in 2 children. Tocilizumab was introduced intravenously every 2 or 4 weeks in dose of 12 mg/kg for children <30 kg or 8 mg/kg for children ≥30 kg. Therapy duration was from 3 months to 5 years (average duration 23 months). Assessment of disease activity and therapy efficiency was conducted in accordance with ACR pedi criteria. Nonparametric statistical methods were used to compare results.

Results: Prior to tocilizumab use high disease activity was observed in all children. Average number of joints with active arthritis was 13.5 [6;15] (Me [25.75%]). Average number of joints with functional impairments – 12.5 [6;15]. Average ESR (according to Panchenko) – 50 [40;60]mm/h, CRP 98.6 [55;139]g/L. Assessment of functional activity according to CHAQ questionnaire – 2.08 [2.25]. Activity assessment according to VAS by doctor – 82 [75;90]. No eye lesions were found in children under monitoring. All 16 children with sJIA had fever, hepatosplenomegaly and lymphadenopathy, the rash had 11 children, polyserositis - 8. In 5 children there was a complication in the form of a syndrome of macrophage activation.

During the tocilizumab therapy a decrease in disease activity was observed

in all patients. Mean number of joints with active arthritis was 1 [0;2] (Me [25.75%]) (P=0.0002). Mean number of joints with functional impairments – 3 [0;3] (P=0.0003). Average ESR was 4 [3.5;5]mm/h (P=0.0002), CRP 0.75 [0;1]g/L (P=0.0003). Assessment of functional activity according to CHAQ questionnaire was 0.25 [0.0;0.5] (P=0.0004). Activity assessment according to VAS by doctor – 16 [10;20] (P=0.0002). Assessment of parents according to VAS 18 [10;20] (P=0.0002).

Clinical disease remission (according to ACR pedi criteria – ≥90%) was observed in 11 patients after 6–9 months of treatment. Remission duration up to now is from 3 months to 4 years. Efficiency according to ACR pedi criteria is 70% in 6 children, 50% in 1.

The drug was well-tolerated. Undesirable effect such as allergic skin reactions were observed only in one child. In one child the lack of efficiency produced by switching to canakinumab. Drug was cancelled in 3 patients due to long-term remission (≥3–4 years), before of them after a year needed the resumption of therapy in connection with the aggravation of the disease.

Conclusions: Tocilizumab therapy was highly effective and safe in patients with JIA. Clinical remission was achieved in 61,1% children. Decrease in disease activity was observed in 39.9% of children. No serious undesirable effects were reported.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4011
AB0954 RELATIONSHIP BETWEEN SERUM COMPLEMENT LEVELS AND RENAL PATHOLOGICAL CLASSIFICATION IN CHILDREN WITH SILENT LUPUS NEPHRITIS

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Background: Silent lupus nephritis is defined by some pathological evidence of lupus nephritis with normal urinary findings. It is therefore apparent only upon renal biopsy. Serum complement levels have been associated with overall lupus disease activity. Despite recent progress in understanding the pathogenesis of lupus nephritis, including complement, our understanding of silent lupus nephritis, especially in children, remains limited.

Objectives: To study whether serum complement levels are associated with renal pathological classification in children with silent lupus nephritis.

Methods: We determined serum C3 and C4 levels and International Society of Nephrology/Renal Pathology Society classification in 25 patients with paediatric silent lupus nephritis before initial therapy who were admitted to our hospital. Patients were classified as having silent lupus nephritis based on normal urinary findings at baseline renal biopsy in juvenile systemic lupus erythematosus.

Results: Serum C3 levels varied between International Society of Nephrology/Renal Pathology Society classes, with significantly lower levels for silent lupus nephritis patients in class III compared to class II, and for class II compared to class I. There was no significant difference in serum C4 levels between International Society of Nephrology/Renal Pathology Society classes in patients with silent lupus nephritis.

Conclusions: Our results suggest that serum C3 levels were associated with renal pathological classification in children with silent lupus nephritis. We propose that serum C3 levels would provide a useful tool for predicting latent severe nephritis in patients with juvenile systemic lupus erythematosus who have normal urinary findings before initial therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1012

AB0955 NEW ONSET OF UVEITIS, PSORIASIS OR IBD AS PARADOXICAL EFFECTS OF BIOLOGICS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: SINGLE CENTER EXPERIENCE

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Background: Biological agents (BA) are high efficacy options for current therapy for patients (pts) with juvenile idiopathic arthritis (JIA). They are successfully used not only for the arthritis but also for uveitis, psoriasis and inflammatory bowel disease (IBD). However, paradoxical induction of these conditions in pts treated with BA is a well-established phenomenon.

Objectives: To evaluate the frequency of new onset of uveitis, psoriasis or IBD occurring under BA therapy in JIA pts, to establish clinical features, which may be associated with such effects.

Methods: Retrospective cohort study involved all JIA pts (740) who were treated with BA in our clinic from 2004 to 2016. All cases of new onset (no)-uveitis/psoriasis/IBD collected; clinical features of disease onset and course, activity level, JIA category, exposure to Methotrexate (MTX) and BA, presence of ANA, HLA B27 were studied.

Results: We identified 20 (2.7%) pts (11 female/9 male) with new onset of uveitis, psoriasis or IBD occurring under BA therapy in JIA pts, 10 (50%) of pts received MTX. In all cases of new onset of uveitis the Z-score (by AAO) was &lt; 2 SD to Z-score &lt; 2,1 SD. Therapy may be discontinued under BA therapy in JIA pts, but - for IBD - BA therapy should be started at the beginning of disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1013

AB0956 INFLUENCE OF BIOLOGICAL THERAPY ON BONE MINERAL DENSITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is one of the most common and most disabling rheumatic diseases in children. JIA is a systemic chronic inflammatory immunopathological disease, which leads to dysfunction of the joints, their deformation and limitations of life of the child, violates the child's growth and development. One of the complications of systemic JIA in children is osteoporosis. In the pathogenesis of osteoporosis important place is given to the use of glucocorticoids. In world Rheumatology successfully used drugs aimed at the major pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and others.

Objectives: The purpose of research - to determine the influence of biological therapy on bone mineral density in children with JIA.

Methods: 15 children with systemic JIA (mean age 11.9±3.4 years) were examined in the rheumatological department of 4th city clinical hospital of Minsk. Bone mineral density was assessed by 2-energy X-ray absorptiometry (DEXA) to two points of the skeleton. The level of mineralization of skeletal mineral content was assessed using the bone mineral density (BMD) and parameter Z-score. Z-score was used to determine the incidence of osteopenia and osteoporosis in children surveyed. In accordance with the WHO criteria for normal bone mineral density was diagnosed with the Z-score - &lt; 1 SD, osteopenia - &lt; Z-score - &lt; 1 SD, but - &lt; 2.5 SD, osteoporosis - with Z-score &lt; -2.5 SD.

Results: In a study of children osteopenia was diagnosed in 9 patients with systemic JIA (mean Z-score -2.3 SD) Osteoporosis was diagnosed in 6 patients with systemic JIA (mean Z-score -2.7 SD). All children received a mean dose of methotrexate 12.7 mg/m² of body surface area, an average dose of methylprednisolone 0.34 mg/kg body weight per day and treatment of IL-6 inhibitor - tocilizumab 8 mg/kg body weight every 2-4 weeks. Bone mineral density was measured prior to initiating therapy tocilizumab and after 2 years of therapy. During tocilizumab therapy achieved remission of the disease, all children was canceled methylprednisolone. After densitometry of 2 years after the beginning of therapy improvement noted tocilizumab Z-score in children with osteopenia with Z-score -2.3 SD to Z-score &lt; -1.4 SD, and children with osteoporosis with a Z-score -2.7 SD to Z-score &lt; -2.1 SD.

Conclusions: The results indicate a positive influence tocilizumab therapy to bone mineral density in children with JIA.

Acknowledgements: This study would not have been possible without the collaboration of numerous Belarusian pediatric rheumatologists, patients and their parents.

Disclosure of Interest: None declared


AB0957 IS THERE A DIFFERENCE IN THE CLINICAL PRESENTATION OF JUVENILE SYSTEMIC SCLERODERMA PATIENTS ACCORDING THE AGE OF ONSET: RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

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Background: Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease. It was rarely looked at the differences between the clinical presentations of patients at different paediatric age groups. The juvenile scleroderma inception cohort (www.juvenile-scleroderma.com) is a prospective standardized register for patients with jSSc.

Objectives: Comparison of clinical characteristics of patients with different age range at the time of inclusion in the registry.

Methods: Patients with jSSc were included worldwide to the juvenile scleroderma inception cohort. We compared the demographics and clinical characteristics of
AB0958 PROPOSAL FOR A JUVENILE SYSTEMIC SCLEROSIS RESPONSE INDEX (JSScRI): RESULT OF THE CONSENSUS MEETING IN HAMBURG, GERMANY 11TH OF DECEMBER 2016


Background: Juvenile Systemic Sclerosis (JSSc) is an orphan disease. There is increasing interest in testing novel therapies in the management of fibrotic diseases. Therefore, it is very important to develop a Response Index for JSSc (JSScRI) to distinguish effective therapies from placebo. In 2014 at the 1st JSScRI Consensus Meeting in Hamburg, following two rounds of a Delphi process, a core data set items that could change as outcome measures) that will be adopted in the development of a JSScRI.

Methods: Before the 2nd JSScRI Consensus Meeting, the items from the 1st JSScRI Consensus Meeting (2014) were scored via Email, in a Delphi by the participants of the current meeting. Participants included 14 experts in adult JSSc and a patient partner. During the subsequent face to face NGT, participants of the current meeting. Participants included 14 experts in adult JSSc and a patient partner. During the subsequent face to face NGT, the participants after a nominal group discussion. The domains and items were scored regarding their importance for 1 year clinical trial from 1 (not relevant at all) to 9 (most relevant). A priori, it was agreed by the participants that the goal of the NGT was to exclude items that: 1. Are not feasible and 2. do not represent the impact of the disease on quality of life, vocational or recreational activity. Items with a median score less than 4 were excluded as they were felt to not represent an outcome measure or were non-feasible and items received a median score less than 4.

Results: Seventy-one items in 13 domains were scored. Six items were not scored as they were felt to not represent an outcome measure or were non-feasible and six items received a median score less than 4.

Table 1. Assessment of the Activity of the Musculoskeletal domain

<table>
<thead>
<tr>
<th>Whole Group</th>
<th>1–3</th>
<th>4–6</th>
<th>7–9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swollen joints</td>
<td>7</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Limited range</td>
<td>7.5</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>3a) MMT</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>3b) CMAS</td>
<td>7</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>4) Presence of tendon friction rub</td>
<td>7</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>5a) CK</td>
<td>8</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>5b) Aldolase</td>
<td>7</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3419

AB0999 EVALUATE THE CARDIOVASCULAR RISK THROUGH CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN THE YOUNG ADULT AGE

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Background: The relationship between inflammation and atherosclerosis has been demonstrated, so it is important to identify early markers of the disease. Ultrasound carotid intima-media thickness (CIMT) measurement is a non-invasive, consistent, validated technique used as a marker to identify subclinical arteriosclerotic disease.

We aimed to evaluate long-term risk of cardiovascular disease in young adult patients with juvenile idiopathic arthritis (JIA) is unclear and there are no risk management guidelines for these patients.

Objectives: To assess whether there is an increase in CIMT in the young adult with a history of JIA and to relate CIMT with classic cardiovascular risk factors in these patients.

Methods: Observational and cross-sectional study. Follow-up patients from transitional care between 18 and 36 years old, with JIA diagnosis by ILAR classification. Filtration data, anthropometric variables and activity disease scores were collected.

We performed, prior informed consent, CIMT measurement by radiofrequency with Esaote MyLab 70XVG. Three measurements were performed on each carotid artery, according to the protocol of the American Society of Echocardiography.

Results: Of the 20 patients, 17 (85%) women and 3 (15%) men. Subtype distribution was 8 (40%) oligoarticular, 1 of them ANA negative; 8 (40%) poliarticular being 4 seropositive and 4 seronegative; 1 (5%) systemic; 2 (10%) psoriatic arthropathy and 1 (5%) HLA B27 positive arthritis. 66.7% are with disease modifying drugs (26.7% synthetic and 40% biological), while 33.3% do not have specific treatment.

The main variables studied are described in the attached table (Table 1).

Table 1. Abridged description of our series patients.

<table>
<thead>
<tr>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>Typical deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>20</td>
<td>18</td>
<td>36</td>
<td>24,75</td>
</tr>
<tr>
<td>Diagnosis age</td>
<td>20</td>
<td>0</td>
<td>1</td>
<td>9,70</td>
</tr>
<tr>
<td>Evocation time (years)</td>
<td>20</td>
<td>5</td>
<td>27</td>
<td>15,00</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>19</td>
<td>15,5</td>
<td>38,5</td>
<td>24,505</td>
</tr>
<tr>
<td>Abdominal perimeter</td>
<td>20</td>
<td>58</td>
<td>126</td>
<td>81,33</td>
</tr>
<tr>
<td>Waist-hip index</td>
<td>20</td>
<td>44</td>
<td>135</td>
<td>90,40</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>20</td>
<td>96</td>
<td>130</td>
<td>114,05</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>20</td>
<td>60</td>
<td>99</td>
<td>73,90</td>
</tr>
<tr>
<td>Left CIMT</td>
<td>20</td>
<td>394</td>
<td>634</td>
<td>464,15</td>
</tr>
<tr>
<td>Right CIMT</td>
<td>20</td>
<td>337</td>
<td>600</td>
<td>467,45</td>
</tr>
<tr>
<td>HAO</td>
<td>17</td>
<td>0,0</td>
<td>2,25</td>
<td>0,325</td>
</tr>
<tr>
<td>VAI (mm²)</td>
<td>18</td>
<td>1</td>
<td>18</td>
<td>3,17</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>17</td>
<td>3</td>
<td>57,7</td>
<td>9,419</td>
</tr>
<tr>
<td>DSAS8</td>
<td>16</td>
<td>97</td>
<td>3,97</td>
<td>1,856</td>
</tr>
</tbody>
</table>

Conclusions: The carotid intima-media thickness of patients with JIA were lower than the controls previously described in the literature, so we will complement this study with our population controls.

In addition to classic cardiovascular risk factors such as systolic blood pressure and BMI, there is correlation with the evolution time in years of the disease and systolic blood pressure (r =0.621) was observed at the level of 0.01 and with C Reactive Protein (r =0.524) and BMI (r =0.471) at the 0.05 level.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4029
GROWTH AND SEXUAL MATURATION IN GIRLS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases with onset before the age of 16 years and joint inflammation as a main feature. Longitudinal growth is one of the main physical changes in childhood and adolescence. The etiology of delayed growth in children with JIA is multifactorial and strongly associated with prolonged inflammatory activity.

Objectives: To evaluate growth, sexual maturation, and the difference between final and expected height in girls with JIA and no glucocorticoid treatment for at least six months, as compared to a group of healthy girls.

Methods: This cross-sectional study involved 44 girls with JIA, diagnosed according to International League of Associations for Rheumatology (ILAR) criteria, and 59 healthy controls, aged between eight and 18 (incomplete) years with no comorbid chronic diseases. Demographic data were collected from all participants, and disease and treatment variables were compiled for the patient group. Anthropometric measurements were converted into z-scores based on WHO standards. Sexual maturation was classified according to Tanner stages.

Results: BMI and height z-scores were lower in girls with JIA as compared to controls. These values differed significantly in Tanner stage II. Three (6.8%) girls with JIA had height-for-age z-scores < -2 (short stature). Girls with polyarticular JIA and higher cumulative glucocorticoid doses were significantly more likely to present with short stature. The percentage of prepubertal girls in the JIA group was significantly higher than that observed in the control group, p = 0.012. Age of menarche, adult height, and the difference between actual and expected height did not differ between groups.

Table 1. Comparison of pre- and postmenarcheal growth parameters between groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n=44)</th>
<th>Control participants (n=59)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menarche – n (%)</td>
<td>17 (38.6)</td>
<td>37 (62.7)</td>
<td>0.026</td>
</tr>
<tr>
<td>Age of menarche (years)</td>
<td>12.2±5.1</td>
<td>11.5±1.2</td>
<td>0.066</td>
</tr>
<tr>
<td>Menarche &gt;2 years – n (%)</td>
<td>13 (76.5)</td>
<td>22 (37.5)</td>
<td>0.363</td>
</tr>
<tr>
<td>Δ Target height (father/mother)</td>
<td>-3.15±8.7</td>
<td>1.31±5.4</td>
<td>0.112</td>
</tr>
<tr>
<td>Nutritional data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI z-score</td>
<td>-0.10±1.29</td>
<td>0.92±1.19</td>
<td>0.007</td>
</tr>
<tr>
<td>Height/age z-score</td>
<td>0.14±1.24</td>
<td>0.27±1.17</td>
<td>0.253</td>
</tr>
<tr>
<td>Bone age z-score</td>
<td>-1.53±1.29</td>
<td>-1.42±1.17</td>
<td>0.928</td>
</tr>
</tbody>
</table>

Conclusions: These findings suggest that even six months after the suspension of glucocorticoid treatment, children with more severe forms of JIA and exposure to higher doses of glucocorticoids are still susceptible to growth impairment and delayed puberty.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6912

AB0961 A COHORT OF PATIENTS WITH AUTOINFLAMMATORY DISEASES FOLLOWED-UP IN A UNIT OF PAEDIATRIC AND TRANSITIONAL RHEUMATOLOGY: A DESCRIPTIVE STUDY

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Background: The autoinflammatory diseases (AD) are uncommon, most of them are presented as episodes of recurrent fever and may be accompanied by other inflammatory symptoms. This group of diseases includes polygenic entities (without a single known genes mutation) such as Behcet’s disease (BD), systemic-onset juvenile idiopathic arthritis (soJIA), Chronic recurrent multifocal osteomyelitis (CRMO) and PFAPA syndrome. On the other hand, we found the entities that present with specific monogenic monomutations, such as Familial Mediterranean Fever (FME), TNF receptor-associated periodic syndrome (TRAPS), hyper-IgD syndrome and periodic fever (HIDS), cryopyrinopathies (FCAS, MWS, CINCA). Blau’s syndrome and PAPA. A group of patients who can not be classified into a specific diagnosis are clustered as recurrent fever without known genetic anomaly (RFW).

Objectives: To describe and compare the clinical features of monogenic and polygenic AD and RFW seen in a paediatric and transitional rheumatology unit of a Spanish tertiary care hospital.

Methods: We performed a retrospective study including 39 patients with AD followed in our center.

Results: The distribution of diagnoses was: soJIA 19 patients (48.72%), BD 5 (12.82%), PFAPA 6 (15.38%), CRMO 3 (7.69%), RFW 4 (10.26%), HIDS 1 (2.56%) and CINCA 1 (2.56%). Patients came from different regions of Spain, being 22 of them boys (56.41%) and 17 girls (43.59%). The genetic study was performed in 10 patients, being positive in 7 (17.95%). Mean age at onset of symptoms was 5.5±6.5 years in monogenic diseases, 7.96±4.8 years in polygenic disorders and 9.5±5.91 years RFW. Delay in diagnosis in monogenic diseases was higher than in polygenic diseases (67.69±29 months vs. 24.03±30.33 months, respectively). The clinical manifestations more frequently found were fever, followed by joint involvement, being more common in monogenic diseases than in polygenic disorders (table). Haemoglobin levels were lower in monogenic than in polygenic diseases 9.9±2 g/dL vs. 11.9±0.63 g/dL, ESR and CRP was higher in monogenic diseases 106 mm/h±6.5±80.5 μg/dL vs. 84.14±56.1 mm/h±33.78 and 57.9±59.5 mg/L, unlike ferritin that was more elevated in polygenic disease 896 μg/dL±1788.34 than in monogenic diseases 183 μg/dL±195.7. During his follow up 84.62% of patients received corticosteroids, 51.8% metronexthate and 46.15% biological therapy.

Conclusions: soJIA was the most frequent AD in our center. All the patients had a similar gender distribution. Delay in diagnosis was greater in monogenic diseases compared with polygenic disorders. Fever and joint involvement were the more common clinical manifestations, especially in monogenic diseases. Ferritin levels were higher in polygenic diseases, whereas CRP and ESR which were higher in monogenic diseases. During the follow-up most patients required treatment with corticosteroids and approximately half of them required biological therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6912

AB0962 CLINICAL AND LABORATORY CHARACTERISTICS OF NON-BACTERIAL OSTEOMYELITIS: DATA ANALYSIS OF 91 PATIENTS

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Background: Non-bacterial Osteomyelitis (NBO) is a sterile inflammatory bone disorder of unknown etiology. It typically affects children and most commonly presents with bone pain and/or swelling.

Objectives: The aim of study is to evaluate clinical and laboratory features of non-bacterial osteomyelitis in children.

Methods: Our retrospective – prospective study was included 91 patients with NBO. A routine blood test (WBC, platelets, ESR, C-reactive protein (CRP) and hemoglobin levels), a radiological examination and a bone biopsy with evaluation bacteriological and morphological data were performed in all patients.

Results: The mean age of onset NBO was 7.3 years (2.5; 10.6). We did not reveal any gender peculiarities in our study. Family history of immune-mediated diseases is found in 5/75 (6.7%) in prospective group. Concomitant immune-mediated diseases were noted in 62/89 (68.1%). Diagnostic delay was 6.3 (2.0; 17.8)
Lipid abnormalities in children and adolescents with systemic lupus erythematosus

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Background: Systemic lupus erythematosus is an autoimmune disease that leads to the progressive destruction of the vital organs and systems, promotes early disability, premature mortality. The main reasons for the latest adult population of patients have complications of atherosclerotic vascular lesions such as the myocardial infarction and the stroke. The greatest effectiveness of the population of patients have complications of atherosclerotic vascular lesions, and (1,64±0,54) mmol/L (1,45±0,19) mmol/L vs (0,72±0,08) mg/L (p<0,05). In parallel, the concentration of HDL cholesterol patients of the disease before treatment (r = -0,59). During the treatment, exacerbations were marked only in 1 case, adverse events in 3 cases (skin infections, leukopenia). TCZ therapy allowed to completely discontinue CS in 63,6% cases, minimize them to 4 mg/day in others. DMARDs are discontinued in 9% cases.

Conclusions: Administration of TCZ is rather effective towards the drug induced remission even in long-time JIA process, but the least joint damage, osteoporosis and stunted growth can be obtained with earlier tocilizumab prescription. Reclassification of patients according to specific clinical and immunological features leads to optimization of the selection of targeted therapy.

References:
[1] While identifying in onset of JIA polycellular destruction and systemic features (hyperthermia, anemia, leukocytosis, high laboratory activity and severity of osteoporosis) one should consider the feasibility of early administration of tocilizumab.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2715

EVALUATION OF BONE MINERAL DENSITY IN CHILDREN WITH CHRONIC RECURRENT MULTIFOCAL OSTEOYELITIS AT DIAGNOSIS

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Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare autoinflammatory disorder that has sterile bone inflammation as a main phenotypic feature. Diagnosis of CRMO is based on typical clinical and radiologic findings and presence of some inflammatory markers. Plain radiographs, technetium bone scan and MRI may be used for diagnosis of children with suspected CRMO. Despite data for other imaging methods in children with CRMO, little information is available regarding the bone mineral density.

Objectives: The aim of the study was to evaluate bone mineral density (BMD) findings in children with CRMO at time of diagnosis.

Methods: The medical records of children with CRMO were reviewed retrospectively. Children who met Bristol diagnostic criteria were included in the study. Clinical and laboratory findings, bone scan and MRI features were analyzed. Bone mineral density was measured by DEXA technique at femoral neck and lumbar spine regions; a Z-score was considered as osteoporosis.

Results: Among children treated with TCZ 63,6% were sJIA cases, 63,6% were female. Age of onset 6,1±4,7y (6m–10,5y), all had acute onset, hyperthermia, severe pain syndrome, exudative arthritis in all pJIA cases and half of sJIA cases. ESR 39,7±11,2 mm/h, CRP 53,8±16,1 mg/L, all patients had anemia, leukocytosis and were seronegative for RF and anti-CCP. 3 of pJIA patients revealed ANA (1:1200–2400), 1, IL-6 19,78±5,7 pg/mL. Before biological therapy has begun, SJC courses were continuously relapsing in all cases with 4,7±2,1 exacerbations per y; during the 1st y of illness 8 cases run with coxitis, 7-cervical spine involvement, 9-wrists damage. All patients received CS therapy before initiating TCZ, 45,4% of them with pulse therapy, all marked by the inability to minimize the CS dose, all received 2–4 DMARDs in high doses. 2 patients received adalimumab before TCZ treatment. Elapsed time from the onset to biological agent prescription was 5,3±5,1 years. At the start of biological therapy JADAS was 19,6±5,7, stunted growth -1,88±0,3, α, according to densitometry, osteoporosis took place in every case (Z=−2,7±1,1). After 6 month JADAS was 1,8±1,1, ESR and CRP normalized, IL-6 rate remained high in 36% cases. After 1 year the severity of osteoporosis decreased (Z = −1,17±0,8), bone deficiency on duration of TCZ exposure (r = −0,72) and on the elapsed time from onset of JIA before the start of biological therapy (r = −0,84). The mean increase in height was 7,73 cm/patient-year (−1±0,8). Stunted growth depended on the duration of TCZ course (r=0,81) and the elapsed time from the onset of the disease to the start of biological therapy (r=0,72). After 1 y of TCZ all children had normal weight and BMI for age (19,89±1,9). After 1–5 y of treatment JADAS was evaluated 2,1±2,9 (0–7), the degree of joint damage didn’t depend on the duration of the biological therapy (r=0,24) and correlated with the time elapsed from the onset of the disease before treatment (r = 0,59). During the treatment, exacerbations were marked only in 1 case, adverse events in 3 cases (skin infections, leukopenia). TCZ therapy allowed to completely discontinue CS in 63,6% cases, minimize them to 4 mg/day in others. DMARDs are discontinued in 9% cases.

Conclusions: Administration of TCZ is rather effective towards the drug induced remission even in long-time JIA process, but the least joint damage, osteoporosis and stunted growth can be obtained with earlier tocilizumab prescription. Reclassification of patients according to specific clinical and immunological features leads to optimization of the selection of targeted therapy.

References:
[1] While identifying in onset of JIA polycellular destruction and systemic features (hyperthermia, anemia, leukocytosis, high laboratory activity and severity of osteoporosis) one should consider the feasibility of early administration of tocilizumab.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2715
AB0965  THE CLINICAL OBSERVATION OF IMMUNOADSORPTION IN TREATMENT OF CHILDREN WITH REFRACTORY AUTOIMMUNE DISEASES

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Objectives: Explore the clinical efficacy and safety of the immunoadsorption assisted treatment of children with refractory autoimmune diseases.

Methods: Use HA280 type resin perfusion machine for four times of whole blood immunoadsorption treatment for one case of a 4-year-old child combined with severe dermatomyositis and pulmonary infection, one case of 9-year-old child with severe allergic purpura combined with gastrointestinal bleeding, intestinal perforation and subcutaneous tissue.

Results: Four cases were treated with partial hepatectomy, one case of 11-year-old child with systemic juvenile idiopathic arthritis combined with head and facial cellulites and macrophage activation syndrome. Observe the improvement of its clinical manifestations, serum immunoglobulin, complement, liver and kidney function, myocardial enzymes, autoantibodies.

Conclusions: The whole blood immunoadsorption treatment is able to reduce blood plasma IGG, improvement complement C3 and C4 level, eliminates anti-CCP immune body in vivo, reduce the cardiac muscle zymogrom and the liver enzyme in a short time, increase sensitivity to the adrenal cortex hormone, alleviates immunological disease's symptom in active stage, have the advantage of operation simplicity, high efficiency.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2119

AB0966  HYPOVITAMINOSIS D IN JUVENILE IDIOPATHIC ARTHRITIS: PREVALENCE AND RELATED FACTORS

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Background: 25hydroxy-vitamin D not only plays a key role in calcium homeostasis, but also has antiinflammatory and immunomodulatory properties. Hypovitaminosis D prevalence in children suffering from Juvenile Idiopathic Arthritis (JIA) ranges from 6% to 30% according to different publications.

Objectives: Evaluate hypovitaminosis D prevalence in JIA pediatric patients in Spain and assess involved factors.

Methods: Observational cross-sectional study in JIA Spanish patients from 4 to 15 years, monitored by a Pediatric Rheumatology Unit. Monocarticular forms and patients with other chronic diseases or receiving different treatments from those indicated for JIA were excluded.

Results: 76 children participated. Their characteristics are included in table 1. The population’s prevalence estimation of hypovitaminosis D in children with JIA was 16 - 35% (CI 95%). We found no relationship between 25 hydroxy-vitamin D levels and sex, JIA subtype neither duration or dose of systemic glucocorticoids.

Conclusions: Hypovitaminosis D was defined as 25hydroxy-vitamin D plasma levels lower than 30 ng/ml

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4120

AB0967  CLINICAL, LABORATORY PROFILES AND LONG-TERM OUTCOME OF JUVENILE CUTANEOUS PAN: A SINGLE CENTER EXPERIENCE

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Background: Cutaneous polyarteritis nodosa (cPAN) is an immune complex-mediated rare disease that affects small and medium sized vessels in the dermis and subcutaneous tissue.

The clinical course is characterized by periodic exacerbations and remissions that may persist for many years. Most patients respond to NSAIDs and glucocorticoids (GC), whereas some may require DMARDs and/or immunomodulatory therapy.

Objectives: To describe the different clinical patterns, laboratory findings and long term outcomes of juvenile cPAN in a tertiary care hospital.

Methods: Retrospective observational study, including all patients diagnosed with cPAN between 2002–2016. Diagnosis relied on clinical features confirmed by histological study. Recorded data included clinical features, laboratory results and long-term outcomes.

Results: 10 children were included (7 female), mean age at onset was 9.9 years (r:4.1–16.3). Delay from symptoms onset to biopsy confirmed diagnosis was 2±2.3 months; 4 patients underwent a second biopsy due to inconclusive results in the first performed.

Clinical features included cutaneous (100%) and osteomuscular involvement (50%), fever (40%), neuropathy (10%) and weight loss (10%). Reported cutaneous symptoms were 8 patients with nodules, 4 livedo, 4 purpura, 1 ulcer and 1 necrosis. Most lesions were localized in the lower limbs (8), even though it was also reported in upper limbs (3) and trunk (3). Most cases exhibited raised CRP, ESR and symptoms were 8 patients with nodules, 4 livedo, 4 purpura, 1 ulcer and 1 necrosis.

Conclusions: Clinical and laboratory findings in our series was similar to previous reports. However, our patients presented a greater number of relapses and DMARDs requirement.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2119

AB0968  HYPOVITAMINOSIS D IN JUVENILE IDIOPATHIC ARTHRITIS: PREVALENCE AND RELATED FACTORS

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Background: 25hydroxy-vitamin D not only plays a key role in calcium homeostasis, but also has antiinflammatory and immunomodulatory properties. Hypovitaminosis D prevalence in children suffering from Juvenile Idiopathic Arthritis (JIA) ranges from 6% to 30% according to different publications.

Objectives: Evaluate hypovitaminosis D prevalence in JIA pediatric patients in Spain and assess involved factors.

Methods: Observational cross-sectional study in JIA Spanish patients from 4 to 15 years, monitored by a Pediatric Rheumatology Unit. Monocarticular forms and patients with other chronic diseases or receiving different treatments from those indicated for JIA were excluded.

Anthropometric, clinical and treatment data were recorded. Bone metabolism parameters and validated diet (KIDMED) and exercise (PAQ-C/PAQ-A) questionnaires were obtained.

Hypovitaminosis D was defined as 25hydroxy-vitamin D plasma levels lower than 30 ng/ml

Results: 76 children participated. Their characteristics are included in table 1. The population’s prevalence estimation of hypovitaminosis D in children with JIA was 16 - 35% (CI 95%). We found no relationship between 25 hydroxy-vitamin D levels and sex, JIA subtype neither duration or dose of systemic glucocorticoids.

In bivariate analysis we found direct association between hypovitaminosis D and Body Mass Index percentile (BMI(%) (p=0.05), received dose of prednisone (p=0.03) and clinical activity duration (p=0.04) and an inverse relationship with physical activity level (p=0.04).

In multivariate analysis, relationship between hypovitaminosis D and BMI(%) (B 0.024; p 0.016) and with disease activity (B 0.015; p 0.01) were maintained. Moreover, we found an inverse association with biological disease-modifying antirheumatic drugs (B=-4.69; p 0.048), specifically with anti-tumoral necrosis factor (antiTNFα) (B=-4.7; p 0.042)

Conclusions: Hypovitaminosis D prevalence in our population is similar to previously described.

JIA patients with higher BMI(%) have more hypovitaminosis D, as it has been reported in other inflammatory diseases.

A direct relationship exists between inflammatory activity and vitamin D, but we need more studies to assess if one is cause or consequence of the other.

Patients treated with antiTNFα have better plasma levels of 25 hydroxy-vitamin D, this can be explained because these drugs may increase 25 hydroxy-vitamin D
levels or due to a better response to anti-TNF of those patient with higher plasma levels of 25 hydroxy-vitamin D.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6232

AB0969 IMPACT OF JUVENILE IDIOPATHIC ARTHRITIS ON SCHOOLING
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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children and is one of the major causes of morbidity and physical disability.Due to frequent absences,children with chronic health impairments are confronted with educational difficulties.

Objectives: The aims of this study were to assess the impact of JIA on children’s schooling and to determine the factors that influence their school level.

Methods: This is a cross-sectional study including patients with JIA (ILAR criteria). A detailed questionnaire was completed for each participant by interviewing them or their parents as well as by information obtained from their medical records.Collected data included age,sex,subtype of JIA,disease duration,level of disability according to the Childhood Heath Assessment Questionnaire (CHAQ),visual analog scale for patient’s overall assessment of disease activity,duration of morning stiffness, joint counts,erythrocyte sedimentation rate,C-Reactive Protein,Disease Activity Score (DAS28).Medications used for JIA treatment were also documented.

Data on the school performance of patients and their siblings were obtained using telephone interviews (educational level, absenteeism, school delay by repetition, drop-out).

The comparison of quantitative variables was performed with the Mann-Whitney test and the comparison of qualitative ones was performed with the chi square test. The significance level was set at 0.05.

Results: A total of 38 patients with JIA were included, 23 female and 15 male, with a mean age of 26 years [12–51] and a mean disease duration of 237 months [5–496].The average age of the onset of the disease was 7.4 years [1,15–16].

The most common subtype was rheumatoid factor-positive polyarthritis (n=16) followed by systemic (n=7), oligoarticular (n=4), rheumatoid factor-negative polyarthritis (n=5) and Enthesis-related arthritis (n=4). The mean DAS28 was 2.63 [0.76 - 5.55] and the median CHAQ was 0.528 [0–3].Twenty-seven of the children were receiving corticosteroid. Disease-modifying anti-rheumatic drugs were used by 34 of the 38 patients: methotrexate (n=22), sulfasalazine (n=8),lefunomide (n=7).Ibrotherapies had complications:Hip arthritis (n=15), growth stunting (n=12), uveitis (n=4). Joint replacement was required in 9 cases. Four patients were illiterate,12 had dropped out of school,21 reported repeated absences due to illness.A year of schooling was repeated by 61.7% of patients.Ten out of 32 patients over the age of 20 had an university level.Almost 80% of patients were exempted from physical education.

There were no significant associations between the school-related problems, the socio-demographic characteristics and the various parameters of clinical and biological activity studied.

School failure was similar among patients and their family members.

Conclusions: Our study suggested that JIA negatively affects schooling of children.More studies with a larger sample are needed to identify the variables associated with school failure in order to ensure the proper management of these patients and to increase their academic performance.

References:


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6037

AB0970 CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH RITUXIMAB
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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that is more severe in pediatric population than in adults. Biological therapy with anti-CD20 (rituximab) is an option in patient that do not respond to conventional therapy.

Objectives: The aim of this study is to determine the clinical and immunological response in 9 patients with childhood-onset systemic lupus erythematosus (cSLE) that received treatment with rituximab in a third level hospital

Methods: This is a retrospective observational study. 9 patients treated with Rituximab between November 2007 and October 2016 were included and their medical records were reviewed. The response to treatment at 6 months and one year after the first infusion of Rituximab were assessed. Patients with overlap syndromes were excluded. All patients fulfilled four or more of the 1982 revised American College of Rheumatology criteria for the diagnosis of SLE (<16 years).

Results: Nine pediatric patients with SLE treated with rituximab were included, all of them were female. The age at diagnosis of SLE was a mean of 15.22 years.

Two patients and the median time duration of disease was 87.55months (5–255m). 7 patients were Caucasians. Rituximab was indicated in 6 patients with class IV of lupus nephritis (LN) 1/9 with class III LN, 1/9 with severe cutaneous lupus, and with severe hematological manifestations in 1 case (haemolytic anaemia). In addition, 6/9 patients had mucocutaneous and articular manifestations. The disease activity of all patients was assessed using SELENA-SLEDAI index pre rituximab infusion, the mean was 17.11 (8–33). All patients had low level of complement C3 and C4 and 8/9 increased anti-DNA. In 8/9 patients Rituximab was used as a rescue treatment and in a single case as a first-line treatment.

4/9 patients with renal involvement were previously treated with cyclophosphamide (CYC) IV and mycophenolate, 2/6 CF. In case of cutaneous involvement the previous treatment was methotrexate, azathioprine (AZA) and dapsone and in case of hemolytic anaemia was AZA.

The treatment protocol was 1 gram x 2 (1 cycle) in 7 patients, 75mg/m2 x 4 in 1/9 cases and 600mg monthly for 5 months in the case of haemolytic anemia. Five patients received more than 1 cycle. After the administration of Rituximab, the SELENA-SLEDAI activity index was 4.5 points. At 6 months a complete response was observed in the case of hematological and cutaneous manifestations, in 2 cases of lupus nephritis, in 1 case of severe cutaneous lupus and in 2 cases of cutaneous involvement. Mortality was 11.11% (1/9 patients, per infection and lupus activity, SLEDAI pre rituximab =33).

Conclusions: In our study, although it consisted of few patients, it was objected that Rituximab therapy in patients with cSLE is effective, reduces lupus activity index, especially in cases of renal, cutaneous and hematologic involvement, that 2/9 responded to conventional therapy. It may be consider in the future as an effective alternative treatment at first line treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6846

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Background: The issue of transition from pediatric to adult rheumatology service is an emerging important topic. In 2012 a transition clinic was established according to the “Berliner Transitionsprogram” [1] in cooperation of the Hamburger Zentrum für Kinder- und Jugendrheumatologie and the Rheumatology Unit of the Marien Hospital in Hamburg. The Berliner programme suggests three visits of the patient in transitionprocess, in the presence of the pediatric and an adult rheumatologist together, and the fourth visit conducted by the adult rheumatologist alone. We present the characteristics of the patients at the time of the 4th visit.

Objectives: To characterise the patient population at the time of enrollment into the adult service in the frame of our transition programme.

Methods: We collected patient data starting 8/2012 to 11/2016. We summarized the patient population, who successfully transitioned from pediatric to adult rheumatologic service, concerning diagnosis, sex, age at the time of diagnosis, disease duration at the time of transition, JADAS, HAQ, VAS globular assessment, VAS pain, medication and disease activity.

Results: 73 patients were transitioned. 65% of them female. Mean age at diagnosis of the patients was 12.5 years. Mean disease duration at time of transition was 10.8 years. The mean JADAS Score was 3.18 and the mean HAQ Score was 0.136. The patients global activity score was, on a VAS of 0 to 100, 14.03 and the global pain score, on a VAS of 0 to 100, 12.33. 39.7% of the patients received synthetic DMARDS and 34% biologic DMARDS: Only 1 patient received steroids. 24.6% of the patients were off medication. 63% of the patients were in remission, 31% of them on medication and 39% off medication.

Conclusions: In this monocenter cohort 63% of patients were in remission, and with the mean JADAS Score of 3.18 most of them have low disease activity under the current treatment. The mean HAQ Score with 0.136 reflects a score, which is expected in healthy controls. But 75.4% of the patients needed medication to
AB0972 CHILDHOOD ONSET STROKE AND VASCULITIS ASSOCIATED WITH DEFICIENCY OF ADENOSINE DEAMINASE 2 (DADA2)

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Background: The deficiency of Adenosine Deaminase 2 (DADA2) is a rare autosomal recessive condition resulting from mutations in CECR1 (Cat Eye Syndrome Chromosome Region 1) gene, mapped to chromosome 22q11.1. It is a type of autoinflammatory disease, mainly characterised by early-onset polyarteritis, haemorrhagic, ischemic strokes and hypogammaglobulinemia (1). We report a case of a 7 year boy presenting with haemorrhagic stroke and vasculitis responding to immunosuppression with Anti-TNF drug.

Objectives: A 7 year boy presented to the emergency department with reduced consciousness, headaches and nose bleeds. Initial imaging showed an intraparenchymal haemorrhage requiring frontal craniotomy and evacuation of the haematoma. This acute presentation was preceded by a history of recurrent fevers, weight loss, testicular pain, erythema nodosum and tender lymph nodes.

Methods: The laboratory findings revealed anaemia, ESR of up to 61mm/h, Complement C3 and C4 levels, positive Anti nuclear antibody (ANA), mildly raised antibodies to double stranded DNA (dsDNA) and Proteinase 3 antibody. Skin biopsy confirmed panniculitis. CT imaging and angiography of the head at the time of acute presentation showed intraparenchymal haemorrhage and aneurysm of the left middle cerebral artery. Further CT angiography of the whole body revealed renal and liver microaneurysms. A provisional diagnosis of Polyarteritis nodosa was made and started on steroids and cyclophosphamide. He had further genetic testing, showing mutation in CECR1, leading to Adenosine deaminase 2 deficiency. Patient responded to cyclophosphamide induction regime, which was followed by Etanercept.

Results: We report a case of ADA2 deficiency presenting initially with features of an autoinflammatory disorder, complicated by acute stroke secondary to haemorrhage. Our patient exhibited most of the clinical symptoms previously reported in ADA2 deficiency, including its association with polyarteritis nodosa (2). Although, he did not exhibit hypogammaglobulinemia (3) which has been reported, interestingly, he was positive for markers of autoimmunity (ANA, ANCA) (4). It has been reported that treatment with anti-TNF and IL-6 (5) could lead to improvement, and our patients initial response to cyclophosphamide was excellent, followed by continued treatment with Etanercept.

Conclusions: Screening for adenosine deaminase 2 deficiency should be considered in all children presenting with neurological symptoms and features of vasculitis.


References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5098

AB0973 ANTIPHOSPHOLIPID ANTIBODIES IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND JUVENILE IDIOPTATIC ARTHRITIS

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Background: Antiphospholipid antibodies (aPL) are a family of autoantibodies that present in a small percentage of the population but occur more commonly in patients with Antiphospholipid syndrome (APS) and Systemic lupus erythematosis (SLE).

Objectives: We aimed to determine of the level of anti-β2-glycoprotein I (anti-β2GPI) (IgG and IgM) isotypes and anticardiolipin antibodies (aCL) as inflammatory markers in children with SLE and Juvenile Idiopathic Arthritis (JIA) and figure out their relation to the clinical manifestations and activity of the disease.

Methods: This prospective study included one hundred twenty children, sixty five having SLE and fifty five having JIA, their ages range between 4.5 – 16 years (37 males and 83 females). In addition, twenty apparently healthy children of comparable age, sex and nutritional status were used as a control group. All patients and normal controls were subjected to full clinical and laboratory investigations included aCL and anti-β2GPI level (IgG and IgM) measured by a standardized ELISA.

Results: IgG isotype of anti-β2GPI was found to be positive in 27.7% and 14.5% for SLE and JIA groups respectively. However IgM isotype of anti-β2GPI was found to be positive in 24.6% and 7.25% for SLE and JIA groups respectively. The mean levels of both IgG and IgM isotypes of anti-β2GPI were found to be significantly increased in comparison to controls (P<0.001) in both SLE and JIA groups. IgG isotype of aCL was found to be positive in 23.1% and 18.2% for SLE and JIA groups respectively. However IgM isotype of aCL was found to be positive in 19.5% and 18.2% for SLE and JIA groups respectively. A significant positive correlation was found between IgM and IgG isotypes of anti-β2GPI and with their corresponding class of aCL in both SLE and JIA groups. A significant positive correlation was found between the elevation of anti-β2GPI (IgG) and thrombocytopenia together with neuropsychiatric disease in SLE. While in JIA elevation of anti-β2GPI was found to be correlated only with elevation of aCL irrespective to clinical or laboratory data.

Conclusions: The study reported a higher prevalence of aPL in children with SLE and JIA. Elevated levels of anti-β2GPI (IgG) correlated with thrombocytopenia together with neuropsychiatric disease in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1593

AB0974 ETANERCEPT TREATMENT FOR A PATIENT WITH REFRACTORY MACROPHAGE ACTIVATION SYNDROME IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOUS

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Background: Macrophage activation syndrome (MAS) is a serious, potentially fatal complication of childhood systemic inflammatory disorders, and it is most frequent in Systemic Juvenile Idiopathic Arthritis, for instance, it is increasingly reported in other pediatric rheumatic diseases as lupus erythematous and Kawasaki disease.

Objective: To describe clinical case report of a 16 year old girl with Juvenile Systemic Lupus Erythematosus and Macrophage Activation Syndrome refractory.

Methods: A 16-year-old woman with recent diagnosis of Systemic Lupus Erythematosus in November 2015. At admission with continuous fever lasting 2 months, with initial laboratory studies with Triglycerides 395 mg/dl, Ferritin 3.300 ug/l, soluble receptor IL-2 2.838 U/ml, fibrinogen 166 mg/dl, Hemophagocytes in bone marrow, presence of persistent cytopenias. Initial management with methylprednisolone 30 mg/kg/day (3 days) without clinical response was initiated. Management is added to Cyclosporin A (10 mg/kg/day), reporting subtherapeutic serum levels despite high doses without clinical response and improvement of laboratory controls. During the hospital stay complete 13 months of treatment with Etoposide 180 mg/l/day, with ferritin levels in 4,180 ug/l, triglycerides 438, Fibrinogen 455 mg/dl, WBC 5,000 u1 (3,400 neutrophils, lymphocytes 1,050), platelet count 78 x 103 ml-1, hemoglobin 7.2 g/dl. After three months of treatment, she was given with Etanercept 0.4mg/kg/dose, 2 times a day. Currently in week 3 of treatment with WBC 6,500 ml-1, hemoglobin 9.7 g/dl, platelet count 140 x 103/ml-1 and ferritin 4,270 ng/ml. The patient remains disease with costicosteroid, cyclosporine, and etanercept, without adverse events.

Results: Patient treated with Etanercept during 5 weeks, presenting clinical response for MAS.

Conclusions: A general therapeutic protocol for MAS is not available: first line treatment is usually represented by parental administration of high dose corticosteroids. Mild forms are reported to respond to steroids alone in association with supportive medications. Steroid-resistant cases or the most severe forms of MAS, the addition of cyclosporine A, other therapeutic regimens have been studied such as high-dose intravenous immunoglobulin, antithymocyte globulins, etanercept, etoposide and plasmapheresis.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5636
AB0975  
INCIDENCE OF INFECTIONS WITH BIOLOGICAL THERAPIES IN PARAGUAYAN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: BIOBADAGUAY (BIOLOGICAL THERAPIES ADVERSE EVENTS PARAGUAYAN-URUGUAYAN REGISTER)


Background: Biological Therapies (BT) are important in the therapeutic arsenal of rheumatic diseases; however there is an increased risk of infections with their use.

Objectives: To determine the frequency and type of infections in Paraguayan patients with Juvenile Idiopathic Arthritis (JIA), included in the BIOBADAGUAY Register.

Methods: A prospective observational study of patients with JIA treated with BT, included in the BIOBADAGUAY Register. Patients at the onset of BT were included. The change and/or discontinuation of BT and the occurrence of adverse events (AEs) were recorded. Infectious events as affected organ, type, severity, outcome and need of temporary or permanent suspension of the biological agent were analyzed.

Results: 59 patients with JIA and 69 BT were identified between May 2012 and December 2016. Female: 63% (37); Men: 37% (22). The mean age was 10 (3–18) years old. Mean disease progression of 2.8 (0.2–12) years from the diagnosis to BT beginning. JIA subtypes: poliarticular negative RF (27%), oligoarticular (27%), systemic (12%), polyarticular positive RF (7%), psoriatic (3%), other (indeterminate) (3%). Biologic treatments: Adalimumab (ADM) 41 (59%), Etanercept (ETN) 19 (28%), Infliximab (IFX) 14 (21%), Tocilizumab (TCZ) 9 (13%). There were 83 AEs of all treatments, 80 (96%) non-serious and 3 (4%) severe with 1 death. Infections and infestations 54 (65%) of AEs were recorded. Of all TB infections: the 94% (51) were not serious and recovered without sequela. Most infections recovered without sequelae, except one death due to pneumonia (Table 1).

Table

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<th>Type</th>
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<td>54</td>
<td>28</td>
<td>ADM</td>
<td>34</td>
<td>Temporal</td>
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Conclusions: 1) Infections and infestations (65%) were the AEs more frequently observed. 2) Of all infections, respiratory tract were the most frequently observed. 3) Most of the infections were not serious and recovered without sequela. 4) Although the frequency agent involved in infectious events wasADM (52% of all infections); even so it is the most frequently administered agent. 5) Increased number of patients, greater diversity of treatment as well as a longer data to corroborate the observation period is required.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3228

Other orphan diseases

AB0976  
REMISSION OF MULTICENTRIC RETICULOHISTIOCYTOSIS WITH COMBINATION TOCILIZUMAB AND ZOLEDRONATE

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Background: Multicentric reticulohistiocytosis (MRH) is a rare non-Langerhans cell histiocytosis. It can affect any organ but predominantly skin and joints. Joint involvement usually precedes skin involvement and can be very destructive. Early diagnosis and treatment is therefore important but can be difficult.We describe a woman with MRH and severe erosive joint disease who responded to combination tocilizumab and zoledronate.

Objectives: A 43 yr old woman presented in 2012 with a 3 mth history of rash on her face, chest and ears and fingers, and arthralgia affecting shoulders, wrists, fingers and knees. On examination she had diffuse hand swelling, right knee effusion and erythematous eruption affecting her face, chest and ears with papules on the sides of her fingers. Investigations: normal FBC; CRP; U-Es, LFTs. ESR 12 mm/hr. ANA +ve at 1:1280 (finely speckled). Ro +ve; ENA including Jo-1, ANCA and dsDNA antibodies -ve, C3/C4, lgs all normal/-ve. Hand XR: periarthritis DIP erosions. Skin biopsy: large multinucleate cells with abundant cytoplasm staining positive with CD68 (histiocyte marker); CD1a negative (Langerhans cell marker), consistent with MRH. PET-CT body: incidental finding of thymic remnant.

Methods: Initial Rx:prednisolone 20 mg od + HCQ 200mg bd with initial good response of joint and skin symptoms, but recurrence of symptoms on reducing steroid dose. Nov 2012: MTX up to 20mg /week added. Stopped after 4 mths because of a linear rise in P3NP levels to 11.2. Fibroscan showed slightly raised stiffness of 7.4kPa. AZA 75mg od introduced in Feb 2013, then etanercept 50mg weekly. This led to good control of symptoms for approximately 4 mths on single agent therapy. March 2014: relapse of joint and skin symptoms. June 2014: tocilizumab 8mg/kg iv 4 weekly started. After 5 infusions, her skin cleared for the first time. December 2014: relapse of joint and skin symptoms. Tocilizumab was adjusted to 650mg per mth from 620mg in view of slight weight gain. Annual iv zoledronate 5mg was started. She has had no further joint or skin exacerbations.

Conclusions: The pathogenesis of MRH is poorly understood. The overexpression of cytokines including TNFα, IL-1 and IL-6 in inflammatory lesions gives a number of logical drug options, including tocilizumab. The observation that mononuclear cells in both skin nodules and synovium in MRH exhibit some properties of osteoclasts might explain the mechanism behind reported success using bisphosphonates. To our knowledge, this is only the second case to report success with using tocilizumab in the treatment of MRH and the first to report on concomitant treatment with a bisphosphonate. No adverse effects have been observed throughout treatment, and remission appears to be sustained. Without withdrawing treatment we cannot know if the remission is natural or drug induced, though the relatively short timescale suggests a drug effect.

Disclosure of Interest: None declared

AB0977  
DETERMINATION OF A CUT-POINT BETWEEN LOW/HIGH ANTI RNP ANTIBODIES TITRES, IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE

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Background: Sharp described Mixed Connective Tissue Disease (MCTD) in 1972[2]. MCTD is characterised by the presence of Raynaud phenomenon, puffy hands, synovitis, acrosclerosis, myositis and positive ribonucleoprotein (RNP) antibodies. Classification criteria for MCTD except for Kasukawa’s criteria demand the presence of high titres of anti-RNP antibodies (measured by hemagglutination). As a result, the cut-point between low and high anti-RNP titres must be well defined. In best of our knowledge, this cut-point have not been established for modern laboratory techniques.

Objectives: Determine a cut-point between low/high anti-RNP titles measured by ELISA, for the diagnosis of Mixed Connective Tissue disease. Describe the clinical and immunological characteristics of patients with positive titres of anti-RNP antibodies.

Methods: It was a Retrospective cohort study of patients with positive anti-RNP antibodies (>10) measured by ELISA. We had identified all patients with positive anti-RNP antibodies titles in the last five years, using our laboratory base date. Clinical histories were reviewed, we recollected clinical and paraclinical data. We performed descriptive analysis and ROC curves for diagnostic tests with STATA software.

Results: We detected 75 patients with positive antiRNP antibodies, we obtained 65 clinical records. 89,23% (58) of patients were women and 10,77% (7) men.
ASSOCIATION OF INFLAMMATORY ARTHRITIS WITH VOGT-KOYANAGI-HARADA SYNDROME (VKHS)

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Background: VKHS is a rare cause of granulomatous uveitis leading to significant visual loss in patients who develop it, usually accompanied by extracocular manifestations that include meningitis, vitiligo, poliosis, and hearing loss. In our country it is responsible for 13% to 27% of all uveitis, affecting mainly young women.

Objectives: To describe the presence of inflammatory arthritis in patients with VKHS at a third level hospital.

Methods: A cross-sectional study of 4 patients with established VKHS that fulfilled the 2001 revised diagnostic criteria for Vogt-Koyanagi-Harada disease (1) was rolled out. Ultrasoundography was performed to all patients by a trained rheumatologist in carpal, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints evaluating presence of power Doppler (PD) signal, bone erosions, and cartilage changes.

Results: We included 3 women and 1 man, mean age was 34.7±10.3 years, and they all had characteristics of complete VKHS. Mean disease duration (since first manifestation of ocular symptoms) was 5.2±3.5 months. One patient had synovitis (36.8%) and in the majority one did not find trigger factor. There was presence of arthritis in a significant percentage of patients. In the last years the use of the RMN has been added to the diagnosis and to the follow-up. Throgh there are no clinical tests that support it the use of the metotrexato has been generalized as adjuvant treatment to the steroids.

Conclusions: The prevalence of inflammatory arthritis in patients with VKHS has only been described in one case (2). Despite the exceptionality, we propose that polyarthritis and probably erosive arthritis can represent part of the spectrum of the disease, processes that share some features of the genetic susceptibility with rheumatoid arthritis as HLA-DR4, CTLA-4 and STAT4.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6914

EOSINOPHILIC FASCITIS: CLINICAL EXPERIENCE IN A SERIES OF 21 PATIENTS

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Background: The Eosinophilic fascitis (EF) is an uncommon sclerodermiform syndrome with unknown etiology and poorly understood pathogenesis and natural evolution. The published cases are short, with a total of 280 cases described in the literature from 1974. There is neither clinical tests nor consensus on the EF treatment.

Objectives: To describe a series of 21 patients with EF.

Methods: Multicentric, retrospective Case Series Study

Results: We reviewed 21 patients diagnosed of EF (cutaneous induration-consistent biopsy) between January 1998 to January 2015. A total of 13 males and 8 females.

Conclusions: In our series, the EF prevals in males, in the decade of the 40 and in the majority one did not find trigger factor. There was presence of arthrits in a significant percentage of patients. In the last years the use of the RMN has been added to the diagnosis and to the follow-up. Throgh there are no clinical tests that support it the use of the metotrexato has been generalized as adjuvant treatment to the steroids.

Disclosure of Interest: None declared


Disclosure of Interest:

Other clinical and analytical manifestations (N=21).

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</tr>
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<td>8 (37)</td>
</tr>
<tr>
<td>Elevated ESR</td>
<td>4 (16)</td>
<td>17 (64)</td>
</tr>
<tr>
<td>Elevated LD</td>
<td>8 (37)</td>
<td>13 (63)</td>
</tr>
<tr>
<td>Elevated CK</td>
<td>0</td>
<td>21 (100)</td>
</tr>
<tr>
<td>Systemic symptoms</td>
<td>7 (32)</td>
<td>14 (68)</td>
</tr>
<tr>
<td>Pericardial affection</td>
<td>3 (11)</td>
<td>18 (89)</td>
</tr>
<tr>
<td>Autimmune thyroid</td>
<td>2 (5)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>4 (16)</td>
<td>17 (84)</td>
</tr>
</tbody>
</table>

Conclusions: In our series, the EF prevals in males, in the decade of the 40 and in the majority one did not find trigger factor. There was presence of arthrits in a significant percentage of patients. In the last years the use of the RMN has been added to the diagnosis and to the follow-up. Throgh there are no clinical tests that support it the use of the metotrexato has been generalized as adjuvant treatment to the steroids.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4483

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6914
AB0981 CLINICAL FEATURES OF 28 CASES OF LIMB RESTRICTED VASCULITIS AND FASCITIS
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Background: We sometimes experience the cases with fever and muscle pain of lower limbs without any specific features. There are sporadic case reports of eosinophilic fasciitis and limb restricted vasculitis. However, few reports compare and discuss such cases.

Objectives: To describe the clinical features, MRI findings, histopathology, diagnosis and response to treatment of these cases.

Methods: We retrospectively analyzed the clinical features of 28 patients who were admitted to our hospital because of fever and muscle pain of lower limbs from 2004 to 2016.

Results: Among the 28 patients, 17 were vasculitis syndrome; eleven were limb restricted small vessel vasculitis (LrSvv), six were microscopic polyangiitis (MPA). Seven were fasciitis; three were eosinophilic fasciitis, three were diffuse fasciitis without eosinophila and one was tuberculosis fasciitis. One was relapsing polychondritis. The other 21 patients were without a specific diagnosis. In our study, average age was 57.5±19.9 years old and older than in previously reported cases of limb restricted vasculitis.[1,2] Sixteen were female; twelve were male. Abnormal MRI findings in non-inflammatory fasciitis and vasculitis syndrome were bilateral. Tuberculous fasciitis showed specifically abnormal intensity and fluid collection in unilateral thigh. Unilateral lesion and fluid collection may indicate infectious disease and bilateral lesion may indicate autoimmune or autoinflammatory diseases. MRI of vasculitis syndrome and fasciitis showed hyperintense T2-weighted signals in muscles of either legs, or thighs, or both. Twenty-three patients (n=23) showed atypical abnormal signal intensity in most cases with fasciitis and 6 (40%) with vasculitis syndrome. It was difficult to differentiate between vasculitis and fasciitis by MRI findings. Muscle biopsy was performed in 25 patients. In most cases, we performed en bloc biopsy, including muscle, fascia, skin and subcutaneous tissue. MRI was useful to determine the location of biopsy. All patients were treated with glucocorticoids. Immunosuppressive agents (azathioprine, n=10; methotrexate, n=5; cyclophosphamide, n=1; tacrolimus, n=1) were added in 15 patients and anti-tuberculosis drugs in one. None of the 11 patients with LrSvv showed positive blood tests of anti-nuclear, cytoplasmic antibody or developed any other organ involvement during follow-up period (median 96 months; range 3–125). They responded well to glucocorticoid therapy (oral prednisolone 0.5–6.0mg/kg/day or intravenous methylprednisolone at doses of 1g/day). Recurrence rate of LrSvv was 0%, although that of MPA patients was 50% (n=3). In four patients with LrSvv, treatment was ceased and they achieved drug-free remission. There were no apparent differences between the patients who achieved drug-free remission and who didn’t.

Conclusions: MRI and muscle biopsy were useful for diagnosis of disease with fever and muscle pain of lower limbs.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4169

AB0983 MEFV MUTATIONS IN ARMENIAN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES
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Background: The systemic diseases of connective tissue have autoimmune mechanism in development. While autoimmunity involves adaptive immune activation, autoinflammation involves innate immune activation. The prototype of autoinflammatory diseases is familial Mediterranean fever (FMF), which is the global medical problem for Armenian ethnics on the whole, affecting 1–2% of population.

Objectives: The aim of this study was investigation of MEFV mutations and their possible influence on the systemic diseases in Armenian patients.

Methods: We have examined 183 patients with FMF. All patients with FMF fulfilled Tel-Hashomer FMF diagnostic criteria. Molecular-genetic detection of 12 MEFV mutations common for Armenians carried out in Medical Genetic Centre of Armenia. In 49 patients one of autoimmune systemic diseases was diagnosed: in 24 patients-sarcoidosis, in 23 - systemic lupus erythematosus (SLE), in 1 - systemic sclerosis.

Results: In the SNSA group from 21 patients 16 were male, 8 were female, the mean age of patients was 35.4±12.2. The mean age at the beginning of the disease was 14.91±12.6. In all cases the symptoms of FMF were preceded by specific symptoms of arthritis. Unilateral saccroilitis was revealed in 6 patients, bilateral saccroilitis in 18 patients. The limitation of lumbar motion was assessed by Schober’s test. 7 patients with Schober’s test 1–2 cm had bilateral sacroiliitis grade III-IV and fulfilled the modified New York criteria for analysing spondylitis. HLA B-27 was examined in 7 patients. In 5 cases it was negative, and in 2 cases –positive. MEFV gene analyses were carried out in 21 cases: 7 patients had one heterozygote mutations: 6-M694,1-M680I; 5 patients -M694V/M694V, 9 patients had compound heterozygote mutations: 5- M694V/VT268A, 3 - M694V/E148Q, 1 - M690/V148Q. So, the prevalent mutation was M694V.

In SLE group from 23 patients female were 21 (91.3%), male – 2 (8.7%). Mean age of patients was 37.4±2.5 years. The beginning of FMF was earlier than SLE. The activity of SLE estimated by SLEDAI index was significant lower than in FMF. SLE and FMF co-occurring with M694V. M694V co-occuring lupus according to both clinical and laboratory findings including serological markers of SLE -ANA, anti-dsDNA. The prevalent mutation was M694V - 44.6%; VT268A was 21.7%, M680I-9.8%. Most common variations with M694V were M690I/V148Q. None of patients had mutation V726A.

Conclusions: MEFV is involved in the development of SLE. M694V is the main mutation in SLE patients in Armenia.

References:
Results: All patients were males with a mean age of 67 years (range 53–78). Two had pancreatic involvement; one had lymph node enlargement; one had pancreatic and lymph node involvement; one had pancreatic, aortic, submandibular gland and lymph node involvement. Patients with pancreatic involvement presented with increased serum amyloses or abdominal discomfort; none had obstructive jaundice; all had overt diabetes. The mean IgG4-RD RI, serum IgG4 concentration and plasmablasts counts at baseline were 8 (6–15), 483 mg/dL (136–983) and 3336/mL (330–9330 /mL), respectively. All patients had increased 18F-FDG uptake on PET/CT scan within the affected organs. After 6 months of methotrexate, Patients 1, 2, and 3 were on CR with improved or normalized PET/CT findings, serum IgG4 and plasmablasts levels. Patient 5 achieved PR, showing in loved 18F-FDG-PET/CT findings, normal plasmablasts level, but stable serum IgG4 concentration; after 10 months of methotrexate, persistence of disease activity prompted the introduction of glucocorticoids. Methotrexate was stopped in Patient 4 after 5 months of nausea and vomiting; at 6 months he showed persistently increased plasmablasts count and 18F-FDG uptake on PET/CT, thus requiring a rescue therapy with glucocorticoids. (Table 1)

Conclusions: In localized forms of IgG4-RD with mild manifestations, methotrexate represents a promising alternative strategy for inducing disease remission, especially in the presence of contraindications to glucocorticoids.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4499

AB0986 FAMILIA MEDITERRANEAN FEVER GENE MUTATIONS: A POORLY STUDIED CAUSE OF INTERMITTENT HYDARTROSIS

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Background: Familial Mediterranean Fever (FMF) is an inherited autoinflammatory disorder caused by mutations in the MEFV gene encoding pyrin, characterized by recurrent episodes of fever and serositis. Some patients with FMF present incomplete and atypical manifestations of FMF disease and pyrin manifests only as intermittent arthritis.

Objectives: Characterization of musculoskeletal clinical manifestations in patients with mutations of the MEFV gene in our hospital.

Methods: We retrospectively reviewed clinical records of patients with mutations detected in the Family Mediterranean Fever MEFV gene in our hospital from January 1, 2008 to October 1, 2016. We collected parameters such as age at diagnosis, age of onset Of the symptoms, sex, affected joints, other extra-articular manifestations and type of MEFV gene mutation.

Results: Eight patients (5 males, 3 females) aged from 3 to 51 years (mean 36) were identified. All patients had fever, polyarthritis or pericarditis and serositis (pericarditis 7/8, pleuritis 6/8, abdominal pain 5/8). Four patients had pericarditis, pleuritis and serositis. Five patients were treated with colchicine, two with glucocorticosteroids. Three patients had a complete response, one a partial response and four a poor response to treatment.

Conclusions: Few case reports have already shown the efficacy of tocilizumab (TCZ) in PMR patients. IL-6 is involved in the pathogenesis of PMR and quite a few case reports have already shown the efficacy of tocilizumab (TCZ) in PMR patients and some of them received TCZ mono-therapy without GC. TCZ mono-therapy may be a good alternative therapy instead of GC for elderly patients with various comorbidities.

Disclosure of Interest: None declared


AB0985 METHROTAXITE AS INDUCTION OF REMISSION THERAPY FOR LOCALIZED MANIFESTATIONS OF IGG4-RELATED DISEASE

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Background: Medium to high dose glucocorticoids represents the treatment of choice for inducing remission in patients with IgG4-related disease1. However, clinicians might prefer alternative equally effective drugs in clinical settings where long-term corticosteroids treatment is contraindicated, such as diabetes or osteoporosis. We recently reported the efficacy of methotrexate in maintaining glucocorticoid-induced IgG4-RD remission2.

Objectives: To evaluate the efficacy of methotrexate as induction of remission therapy in selected cases of mild and localized IgG4-RD complicated by clinical scenarios that might advise against corticosteroids treatment.

Methods: Five patients with active untreated IgG4-RD were started on oral or subcutaneous methotrexate (up to 15–30 mg/week). Efficacy of methotrexate in inducing remission was assessed at 6 months by 18F-FDG PET/CT scan and by measuring the IgG4-RD Responder Index (RI)3 and circulating plasmablasts4. Partial response (PR) corresponded to an improvement of the IgG4-RD RI > 2 points. Complete response (CR) corresponded to an IgG4-RD RI score < 3.

Conclusions: In localized forms of IgG4-RD with mild manifestations, methotrexate represents a promising alternative strategy for inducing disease remission, exceptionally in the presence of contraindications to glucocorticoids.

References:

Disclosure of Interest: None declared

Results: Seven patients with MEVF gene mutations were reviewed, all of them were women, ranging in age from 14 to 61 years old. Two of them had recurrent knee monoarthritis, one had a history of arthritis in the hands and erratic arthralgias, one had erratic arthralgias and two had no musculoskeletal manifestations. The 2 patients with intercurrent hydrarthrosis responded satisfactorily to colchicine, but not the other patients with other musculoskeletal manifestations.

Conclusions: Genetic testing of the common mutations of the MEVF gene should be considered in patients with recurrent episodes of monarthropathy without justifying cause (palindromic rheumatism, intermittent hydrarthrosis, etc.)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6487

AB0088 BEHÇET’S DISEASE IN A DEFINED AREA OF NORTHERN WESTERN SPAIN

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Background: Behçet’s disease (BD) is a multisystemic inflammatory chronic disease. There is a wide variation in the clinical features of BD among geographical groups.

Objectives: To determine the demographic and clinical characteristics of BD in a defined area of northwestern Spain (Vigo).

Methods: Patients with BD (International Criteria BD) and seen in the University Hospital of Vigo in Spain, from 1994 to 2016, were retrospectively enrolled. Demographic, clinical, treatment and evolution data were recorded and analyzed using SPSS 22.0.

Results: Our patients were 26 male and 25 female. The mean age at the onset of the disease was 33±11.95 years (11–62). Oral and genital ulcers were seen in 100% and 84.3% respectively and skin lesions in 88.2%. Ocular involvement occurred in 35.3%, neurological disease in 39.2% and gastrointestinal involvement in 29.4% (the area worst affected was colon and small bowel). Vascular disease was present in 33.3%. See table 1. Pathergy test was performed in 18 patients (35.29%) and 10 (55.5%) were positives. HLA BS1 was studied in only 13 patients (25.5%) and 8 (61.5%) were positives. 62.7% of patients had no cardiovascular risk factors (CVRF), 27.4% were smokers, 7.8% were hypertensive and 3.9% were hyperlipidemic and diabetic respectively. CVRF were not related to thrombotic events (p<0.05). In regard to gender influence, only pseudofolliculitis was significantly more frequent in men (p<0.001). There was a trend for increased prevalence of ocular disease and elevated erythrocyte sedimentation rate/serum C-reactive protein in men, and anemia in women, which, however, did not reach statistical significance. Treatment consisted of corticosteroids (92.2%), colchicine (88.6%) and another immunosuppressive agent (35.3%). During the disease course 78.4% of the patients had an outbreak, 45.1% initiated or changed to immunosuppressive agent and 19.6% used biological drugs. Most of our patients (92.1%) were admitted to hospital and these constitute an evident bias. Two patients died during the follow-up period, but only one in relation of BD (upper gastrointestinal bleeding and seizures).

Conclusions: Our series has some particular aspects especially the high frequency of gastrointestinal lesions and neurologic involvement. CVRF do not seem to play a role in the development of thrombotic events. Our results confirm the high geographic variation of BD expression.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3983

AB0089 RHEUMATOLOGIC COMPLICATIONS OF THALASSEMSIA: SHOULD RHEUMATOLOGISTS JOIN THE MANAGEMENT TEAM?

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Background: Beta-thalassemia major is accompanied by progressive multi organ systems involvement due to the disease pathophysiology as well as iron overload from blood transfusions on a regular basis. Rheumatologists are not frequently involved in the multidisciplinary management of the disease, in which rheumatologic complications are relatively common.

Abstract AB0089 – Table 1. Clinical manifestations of our BD patients

| Abstract AB0088 – Table 1. Clinical manifestation of our BD patients |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Skin lesions | Ocular disease | Neurologic disease | Vascular disease | Gastrointestinal involvement |
| 41/55 (88.2%) | 19/51 (35.3%) | 20/51 (39.2%) | 17/51 (33.3%) | 15/51 (29.4%) |
| Pseudofolliculitis | 58.8% | Venous thrombosis 21.6% | Pain 11.7% |
| Erythema nodosum | 39.2% | Arterial thrombosis 7.8% | Bleeding 9.8% |
| Avascular necrosis | 5.9% | Cerebral venous thrombosis 5.9% | Diarrhea 5.9% |
| Paresthesias | 3.9% | White matter lesions 5.9% | Fever 2% |
| Venous occlusion 2% | | Stroke 3.9% | | |
| Others 5.9% | | Migraine 3.9% | | |
AB0990

PERI-ARTERITIS AS A NOVEL PARANEOPLASTIC PRESENTATION OF MYELODYSPLASTIC SYNDROME: A CASE SERIES AND REVIEW OF THE LITERATURE

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Background: Myelodysplastic syndromes (MDS) are characterized by ineffective and dysplastic hematopoiesis resulting in peripheral blood cytopenias with varying risk for progression to acute myelogenous leukemia (AML). Autoimmune manifestations have been well described in association with MDS1. Peri-arteritis has rarely been reported.

Objectives: Here, we present a novel association of MDS with peri-arteritis.

Methods: Three patients within our institution and one in the literature were identified. Patients were diagnosed with MDS according to 2008 World Health Organization classification with concomitant occurrence of peri-arteritis on imaging2.

Results: See Table 1.

Conclusions: Autoimmune manifestations associated with MDS occur in 7–25% of patients. The most commonly reported conditions include vasculitis, inflammatory arthritis and connective tissue disease. There is a paucity of literature describing peri-arteritis associated with MDS. Review of the literature revealed only one other case of peri-arteritis associated with MDS outside of those identified at our facility3.

With this case series, we report peri-arteritis as a novel presentation of MDS. Peri-vascular inflammation may mimic idiopathic retroperitoneal fibrosis, however, may be attributed to genetic factors. Arthritis may develop secondary to iron deposition in the synovial tissue or due to iron chelators such as deferoxamine, which may provoke a self-limited arthritis due to synovial destruction sustained by free radicals production during iron interchange. Several studies reported increased incidence (16%–30%) of arthropathy in beta-thalassemia patients on deferoxamine therapy. Multiple etiologies contribute to osteoarthritis in thalassemia patients such as bone marrow expansion, iron deposition within the joint, and hypoparathyroidism. Only few cases of Salmonella enteriditis septic arthritis were described in thalassemia patients. The associations between osteopetrosis and hypogonadism, diabetes, and vitamin D and calcium deficiency were found significant. Skin lesions of PXE were reported in up to 16% in beta-thalassemia.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3332

Patient 1

Age 67
Sex Female
MDS type CMML-1

Presenting Symptoms Hydropnephrosis, abdominal pain, weight loss
Bone Marrow Biopsy Hypercellular features of CMML-1

ANCA and ANA Negative
ESR (0–15mm/hr) 21
CRP (<0.9mg/dL) 5.4

Treatment Corticosteroids

Clinical Course Unilateral stenosing and nephrostomy tube placement improved symptoms. Inflammatory markers remained elevated despite treatment.

References:
A DIFFICULT DISTINCTION – ERDHEIM-CHESTER DISEASE MIMICKING IGGA-RELATED DISEASE

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Background: Rheumatologists are often confronted with systemic and rare diseases. Even among the rare diseases, clinical features may overlap, but treatment options for different diseases may differ.

Objectives: To illustrate the diagnostic challenges the clinician is confronted with when facing rare and systemic diseases in clinical practice with a case report where clinical features were overlapping.

Methods: A 64-year-old woman was presented to our institution after suffering from two ischemic strokes. Cerebral imaging was suggestive of large-vessel vasculitis. Additionally, imaging also revealed a left-sided retro-orbital mass. Her past medical history was notable for retropertioneal fibrosis with ureteral obstruction requiring percutaneous drainage six months before presentation and placement of a cardiac pacemaker several years ago. Treatment with high-dose prednisone had been initiated but showed no clinical or laboratory improvement.

Results: Clinical examination revealed mild persistent facial hemiparesis and difficulty with ambulation. Mild exophthalmos was present on her left side. On palpation, there were palpable axillary masses bilaterally. Otherwise, her physical examination was normal. Laboratory analysis revealed elevated soluble interleukin-2 receptor levels at 2800 IU/mL (N: 230–770 IU/mL) and mildly increased C-reactive protein at 10 mg/L (N: <5 mg/L). Autoantibodies, including rheumatoid factor, IgG4, ANCA, ANA, and ERA were all within normal range. Plasma cells were normal on flow cytometric analysis. A PET-CT was performed which revealed signs of alveolitis, retropertioneal fibrosis, axillary masses with strong tracer uptake (figure 1) as well as tracer uptake of the left femur and periaortic sheathing. We performed a biopsy of the left-sided axillary mass. Histopathologic analysis showed Touton giant cells and septal fibrosis. Staining was negative for CD1a and S100 but positive for CD68. Molecular pathologic analysis revealed the presence of the BRAFV600E mutation, findings that are consistent with the diagnosis of Erdheim-Chester disease. We initiated treatment with the BRAF-inhibitor vemurafenib and will follow the patient closely. Staining for IgG4 was negative.

Conclusions: Erdheim-Chester disease (ECD) and IgG4-related disease are very rare disorders and can present with similar clinical findings, such as retropertioneal fibrosis, alveolitis or lymph node enlargement. About 500 cases of ECD worldwide have been reported. ECD is a non-Langerhans cell histiocytosis with a reported five-year survival rate of about 68%. Roughly 50% of patients show a BRAF mutation. Various treatment options have been reported and are recommended by the recently published consensus guidelines (1). These include interferon-alpha, vemurafenib and also TNF-alpha inhibitors, such as infliximab, but also interleukin-antagonists, such as anakinra (IL-1) or tocilizumab (IL-6). Rheumatologists have to consider non-Langerhans cell histiocytoses in the differential of systemic diseases because the distinction can be difficult and imaging, as well as meticulous histopathologic analyses, are necessary to correctly diagnose these patients because treatment differs.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8903

ELDERLY - ONSET SARCOIDOSIS: A SINGLE CENTER COMPARATIVE STUDY

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Background: Sarcoidosis is a chronic granulomatous inflammatory disease characterized with non-casefied granuloma formation. It is rarely affects patients older than 65 years old.

Objectives: The purpose of this study is to compare and evaluate the demographic, clinical and laboratory features of elderly-onset (EOS) and young-onset sarcoidosis (YOS) patients.

Methods: One hundred and thirty one patients diagnosed with sarcoidosis according to clinical, radiologic and histopathological evaluation were included in this study. The patients with initial symptoms started after age 65 were accepted as EOS. Demographic, clinic, radiologic, and laboratory data and the medication which the patients received were recorded and retrospectively evaluated.

Results: Twenty (15.3%) of 131 patients were diagnosed as EOS, and 111 (84.7%) patients were evaluated as YOS. Fifteen of 20 EOS patients were female and 5 and 5 of them were male. Average duration of the disease was determined as 38.4months for YOS and 22.5months for EOS (p=0.556). Delay of the diagnosis was 12months for YOS while it was 3months for EOS (p=0.001). Higher rates of fatigue, comorbid diseases and more Hydroxychloroquine (HQ) use were detected in EOS patients comparing to YOS (p=0.010, p=0.003 and p=0.049 respectively). There was obviously more disease modifying anti-rheumatic drugs (DMARDs) use by YOS group but statistical difference wasn’t significant. The 3-year survival rate after diagnosis of sarcoidosis was %95 in the EOS group, compared with %100 in the YOS group.

Conclusions: In this study we showed that EOS and YOS patients may be characterized with different clinical, and laboratory features. EOS patients are characterized with higher rates of fatigue and comorbid diseases, less inflammatory sign and delayed diagnosis, and less DMARDs usage.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1377

ANTI TNF-ALPHA THERAPY WOULD BE LIFESAVING IN DEFICIENCY OF ADENOSINE DEAMINASE-2

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Background: Deficiency of adenosine deaminase-2 (DADA2) is a rare form of autoinflammatory disorder with limited reported cases.

Objectives: In this study, we have characterized the clinico-immunological, radiological and genetic characteristics of eight childhood-onset DADA2 patients. We aimed to compare these features between surviving and deceased patients.

Methods: Demographic features, clinical characteristics, imaging findings, mutations and pharmacological treatments compared between surviving and deceased DADA2 patients.

Results: Eight patients from seven families were enrolled. While five of them were still surviving, three of them had died due to various reasons. Median age of the patients at disease onset and diagnosis were 7 years (range 0.5–13 years) and 14 years (range 5–27 years), respectively. The main clinical manifestations were cutaneous manifestations (7/8), recurrent low-grade fever (6/8), neurological involvement (6/8) and gastrointestinal involvement (5/8). All patients had increased acute phase reactants at presentation and also during flares. Until the diagnosis of DADA2, five patients had been followed-up with the diagnosis of PAN; two patients both with PAN and FMF, and one patient with CAPS and vasculitis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8903

Abstract AB0994 – Table 1. Clinical features and imaging results of DADA2 patients

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<th>9</th>
<th>7</th>
<th>7</th>
<th>1.5</th>
<th>13</th>
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<td>PAN</td>
<td>PAN</td>
<td>PAN</td>
<td>PAN-FMF</td>
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<tr>
<td>GIS involvement</td>
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<td>Yes</td>
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<tr>
<td>Cutaneous findings</td>
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<td>Yes</td>
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<td>No</td>
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<tr>
<td>Neurologic involvement</td>
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<td>Yes</td>
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</tr>
<tr>
<td>Neuroimaging findings</td>
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<td>Hemorrhagic stroke</td>
<td>Periventricular leucomalasia</td>
<td>Normal</td>
<td>Normal</td>
<td>Cerebral atrophy</td>
<td>Ischemic stroke</td>
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Scientific Abstracts: Disclosure of Interest:
Demographic, clinical, neurological features and genetic mutations did not differ in surviving and deceased DADA2 patients. Deceased and surviving subjects differed in terms of medication usage after the diagnosis of DADA2. Anti-TNF alpha treatment has been initiated in 5 surviving patients soon after the diagnosis of DADA2. However, unfortunately three patients who have died, were able to use either a few dosage of anti-TNF alpha treatment or none; one patient due to reluctance of patient and two patients due to establishment of a definite diagnosis with genetic analysis after the patients had died.

Conclusions: Although this study includes limited number of patient, to our knowledge this study for the first time compares the phenotypic, genotypic and medication differences between surviving and deceased DADA2 patients. Anti-TNF alpha treatment seems to be very efficient and lifesaving in DADA2 patients.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4254

AB0995
CLINICAL, THERAPEUTIC, AND GENETIC ANALYSES IN A PATIENT WITH PAPA SYNDROME COMPLICATED WITH INFLAMMATORY BOWEL DISEASE

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Background: PAPA syndrome is an autoinflammatory disease linked to mutations in the PSTPIP1 gene [1]. These mutations produce a hyper-phosphorylated PSTPIP1 protein and alter its participation in the activation of the "inflammases" [2]. PAPA syndrome is characterized by pyogenic arthritis with pyoderma gangrenosum and acne, and usually treated with corticosteroids. Reports from the literature suggest that patients with poorly controlled PAPA syndrome may benefit from IL-1 alpha treatment. We herein reported a Japanese PAPA syndrome patient who have been affected by a mutation of the PSTPIP1 gene.

Methods: We herein report a 25-year-old Japanese male who suffered from recurrent arthritis in his knee and ankle joints, pyoderma gangrenosum, and acne. He had experienced melena and multiple colonic ulcers had been detected by colonoscopy. His ulcerations resembled ulcers associated with Crohn’s disease. A biopsy of colon was performed for the evaluation of this colonic lesions. Histopathologically, the ulcer appeared as a deep ulcer leading to the submucosal tissue. The surface of the ulcer remained intact. Isolation of microorganisms from the ulcer was not carried out. The 45-year-old father of this patient had the same mutation, thus suggesting that this mutation of PSTPIP1 gene might not be related to his phenotype. We are currently carrying out genetic analysis to confirm this hypothesis.

Results: 1) A histological analysis revealed that a large number of neutrophils had accumulated in the skin lesions; however, very few neutrophils were detected in the pathological lesions of the knee joints and colon. 2) According to a gene analysis, we detected a novel heterozygous mutation (E101G) in the PSTPIP1 gene. This mutation was also found in the healthy father also had the same mutation, thus suggesting that this mutation of PSTPIP1 gene might not be related to his phenotype. A search of other affected genes besides the PSTPIP1 gene for PAPA syndrome in this case. 3) After treatment of biologics (infliximab), the clinical symptoms, such as arthritis and multiple colonic ulcers, were considerably improved and the serum level of IL-6 and TNF-α were decreased in this patient.

Conclusions: We herein reported a Japanese PAPA syndrome patient who was complicated with inflammatory bowel disease and had a good response to biologics. A genetic analysis suggested that this particular phenotype might not have been affected by mutation of the PSTPIP1 gene.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3986

AB0996
FREQUENCY OF HLA-B*51 AND THE ASSOCIATION WITH CLINICAL MANIFESTATIONS IN ARABIAN PATIENTS WITH BEHÇET DISEASE

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Background: Behçet disease (BD) is a systemic inflammatory disease mostly characterized by oral and genital ulcers and variable manifestations affecting other organs, mainly skin and eye. The HLA class I molecule HLA-B*51 allele is strongly associated with BD in many different ethnic groups and appears to be a significant risk factor for BD in the ancient Silk Route areas in contrast with Western and Northern Europe and U.S.

Objectives: Our purpose was to show the frequency of presence of HLA-B*51 allele in Arabian patients with BD and estimate any correlation with common symptoms of disease depended on presence of HLA-B*51.

Methods: Forty-seven patients of Arabian origin (28 males, 59.6% and 19 females 40.4%) fulfilling the International Criteria for BD (ICBD) with mean age 29.7±11.3 years; disease duration – 5±12.4 years were enrolled. We observed the clinical manifestations of BD of both HLA-B*51 carriers and non-carriers.

Results: HLA-B*51 was detected in 38 (80.8%) patients, of whom 25 male and 13 female (65.8% and 34.2%, respectively). Arthritis, erythema nodosum and genital ulcers were significantly more common in HLA-B*51-positive patients (83.3%, 83.3% and 80.6% respectively) than in HLA-B*51-negative ones (16.7%, p=0.032, 16.7% p=0.032 and 19.4% p=0.023 respectively).

Conclusions: In the HLA-B*51 first estimation of frequency gene in patients with BD in Armenia, our result indicated that the frequency of HLA-B*51 allele in BD is 80.8% which is higher than elsewhere (In Japan 58.9%, Iran 61.9%, Turkey 75%, Saudi Arabia 76.9% Greece 78.9%)5. Furthermore, this investigation revealed HLA-B*51 carriage much more often in male than in female BD patients. In addition HLA-B*51 carriers are in significant higher risk of development of arthritis, erythema nodosum and genital ulcers.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4715

Diagnostics and imaging procedures

AB0997
ULTRASONOGRAPHIC EVALUATION OF ANTERIOR KNEE PAIN IN YOUNG ADULTS

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Objectives: The Primary outcome of the present work is to detect type and frequency of Ultrasonographic changes in patients with anterior knee pain. Secondary outcome is to determine the role of MSUS in early detection of causes of anterior knee pain (AKP).

Methods: Sixty patients with AKP and 20 sex and age matched healthy control were included in this study obtained from the outpatient of Physical Medicine and Rheumatology Department of El Hussein and Bab El-Sharia university hospitals. Inclusion criteria: age between 20–40. Exclusion criteria: trauma, Crystal induced arthritis, connective tissue diseases (RA, SLE, SpA), chronic liver or kidney disease and previous surgery. Full medical history and clinical examination (EMG, knee Conventional Radiography and Musculoskeletal Ultrasonography (MSUS) were done to all patients. Bilateral MSUS examination of the following common sites: Insertion of quadriceps tendon, Ligamentum patellae and Anterior aspect of the knee from medial to lateral. According to EULAR guide lines for musculoskeletal ultrasonography.

Results: The mean duration of knee pain in patients group was 11.4±9.134 months. ESR, CRP and WOMAC were higher in patients group (p<0.01). MSUS showed significantly more frequent Supra-patellar and Infra-patellar bursitis in patients than control group (p=0.000). Patients had higher frequency of cartilage thickness than control, 2.2±0.5 mm vs 2.7±0.261 mm respectively (P<0.000, 95% Cl: 0.31 to 0.58).

Conclusions: The degree of Knee pain, measured by WOMAC, is positively correlated with inflammatory biomarkers (ESR and CRP) in patients with Anterior knee pain. MSUS revealed a positive correlation between Femoral Articular Cartilage thickness and the periarticular tendon- thickness, namely Patellar origin, patellar insertion and Quadriceps insertion. Interestingly, our data present an evidence of the negative impact of the duration of knee pain over Femoral Articular Cartilage thickness as well as Patellar origin thickness. (FACh thickness get worse with longer duration of pain)
AB0998 DIAGNOSTIC VALUE OF 14-3-3 (ETA) IN RHEUMATOID ARTHRITIS

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Background: Protein 14-3-3 (eta) involved in the upregulation of inflammatory and joint damage factors [1]. 14-3-3 is the candidate biomarker of rheumatoid arthritis (RA) [2].

Objectives: To evaluate the clinical utility of 14-3-3 for diagnosis of RA.

Methods: We studied 44 patients (pts) with RA, 5 men and 39 women, median age (25-75 percentile) of age 45 (35-59) years; disease duration is 10 (5-20) months. DAS28 5.2 (4.4-6.2); 5 pts with systemic lupus erythematosus, 4 – ankylosing spondylitis, 5 – OVERLAP; 4 with psoriatic arthritis and 20 healthy individuals.

14-3-3, anti-cyclic citrullinated peptide autoantibody (anti-CCP) was measured in serum by commercial enzyme-linked immunosorbent assays, IgM rheumatoid factor (IgM RF). Measured by immunonephelometry.

Results: The diagnostic sensitivity of 14-3-3 for RA (cut off 0.19 ng/ml) is 70.5%, specificity – 83.7%; positive likelihood ratio – 4.33, negative likelihood ratio – 0.35; positive predictive value – 81.6%, negative predictive value – 73.5%; AUC = 0.78 (CI 0.68–0.88). Concomitant presence of 14-3-3 and IgM RF, anti-CCP was determined in 66%, 73% of the patients with RA respectively. 14–3–3 had correlation with IgM RF (r=0.7, p<0.05).

Conclusions: Serum 14-3-3 correlation with IgM RF (r=0.7, p<0.05) for RA (cut off 0.19 ng/ml) is 70.5%, specificity – 83.7%; positive likelihood ratio – 4.33, negative likelihood ratio – 0.35; positive predictive value – 81.6%, negative predictive value – 73.5%; AUC = 0.78 (CI 0.68–0.88). Concomitant presence of 14-3-3 and IgM RF, anti-CCP was determined in 66%, 73% of the patients with RA respectively. 14–3-3 had correlation with IgM RF (r=0.7, p<0.05).

AB0999 FINNISH COHORT OF PATIENTS WITH RAYNAUD’S PHENOMENON-NAILFOLD VIDEOKAPILLAROSCOPY FINDINGS AND AUTOANTIBODY VALUES

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Background: Raynaud’s phenomenon (RP) is very common all around the world, especially in cold climates (from 3 to 22%) (1). Nailfold capillaroscopy and autoantibodies have a pivotal role in diagnosing of different diseases in the context of RP (2). This is a first study of patients with RP in Finnish tertiary care hospitals.

Objectives: Aim is to investigate nailfold videokapillaroscopy (NVC) findings and autoantibody-values in patients with Raynaud’s phenomenon first time in Finnish prospective multicenter study cohort.

Methods: We enrolled consecutive 160 patients with Raynaud’s phenomenon who underwent NVC 3/2012–4/2015. Nailfold capillaries of II-V fingers of both hands were examined by using an optical probe videokapillaroskope mounted with x200 magnification lens. Images where analyzed with Videoccapt software (DS Medigroup, Milan, Italy). NVC findings were classified with qualitative scoring, whereas the other 30% had symmetrical axonal neuropathies (entrapment neuropathies), whereas the other 30% had symmetrical axonal neuropathies (entrapment neuropathies). Ultrasound diagnosis of posterior tibial entrapment at the ankle was encountered in 20 (40%) patients. In addition, a positive power Doppler (PD) signal and medium titers of ANA and 76.0% (n=19) had high titers of ANA. 69, 2% (n=18) had anticitrulline antibodies (ACA) and 3, 8% (n=1) had antitopoisoenermase I antibodies (anti-Scl-70). Those patients who had positive ACA or anti-Scl-70 also had a NVC scleroderma-pattern.

Conclusions: The main reason for NVC in this cohort was differential diagnosis of Raynaud’s phenomenon, and in most patients in diagnostic group primary Raynaud’s phenomenon was diagnosed. NVC is useful method for differential diagnosis of Raynaud’s phenomenon.

References:
erosions of the ankle joint were prevalent among the active group in comparison with patients in remission (p<0.001), as shown in figure (1).

Conclusions: Peripheral nerve affection is common in the rheumatoid foot, irrespective of the disease activity level. The most common foot neuropathies are; posterior tibial entrapment at the ankle, peroneal entrapment at the fibular neck and pure median neuropathy. MSUS is valuable for diagnosis of posterior tibial entrapment at the ankle. In addition, a positive PD signal and erosions of the ankle joint are associated with disease activity.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.8184

AB1001

CLINICAL VERSUS ULTRASOUND EVALUATION OF PERIPHERAL ENTHESITES IN A COHORT OF SPONDYLOARTHRITIS
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Objectives: Clinical versus ultrasound evaluation of peripheral entheses in a cohort of spondyloarthropathy

Methods: A monocenter prospective study of all SpA >18 years meeting the ASAS criteria for SpA followed in a rheumatology center over a period from January 2015 to April 2016. Demographic, clinical, lab and ultrasound characteristics were noted. Fifteen enthesal sites were investigated bilaterally: insertions of sub-scapular, medial and lateral epicondylar tendons, triceps brachialis, Achilles tendon, plantar aponeurosis. These sites were assessed clinically and with US during the same visit and then results were compared between the clinical and the US examination.

Results: A total of 208 patients were included, mainly men (63.5%). The mean age was 40.2±11.7 years and the mean duration of the SpA was 11.8±8.7 years. Axial radiographic SpA was the most frequent phenotype (69.2%) and ankylosing spondylarthritis was the most frequent sub-group (57.7%). At examination, 88.9% had an active disease (ASDAS-ESR and/or ASDAS-crp >2.1) and 64.4% of SpAs were taking NSAID. Clinical examination and US revealed at least one abnormal enthesis in 55.3% and 86.1%, respectively.

Table 1. The global and site-specific clinical and ultrasound prevalence of peripheral entheses

<table>
<thead>
<tr>
<th>Entheses</th>
<th>Clinical%</th>
<th>Ultrasound%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcaneal tendon</td>
<td>13.9</td>
<td>68.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Quadricipital</td>
<td>9.9</td>
<td>49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supra Spinatus</td>
<td>17.8</td>
<td>45.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gluteus Medius</td>
<td>11.3</td>
<td>34.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patellar Inf</td>
<td>8.9</td>
<td>32.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plantar Aponoeurosis</td>
<td>14.7</td>
<td>32.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triceps Brachialis</td>
<td>10.3</td>
<td>26.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral Epicondylar</td>
<td>23.8</td>
<td>24.5</td>
<td>NS</td>
</tr>
<tr>
<td>Medial Epicondylar</td>
<td>12.7</td>
<td>3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Int Collateral Lat Ligt</td>
<td>6.5</td>
<td>2.6</td>
<td>0.009</td>
</tr>
<tr>
<td>Sup Collateral Lat Ligt</td>
<td>5.8</td>
<td>1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Collateral Med Sup Ligt</td>
<td>5.8</td>
<td>0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Collateral Med Inf Ligt</td>
<td>5</td>
<td>0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All sites</td>
<td>44.2</td>
<td>83.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: In this cohort and as expected, ultrasound (with at least one elementary lesion) was superior to clinical examination for the detection of peripheral entheses (83.2 vs. 44.2%, P<0.001). Interesting sites to explore according to the prevalence and to the presence of a Doppler signal (<2mm cortical) would be insertions of the calcaneal, quadricipital, patellar, gluteal, plantar aponeurosis and triceps brachialis tendons.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1572

AB1003

MEDIUM AND ULNAR NERVE CROSS-SECTIONAL AREA IN CARPAL TUNNEL SYNDROME WITH EXTRATERRITORIAL SPREAD OF SENSORY SYMPTOMS
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Objectives: To evaluate the relationship between extramedian spreading of sensory symptoms and median and ulnar nerve cross-sectional area in patient with carpal tunnel syndrome (CTS), to compare the ultrasonographic and electrophysiological findings in patients with CTS whose sensory symptoms are extramedian spreading or median distribution only.

Methods: Patients with CTS were divided into two groups as with and without extramedian symptoms and were assessed clinically, electrophysiologically and ultrasonographically by three blind investigators. In electrophysiological tests, median and ulnar nerve conduction studies were performed. Nerve cross-sectional areas were measured at hamatum hook, pisiform bone, radio-ulnar joint, one-third distal part of forearm, and medial epicondyle for median nerve; radio-ulnar joint, pisiform bone, one-third distal part of forearm, and medial epicondyle for ulnar nerve by ultrasonography.

Figure 1 summarizes the prevalence of elementary ultrasound lesions per site.

Elementary Lesions

Hypo-hypo-echoicn (Thickening
Enthesophytes Erosions Calcification

Conclusions: This study demonstrated that extramedian spreading of sensory symptoms is associated with increased nerve cross-sectional area.
Results: The study was completed with 61 patients (108 hands). Extramedian symptoms were present in 31 patients (54 hands). Finger grip strength was lower, pain values evaluated with visual analogue scale were higher in these patients (p<0.05). There was no statistically significant difference in electrophysiological and ultrasonographic parameters between two groups.

Conclusions: These results suggest that extramedian spread inCTS patients is more related to central and peripheral sensitization than peripheral causes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6551

AB1004 NOMENCLATURE ON MEDICAL, DIAGNOSTIC, AND THERAPEUTIC PROCEDURES IN RHEUMATOLOGY

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Background: One of the missions of the Spanish Society of Rheumatology (SER) is to provide professionals involved with the necessary tools to ensure a better care for patients suffering from a rheumatic disease. Up to now, there is no benchmark that quantifies the complexity of medical acts in this specialty. Therefore, there is a need to adopt a physician activity scale that would allow assessment of their professional activity and skills regarding patient care.

Objectives: To compile a nomenclature of medical, diagnostic, and therapeutic procedures in the field of rheumatology; and to establish a hierarchical classification system according to a complexity index which was calculated by two factors: time of completion and degree of complexity of each act.

Methods: A list of care, diagnostic, and therapeutic acts was compiled based on the nomenclature created by Drs Fernandez and Oliver. The hierarchical classification system was based on the construction of a complexity index which was calculated by two factors: time of completion and degree of complexity of each act.

Results: The total of included acts was 54. The results obtained with the Delphi method tended to show a consensus of opinion (media IQR2 – IQR1=0.8–1.9=-1.1). Furthermore, a validation of these results was carried out through a massive survey among the partners of SER. The survey results showed a high degree of agreement (at least 70.0 per cent of the partners agreed or strongly agreed with the complexity of each act).

The degree of complexity in successive visits was 100. In the query section for consultations, the highest scores were obtained by first visit to hospitalized patient (366) and home visit (369). Regarding diagnostic techniques, the highest scores were obtained with biopsies: bone (465), sural nerve (416), and synovial (380). Also worth mentioning the scores obtained by ultrasound scan (204), capillaroscopy (113) and densitometry (112). Regarding therapeutic techniques, intra-articular injection under sedation in children obtained a score of 388; while intra-articular injection with ultrasound control obtained a score of 163. The clinical report of disability was agreed to have a score of 323, and the expert report obtained a score of 370.

Conclusions: This work has made it possible to create a nomenclature of 54 acts in Rheumatology, where biopsies (bone, sural nerve, synovial), visits to hospitalized patients, home visits, infiltration under sedation in children, and expert reports are identified as the most complex acts. Musculoskeletal ultrasound is considered twice as complex as a successive visit, capillaroscopy, or bone densitometry. These results will make it possible to improve patient care and establish a solid and agreed foundation to negotiate the provision of public and private services.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4353

AB1005 HYPERTHYROID AND HY珀THYROID STATUS WAS STRONGLY ASSOCIATED WITH MUSCULOSKELETAL ULTRASONOGRAPHIC ABNORMALITIES WITH ARTHRALGIA

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Background: Thyroid dysfunction can cause musculoskeletal symptoms and sign. Ultrasonography is a useful tool for the evaluation of synovitis and is more accurate than clinical examination.

Objectives: The purpose of the study was to determine whether musculoskeletal ultrasonographic (MSUS) abnormalities were observed according to the state of thyroid disease.

Methods: Patients with thyroid disease were categorized as euthyroid, hypothyroid, or hyperthyroid status according to thyroid hormone levels and evaluated the association with MSUS abnormalities. In addition, the association of the presence of thyroid autoantibodies with MSUS abnormalities was also studied. In MSUS, an experienced rheumatologist examined the presence of synovial fluid, synovial hypertrophy, and grade of power doppler in the knee joint.

Results: Table 1. Patient characteristics

| Age – mean ± SD (years) | 58±13.0 |
| Sex – n (%) | Male 13 (11.9) Female 96 (88.1) |
| Thyroid diseases duration – median (range), (years) | 4 (0–13) |
| Distribution of thyroid diseases - n (%) | Euthyroid status 61 (56) Hypothyroid status 11 (10.1) Hyperthyroid status 37 (33.9) |
| Positive thyroid autoantibodies – n (%) | 68 (62.4) |
| Taking thyroid medication – n (%) | 100 (91.7) |
| Patient’s Knee VAS (100mm) – median (range) | 10 (0–80) |
| MSUS finding – n (%) | Normal 72 (66.1) Abnormal 37 (33.9) |

Conclusions: Both hypothyroid and hyperthyroid status was significantly associated with MSUS abnormalities with knee arthralgia. MSUS is a useful tool to detect clinically early joint abnormalities. We suggest that patients with diagnosed thyroid dysfunction and who remain uncontrolled, should assess the MSUS examination in patients with arthralgia. Moreover a thyroid function test for unexplained arthritis might be warranted.

References:

Disclosure of Interest: None declared


AB1006 POWER-DOPPLER TECHNIQUE IN PAGET’S DISEASE OF BONE: A NEW MONITORING TOOL OF THERAPEUTIC RESPONSE. STUDY ON 43 PATIENTS

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Background: To date the evaluation of the disease activity and the monitoring of the therapeutic response of patients affected by Paget’s disease of bone is based only on clinical and hematological data. However, in clinical practice the management of these patients is still challenging. Previous angiographic
and histological studies have revealed that the accelerated bone turnover is associated with an increased blood flow and hypervascularity, suggesting a role of high-resolution sonography with power-Doppler (PD) and color-Doppler (CD) in Paget's disease. Our preliminary data demonstrated that this technique shows not only the alterations of the pagetic bone profile, but also the hypervascularization of the osteoperiosteal-layer before the diagnosis and during follow-up.

**Objectives:** To validate the PD technique as a useful tool not only for the diagnosis of Paget's disease of bone but also for the evaluation of the disease activity and for the monitoring of the therapeutic response.

**Methods:** Forty-three consecutive patients affected by Paget's disease of bone and treated with neridronate were followed up over the last ten years. Patients were classified in eight clinical patterns defined by the presence of bone alkaline phosphatase elevation over the normal range (BAP+), bone pagetic pain as visual analogue scale $≥$70 (VAS+) and PD alterations of osteoperiosteal vascularization (PD+). Data were analyzed by Fisher exact test (two tails) to assess the associations between BAP+, VAS+ and PD+ at different times during follow up: before the start of the therapy, after the first, the second and the third neridronate cycle of therapy, and at the end of all cycles.

**Results:** At any time BAP+ and VAS+ were not associated. A trend of association between VAS+ and PD+ could be observed only after the first neridronate cycle. In contrast, the association between BAP+ and PD+ was statistically significant before the therapy, at the end of all cycles of therapy and after the second one, but not after the first one.

**Table 1. Associations between BAP elevation over the normal range, VAS and PD alterations of osteoperiosteal vascularization, $p<0.05$**

<table>
<thead>
<tr>
<th></th>
<th>BAP+/VAS+</th>
<th>BAP+/PD+</th>
<th>VAS+/PD+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before therapy</td>
<td>40</td>
<td>1.000</td>
<td>35</td>
</tr>
<tr>
<td>After first therapy cycle</td>
<td>40</td>
<td>0.6225</td>
<td>35</td>
</tr>
<tr>
<td>After second therapy cycle</td>
<td>22</td>
<td>0.4701</td>
<td>21</td>
</tr>
<tr>
<td>After third therapy cycle</td>
<td>9</td>
<td>1.000</td>
<td>9</td>
</tr>
<tr>
<td>At the end of all therapy cycles</td>
<td>40</td>
<td>1.000</td>
<td>35</td>
</tr>
</tbody>
</table>

Conclusions: The lack of association between VAS+ and PD+ or BAP+ or BAP+ may be due to the difficulty of the patients in identifying and quantifying the pagetic pain, and suggests the weakness of the clinical criteria in defining the disease activity. Otherwise, PD technique proves to be a fast, reliable and not expensive tool, which is also very useful for monitoring/achieving better control of Paget's disease of bone.

**References:**


**DOI:** 10.1136/annrheumdis-2017-eular.5963

**Conclusions:** The SLE-key® RuleOut test detects a serologic signature which remains stable between sampling dates and over a long period of time after diagnosis in 84% of subjects. Subjects who were ruled out at T1 were generally ruled out at T2. Patients not ruled out at T1 remained not ruled out at T2. The clinical implications of a changing SLE-key® RuleOut score in the remaining 16% of patients may be meaningful, and are currently being carefully investigated.

**References:**

1. Fattal et al; Immunology 2010.

**Acknowledgements:** The authors wish to acknowledge the invaluable contributions of Cohen-Gindi O, Lerner M, Tarnapolski O, Blumenstein Y, Javaherian A, Pitts J, Barton M and Wong E and Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115308/BIOVASCSAFE.


**DOI:** 10.1136/annrheumdis-2017-eular.5963

**DISTRIBUTIONS OF ANTIBODIES IN SLE PATIENTS IN DIFFERENT ETHNIC GROUPS IN XINJIANG**

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**Objectives:** The aim of this study was to explore distributions of antibodies in SLE patients in different ethnic groups in xinjiang.
MRI CONTRIBUTES TO ACCURATE DIAGNOSIS OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH SERUM NEGATIVE HLA-B27


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Background: Based on ASAS axial spondyloarthritis (SpA) criteria, the presence of structural changes of sacroiliac (SI) joints such as sclerosis, bone erosion, joint space widening or ankyloses does not meet the definition of active sacroiliitis on magnetic resonance imaging (MRI), if there is no bone marrow edema (BME). However only less than half Asian patients with SpA were characterized by BME. Neither serum inflammatory markers such as c reactive protein (CRP) nor erythrocyte sedimentation rate (ESR) is able to be useful as diagnostic markers in the early phase of SpA. HLA-B27 is associated with early diagnosis of SpA and axial inflammation of SI joints on MRI. Nonetheless, HLA-B27 is not associated with structural lesions of SI joints. All factors contribute to difficult defining early Asian SpA patients in the absence of serum HLA-B27 and active imaging inflammation.

Objectives: The aim of this study is to evaluate the prevalence of structure changes of SI joints on MRI in Taiwanese SpA patients in the absence of serum HLA-B27.

Methods: Thirty-three patients with inflammatory back pain and morning stiffness (disease duration more than 3 months) and high disease activity (BASDAI>4) who had to be either serum HLA-B27 positive (10 patients) with >1 SpA-feature or HLA-B27 negative with ≥2 SpA-features (22 patients) were included in this prospective study. All patients did not meet the definition for a positive radiograph according to the modified New York criteria. MRI was performed with multiple sequence (Coronal and axial T1-weighted spin echo, coronal and axial short-tau inversion recovery). SI joints were evaluated for the prevalence of subchondral BME and structure changes (sclerosis, bone erosion, joint space widening and ankylosis). All patients were tested for X-rays of the pelvis and serum levels of ESR and CRP. Correlation analysis was performed among the different collected variables.

Results: Subchondral BME was only present in 8 of 23 patients with SpA in the absence of serum HLA-B27 (34.8%), while 7 of 10 (70%) HLA-B27 serum positive SpA patients revealed ≥1 BME on MRI. Although, including sclerosis, bone erosion and joint space widening were identified in 8 (80%), 10 (100%) and 5 (50%) SpA patients with positive serum HLA-B27, respectively. Nevertheless, these structural changes of SI joints on MRI were more common in HLA-B27 serum negative patients, as 15 (65.2%), 20 (87.0%) and 7 (30.4%) of 23 serum negative patients, respectively.

Conclusions: MRI contributes to detect structural changes of SI joints for patients with nonradiographic axial SpA in the absence of serum HLA-B27.

REFERENCES:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6069

ULTRASOUND MORPHOSTRUCTURAL PATTERN OF THE TIBIOFIBULAR JOINT: PRELIMINARY RESULTS

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Background: The anatomy of the proximal tibiofibular (TF) joint is directly related to its ability to withstand stress applied in either a longitudinal or axial fashion. It is traditionally evaluated by CT scan, however, in certain conditions, it could be evaluated by ultrasound (US) conveniently; so far US has not been using to evaluate the TF joint. US is an innocuous, accessible and cheap image technique, that has demonstrated its utility for evaluating joints in several pathologic conditions, and might have an important role in the early diagnosis of inflammatory, degenerative or even traumatic lesions at the level of the TF joint; there are no studies that have evaluated the morpho-structural pattern of the TF joint.

Objectives: To describe the morphostructural pattern of the tibiofibular joint in healthy subjects.

Methods: Subjects older than 18 yrs old, with no history of past/present lesion of the knee, without any joint or neurovascular disease were included. A short questionnaire related to physical activity applied, and clinical evaluation to discard instability performed. US of both knees in extension done, using an Esaote 6 MyLab 70 ultrasound equipment with a 7.5 - 12 MHz linear transducer. Descriptive statistics applied.

Results: Thirty-six patients (27 women, 75%) included, mean age 41±2.8±9 years, mean weight 71±12.46 kg, mean height 1.61±0.09 ms and BMI 71.07±12.40. 69% of the subjects practice mild exercise activities. By US mean distance between tibia and fibula were 3.2±1.7 cm; the mean thickness of the ligaments (superior and inferior tibiofibular ligaments 3.2±1.3, 3.6±1.6, 3.2±1.6 cm respectively and in the superior and inferior fibular ligaments 3.2±0.90 cm and 3.2±0.89 cm respectively. Ligaments were hyperchoic in 61.1%, a well-defined border was seen only in 48.6%. Inside of joints a hypoechogenic tissue was observed.

Conclusions: These preliminary results suggest that US can be a useful tool for evaluating the tibiofibular joint.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6840

RELIABILITY OF SONOGRAPHIC PERITENON EXTENSOR TENDON INFLAMMATION PATTERN IN PSORIATIC ARTHRITIS

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Background: Preliminary results demonstrate that the peritenon inflammation of extensor digitum tendon (PTI) is a specific ultrasonic (US) pattern of Psoriatic Arthritis (PsA) and is associated with the presence of PsA. Nonetheless, PTI was suggested as a pattern playing a key role in the differential diagnosis between Rheumatoid Arthritis and PsA 1,2.

Objectives: In spite of PTI’s clinical impact, there are no data regarding the reliability of US PTI evaluation. The present study addressed this topic by testing the reliability of US on evaluation of PTI.

Methods: 27 consecutive non selected PsA patients with clinical involvement of at least one 2nd to 5th MTPJ were included. A rheumatologist trained in PTI assessments obtained the US images exploring the dorsal aspect of MTPJ from 2nd to 5th of both hands using a MyLab 70 XVG machine, Esaote, Genova, Italy, with a greyscale (GS) 13 MHz probe and a 7.1 MHz power Doppler (PD) frequency, PRF 750 Hz and a 60 Gain. 3–5 seconds videos of each MCPJ were obtained in transversal and longitudinal views for further reliability analysis. In the inter-reader performed by 5 readers from 5 different hospitals and four countries, it was scored as present or absent 1) PTI (defined as an hypoechoic swelling of the soft tissue surrounding the extensor tendon at MCPJ level with or without PD) and 2) intra-articular synovitis (IAS, OMERACT definition), both in PD and GS. The consensus of true US results for every joint and lesion was achieved when at least three readers had the same opinion.

Cohen’s Kappa test was used for statistical analysis.

Results: Clinical MCPJ involvement was present in 60 (27.7%) of the 216 joints whereas US detected IAS and/or PTI in 75 (34.7%), US showed GS PTI in 41 (19%) of the joints, while GS IAS was found in 63 (29.2%) with PD activity in 41 (19%) of the joints. The inter-reader reliability is shown in the Table. Intra-reader reliability results expressed as mean Kappa were 0.826 for PTI PD, 0.784 for PTI GS, 0.743 for IAS PD and 0.637 for IAS GS.

Conclusions: US examination of MCPJ shows that PTI is near as frequent as PsA with reliability of US evaluation. The present study addressed this topic by testing the reliability of US on evaluation of PTI.

References:
Clinical Utility of Antihistone Antibodies: A Descriptive Study

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Background: Antihistone antibodies (AHA) have been linked to Drug-Induced Lupus Erythematosus (DILE) for decades. However, for some authors this relationship is not so clear and suggest that the presence of these autoantibodies is related to other autoimmune diseases more frequently.

Objectives: The main objective of this work was to study the association of AHA with different autoimmune entities (including DILE) and to look into which clinical manifestations and which autoantibodies are more frequently related to AHA.

Methods: We performed a descriptive study. A database was constituted using all patients with AHA+ in any blood analysis between years 2000 and 2016 in the University Hospital Complex of Vigo. The variables of the study were: presence of autoimmune disease, clinical manifestations and related autoantibodies.

Results:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men</th>
<th>Women</th>
<th>All</th>
<th>% Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50</td>
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<td>Gender</td>
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<td>100</td>
</tr>
<tr>
<td>SLE</td>
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<td>DILE</td>
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<tr>
<td>Scleroderma</td>
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<td>9</td>
<td>12</td>
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<tr>
<td>No diagnosis</td>
<td>5</td>
<td>19</td>
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<td>33</td>
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<tr>
<td>Malar rash</td>
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<td>11</td>
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<tr>
<td>Photosensitivity</td>
<td>2</td>
<td>11</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Arthritis</td>
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<td>31</td>
<td>37</td>
<td>51</td>
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<tr>
<td>Lupic nephropathy</td>
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<td>13</td>
<td>17</td>
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</tr>
<tr>
<td>Raynaud</td>
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<td>11</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Hematological abnormalities</td>
<td>5</td>
<td>20</td>
<td>25</td>
<td>34</td>
</tr>
</tbody>
</table>

None of the 73 patients AHA+ developed DILE while almost 50% of them suffer any other autoimmune disease. We found a high percentage of AHA+ patients with lupus erythematosus complications such as arthritis and hematological abnormalities. AntiDNAds antibody was the more frequent coexpressed autoantibody.

Conclusions:
- AHA detection is not useful as DILE screening.
- AHA+ suggest the presence of other autoimmune disease rather than DILE.
- AHA+ may be related to lupus erythematosus systemic complications.

References:
Conclusions: The novel FOI RA synovitis scoring system showed high reliability and moderate to good responsiveness in the wrist and hand. Future studies should focus on assessing the sensitivity and specificity of the FOI synovitis score with ultrasound and magnetic resonance imaging as gold standard.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4633

AB1014 SAFETY OF OUTPATIENT PERCUTANEOUS NATIVE RENAL BIOPSY IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES: RESULTS FROM A MONOCENTRIC COHORT

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Background: Renal involvement is common in patients with systemic autoimmune conditions, mainly systemic lupus erythematosus (SLE) and vasculitis, including cryoglobulinemia. Despite the advances in percutaneous kidney biopsy (PKB) techniques and overall improved safety of the procedure, clinically significant bleeding complications do occur.

Objectives: to investigate the safety of performing percutaneous native kidney biopsy (PKB) as an outpatient procedure (implying an observation period of 6 hrs) compared to the traditional inpatient policy in patients with systemic autoimmune conditions.

Methods: Group I, in whom PKB was performed was included in the outpatient department (2012–2016) and followed by 6 hours’ observation period and then by regular outpatient visits and group II, in whom PKB was performed and followed by at least 1-day hospital admission. Group II included retrospectively retrieved patients who underwent PKB in our Institution between January 2000 and November 2012 as in patient procedure. All biopsies were performed by a single nephrologist following a structured protocol.

Results: A total of 81 biopsies (group I and group II) were included in this study, 44 (54%) of patients were female and the mean age was 49.9±17.6 years. Twenty-six percent of biopsies were performed for the diagnostic workup of nphrotic range proteinuria, 21% for rapidly progressive renal insufficiency, and the remaining 53% for non-nphrotic proteinuria and/or hematuria. No patient suffered for a major complication and only 3 (3.7%) patients (one with cryoglobulinemic vasculitis and 2 with ANCA associated vasculitis) developed a minor complication, including gross hematuria in one case and sub-capular perinephric hematoma on sonography not requiring intervention in 2 patients.

Conclusions: The lack of major complications and the very limited rate of minor bleeding support that outpatient biopsy could be a valuable, safe, and perhaps cost-effective method of obtaining diagnostic renal tissue in the majority of patients with systemic autoimmune diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3318

AB1015 AUTOMATED SQUEEZE TEST (GAENSLEN'S COMPRESSION MANEUVER) IN RHEUMATOID ARTHRITIS PATIENTS. A PRELIMINARY STUDY

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Background: The squeeze test (a.k.a Gaenslen’s Compression Maneuver) consists on the compression of the metacarpal-phalangeal (MCP) joints to elicit pain in a patient with active synovitis. The squeeze test has three main purposes: Screening of inflammatory arthritis, as a predictor of rheumatoid arthritis in arthralgia patients, and as a quick and practical evaluation of the presence/absence of synovitis in patients already diagnosed with RA. The force and the way to perform the squeeze test had been evaluated in rheumatologists on a biomechanical device, with conflicting results. We developed a biomechanical device to perform the squeeze test.

Objectives: Our aim is to determine the force whether the automated squeeze test discriminate patients with active RA from inactive ones. And the force that differentiates a healthy patient from a RA patient.

Methods: Observational study in RA (ACR/EULAR 2010) patients and healthy persons. We perform 3-squeeze test on the device in the MCP joints and record the force enough to elicit pain. And then compare them with the joint counts by the clinician.

Results: Two hundred MCP joints from 50 hands were tested. From 25 RA patients with a mean age of 54.6 years (SD 11.22), with a mean disease latency of 1.2 years (SD 2.7). The total swollen joint count was 16 (7 right joints + 9 left joints) and 70 total tender joint count (30 right joints and 40 left joints). The median of force that caused pain in the RA patient’s right hand was 3.07 kg (IQR 2.4) and the left hand was 2.78 kg (IQR 3.8). The cut-off for the force to detect a tender right hand joint was 1.020 grams with a sensitivity of 100% and specificity of 73.3%; for a swollen right hand joint was 1,400 grams with a sensitivity of 100% and specificity of 28.6%. For a tender left hand joint was 1620 grams with a sensitivity 70% and specificity of 6.7%; and for a swollen left joint was 1990 grams with a sensitivity of 100% and specificity of 27.3%. In the second phase, 560 MCP joints of 140 hands from 70 healthy volunteers were compressed. The median force to elicit pain in the right hand was 4.2 kg (IQR 9.5) vs. 3.07 kg (IQR 8.7) from RA patients (p=0.003), and for left hand 4.6 kg (IQR 9.7) vs. 2.78 kg (IQR 9.2) from RA patients (p=0.014).

Conclusions: It is necessary to continue the exploration of the maneuver in different clinical settings. Validate the strength in patients with different arthropathies, activity levels and different clinical stages (screening, activity, prediction) and also with imaging methods for evidence of inflammation (US, MRI).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2162

Abstract AB1016 – Table 1

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<td>Polyarthralgias</td>
<td>Arthremalgias</td>
<td>Polyarthralgias</td>
<td>Fatigue</td>
<td>Hand pain and deformity of 2nd PIPs</td>
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<td>4th interphalangeal joint</td>
<td>Dry eye and dry mouth</td>
<td>Back pain</td>
<td>Back pain</td>
<td>Back pain</td>
<td>Fatigue</td>
<td>Oral aphthosis</td>
<td>Left foot edema</td>
</tr>
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<td>Graves Basedow</td>
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<td>Degenerative axial and joint signs</td>
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<td>OA</td>
<td>OA</td>
<td>OA</td>
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</tr>
</tbody>
</table>

NP: not performed; N: normal; OA: osteoarthritis, PsA: psoriatic arthritis, CPPD: chondrocalcinosis.

AB1016 ANTI-DFS70, A TOOL IN USUAL CLINICAL PRACTICE: A CASE SERIES

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Background: The presence of anti-nuclear antibodies (ANA) has been considered a characteristic of systemic autoimmune diseases (SAD). Patients are frequently referred for study because they have ANA and are followed because of the possibility to develop SAD. Approximately, 20% of healthy individuals with ANA detected by indirect immunofluorescence (IFI), especially at low titers, have a dense, line speckled pattern (DFS) that frequently corresponds to the presence of anti-DFS70 antibodies. The importance of this antibody is due to its low prevalence in subjects with ASD (1%) compared to its presence in 33.1% of healthy subjects with ANA.

Objectives: To describe the usefulness of Anti-DFS70 in a series of patients presenting ANA.

Methods: We collected prospectively throughout the year 2016 all the patients referred to a tertiary hospital for ANA study and in whom the presence of anti-DFS70 antibodies was confirmed. All patients underwent a thorough medical history, physical examination, and relevant follow-up tests were performed according to the clinical presentation. The IFI was performed in a Menarini Zenit-Up/GSight system, as well as ANA screening in Hep-2000 (Fluorescent IgG ANA-Ro Test System-immunocconcepts) and the detection of anti-DFS70 antibodies by immunoblot (ANA + DFS70 Dot Blot-Alphadia).

Results: We collected in a period of 12 months a total of 7 patients with anti-DFS70 antibodies. Most of them (6/7) were referred because of non-specific symptoms such as arthralgia, fatigue, thrush, edema, ... and the presence of ANA. The findings are detailed in Table 1.
Conclusions: Anti-DFS70 is a valuable biomarker, with a very low prevalence in SAD, which gives it a role as a negative predictive marker of developing SAD when it is absent. Its detection in serum with a dense fine speckled pattern ANA (IFI) should be part of the protocol of the immunology laboratory. It is a cost-effective determination, as demonstrated in a recent study, by avoiding the costs associated with the follow-up of these patients. In our case, its finding allowed us to reassure the patient and avoid the accomplishment of further complementary tests, as well as an unnecessary monitoring.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3410

AB1017 THE DEFEAT OF THE HIP JOINT IN ANKYLOSING SPONDYLITIS BY MAGNETIC RESONANCE IMAGING

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Background: According to the carried out epidemiological studies in Russia of patients with ankylosing spondylitis (AS) defeat of the hip joints was impairment in 46% of cases, but was the reason for the replacement in 7% of cases. Objectives: To compare the clinical manifestations of hip arthritis (coxitis) with the results of magnetic resonance imaging (MRI) of the joint hip (HJ) in patients with ankylosing spondylitis (AS). Methods: Examined 117 patients (mean age 31.7±12.7 y, age range 7–84 y), complaining of pain in the hip joints. The average age of onset of disease was 26.3±20.3 y, HLA-B27 identified in 93% of patients. The median duration of AS – 57 [2–384] months. RESULTS: BasDAI 5.7±5.1, Diagnosis of hip septic arthritis were made based on clinical signs – the presence of pain in hips and/or restriction of movements in HJ at the time of patient admission to the clinic. In addition to clinical and radiographic examination all patients were performed MRI of hip joints T1 and T2.

Results: The Median duration of clinical manifestations of coxitis by the time of the study was 60 months. [25%; 75%], evaluation of pain in HJ for numeric rating scale (NRS) – 4 [2; 8], According to MRI identified the following inflammatory changes (IC): synovitis-71 (83%) patients, bone marrow edema (BME) – 44 (31.6%) patients. In BME acetabulum 36%, BME heads 63%, a combination of synovitis and BME were 7 patients (9%). Depending on radiological stage (estimated by BASRI hip), patients were divided into two groups (table 1).

Table: Results

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>BASRI hip T1 (n=48)</td>
<td>20(28)</td>
<td>33(36)</td>
<td>0.04*</td>
</tr>
<tr>
<td>AS duration, mo, T2 (n=48)</td>
<td>43 [19;80]</td>
<td>102 [24;120]</td>
<td>0.006</td>
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<tr>
<td>BASDAI, n (%)</td>
<td>4 [2; 8]</td>
<td>5 [4; 11]</td>
<td>0.005</td>
</tr>
<tr>
<td>BASRI hip T1 (n=60)</td>
<td>9 [91]</td>
<td>84 [91]</td>
<td>0.7*</td>
</tr>
<tr>
<td>ASDS (CRP) Me, n (%)</td>
<td>4 [2; 8]</td>
<td>6 [5; 7]</td>
<td>0.002</td>
</tr>
<tr>
<td>BASRI hip T1 (n=60)</td>
<td>10 [5; 25]</td>
<td>25 [8; 35]</td>
<td>0.001</td>
</tr>
<tr>
<td>NRS, Me, n (%)</td>
<td>0 [0; 2]</td>
<td>20 [4; 43]</td>
<td>0.05*</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>5 (3;9)</td>
<td>5 [2; 8]</td>
<td>0.01*</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>44 (92%)</td>
<td>27 (45%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Synovitis</td>
<td>6 (12.5%)</td>
<td>39 (64%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusions: MRI allows to clarify the cause of the pain and limitations of movement in HJ with AS, determine the patient has inflammatory changes, including in the absence of radiographic changes in these joints. Patients with severe radiological change (BASRI II-V), have a greater duration of the disease, severe functional abnormalities in the BASFI index. With increasing radiological stage (BASRI hip I-V) increased the detection rate of osteos (MRI). Further research to clarify the relationship of clinical manifestations of coxitis (pain level) from MRI data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4008

AB1019 ASSOCIATION OF INFLAMMATORY DISEASES – A CURRENT TOPIC FOR THE PRACTITIONER

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Background: Autoimmune, infectious, traumatic or neoplastic inflammation represents a warning for the practitioner. Numerous clinical specialities face daily with the presence of inflammation. The efforts of medical staff must aim to establish the pathogenesis, the expansion and to find the most effective ways of treatment. Objectives: Our study objective is to highlight the correlations between Spondyloarthropathies (SpA) and intestinal manifestations, the link between the antigen HLA B27 and joint and intestinal inflammatory changes and also the relationship between the presence of sacroiliitis and bowel disorders.

Methods: The study included 42 patients (28 men, 14 women). Of the 42 patients, 31 were diagnosed with ankylosing spondylitis (AS) (according to modified New York criteria), 8 with psoriatic arthritis (PsA) (using CASPAR diagnosis criteria) and 3 patients had had reactive arthritis (ReA) (according to ASAS criteria). All subjects enrolled in the study were screened for the presence of the antigen HLA-B27. The diagnosis of PsA was confirmed through helvis X-ray centered on the SI joints. All patients diagnosed with AS presented radiological sacroiliitis, only 5 cases in the group of PsA and 1 patient diagnosed with ReA. To investigate the presence of intestinal inflammation, a colonoscopy with biopsy was performed to all subjects included in the study. Among patients with AS, 5 of them had inflammatory changes suggestive of Crohn’s disease (CD) and 2 for ulcerative colitis (UC). Subclinical intestinal inflammation was evaluated in 15 cases: 12 of SA group and 3 of PsA group. We also highlighted 7 cases of irritable bowel syndrome: 1 patient with PsA and 6 patients with UC. Results: After the statistical analysis of the collected data, the following statistically significant correlations were found (p<0.05): radiological sacroiliitis correlated with AS and PsA; the antigen HLA-B27 is in close relation with all 3 forms of spondyloarthritides; subclinical intestinal inflammation was positively correlated with AS and PsA. No associations were found between the presence of intestinal inflammation and sacroiliitis.

Conclusions: This study points the link between intestinal and joint inflammation, primarily due to a common pathogenic mechanisms. A careful monitoring and a close collaboration between gastroenterologists and rheumatologists contributes to an optimal management of these patients.

References:
MULTIFREQUENCY BIOIMPEDANCE COMBINED WITH VIDEOCAPILLAROSCOPIC FINDINGS IN PATIENTS WITH MUSCULOSKELETAL DISEASES

E.M. Bartels, J. Kvistgaard Olsen, H. Bliddal, L.E. Kristensen

Background: Musculoskeletal diseases may involve muscle function, which often deteriorates due to a combination of pain and lack of exercise. Possible correction of this by training, or at least achievement of optimal efficiency of involved muscles with therapy, taking age and affecting disease into account, is an area which needs easily applicable and non-invasive pain-free assessment methods capable of monitoring daily living tasks outside a strict laboratory setting. Multi-frequency bioimpedance (mfBIA), assessing muscle health prior to exercise, in combination with Acoustic Myography (AMG), which allows real-time tests while e.g. walking on a treadmill, may be such a method.

Objectives: To validate AMG combined with mfBIA for muscle-use assessment during a series of daily activity movements and exercise with the aim of introducing the method in the clinic.

Methods: 10 healthy subjects aged 25-68 years were assessed with mfBIA (beamformer, Brisbane, Australia) prior to and following exercise of m. gastrocnemius during walking, stair climbing and descending, and cycling with increasing load. AMG was recorded with a CURO unit (MyoDynamik ApS, Frederiksberg, Denmark), and data handling was carried out with software belonging to the devices. The mfBIA parameters considered were resistance (R), internal (Ri) and external (Re) conductance, central frequency (fc), and the AMG parameters were Efficiency (E) – synchronization of motoric units, Temporal summation (T) – how frequently do you use a particular muscle fibre, and Spatial summation (S) – how many fibres in use at a given time, all given as Median; Min.Max.

Results: The mfBIA data, showing the health state of the muscle, showed changes in R, Ri, Re and fc as expected for a healthy muscle as an effect of the exercise. The AMG data showed good reproducibility with repeated measurements. Walking on flat ground was less synchronized (E 2; 1.4) as were walking up (E 4; 1.6) and down stairs (E; 1.6), than cycling (E 5.5; 5.9). With increasing load during cycling, E decreased with the higher demand to E 5.5 (range 1-7). The T-score was similar around 7 for all types of walking, while overall decreasing with increasing load during cycling from 6.5 to 5.5. The S-score was low during the three types of walk, indicating use of many fibres (S around 3), which is in line with the low E-score. For cycling the S-score decreased slightly with increasing load, from 8 to 7.5.

Conclusions: The combined method of mfBIA and AMG shows good reproducibility. This method has the potential to assess training possibilities in patients with musculoskeletal diseases by testing directly on muscles during the movements of daily function. The method is applicable in real life settings outside the laboratory.

Acknowledgements: The Parker Institute is supported by the Oak Foundation

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2228

AB1020

MULTIFREQUENCY BIOIMPEDANCE COMBINED WITH ACOUSTIC MYOGRAPHY – A NON-INVASIVE PAIN-FREE ASSESSMENT OF MUSCLE USE


Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that can present, as other collagen vascular disorders, changes in blood vessels. It can be evaluated by a non-invasive technique called periungual nailfold videocapillaroscopy (VCP). This technique is helpful in the diagnosis of systemic sclerosis (SSc), being part of the new classification criteria, and identifies individuals with Raynaud’s phenomenon who are at a higher risk for developing SSc.

Methods: This study aims to describe the videocapillaroscopic profile of a series of SLE patients and investigate if the VCP pattern is different among those with Jaccoud’s arthropathy (JA) compared to the patients without this complication.

Results: In a population of 113 female patients with SLE (67 without JA and 46 with JA), at least one alteration was observed in VCP in 89.40% of patients, and the “nonspecific changes” were the most prevalent. Minor changes were seen in 39 (58.2%) and 26 (56.5%) patients, and major changes were seen in 21 (31.3%) and 11 (23.9%) patients without and with JA, respectively. The SD patterns were observed in 02 (3.0%) and 03 (6.5%) patients without and with JA, respectively (p<0.05).

Conclusions: The majority of patients of SLE present changes in the VCP exam, but such a tool does not allow distinguishing those with or without JA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6627

AB1021

ACOUSTIC MYOGRAPHY – A NON-INVASIVE PAIN-FREE ASSESSMENT OF MUSCLE USE

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Background: Ultrasound (US) has shown to be a sensitive imaging tool for the detection of subclinical signs of synovitis in patients (pts) with rheumatoid arthritis (RA); further studies are still required to delineate the impact of US findings in the management of RA pts in daily clinical practice.

Objectives: To investigate the relationship between US findings indicative of joint inflammation and US bone erosions at joint level in pts with RA.

Methods: In 2015 an educational event focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy. In every center, the local rheumatologists provided RA pts to be examined by US. Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). Bilateral US examinations of wrists, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, using a Logiq E R7, General Electronics, with a 4.2–13 MHz linear probe. All US findings were scored using a 4 degree semiquantitative scoring system.

Results: In 465 RA pts, a total of 10.230 joints were scanned. Of these joints, 3.999 (39%) showed joint effusion and/or synovial proliferation and 1.784 (17%) were found positive for PD signal. The most frequently involved joints were the wrists followed by the second MCP joints and first MTP joints. In 749 joints US detected at least one bone erosion. The most frequently eroded joints were the wrists, the second and fifth MCP joints and the first and fifth MTP joints. A total of 226 RA pts showed at least one bone erosion and in 181 (80%) of these pts the eroded joints were found positive for PD signal.

Conclusions: A high prevalence of PD signal was found in the joints found eroded by US. This is the first study providing such an evidence using a portable US equipment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3369

AB1022

THE RECALL SURVEY: THE RELATIONSHIP BETWEEN ULTRASOUND SYNOVITIS AND BONE EROSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6827

AB1023

QUANTIFERON®-TB GOLD IN-TUBE ASSAY CAN BE USED FOR THE LATENT TUBERCULOSIS SCREENING BEFORE BIOLOGICAL DRUG TREATMENT IN A BCG VACCINATED COUNTRY: HUR-BIO SINGLE CENTER REAL LIFE RESULTS

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Background: Patients treated with biologic agents have increased risk of
AB1024 ULTRASOUND IN GIANT CELL ARTERITIS: CUT-OFF AND PITFALLS IN THE HALO SIGN

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Objectives: The objective of this study was to assess reliability of QFT test for latent TB before biological treatment.

Methods: Hacettepe University Rheumatology Biologic Registry (HUR-BIO) is a single center biological registry since 2005. Between Nov 2011 and July 2015, 1347 patients were assessed by QFT for latent TB. All consecutive patients were evaluated by a standard questionnaire between July 2015 and October 2016. The questionnaire included demographics, characteristics, medical history, symptoms of active TB. 671 patients were assessed by the physicians. TB status of other 676 patients were checked from Turkish national tuberculosis registry records. It’s an obligatory disposition for physicians to inform health ministry about TB cases and all TB patients must be recorded in those registry. The mean TB incidence per year was calculated for every anti-TNF agents and non-TNF biological agents.

Results: Total 1347 (58.1% female) patients were recruited to study. Mean age was 42±12 years. Diagnosis were followed; RA 436 (32.4%), SpA 844 (62.9%), others 67 (5.1%). Total biological drug exposure was 2329 patient-years; adalimumab (660 years), etanercept (630 years), infliximab (426 years), golimumab (283 years), certolizumab (78 years), and total anti-TNF duration (2071 years). Non-TNFi exposure was 258 patient-years. Positive and indeterminate QFT results were found in 267 (19.0%) and 20 (1.5%) patients, respectively and therefor were prescribed INH prophylaxis. In addition, INH was prescribed to 37 (2.7%) patients according to chest X-ray and physician decision. Pulmonary TB was found in 3 of 1347 (0.22%) patients. TB was developed 38, 28 and 21 months after QFT. The mean TB incidence per year was 128.8/100,000 for all biological drugs. The mean TB incidence per year according to QFT positive and negative patients were 181.8/100,000 vs 112.4/100,000.

Conclusions: According to QFT screening for latent TB, INH was started almost 20% of patients. However, if we used TST for latent TB test in BCG vaccinated countries, INH would started almost 70–80% of patients. Therefore QFT was a good tool for latent TB screening in BCG vaccinated countries. Consequently, QFT test seems acceptable to determinate latent TB during biological drug usage. In addition, TB incidence has increased almost 7 times of our national TB incidence.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4080

AB1025 THE SUPERB MICROVASCULAR IMAGE IS MORE SENSITIVE THAN CONVENTIONAL POWER DOPPLER IMAGING IN DETECTION OF ACTIVE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Precise evaluation of synovial inflammation and bony deformity is very important for the management of rheumatoid arthritis (RA). One of the most popular used methods to detect synovial inflammation and bony erosion is ultrasonography. Previous literatures revealed that US using power Doppler imaging (PDI) could detect more sensitive synovial inflammation than conventional radiography. However, there are still some limitations in ultrasonography. The superb microvascular imaging (SMI) is a new software technology introduced by Toshiba, which can detect a vascularity more sensitively without artifacts.

Objectives: In this prospective study, we evaluated the clinical usefulness of the SMI compared to PDI for the detection of active synovits in patients with RA.

Methods: This prospective observational study includes 56 patients with RA (42 females; mean age), from June 2015 to October 2016. The mean age of RA patients was 53.2±17.6 years, and 42 patients were female (75.0%). All included patients underwent ultrasound about both wrists and hands (total 22 joints; wrist joints, metacarpophalangeal joints, and proximal interphalangeal joints). All the ultrasound examinations were performed at the volar side of the wrists and hands using both conventional PDI and SMI which use Aplo Tim 500 Ultrasound (Toshiba Medical Systems Corporation). Their results were scored for each joint from grade 0 to grade 3 according to the vascularity (grade 0, no vascularity; grade 1, single vessel; grade 2, vascular flow less than 50% in field of view; grade 3, equal to 50% or more). The sum of grades for 22 joints was compared between PDI (PDI-sum) and SMI (SMI-sum). The correlation between the sum of grades values and inflammatory laboratory parameters including the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and disease activity score 28 (DAS28) were also evaluated.

Results: The mean values of ESR, CRP and DAS28 were 27.13±18.06 mm/hr, 6.78±9.14 mg/L, and 2.71±1.11 respectively. The positive rates of rheumatoid factor and anti-cyclic citrullinated antibody were 73.2% and 75.0%, respectively. The sum of grades for 22 joints was significantly higher in SMI-sum compared to PDI-sum (10.27±8.20 vs. 5.89±3.76, p<0.001). The SMI-sum was highly correlated with the PDI-sum score (γ=0.800, p <0.001). The SMI-sum showed positive correlation with DAS28, tender joint count, swollen joint count, visual analogue pain scale, and CRP level (γ=0.486, p<0.001; γ=0.385, p=0.003; γ=0.467, p<0.001; γ=0.351, p=0.008; and γ=0.329, p<0.001, respectively).

The number of clinical remission (DAS28 score below 2.6) was 28 (50.0%). The SMI-sum was significantly higher than PDI-sum in patients with clinical remission (7.96±3.59 vs. 4.6±3.03, p<0.001). All of the patients with clinical remission showed active synovitis at more than one joint in SMI.

Conclusions: SMI showed a more sensitive vascularity in RA patients than PDI. We could detect active synovitis through SMI in the RA patients with clinical remission. SMI could be a useful technology for the evaluation of synovitis in RA patients, especially for the detection of clinically subtle, but active synovitis in RA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4571
AN ANA SCREENING ASSAY (ELIA®, CTD SCREEN) CONTAINING MULTIPLE ANTIGENS INCREASES THE SENSITIVITY AND SPECIFICITY OF ANA TESTING BY INDIRECT IMMUNOFLUORESCENCE

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Background: Antinuclear antibodies (ANA) are the serological hallmark of connective tissue diseases (CTD) and indirect immunofluorescence (IIF) on Hep-2 cells is the gold standard for ANA screening. While this method is sensitive it lacks specificity. Moreover, lower-titer ANA subspecificities may escape detection by IIF.

Objectives: To investigate the usefulness of an ANA screening assay containing multiple diagnostic antigens for CTD diagnosis.

Methods: Sera from 265 consecutive patients presenting with symptoms characteristic of connective tissue diseases (but without a clear diagnosis yet) were analysed by IIF and the ELIA® CTD Screen (Thermo Fisher Scientific) containing the following antigens: dsDNA, U1-anRNP, Sm, Ro60, RRo52, La, Rib-P, topoisomerase I (ScI-70), centromere B, DNA polymerase III, fibrillarin, Jo-1, Mi-2, Pm-Scl. All positive sera were further analyzed by monospecific assays (Thermo Fisher Scientific).

Results: Among the 265 patients, 90 were positive by IIF and 78 by CTD Screen; 61 sera were positive in both systems, 17 only in the CTD Screen and 29 only in IIF. In double positive patients at least one relevantly reactive antibody was detected, with anti-Ro and anti-dsDNA antibodies being most frequently detected. Importantly, antibodies were also detected in 15 of the 17 patients who were exclusively positive in the CTD Screen: 7 patients had anti-dsDNA, 4 anti-Ro, 1 anti-La and 1 anti-U1RNP, and 1 patient had anti-Jo-1 antibodies. In contrast, among the 29 sera exclusively positive by IIF only two contained a diagnostically relevant antibody. Clinical evaluation revealed that 16 out of the 17 CTD Screen pos/IIF negative patients presented with at least one clinical sign commonly associated with systemic rheumatic disease (sccia syndrome, 12 patients; anti-Ro, 1 patient; anti-U1RNP, 13 patients; antibodies, 2 patients; levokucytopenia, 2 patients; Raynaud’s phenomenon, 5 patients; pericarditis, 1 patient; thromboembolic events, 2 patients). These patients may be at higher risk for developing a CTD, or, alternatively, may be at an early stage of a CTD in which a definite diagnosis is not yet to be made. The combination of distinct autoantibodies with clinical signs of systemic rheumatic disease, however, warrants a careful follow up in these patients.

Conclusions: ANA screening assays containing multiple antigens such as the ELIA® CTD Screen seem to be helpful diagnostic tools that should be used in addition to IIF for detection of disease-associated autoantibodies enabling the physician to substantially improve diagnostics of connective tissue diseases.


DOI: 10.1136/annrheumdis-2017-eular.6053

THE UTILITY OF LIP BIOPSY IN PATIENTS DIAGNOSED OF IPAF (INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES)

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Background: The European Respiratory Society/American Thoracic Society Task Force has defined a classification criteria for interstitial pneumonia with features of autoimmune disease that does not accord to a specific systemic disease. This criteria combines clinical, serological and radiological domains. The clinical criteria does not include dry syndrome even though the serological criteria does include anti-Ro and antiLa antibodies. It is known that some patients with dry syndrome with antibodies negativity undertake lip biopsy to confirm Sjögren Syndrome (SS). Therefore lip biopsy could be useful to IP AF if SS is suspected.

Objectives: The aim of this study was to identify the prevalence and distribution of sesamoid bones detected on CR and DTS in patients suffering from PsA. We also aimed to identify the sesamoid bones in the hand using digital tomosynthesis (DTS).

Methods: Using CR and DTS, hand images (81 left and 100 right) were taken at a tertiary hospital were retrospectively reviewed. The sesamoid bones were identified in the distal interphalangeal (DIP), interphalangeal (IP), and metacarpophalangeal (MCP) of the thumb (I), index (II), long (III), ring (IV), and small (V) fingers. Differences in number of sesamoid bones detected on CR and DTS were analyzed.

Results: Sesamoid bones were observed in MCP I (100%), MCP II (46%), MCP III (2%), MCP IV (2%), MCP V (53%), and IP (59%) on CR. Using DTS, sesamoid bones were found more often in DIP (100%), MCP II (54%), MCP III (2%), MCP IV (1%), MCP V (59%), and IP (75%). Differences in the mean number of sesamoid bones detected on CR and DTS were statistically significant. Sesamoid bones in DIP joints were frequently observed on DTS, but rarely found on CR.

Conclusions: Most sesamoid bones in the hand were detected in MCP I, II, V, and IP joints, and were more often detected on DTS than CR. DTS is a reliable tool to evaluate bony structures in the hand.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4553

ULTRASOUND NAIL ASSESSMENT IN PSORIATIC ARTHRITIS AND PSORIASIS COMPARED WITH HEALTHY CONTROLS

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Background: Assessment of nail involvement is currently made by clinical assessment using nail psoriasis severity index (NAPSI). Whilst clinical assessment can detect superficial nail changes, the matrix and the extensor tendon region are not accessible for clinical assessment. In myositis (MS) ultrasound (US) is playing an important role in the evaluation of psoriatic arthritis (PsA) patients. Recently, MSUS has been more used in the evaluation of nail involvement in psoriasis (PsO) and PsA patients.

Objectives: The primary objective of this observational, cross-sectional study was to assess the MSUS morphological and vascular abnormalities in nail in PsA and PsO patients compared with healthy controls. The secondary objective was to compare MSUS and clinical assessment of the nail in PsA and PsO patients.

Methods: We included patients with PsA (diagnosed according to CASPAR criteria) and patients with PsO without joint involvement (diagnosed by an experienced dermatologist according to clinical findings) and healthy controls.
Clinical evaluation consisted in the evaluation of the NAPSI and PASI scores. The MSUS evaluation consisted in the evaluation of 10 hand nails. In B-mode (BM) we evaluated the followings: thickness of the nail bed from the distal phalanx bone surface to the ventral plate (PB) according to Worstman X et al.; thickness of the nail from dorsal to ventral plate (IP); dorsal and ventral plate morphology, echogenicity and integrity. Additionally, we performed a color Doppler (CD) evaluation for the presence of CD signal at the nail bed and matrix level. A score for BM and different scores for CD were calculated for each nail sums and of all nails for BM and CD scores were calculated for each patient.

Results: We evaluated 60 patients with PsA, 23 with PsO and 20 controls. 52.4% were female. The mean age (SD; range) was 50.2 (13.6; 23–83). The age was higher in patients (PsO and PsA) than in controls (p<0.001). Patients with PsA were more treated with DMARD (81.7%) while patients with PsO were more treated with topics (73.9%) than DMARDs (13%), (p<0.001). The majority of the patients (96%) had a PASI score less than 12. The NAPSI was higher in PsO patients than in PsA patients (p<0.001): for all controls the NAPSI was 0. US measurements of IP and PB were significantly higher in patients than in controls in the majority of the nail (p<0.045). Total US score for BM was significantly higher in patients than in controls (p<0.001). There were no significant differences for the majority of CD scores between patients and controls. Overall we found weak to moderate positive correlations between NAPSI and US scores for BM, both for matrix and bed. For most of the nails we found no correlation between NAPSI and CDUS scores; for the rest of the nails the US scores for BM, both for matrix and bed. For most of the nails we found no correlation between NAPSI and CDUS scores; for the rest of the nails the US scores for BM, both for matrix and bed. For most of the nails we found no correlation between NAPSI and CDUS scores; for the rest of the nails the US scores for BM, both for matrix and bed. For most of the nails we found no correlation between NAPSI and CDUS scores; for the rest of the nails the US scores for BM, both for matrix and bed.
AB1033 THE EXPRESSION OF IMMUNOGLOBULIN G AND IMMUNOGLOBULIN G4 IN LYMPHOMA

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Background: Although IgG4-related disease has been gradually recognized, its relationship with malignant diseases, especially lymphoma has been an area of concern.

Objectives: To explore the expression of IgG4 positive cells in lymphoma.

Methods: Surgical excision specimens with definite diagnosis of lymphoma from January 2010 to December, 2013 were collected. Hematoxylin-eosin staining and immunohistochemical staining of IgG and IgG4 were then evaluated on dense lymphoplasmacytic infiltration, storiform fibrosis and obliterative phlebitis. For the quantification of IgG and IgG4 positive cells, the areas with the highest density of positive cells were evaluated. Three high-powered fields (hpf) in each section were analyzed, and the average number of positive cells per hpf was calculated.

Results: 16 patients with lymphoma were selected in our study. There were 9 males and 7 females with an average age of 51 years old. The pathological type included 13 cases of non-Hodgkin lymphoma and 3 cases of Hodgkin lymphoma. Sub types of Non-Hodgkin lymphoma contained 8 cases of diffuse large B cell lymphoma, 2 cases of small B cell lymphoma, 1 case of mucosa associated lymphoid tissue marginal zone B cell lymphoma (MALToma), follicular lymphoma, peripheral T-cell lymphoma and hepatosplenic T-cell lymphoma. The 16 specimens all manifested as dense lymphocytic infiltration, accompanied by atypical lymphocytes. Proliferation of fibrous tissue was only seen in one specimen. 14 cases were IgG positive with the highest cell count from 20–350/hpf. IgG4 can be expressed in both cytoplasm and cytomembrane. 2 cases of IgG4 positive were Hodgkin lymphoma and the highest cell counts were 11 and 12/hpf respectively.

Conclusions: IgG4 positive cell, fibrosis and obliterative phlebitis seldom appear in lymphoma. Among specific tumor signature molecules, it may not be difficult to distinguish lymphoma from IgG4-related disease.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3899

AB1034 SCORING SYSTEMS OF MUSCLE MRI IN IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: MRI is a widely used radiological method for assessing muscle involvement in idiopathic inflammatory myopathies (IIM). There is still no universally accepted and validated scoring protocol for the quantification of pathological changes in muscles.

Objectives: To identify MRI scoring systems used in previous studies. To summarize the most frequently evaluated MRI features and to suggest parameters for a unified scoring system, that has to be validated in the future.

Methods: A detailed literature search was conducted in the standard medical databases. Information regarding individual MRI scoring systems were obtained from the methodological explanations and their parameters were compared.

Results: We identified different scoring systems with a large variability of assessed localizations and parameters (Table 1). Muscle oedema as a sign of active muscle inflammation was evaluated in all studies. There were some studies using modified Mercuri score for evaluation of the fatty infiltration as a marker of chronic muscle damage or the Goutallier grading (1,2), developed originally for the assessment of inherited neuromuscular disorders or structural changes in orthopedics. Perifascicular oedema or soft-tissue oedema were also assessed in some cases. There was no concordance between evaluated muscle groups.

Conclusions: MRI plays a significant role in the evaluation of pathological changes in IIM. This research demonstrated, that there is no widely used, standardized method for assessment of a MRI finding. According to our results, a future concept of MRI scoring system should include evaluation of muscle oedema, fatty infiltration and possibly also the presence of perifascicular (-fascial) and subcutaneous tissue inflammation. Muscle groups most convenient for evaluation have to be determined as well.

References:

Acknowledgements: Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00023728 (Institute of Rumatology).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3656

Figure 1. Logistic regression analysis of ultrasound findings for the contribution of diagnosis of dactylitis

Odds Ratio [95%CI]

PD signals of the collateral ligament

5.3

PD signals of the flexor tendons

7.2

0.1 1 10 100

AB1035 EXAMINATION OF ULTRASOUND FINDINGS IN UNDIFFERENTIATED SPONDYLOARTHRITIS PATIENTS WITH DACTYLITIS

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Objectives: To evaluate the ultrasound findings in undifferentiated spondyloarthriti- (uSpA) patients with or without dactylitis.

Methods: Between April 2014 and December 2016, sixty-six patients with uSpA diagnosed at our center were consecutively enrolled. The diagnosis of uSpA was made by the Japan College of Rheumatology (JCR)-certified rheumatologists and dactylitis was defined as sausage-digit appearance. Ultrasound, clinical and laboratory findings at diagnosis in patients with dactylitis (dactylitis group; n=30) were compared to those without dactylitis (non-dactylitis group; n=36). Grey scale (GS) and power Doppler (PD) signals of the wrist and finger joints, PD signal of extensor and flexor tendon sheaths, and PD signals of the collateral ligament of the fingers in both hands were assessed by ultrasound. Ultrasound assessment was made by JCR-certified sonographers.

Results: There were no significant differences in clinical and laboratory findings, including inflammatory back pain, arthritis of the lower limbs, tenderness of the entheses, radiographic/MRI changes of sacroiliac joint and HLA-B27 allele frequency, between two groups. In ultrasound findings, the dactylitis group had significantly more PD signals of the flexor tendon sheaths (83% vs. 22%, p<0.0001), the collateral ligament (83% vs. 25%, p<0.0001), and the MCP joint (30% vs. 3%, p<0.01) as compared with the non-dactylitis group. In logistic

Table 1. Muscle MRI scoring systems

<table>
<thead>
<tr>
<th>Author</th>
<th>Muscle MRI scoring systems</th>
</tr>
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<tbody>
<tr>
<td>Pipitone 2016</td>
<td>1 = present, 0 = absent</td>
</tr>
<tr>
<td>Andersson 2015</td>
<td>1 = present, 0 = absent</td>
</tr>
<tr>
<td>Malattia 2014</td>
<td>0 = no abnormalities, 1 = mild, 2 = moderate, 3 = severe</td>
</tr>
<tr>
<td>Davis 2011</td>
<td>0 = absent, 1 = mild, 2 = moderate, 3 = severe</td>
</tr>
</tbody>
</table>

STR = short tau inversion recovery, NS = not specified, T1W = T1 weighted sequences, VAS = visual analogue scale.

STIR = short tau inversion recovery, NS = not specified, T1W = T1 weighted sequences, VAS = visual analogue scale.
AB1036 PREDICTIVE VALUE OF BASAL REACTANTS IN AN EARLY ARTHRITIS CLINIC. DOES ESR ELEVATION CRITERIA MAKE A DIFFERENCE?

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Background: The presence of high acute phase reactants may help the diagnosis and classification of patients with rheumatoid arthritis, specially in seronegative patients.

Objectives: Our objective was to establish if the presence of high basal reactants in early arthritis may help to establish the diagnosis of rheumatoid arthritis following criteria of ACR 1987 (which does not include positive reactants in diagnostic criteria) at 12 months of follow-up.

Methods: The presence of acute phase reactants at the baseline visit (elevated CRP and elevated ESR according to two different criteria) was studied in a population of 70 patients referred to the arthritis clinic with criteria for suspicion of early arthritis to meet at least one of the Following criteria: a) Swelling in 2 or more joints) b) Pain in MCFs, MTFs and/or wrists c) Morning stiffness greater than 30 minutes (* SERAP study criteria), with <12 months of evolution of symptoms. None of the patients had previous diagnosis of rheumatoid arthritis or other inflammatory joint disease nor had previous treatment with steroids or DMARDs. The presence of high VSG (mm/h) was considered according to two criteria: a) ESR 1: VSG ≥20 in men and VSG ≥15 in women; b) ESR 2 (criterion according to age and sex) (1): Age ≤50 years ESR 20 in men and ESR 30 in women; Age ≥50 years of age, ESR 15 in mm/h in men and ≥20 in women. Statistics: Chi-square or Fisher test (for any value ≤5). Odds ratio (OR) calculation.

Results: 70 patients, 45 women (64%), x age 51,5/6,16,0,8 y (18–85) were included, x disease duration 3,47 meses ± 2,59 (0,53–11,73), 48/70 (68,5%) of RA, 23/70 (32,9%) were classified in non-RA group because they meet criteria of other inflammatory conditions (eg. psoriatic arthritis RA-like). 45/70 patients had high baseline CRP (64,3%), ESR 1 38/70 (54,3%) and ESR 2 35/70 (50%). Basal CRP ≥5 showed statistically significant differences for RA diagnosis (ACR 1987 criteria) p ≤0.003, OR = 4,64 (1,62–13,24) but basal positive ESR 1 criteria did not (p =0.122). Basal positive ESR2 showed significant differences for diagnosis of RA, with p =0.036, OR =2,78 (0,99–7,47). In the subgroup of seronegative patients, basal CRP could predict ACR 1987 RA diagnosis at 12 months follow-up p =0,019, OR 4,2 (1,23–14,36), but ESR (both ESR1 and ESR2) not (p =1,000). If the 5 patients ACR 1987 meeting criteria RA-like but diagnosed on other inflammatory conditions were included, the results are similar but ESR2 reached p =0,019, OR 4,2 (1,23–14,36), but ESR (both ESR1 and ESR2) not (p =1,000).

Conclusions: The presence of elevated basal CRP-≥5 may be used as a factor that helps to predict the diagnosis of rheumatoid arthritis according to ACR 1987 criteria for RA. The baseline elevated ESR according to the sex and age criterion could be useful as a predictor factor for the diagnosis of rheumatoid arthritis, while the VSG criterion ≥20 in all patients does not demonstrate differences in the study between the two groups with final diagnosis AR and non-RA. In seronegative patients, only CRP demonstrated predictive value but ESR not.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3170

AB1037 INTEROBSERVER RELIABILITY OF KNEE OSTEOARTHRITIS LESIONS USING MUSCULOSKELETAL ULTRASOUND: DIFFERENCES BETWEEN STATIC VERSUS REAL TIME READING

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Background: Musculoskeletal ultrasound (MSU) is an imaging technique proved to be valid in several musculoskeletal conditions. In osteoarthritis (OA) it allows the identification of inflammation and structural damage. However, MSU is an operator dependent method and its widespread use has been hampered by questions related to the reliability of both, image acquisition and image interpretation.

Objectives: The objective of this study was 1) to evaluate the interobserver reliability of knee OA according to the definitions used by the OMERACT reliability exercise of inflammatory and structural abnormalities in patients with knee osteoarthritis using ultrasound and 2) to compare the interobserver reliability on previous collected images (static reading, thereafter) versus after the acquisition and interpretation of images in real time (real time reading, thereafter).

Methods: A reliability exercise based on the reading of US images was conducted by two experienced rheumatologists in MSU. A set of 59 images of both, normal and OA knee lesions were collected for the static reading. A set of 20 knees were scanned by each rheumatologist for the real time reading. Dichotomous and semi-quantitative scoring (0–3) was performed for the presence of damage on the condrosynovial margin, osteochondral margin and matrix of the trochlear cartilage, osteophytes at the lateral and medial femoral condyle and proximal tibia, medial and lateral meniscal extrusion and Baker’s cyst. Interobserver reliability was calculated by the Cohen’s kappa coefficient.

Results: Interobserver reliability scores for the static reading were good for cartilage damage, meniscal extrusion and Baker’s cyst, while they were excellent for the presence of osteophytes. The scores for the real time reading were poor to moderate for cartilage damage, osteophytes and Baker’s cyst and good for meniscal extrusion. These results are shown in Table 1.

Table 1. Interobserver κ values for agreement of the static and real time reading of US abnormalities in knee osteoarthritis

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Static reading</th>
<th>Real time reading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condrosynovial margin</td>
<td>0.588 (0.180)</td>
<td>0.588 (0.180)</td>
</tr>
<tr>
<td>Cartilage matrix</td>
<td>0.732 (0.118)</td>
<td>0.317 (0.143)</td>
</tr>
<tr>
<td>Osteochondral margin</td>
<td>0.658 (0.148)</td>
<td>0.251 (0.163)</td>
</tr>
<tr>
<td>Medial condyle osteophyte</td>
<td>0.508 (0.176)</td>
<td>0.412 (0.213)</td>
</tr>
<tr>
<td>Lateral condyle osteophyte</td>
<td>0.752 (0.184)</td>
<td>0.365 (0.228)</td>
</tr>
<tr>
<td>Medial tibial osteophyte</td>
<td>0.865 (0.129)</td>
<td>0.490 (0.96)</td>
</tr>
<tr>
<td>Lateral tibial osteophyte</td>
<td>0.744 (0.236)</td>
<td>0.432 (0.213)</td>
</tr>
<tr>
<td>Meniscal extrusion</td>
<td>0.673 (0.204)</td>
<td>0.704 (0.159)</td>
</tr>
<tr>
<td>Baker’s cyst</td>
<td>0.714 (0.256)</td>
<td>0.490 (0.860)</td>
</tr>
</tbody>
</table>

Conclusions: This exercise shows that the interobserver reliability of MSU for the detection of knee OA lesions is widely different depending on the type of reading (static versus real time). Although MSU seems to be reliable for the detection of knee OA lesions, caution needs to be taken in the interpretation of published data regarding the type of reading exercise performed.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3863

AB1038 INFLUENCE OF AGE ON ENTHESIS IN TUNISIAN PEOPLE: AN ULTRASOUND STUDY

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Background: By aging, many changes occur in the different components of the locomotor system, leading to a pathological situation such as osteoarthritis or remaining totally asymptomatic.

Objectives: The aim of the current study was to compare, via ultrasound, the entheseal changes in two groups of people having different ages by calculating a modified Madrid sonography enthesis index.

Methods: The study was conducted in the rheumatology department of Mongi Slim Hospital in Tunisia, between July 2015 and December 2016, including 17 healthy subjects. We indentified two groups: (G1) 9 persons aged ≥50 years [51–68] and (G2) 8 persons aged ≤50 years-old [37–50].

All the included persons underwent an enthesis ultrasound exploration (Esaote MyLab 60 machine and a 13–18 MHz linear array transducer) by a rheumatologist.
EXPERIMENTED IN ULTRASOUND. FIVE ENTHESIS LOCATIONS BILATERAL DISTAL ACHILLES TENDON, DISTAL AND PROXIMAL PATELLAR LIGAMENTS, DISTAL QUADRICEPS, AND BRACHIAL TRICEPS TENDONS IN EACH PERSON WERE EXPLORED. THE FOLLOWING ELEMENAL DISECTIONS OF ENTHESIS WERE EVALUATED: THICKNESS, PRESENCE OF CALCIFICATIONS, EROSIONS, ERNATHROPHYES, LOSS OF FIBRILLAR PATTERN, AND POWER Doppler SIGNAL. THE CALCULATED INTRINSIC DISTAL ATHESIS INDEX WAS CORRELATED TO THE DISTAL PATELLAR LIGAMENT改变, SIGNIFICANCE LEVEL WAS SET AT 5%. RESULTS: IN OUR STUDY POPULATION, THE MEDIAN AGE WAS 51.8±2.3 YEARS AND THE MEDIAN BODY MASS INDEX WAS 30.2±1.4 KG/M². THIS LAST WAS SIMILAR BETWEEN THE TWO GROUPS. ALL INCLUDED SUBJECTS WERE FEMALE. THE TOTAL ATHESIS INDEX WAS HIGHER IN GROUP 1 (6.76±0.91) THAN GROUP 2 (3.50±0.73) WITH A STATISTICALLY SIGNIFICANT DIFFERENCE (P<0.01). CONSIDERING EACH EVALUATED ATHESIS, THE DISTAL PATELLAR LIGAMENT ARCHITECTURE WAS HIGHER THAN THE MEDIAN (1.67±0.55 VS. 0.25±0.16 WITH P<0.03). FOR THE OTHER ENTHESIS, THERE WAS A STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN THE 2 GROUPS. CONCLUSIONS: THE DISTAL PATELLAR LIGAMENT ENTHESIS CHANGES SHOWN IN OLDER PERSONS MAY BE THE TRANSMISSION OF A SILENT-STAGE OF KNEE OSTEOARTHRITIS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5630

AB1039 RELATIONSHIPS BETWEEN SONOGRAPHIC AND ELECTROPHYSIOLOGICAL MEASURES IN PATIENTS WITH IDIOPATHIC CARPAL TUNNEL SYNDROME WAITING FOR SURGERY

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Background: Sonography is a diagnostic tool with great development in diagnosing entrapment neuropathy. It’s an easy, painless, fast, non-invasive technique and can explore how the nerve’s morphology and pathologies are associated. An electroencephalogram is used to assess the intensity of nerve involvement.

Objectives: To determine the relationship between the intensity of nerve involvement by electroencephalogram and the measurement of the cross-sectional area (CSA) of the median nerve by sonography in patients with idiopathic carpal tunnel syndrome (CTS) waiting for surgery.

Methods: 56 wrists of 39 consecutive patients waiting for surgery were tested; however, 5 were excluded because were found to have anatomic variants (4 bilateral nerves, 2 median arteries) and 1 fibrolipoma. Therefore, the final sample was 51 wrists of 37 consecutive patients (11 male and 26 females), with a mean age of 49.2 years (25–85), all with electrophysiologically confirmed idiopathic CTS. Patients were classified by their electrophysiologic grade. The median nerve cross-sectional area at proximal and distal carpal tunnel was measured using high frequency ultrasound.

Results: CSA, the severity of the electrophysiologic grade and the duration of symptoms were analysed. Also, a median nerve morphological characteristics examination (hypoecogenicity, loss of fascicular structure, Power Doppler signal and anatomical variants) was undertaken. A comparison between CSA and the severity of the electrophysiologic grade was made using an independent T test and the connection between CSA and the duration of symptoms was calculated using ANCOVA test.

Patients were classified by their electrophysiologic severity grade (8 mild, 13 moderate, 29 severe and 1 very severe). The mean ultrasonic area of distal median nerve was 8.7 mm² in mild/moderate and 9.2 mm² in severe/very severe cases (P=0.52). The average of proximal CSA was 11.6 mm² in mild/moderate and 14.1 mm² in severe/very severe cases with statistical significance differences (P=0.026). Relationship between CSA and symptom’s duration wasn’t identified. In 89.2% of the cases, hypoeccogenicity and the loss of fascicular structure were observed but no cases were found to show positive Power Doppler signal.

Conclusions: The most valid and relevant parameter regarding the electromyogram in the diagnosis of CTS is CSA at proximal carpal tunnel by sonography.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4514

AB1041 ULTRASONOGRAPHY OF NORMAL MUSCULOSKELETAL STRUCTURES IN 100 SECTIONS: A BOOKLET AND A CD-ROM

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Objectives: To present a booklet and a CD-ROM with a mini-atlas including 100 sections illustrating the normal ultrasonic musculoskeletal anatomy.

Methods: We performed an ultrasound examination of large and small joints of the medical staff not suffering from any musculoskeletal disorder. Ultrasound examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. Finally, for the sake of clarity of the presentation of this library, we presented each image accompanied with another showing the valid positioning of the probe and an annotated schema for each section made.

Results: We present in the form of a CD-ROM and booklet a photo library of a cross-section of the flexor digitorum superficialis and profundus tendons.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4591

AB1040 CLINICAL UTILITY OF BONE SCINTIGRAPHY FOR INFLAMMATORY ARTHRITIS

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Background: Bone scintigraphy is often used in the workup of patients with rheumatological disease, in particular for the investigation of inflammatory arthritis. It also has a role in the investigation of malignancy and fractures. As an imaging technique, it is very sensitive but not specific for inflammation. The most common technique used is triple phase scintigraphy, with the 2nd phase (blood pool phase) being the most useful for identifying inflammation.

Objectives: To evaluate the clinical utility of bone scintigraphy in the workup of patients with rheumatological disease, in particular for inflammatory arthritis.

Methods: This was a retrospective study of patients seen in the rheumatology outpatient between January 2011 and July 2014, who had bone scintigraphy as part of their workup. Their clinical record was reviewed to obtain pre- and post-test clinical diagnoses, bone scintigraphy reports and investigations (ESR/CRP, rheumatoid factor/CCP antibodies). For patients who had followup at one year we recorded their clinical diagnosis at this time.

Results: A total of 226 patients had bone scintigraphy, with a median age of 54 years. 63% were female. The main indication for bone scintigraphy was to assess for inflammation in 194 patients. For this group, the most common pre-test diagnosis of inflammatory arthritis (41%), followed by degenerative arthritis (36%), unclear diagnosis (20%) and mixed inflammatory and degenerative arthritis (3%). Overall, 49% (n=111) of patients had their diagnosis changed after bone scintigraphy.

The pre-test diagnosis was compared to bone scintigraphy findings with the highest confirmatory rate for degenerative arthritis (67%), followed by inflammatory arthritis (49%) and mixed arthritis (40%). Bone scintigraphy findings were also compared to post test diagnosis with the highest confirmatory rate for degenerative arthritis (91%), followed by inflammatory arthritis (70%) and mixed arthritis (14%). There was no significant association between patient factors (age, gender, ESR/CRP, RF/CCP) and having confirmatory or conflicting bone scintigraphy findings.

The post test diagnosis was compared to the diagnosis at one year, with the diagnosis being unchanged in 84% for inflammatory arthritis and 45% for degenerative arthritis.

Conclusions: This study showed that bone scintigraphy lead to a change in diagnosis in a large proportion of patients and was better at confirming degenerative arthritis or ruling out inflammatory arthritis.

References:

Acknowledgements: I would like to acknowledge Sara Vogrin (University of Melbourne) for her assistance with statistical analysis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4514
The joints studied are:

- The wrist and hand
- The elbow
- The shoulder
- The ankle and foot
- The knee
- and the hip

100 sections were performed, we presented them together with images showing their normal corresponding musculoskeletal anatomy, the valid positioning of the probe, and also an annotated schema corresponding to each section. We give here below the example of a section illustrating a cross-section of flexor digitorum superficialis and profundus tendons

Conclusions: We hope that we give to rheumatologists a simple tool to recall and standardize the practice of musculoskeletal ultrasound. We intend to enrich it, in the future, with the pathological images and interventional ultrasound videos.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4514
positive: 45.7% (N=21) were RF-ELISA positive and RF-nephelometry negative.

**Conclusions:** ELISA is superior to nephelometry detecting RF in patients with RA, as also in quantifying high-positive values.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2606

**AB1044 EVALUATION OF A FLUOROENZYME IMMUNOASSAY (ELIA-CTD) IN THE SCREENING OF PATIENTS SUSPECTED FOR AUTOIMMUNE CONNECTIVE TISSUE DISEASES**

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**Background:** Detection of auto-antibodies directed against nuclear antigens (antinuclear antibodies or ANA) have important diagnostic and prognostic implications in connective tissue diseases (CTD). The conventional indirect immunofluorescence assay on Hep-2 cell line (ANA-IIF) is the most commonly used method to detect ANA. The ANA-IIF can be labor intensive and suffers from lack of specificity.

**Objectives:** To evaluate the utility of a new fluoroenzyme immunoassay “ELIA-CTD” as an alternative for screening patients suspected for autoimmune connective tissue diseases.

**Methods:** Sixteen Hundred (1600) consecutive patients’ sera submitted for anti-nuclear antibodies testing were used using the ANA-IIF (Diaisorin S.P.A, Saluggia, Italy) and the new ELIA-CTD assay (Phadia GmbH, Frieiburg, Germany). ANA testing was ordered by both primary and secondary care physicians. The ELIA-CTD screening assay is a fluoroenzyme immunoassay which is performed on the Phadia-250 automated platform. The ELIA-CTD assay contains ANA-targeted recombinant antigens including dsDNA, Sm-D, Rib-P, PCNA, U1-RNP (70, A, C), SS-A/Ro, SS-B/La, Centromere B, ScI-70, Fibrillarin, RNA Polymerase III, Jo-1, Mi-2, and PM-scl. The test results are expressed as ratio, with >1.0 considered positive. For ANA-IIF, the cut off for positive results was 1.40 or greater. Additionally, further testing for dsDNA and other extractable nuclear antigens (ENA) was undertaken on a subset of sera that were ANA-IIF+ or whenever there was discrepancy between the two methods.

**Results:** The overall agreement between the two methods was 84.2%. Two hundred and eighty (308) out of 1600 (19.3%) samples tested positive by ANA-IIF as compared to 101/1600 (6.6%) for the ELIA-CTD assay. Additional testing showed that 105 samples were positive for ENA including dsDNA. Of those, 101 were ELIA-CTD positive and 81 were ANA-IIF positive. By incorporating the ENA results, the calculated sensitivity and specificity for the ELIA-CTD were 97.1% and 99.7% respectively with positive and negative predictive values for the ELIA-CTD assay of 96.1% and 99.8%, respectively. The corresponding sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the ANA-IIF assay at different dilutions is shown below:

<table>
<thead>
<tr>
<th>Titer</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1:40</td>
<td>77.7</td>
<td>84.8</td>
<td>26.0</td>
<td>98.2</td>
</tr>
<tr>
<td>≥1:80</td>
<td>60.3</td>
<td>95.3</td>
<td>32.4</td>
<td>98.4</td>
</tr>
<tr>
<td>≥1:160</td>
<td>57.4</td>
<td>97.4</td>
<td>41.3</td>
<td>98.4</td>
</tr>
<tr>
<td>≥1:320</td>
<td>46.5</td>
<td>98.7</td>
<td>48.8</td>
<td>98.5</td>
</tr>
</tbody>
</table>

**Conclusions:** The new automated ELIA-CTD assay shows superior sensitivity and specificity compared to the conventional labor intensive ANA-IIF. The ELIA-CTD can be used as an upfront screening tool for connective tissue diseases. Depending on the clinical details, any ELIA-CTD positive results could be reflexively followed by additional testing including ANA-IIF testing to elucidate the titer and pattern.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1838

**AB1045 MACROPHAGE TARGETED POSITRON EMISSION TOMOGRAPHY (PET) FOR THE IMAGING OF INFLAMMATORY ARTHRITIS: AN IN VIVO AND IN VITRO INVESTIGATION OF TRANSCLECTOR PROTEIN (TSPO) TRACER UPTAKE**

N. Narayan1, H. Mandhair1, C. Coello2, A. Saleem2, A. Sabokbar1, P. Taylor1, 1Clinical Biological Sciences, University of Oxford, Oxford, 1Imanova Centre for Imaging Sciences, London, United Kingdom

**Background:** TSPO targeted PET tracers are increasingly recognised as cellular imaging markers of macrophage infiltration, due to the high expression of TSPO on activated macrophages. Previous work demonstrated the ability of [11C]PK11195 TSPO PET to detect subclinical inflammation in RA, and predict flare in both those with established RA and AGPA positive arthritis. However, high background uptake of [11C]PK11195 in bone, and inability of [11C]PK11195 to detect lesions in AS has driven the investigation of newer TSPO tracers for the detection of inflammatory arthritis.

**Objectives:** Here, we present data confirming the ability of the TSPO tracer [11C]PBR28 to detect and quantify synovitis in both RA and PsA, and in vitro work that assesses more fully what TSPO tracer accumulation in inflamed synovium actually reflects at a cellular level, especially considering TSPO is ubiquitous expressed.

**Methods:** 10 patients (5 with RA, 5 with PsA) with evidence of inflammation in one or both knees (as confirmed by clinical examination and US) and 4 healthy volunteers underwent PET/CT both knees using the TSPO tracer [11C]PBR28. Arthritis patients underwent synovial biopsy of one knee within 7 days of scan. Healthy synovium was obtained from patients undergoing knee arthroscopy for ligamentous injury. Synovial tissue was stained for CD68, CD163 and TSPO. For in vitro work, human monocytes, lymphocytes and synovial FLS from RA patients were harvested, and macrophages differentiated from monocytes. DNA was extracted for PCR. Other cells underwent density centrifugation to extract the cytoplasmic cell fraction, and a radioligand binding assay with [3H]PBR28 was undertaken, to assess tracer binding to TSPO in each cell type

**Results:** Tracer uptake correlated significantly with severity of inflammation on clinical examination and ultrasound, as did synovial sublining staining for CD68, TSPO and CD163 (see table 1). There was negligible staining for all stains in healthy control synovium. qPCR demonstrated highest TSPO mRNA in stimulated FLS (fold change 62.75±10.03) and M2 macrophages (60.69±2.38), with lymphocytes having the least TSPO expression. PBR28 saturation binding confirmed these findings at protein level (see graph 1).

**Conclusions:** Our data demonstrates that the TSPO tracer PBR28 is capable of detecting and quantifying synovitis in RA and PsA. PBR28 tracer uptake correlates with macrophage marker staining, but not with fibroblast marker staining in our patient cohort. mRNA and protein data demonstrate, however, that there is a similar expression of TSPO in activated macrophages and activated FLS, hence TSPO tracer accumulation is as likely to represent FLS activation as it is macrophage activation.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1838

**AB1046 COULD SERUM TWEAK LEVEL BE AN INDICATOR OF SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS?**

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**Background:** TWEAK is a type 2 transmembrane glycoprotein of TNF family that has multiple functions such as angiogenesis, regulation of tissue production-
CAN THE ACR/EULAR 2010 CLASSIFICATION CRITERIA BE USED AS DIAGNOSTIC TOOL FOR RHEUMATOID ARTHRITIS IN REAL LIFE?

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Background: To date, due to the large variability in its clinical manifestations, early identification of rheumatoid arthritis (RA) relies on practice-based evidence. Moreover, this variation hampers the comparability and accurate stratification of the base population within and between RA trials. In 2010 the ACR/EULAR working group developed RA classification criteria that were primarily intended for research purposes. Despite its use in scientific settings, one can speculate on the effectiveness of these criteria when used in the routine clinical practice of diagnosing RA.

Objectives: In this study we aimed to investigate the degree of concordance between the diagnosis of RA in routine clinical practice and the ACR/EULAR 2010 classification criteria.

Methods: All patients who received a diagnosis of RA between 2010–2016 within our hospital were identified according to the financial diagnosis treatment combination (DTC) code, which corresponds to the ICD-10. Clinical and demographic data were extracted from our digital patient records of which 10% of the data were cross-checked by random selection. In retrospect we collected variables at time of RA diagnosis such as: number and type of swollen/painful joints, inflammatory markers, rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), disease duration and patients primary/secondary/tertiary diagnosis according to the rheumatologist. Additionally, all patients were classified according to the ACR/EULAR 2010 criteria for RA. The degree of concordance was determined by descriptive statistics.

Results: The dataset included 977 patients with a DTC RA of which 673 (69%) had RA according to the rheumatologist. From the patients who were clinically diagnosed with RA, 463 (69%) fulfilled the ACR/EULAR 2010 criteria (see figure 1), this is 47% of the total DTC RA patients. The majority of the population was female (72%) and the mean age was 59. A number of 161 (24%) patients were diagnosed with RA according to the rheumatologists, but did not fulfil the ACR criteria. These patients had less inflammation, were more often RF and/or ACPA negative, and had less involved joints. About 5% of the data were missing.

Conclusions: It can be concluded that the DTC codes are not the most reliable source of information about the diagnosis. There is a discrepancy between the DTC code, the diagnosis according to the rheumatologist and the classification criteria. The degree of concordance between rheumatologist and the ACR criteria is comparable to the numbers described in literature. Since in our practice aspects of the ACR classification are used for diagnostic purposes, we will investigate factors that drive the specificity. Furthermore, reasons for the ICD-10/ DTC and final diagnostic mismatch is of great importance and will be studied as well. These factors will indicate the opportunities on the use of the ACR/EULAR criteria in clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2267

SYNTHETASE) DIAGNOSTIC VALUE OF ANTI-JO-1 (ANTI-HISTIDYL-TRNA SYNTHETASE) AUTOANTIBODIES IN PATIENTS WITH HAND OSTEOARTHRITIS

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Background: The destruction of cartilage is one of the basic mechanisms of the progression of hand osteoarthritis (HOA). Radiographic study indicates the thickness of the cartilage indirectly based on the degree of joint space narrowing (JSN). At the same time, the ultrasound (US) method allows to measure cartilage thickness precisely. Objectives: To determine the degree of concordance in the interphysician groups of patients with HOA and to correlate this rate with the degree of JSN, identified by radiologic imaging, and the sonographic changes were assessed using Killman’s method. Next, US investigation was carried out. The thickness of the cartilage was measured in the central part of the 2–5 proximal phalanx heads of both hands in the dorsal longitudinal view in the static image in grayscale with the flexion position no more than 90 degrees. The cartilage is defined as a thin hypoechogenic smooth layer, parallel to the contours of the articular surface. The thickness of the cartilage was defined as the distance between the subchondral bone and the surface layer of cartilage, which was the border between the cartilage and the joint cavity. In the presence of synovial measurement of joint cartilage was carried out before the border and hypertrophic synovial if they differed in the degree of intensity of the US signal. The measurement of cartilage thickness was carried out by a conventional line, which was an exact perpendicular to the surface of the subchondral bone and parallel to the direction of US waves. Measurement was not carried out if visualization of the surface layer of cartilage was not possible. The control group consisted of 45 women 45–75 years old without HOA, but with ultrasound investigation. Data were analyzed using Statistica 10.0 and are presented as mean (standard deviation), ‘odds ratio’ coefficient (OR) and y Pearson’s correlation coefficient. Results: 360 joints of both hands were investigated with successful measurement of the cartilage thickness of 338 (94.7%) joints. The average value of the cartilage in all PIP was 0.31 (0.11) mm. The maximum thickness of the cartilage was obtained in the 2nd PIP joints - 0.34 (0.12) mm on the right hand and 0.36 (0.14) mm on the left hand. For the control group results were 0.38 (0.11) mm and 0.37 (0.13) mm respectively. We have found a reliable relationship between the degree of JSN and cartilage thickness with the OR 1.849 (95% confidence interval 1.198 – 2.855), y = 7.772, p =0.0053. Conclusions: US reduction of the cartilage thickness is a marker of cartilage loss which is correlated with the results of radiologic examination. This makes possible to use ultrasound as an alternative method of diagnosing HOA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6512

CLINICAL UTILITY OF AUTOANTIBODIES AGAINST EXTRACTABLE NUCLEAR ANTIGENS IN ROUTINE CARE: FREQUENCY OF REPEATED TEST REQUESTS AND DIAGNOSTIC VALUE OF ANTI-JO-1 (ANTI-HISTIDYL-TRNA SYNTHETASE)

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Background: High-throughput high-sensitivity ELISAs for autoantibodies associated with CTD, such as extractable nuclear antigens (ENA), are used widely. Anti-Jo-1 (anti-histidyl-tRNA synthetase), one of this panel, is believed to confer a poor prognosis due to an association with interstitial lung disease (ILD) and myositis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6512

Scientific Abstracts
Objectives: To describe: the pattern of anti-ENA positive tests; frequency of repeated requests; stability and repeatability of anti-Jo-1 tests; clinical characteristics of anti-Jo-1 +ves compared with controls; and diagnostic value of anti-Jo-1 for ILD.

Methods: All anti-ENA test requests, from any hospital department, between July 2013 and Dec 2014 were identified. Serum samples are screened forENA (Quanta Lite® ENA profile, Inova Diagnostics) and positive samples have specific ENA antibodies levels quantified. Data from anti-Jo-1 positive patients and controls was extracted from electronic records allowing a minimum of 12 months after first test.

Results:

<table>
<thead>
<tr>
<th>Jo-1 Positive (n=40)</th>
<th>Controls (n=80)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years (range)</td>
<td>53 (19–86)</td>
<td>52 (17–87)</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>70%</td>
<td>79%</td>
</tr>
<tr>
<td>Dead</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Current or previous malignancy</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Raynauds</td>
<td>17.5%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Inflammatory arthritis</td>
<td>20%</td>
<td>19%</td>
</tr>
<tr>
<td>Clinical myositis diagnosis</td>
<td>5%</td>
<td>1.3%</td>
</tr>
<tr>
<td>CPK &gt; 1000 units/liter</td>
<td>5%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>12.5%</td>
<td>6%</td>
</tr>
<tr>
<td>CT chest done during study period</td>
<td>7/40</td>
<td>20/80</td>
</tr>
<tr>
<td>ANA (c=1:100)</td>
<td>10/88 (47.4%)</td>
<td>22/79 (27.8%)</td>
</tr>
<tr>
<td>RF</td>
<td>8/25 (32%)</td>
<td>12/44 (27.3%)</td>
</tr>
<tr>
<td>CCP</td>
<td>0/19 (0%)</td>
<td>3/33 (9.1%)</td>
</tr>
<tr>
<td>Anti-SSA/dsDNA (Crdithia +ve)</td>
<td>7.5%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Scl70</td>
<td>7.5%</td>
<td>0%</td>
</tr>
<tr>
<td>SSA/RO</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>SSB/LA</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>RNP</td>
<td>10%</td>
<td>0%</td>
</tr>
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</table>

*Fisher's exact test, two tailed. **Statistical analyses were not done on these comparisons as by definition controls were negative for ENA antibodies.

Conclusions: 4009 samples from 3581 patients were tested. The first sample tested, chronologically, was designated test of interest. 616 (17.2%) patients were anti-ENA screen +ve, and 40 (1.1%) anti-Jo-1 +ve (≥ 20 AU/mL). Anti-ENA tests were done more once than 350/3581 (9.8%) patients (428/4009 (10.7%) samples) and for 7/40 (17.5%) of anti-Jo-1 +ve patients. The median interval between 1st and 2nd requests: 124 days (IQR 233 days). The Table shows data for anti-Jo-1 patients and randomly selected ENA-ve controls. The frequency of ILD, myositis and Raynaud’s was comparable. Sensitivity and specificity of Jo-1 for anti-Jo1 patients and randomly selected ENA -ve controls. The frequency of ILD, a key feature of “anti-synthetase syndrome”, were 50% (CI 19–81%) and negative predictive value 93.8% (CI 86–98%). Of patients with the highest anti-Jo1 titres (<40 AU/mL, 10/40 patients, 25%): 3 had ILD, 1 myositis and 2 had a malignancy (disseminated melanoma and CML); Bland-Altman plots show that anti-Jo-1 values remained stable when patients were re-tested at another time but re-testing available stored samples from +ve patients showed important variation (Figure).

Conclusions: Our results show the existing discrepancy between the clinical examination and ultrasonographic test in patients in low disease activity/remission by DAS28, even more with the use of doppler. In the comparison of both groups we observed an increase in the difference in those who did not receive biological therapy. In patients with optimized biological therapy, with higher swollen joint count in physical examination, kappa index was near of normality in grayscale. The detection of subclinical joint damage is often undertreated, showing ultrasound as a noninvasive technique of great help reducing joint damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4406
Methods: Fifteen patients with HCVrA & 15 RA patients were subjected to: full history, clinical examination. Ultrasonography assessment using a Philips HDI 5000 system with 12–5 MHz Broadband Linear Transducer. Both knees were examined by one ultrasonographer who was blind to clinical data.

Results: In HCVrA, synovial hypertrophy was detected in 10% of knees (3/30) of which 2 (10%) exhibited Doppler signals, while in RA it was detected in 70% (21/30) of which 95% (20) knees exhibited Doppler signals. Significant difference was found between the two groups (p<0.01). Knee effusion was detected in 80% (24/30), & 86% (26/30), of patients with HCVrA & RA respectively, no significant difference was found. Cartilage degeneration was detected in 76% (23/30) & 83% (25/30), of patients with HCVrA & RA respectively. Bone erosions were detected in 20% (6/30) in the RA group. It was not detected in HCVrA patients. In HCVrA, there was no correlation between the presence of synovial hypertrophy with respect to cartilage degeneration and knee effusion.

Conclusions: We found no specific ultrasonographic feature specific for HCV related knee arthritis, the knee effusion is a predominant feature and the hypertrophied synovium is not frequently found. No destructive lesions were found to be related to the disease itself; however this should be confirmed by histopathological assessment.

References:

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4094

AB1052 QUALITATIVE SYSTEMATIC REVIEW: LACK OF CONSENSUS ON THE CLASSIFICATION CRITERIA FOR DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS

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Background: Diffuse idiopathic skeletal hyperostosis (DISH) is a condition characterized by flowing ossifications of the spine with or without ossifications of entheses elsewhere in the body.1,2 Studies on prevalence and pathogenesis of DISH use a variety of partially overlapping combinations of classification criteria, making meaningful comparisons across the literature difficult.3,4

Objectives: The aim of this study was to systematically summarize the criteria available to classify or diagnose DISH to aid in the development of a more uniform set of diagnostic and/or classification criteria.

Methods: A search was performed in Pubmed, Embase, Cochrane Library and Web of Science using the term DISH and its synonyms. Articles were included when two independent observers agreed that the articles proposed a new set of classification criteria for DISH. All retrieved articles were evaluated for methodological quality and the presented criteria were extracted. The criteria were placed into one of three groups being “descriptive studies”, “sets of criteria for dichotomous diagnosis” or “sets of criteria with consecutive phases”.

Results: A total of 24 articles met the inclusion criteria. Two articles were descriptive studies, 11 contained dichotomous classification criteria and 11 described a set of criteria with consecutive phases. In all articles spinal hyperostosis was required for the diagnosis of DISH. Peripheral, extraspinal manifestations were excluded as a co-requirement for the diagnosis DISH in five articles. Most discrepancies revolved around the threshold for the number of vertebral bodies affected and to defining different developmental phases of DISH. More than half of the retrieved articles described a dichotomous set of criteria and did not consider a consecutive or progressive character of DISH.

Conclusions: In our systematic review we summarize the available different classification criteria for DISH and highlight the lack of consensus on the diagnosis of (early) DISH. Consensus criteria, including consecutive phases of new bone formation that characterize DISH can be developed based upon established diagnostic and classification criteria.

References:

Acknowledgements: None.

Disclosure of Interest: None declared DOI: 10.1136/annrheumdis-2017-eular.4565

AB1053 A NOVEL METHOD FOR IDENTIFYING RADIOGRAPHIC ALTERATIONS IN THE SUBTALAR JOINT USING AN ANISOTROPY-BASED TEXTURE ANALYSIS ALGORITHM: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Background: Osteoarthritis (OA) is the most common form of arthritis and affects disproportionately the knee. Recent developments in imaging technologies showed that OA is not just a joint disease but also involves progressive changes in the subchondral/subarticular bone area of the tibia. On top of the accepted method of measuring the joint space width, assessments of the trabecular bone structure in selected regions of interest (ROI) in conventional X-rays may be offering an alternative method for quantifying the risk and progression of this disease.

Objectives: The accepted method for assessing OA - Joint space width (JSW) and Joint Space Area (JSA) measurements - have limited capabilities in regard to early identification and reproducible follow-ups of the disease. The objective of this abstract is to evaluate the subchondral bone structure as an area for early identification of OA risk, applying texture anisotropy algorithms and subsequently comparing the results to standard JSW and JSA measurements.

Methods: This study was performed using data from the Osteoarthritis Initiative. The analysis data set was restricted to female. OA knee exams recorded with the same modality. Furthermore we selected exams which had a KL grade of 0 at the baseline exam and a deteriorating KL grade ≥2 at the 96 month follow up. 22 cases fulfilled these criteria and we selected 22 matching controls with no signs of OA at the 96 month follow up. The selected region of interest (ROI) for the analysis was the subchondral bone area of the tibia. One additional ROI in each femur condyle – in total 6 ROIs. For each individual ROI, the degree of texture anisotropy was calculated and compared between case/control. In addition, JSW & JSA were calculated in both groups using a proprietary software-based method (ImageBissy Lab, Vienna, Austria).

Results: Whereas the JSW and the JSA measurements did not yield any significant differences with respect to their mean values (Cohen’s d = 0.199 and 0.038), the calculated texture parameters showed that differences in values between cases and controls could be found in text of the subchondral ROIs (ROI1 & 2) with Cohens’d values of 0.625 and 0.831. Respectively. With selected patient criteria, the differences in anisotropy results were significant using these texture parameters.

Conclusions: Our results indicate that using the selected radiographic texture parameters, an early identification of patients at risk for developing OA using conventional X-rays can be achieved. This may offer an additional method for quantifying the risk of baseline OA. This is supported by the Cohen’s d values that are by definition relatively large (0.625 and 0.831). Ongoing research focuses on larger sample set validation and the use of such algorithms for additional applications, such as the early identification of fracture risk.


AB1054 QUANTITATIVE ULTRASOUND FOR ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RELIABILITY AND CONSTRUCT VALIDITY

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Background: Joint ultrasound is an integral part of assessment of patients with rheumatoid arthritis (RA). Semi-quantitative grading of ultrasound is subjective whereas quantitative ultrasound (QUIS) may be more objective.

Objectives: To evaluate the reliability and construct validity of QUIS of wrist joints in patients with RA.

Methods: We studied 95 patients with RA. Following parameters were studied: swollen and tender joint counts (SJC and TJC), patient and evaluator global assessment (PGA, EGA) and disease activity score (DAS28). Patients were classified as active disease and disease in remission as per expert clinician opinion. Colour Doppler ultrasound (CDUS) of wrists was done to obtain semiquantitative grading. Scans were processed in image analysis software (Photoshop CS4) to obtain the following: color fraction of intrasynovial (IS) vascular signals (CF(IS)) = pixel area of IS vascular signals/pixel area of entire IS area (area(IS)), CF(total) (pixel area of both IS and extravasynovial vascular signals/area (IS)) and number of IS (N(IS)) and extravasynovial (N(ES)) vascular signals. Images were stored and independently rated for both CDUS and QUIS by two different raters blinded to each other’s rating.

Results: Demographics of patients were: mean age 48±16.7 years, mean disease duration 24 months (range 4–600), mean DAS28 of 2.98±1.18 and 40% (38/95)
had active disease, CDUS findings were: synovial proliferation: grade 1: 27.4%, grade 2: 54.7%, grade 3: 11.6%; vasculitis: grade 1: 41.1%, grade 2: 32.6% and grade 3: 9.5%. Significant findings of QUS were: CF(IS): 8.6±10.63 (median 6.05, p<0.001) and CF(total): 0.996 (95% confidence interval (CI): 0.994–0.997) and ICC(1,2) for CF(total) was 0.995 (95% CI: 0.993–0.997). CF(IS) was correlated with SJ(C (r=0.22, p=0.029), TJC (r=0.39, p<0.001), PGA (r=0.5, p<0.001) and DAS28 (r=0.47, p<0.001); correlations for CF(total) were: SJ(C (r=0.25, p=0.013), TJC (r=0.41, p<0.001) and PGA (r=0.51, p<0.001) and DAS28 (r=0.5, p<0.001). Significant correlations were also observed for N(SI (r=0.282, p=0.006), TJC (r=0.411, p<0.001), PGA (r=0.48, p<0.001), EGA (r=0.514, p<0.001) and DAS28 (r=0.467, p<0.001). Spearman rank correlations of vascularinity with SJ(C (r=0.25, p=0.011), TJC (r=0.292, p=0.004), PGA (r=0.26, p=0.012), PGA (r=0.186, p<0.103) and DAS28 (r=0.275, p=0.007). Spearman rank correlations of CF(IS) (CF(total) and N(SI with CDUS vascularity were 0.828, 0.864 and 0.689 respectively (p<0.001). Cut-off values for CF(IS), CF(total) and N(SI for distinguishing active RA from RA in remission were 4.78 (AUC: 0.82, 95% CI: 0.73–0.9), 5.75 (AUC: 0.89, 95% CI: 0.69–0.88) and 2.5 (AUC: 0.77, 95% CI: 0.68–0.86) respectively. There were 40 patients with CDUS vascularity ≥2 among which 62.5% (25/40) had active disease. In this group only CF(total) ≥5.75 could distinguish between patients with active disease from disease in remission (p<0.001 (2015 vs. 10/125/2015 vs. 0.046). Conclusions: CF(IS) (CF(total) had excellent inter-rater reliability and construct validity. Simple quantitative cutoffs could distinguish between active RA from remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5842

**AB1055 LEUKOCYTE ESTERASE REAGENT STRIPS FOR RAPID DIAGNOSIS OF INFLAMMATORY SYNOVIAL FLUID**

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**Background:** The analysis of synovial fluid is an important tool for diagnosing joint disease. When synovial fluid is removed, the white cell count (WCC) decreases with time, and an inflammatory liquid could become a false non-inflammatory disease. When synovial fluid is removed, the white cell count (WCC) decreases with time, and an inflammatory liquid could become a false non-inflammatory disease.

**Methods:** Our results demonstrate that leukocyte esterase reagent strips are a rapid, cheap, and sensitive tool to identify inflammatory synovial fluid. Leukocyte esterase reagent strips had an excellent Se but a poor Sp, it could be used as a screening tool in primary care practice. A positive result may indicate an inflammatory process, then the patient should be referred to a rheumatologist.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6482

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**AB1056 RADIOPHARMIC ANALYSIS OF METATARSUS PRIMUS ELEVATUS IN PATIENTS WITH RHEUMATOID FOREFOOT DEFORMITIES**

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**Background:** Metatarsus primus elevatus involves dorsal elevation of the first metatarsal relative to the lesser metatarsals. The role of metatarsus primus elevatus in rheumatoid forefoot deformity is yet to be elucidated. We hypothesise that metatarsus primus elevatus can be attributed to a different pathomechanism than typical rheumatoid forefoot deformities such as hallux valgus, flat foot, and flat foot.

**Objectives:** To clarify the radiographic characteristics of metatarsus primus elevatus in patients with rheumatoid forefoot deformities.

**Methods:** We retrospectively reviewed standing anteroposterior and lateral radiographs of 51 feet (37 patients; mean age 65.7±1.7 years) before toplasty due to metatarsalgia at our hospital. The elevation of the first metatarsal relative to the second metatarsal (MPE), the hallux valgus angle (HVA), the intermetatarsal angle (IMA), talar pitch, and calcaneal pitch were measured. For statistical analyses, the Mann-Whitney U test was used.

**Results:** The group with higher MPE was significantly more under the age (p=0.011). There was no significant difference in HVA between the two groups (p=0.068), although IMA was significantly smaller in the group with higher MPE (p=0.033). In the group with higher MPE, calcaneal pitch was greater (p=0.011) and talar pitch was smaller (p=0.016).

**Conclusions:** In patients with metatarsus primus elevatus, other rheumatoid forefoot deformities such as plantar foot and flat foot were not observed. There was a wide range of hallux valgus severity. Metatarsus primus elevatus may be attributed to greater hindfoot calcaneal pitch.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1945

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**AB1057 MULTIDISCIPLINARY APPROACH FOR DIAGNOSING CONNECTIVE TISSUE DISEASE-RELATED LUNG DISEASE: IS IT USEFUL FOR RHEUMATOLOGISTS?**

S. Peña Montelongo1, A. Monroy Calero1, O. Acosta Fernández2, S. García Hernández1, L. Pérez Martín1, A. Bonilla Arjona4, H. Sánchez Pérez1, B. Bustamante Reyes1, B. Rodríguez-Lozano1, 1Rheumatology; 2Pathology; 3Chest Section, Radiology, Hospital Universitario de Canarias, Tenerife, Spain

**Background:** Many patients with idiopathic interstitial pneumonia (IP) have certain clinical, serological and/or pulmonary morphologic features suggesting an underlying autoimmune disease (AD), but without meeting established criteria for connective tissue disease (CTD), a situation labelled as ‘IP with autoimmune features’ (IPAF)1. To identify an underlying aetiology is important because it may impact on treatment and prognosis, and could be optimised by multidisciplinary approach.

**Objectives:** 1.To identify prevalence of IPAF in routine practice. 2. To determine the value of lung biopsy to diagnose underlying AD.3. To describe the course of IPAF.

**Methods:** Observational, longitudinal retrospective study in a tertiary hospital specific outpatient clinic for IP patients with cough and dyspnea as dominant symptoms requiring co-evaluation by rheumatologists in 2010–2016. Variables included: clinical, serologic and morphological findings by High-Resolution Computed Tomography of lungs assessed by 2011 current guidelines2 and open lung biopsy. Statistical analysis:SPSS 17.0.

**Results:** Of 410 patients evaluated for IP, 93 had rheumatologist assessment, 70 (75.3%), mean age at diagnosis 52.6 years (SD12.13), of whose 48 had no previous diagnosis. Mean follow-up 3.54 (SD2.77)years in undiagnosed patients. The most frequent radiological patterns were: inconsistent with usual interstitial pneumonia (UIP) (67.7%), UIP (22.6%), Possible UIP (4.3%), others (4.3%). Lung biopsy was performed in 15 patients (16%), 11 without previous diagnosis. Histopathology patterns: 8 non-specific interstitial pneumonia (NSIP) in whom final diagnosis of pulmonary fibrosis was confirmed by open lung biopsy. Statistical analysis:SPSS 17.0.

**Results:** Of 410 patients evaluated for IP, 93 had rheumatologist assessment, 70 (75.3%), mean age at diagnosis 52.6 years (SD12.13), of whose 48 had no previous diagnosis. Mean follow-up 3.54 (SD2.77)years in undiagnosed patients. The most frequent radiological patterns were: inconsistent with usual interstitial pneumonia (UIP) (67.7%), UIP (22.6%), Possible UIP (4.3%), others (4.3%). Lung biopsy was performed in 15 patients (16%), 11 without previous diagnosis. Histopathology patterns: 8 non-specific interstitial pneumonia (NSIP) in whom final diagnosis of pulmonary fibrosis was confirmed by open lung biopsy. Statistical analysis:SPSS 17.0.

**Conclusion:** The prevalence of IPAF was 21.1% (19.6%), with IPAF as clinical diagnosis in 24.7% of overall patients. 2. Surgical lung biopsy allowed to diagnose AD in 23% of unlabelled patients with clinical features diagnostic of IPAF. There was no significant difference in HVA between the two groups (p=0.068), although IMA was significantly smaller in the group with higher MPE (p=0.033). In the group with higher MPE, calcaneal pitch was greater (p=0.011) and talar pitch was smaller (p=0.016)

**Conclusions:** 1. Of patients with IP referred for rheumatologist assessment, 31% has no established CTD, with IPAF as clinical diagnosis in 24.7% of overall patients. 2. Surgical lung biopsy allowed to diagnose AD in 23% of unlabelled patients with clinical features diagnostic of IPAF.
patients. After a follow-up time of 3.5 years, 43% of patients that died had been diagnosed as a IAPF.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5550

AB1058 SENSITIVE DETECTION OF DYNAMIC CHANGES OF BONE EROSIONS IN INFLAMMATORY ARTHRITIS BY MUSCULOSKELETAL ULTRASOUND: A COMPARATIVE ANALYSIS WITH HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY

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Background: Bone erosion is a hallmark of inflammatory joint diseases. Its meticulous detection is highly important for correct diagnosis and monitoring of therapy response. Earlier studies showed that musculoskeletal ultrasound (MSUS) has a higher sensitivity than conventional radiography with regards to detection of bone erosions (1) making MSUS more and more popular. The OMERACT ultrasound working group is currently standardizing and validating MSUS as an imaging outcome tool.

Objectives: To investigate the ability of MSUS to sensitively and specifically detect bone erosions in a longitudinal setting using HR-pQCT as a gold standard.

Methods: This is a sequel study to our 2011 cross-sectional comparative analysis on MSUS and HR-pQCT (2). 4/6 healthy individuals, 6/40 psoriatic arthritis patients at study entry, 4/6 patients with erosive RA and 1/6 patients with erosive spondyloarthritis were enrolled. They were assessed for prevalence and severity in MSUS and converted to HR-pQCT. Afterwards, half of the patients were followed up and received an MSUS and an HR-pQCT scan of the clinically dominant hand. Bone erosions at the radial, palmar, and dorsal sites of the second metacarpophalangeal (MCP) joint, as well as the palmar and dorsal sites of the third and fourth MCP joints were assessed for prevalence and severity in MSUS and by HR-pQCT. Afterwards, data were compared to the 2011-dataset. MSUS was graded as described earlier (2).

Results: Datasets without follow-up from the baseline cohort were eliminated. Sensitivity of MSUS in comparison to HR-pQCT regarding correct detection of erosions was 95% and specificity were 79%. For this analysis, grade 1 lesions were included. At follow-up sensitivity was 86% and specificity 79%. At follow-up, 36 MSUS-lesions were no longer detectable in MSUS; 21/36 were false-positive lesions at baseline. Only one false-positive lesion was detected at both time points. One new lesion was detected by MSUS and confirmed by HR-pQCT. Overall severity of bone erosions regressed in MSUS; these findings were confirmed by HR-pQCT (p<0.05).

Conclusions: This is the first study on change of bone erosions over time comparing MSUS and HR-pQCT. MSUS was confirmed being a sensitive imaging tool able to detect changes of erosions over time. Thus, it may be an adept tool to monitor treatment response in inflammatory joint diseases. Correct identification of bone erosions and differentiation from physiological vessel channels requires knowledge of predilection sites of erosions and physiological cortical breaks; this might aid to further increase the diagnostic value of MSUS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5665

AB1060 MEASURING AGREEMENT IN THE ULTRASONOGRAPHIC EVALUATION OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS. A LATIN-AMERICAN MULTICENTER EXPERIENCE ASSESSING THE INFLUENCE OF SONOGRAPHER EXPERIENCE AND EXPERTISE

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Background: Ultrasonography (US) is an important tool in rheumatology practice but it depends on sonographer’s experience.

Objectives: To evaluate the reliability of US assessment among observers across Latin American using a web tool.

Methods: Cross-sectional study. Fifty-one Latin American ultrasonographers took part in a web-based US exercise evaluating images from 20 RA patients. The 4 joints US score was calculated for each patient including bilateral radiocarpal, midcarpal and second metacarpophalangeal joints. PD and GS were graded from 0 to 3, the highest disease activity. Five patients were evaluated twice in order to address intra – rater reliability. The inter and intra-rater reliability was assessed using a two-way random, absolute, individual and average-measures intra-class correlation coefficient (ICC). We stratified sonographers according to experience (defining High experience as: at least 5 years of experience and 80 US assessments/month).

Results: A total of 1020 US image assessments were performed. Mean 4-joints US score was 17.8. The ICC was in the excellent range for intra [individual ICC = 0.945 (CI95% 0.905-0.965); average ICC =0.972 (CI95% 0.950–0.982)] and
inter-reader reliability (individual ICC = 0.867 [95% CI 0.786–0.934]; average ICC = 0.997 [95% CI 0.995–0.999]).

When comparing high with low experience sonographers, there was no significant difference in intra-class correlation coefficient. However, there was a greater variation between the means among low experience readers (13 to 22) and higher experience sonographers (14–18) (Figure 1).

Conclusions: US is reliable to sonographer expertise and experience.


Disclosure of Interest: None declared


AB1061 THE HIGH DOSES GOLIMUMAB BRING BETTER SUPPRESSION OF ULTRASONOGRAPHIC SYNOVIAL INFLAMMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Biologic diseases modifying antirheumatic drugs (bDMARDs) that target cytokines and cytokine receptors such as tumor necrosis factor (TNF)-alpha and interleukin (IL)6 have been established as a standard therapy of rheumatoid arthritis (RA) for patients with conventional systemic DMARDs, such as methotrexate (MTX), resistant disease. Golimumab, one of the bDMARDs, is an antibody targeting to TNF-alpha. In Japan, we can choose the dose of golimumab 50mg or 100mg according to the disease activity. Recent advance of ultrasound (US) equipment allows obtaining high-quality gray-scale (GS) imaging and sensitive or 100mg according to the disease activity. In Japan, we can choose the dose of golimumab 50mg or 100mg according to the disease activity. Recent advance of ultrasound (US) equipment allows obtaining high-quality gray-scale (GS) imaging and sensitive

Methods: Patients with RA treated by golimumab were consecutively included. Ultrasound examination was performed at 52 synovial sites, bilateral first to fifth MTP joints, by using a semi-quantitative scale from 0 to 3.

Objectives: The aim of this study was to compare the ultrasound findings between patients with rheumatoid arthritis (RA) treated by golimumab 100mg and 50mg.

Results: Fifty-five patients with RA (46 female, mean age: 64.2±12.1 years) were included and analyzed. In comparison between the dose of Golimumab at the time of ultrasound examination, disease activity (DAS28-CRP) was significantly higher in 100mg group (100mg, n=15: 3.6±1.0, 50mg, n=40: 2.3±0.9; p < 0.001), disease duration (years) 17.5±9.6 14.2±9.5 0.263, Total GSUS score 16.9±12.6 14.8±12.7 0.572

Conclusions: Even patients have high disease activity, golimumab 100mg suppress the synovitis and tenosynovitis very well. In the condition where disease activity was sufficiently controlled, there was very low level of ultrasound findings of ultrasound at the dose of golimumab.

Acknowledgements: We wish to thank Setsuko Takeda, Ayumi Hashimoto, Emi Isohata, Rika Morinaka, Hatuee Ud a and Tomomi Iwashashi for their special efforts in the sonographic and collecting data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5870

AB1062 PATTERNS OF MUSCULOSKELETAL SYSTEM INVOLVEMENT IN PATIENTS WITH TYPE I AND TYPE II DIABETES MELLITUS

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Background: Diabetes mellitus (DM) is a chronic disease, no known cure except in very specific situations. Musculoskeletal Ultrasoundasonography (MSUS) has a great sensitivity that can help clinical examination for the detection of peripheral enthesis related to DM

Objectives: To study the different patterns of musculoskeletal (MSK) system affection in both types of diabetes mellitus (DM).

Methods: We performed a retrospective single-center study on sixty five patients during the period from May 2014 to February 2015, to evaluate MSK manifestations in diabetic patients at Sayyed Galal University Hospital, Cairo, Egypt. Patients were defined as diabetic on the basis of Diagnosis and Classification of Diabetes Mellitus diagnostic criteria (1997) (1). Clinical data, laboratory investigations, X-ray, musculoskeletal ultrasoundasonography (MSUS) (2) and Bone mineral density was measured using Dual energy X-ray absorptiometry (DEXA) scan (3) were all collected from all patients.

Results: We included 65 diabetic patients; of these 21 patients (32.31%) had type I diabetes while 44 patients (67.69%) had type II diabetes. Age in type I was 25±10.5 years while in type II was 50±18.44 years (P<0.001). DM type II showed higher BMI (P<0.001), fatigue (P<0.005), shoulder periarthritis (P<0.005), ankle periarthritis (P<0.005), large joint arthrosis (P<0.005), anserine bursitis (P<0.001) and planatar fascitis (P<0.003) than type I. Osteoporosis was found in both types but type II showed more prevalence 13/44 patients (29.5%) while type I showed only 3/21 (14.2%). No statistically significant difference between both groups as regard t-score in the three sites. MSUS showed increased prevalence of quadricaps tendon enthesopathy in type I (P<0.033), while Infrapatellar (P<0.023) and retrocalcaneal bursitis (P=0.001) were more prevalent in type II DM.

Conclusions: Early evaluation of any diabetic patient regarding BMD by DEXA scan and soft tissue by MSUS seems to be beneficial for early detection of any abnormality and therefore early management and prevention of complications.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2420

AB1063 ULTRASOUND ASSESSMENT OF SYNOVITIS IN PATIENTS WITH LESSER TOE DEFORMITY DUE TO RHEUMATOID ARTHRITIS

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Background: In recent years, joint ultrasonography has been widely used for the diagnosis and treatment of rheumatoid arthritis (RA), allowing visualization of synovitis. Its clinical usefulness in early diagnosis and evaluation of disease activity has been reported. Continuous inflammation, osteochondral destruction, and soft tissue destruction due to synovitis in toe joints result in various clinical pictures of the foot. In the lateral toes in the forefoot, subluxation or luxation of the metatarsophalangeal (MTP) joints may occur, leading to painful calllosities and resultant disturbance in activities of daily living. Few reports have addressed toe deformity and joint ultrasonographic findings of synovitis in the forefoot.

Objectives: In this study, lateral MTP joints were assessed using joint ultrasonography in RA patients to examine the correlation with deformity.

Methods: Seventy feet of 61 RA patients were examined in the outpatient clinic of our hospital. Patients who underwent surgery were excluded. The mean age of the patients was 66 years (24 to 92 years), and the mean duration of disease was 12 years and 9 months (1 month to 40 years). Biologic products were used for 23 feet. Joint ultrasonography was performed by the same examiner, using the same room and apparatus. Synovitis was defined as Grade 1 or more as determined by Doppler manoeuvre on foot radiographs. In right position obtained before and after ultrasonography, patients with luxation, subluxation, and joint fissure narrowing were classified into the deformity group, those with bone erosion and geode formation into the bone erosion group, and lack of abnormal findings into the normal group.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1415
Carpal tunnel syndrome (CTS) is the only known early clinical manifestation of wild-type transthyretin amyloidosis (ATTRwt), formerly known as senile systemic amyloidosis, which causes an amyloid cardiomyopathy. At the UK National Amyloidosis Centre 98% of those with proven ATTRwt have evidence of median nerve entrapment on neurophysiological studies and 48% have a history of carpal tunnel decompression as much as 12 years prior to heart failure symptoms. ATTRwt is diagnosed in approximately 150 individuals in the UK each year although post-mortem studies suggest presence of ATTRwt amyloid deposits 30% of males over 80 years (yrs)1. A novel bone tracer, Technetium-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) largely abrogates the grade uptake.

Carpal tunnel biopsy can readily identify ATTR amyloid deposition and may identify those at risk of developing cardiac ATTR amyloidosis in the future, permitting earlier intervention with novel therapeutics aimed at preventing accumulation of amyloid. This ongoing study aims to identify the UK prevalence of ATTR amyloid in those with carpal tunnel syndrome and to create a cohort of those who may develop systemic ATTR amyloidosis to further elucidate the disease natural history.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1244

AB1064 CARPAL TUNNEL BIOPSY AND BONE SCINTIGRAPHY USING THE TECHNETIUM-3,3-DIPHOSPHONO-1,2-PROPA NODICARBOXYLIC ACID (99mTc-DPD) TRACER CAN IDENTIFY CLINICALLY SILENT CARDIAC AMYLOIDOSIS AT A POTENTIALLY TREATABLE STAGE

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Background:
Carpal tunnel syndrome (CTS) is the only known early clinical manifestation of wild-type transthyretin amyloidosis (ATTRwt; formerly known as senile systemic amyloidosis) which causes an amyloid cardiomyopathy. At the UK National Amyloidosis Centre 98% of those with proven ATTRwt have evidence of median nerve entrapment on neurophysiological studies and 48% have a history of carpal tunnel decompression as much as 12 years prior to heart failure symptoms. ATTRwt is diagnosed in approximately 150 individuals in the UK each year although post-mortem studies suggest presence of ATTRwt amyloid deposits 30% of males over 80 years (yrs)1. A novel bone tracer, Technetium-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) largely abrogates the grade uptake.

Carpal tunnel biopsy can readily identify ATTR amyloid deposition and may identify those at risk of developing cardiac ATTR amyloidosis in the future, permitting earlier intervention with novel therapeutics aimed at preventing accumulation of amyloid. This ongoing study aims to identify the UK prevalence of ATTR amyloid in those with carpal tunnel syndrome and to create a cohort of those who may develop systemic ATTR amyloidosis to further elucidate the disease natural history.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1244

AB1065 NEEDLE VERSUS FORCEPS TECHNIQUE IN ULTRASOUND-GUIDED SYNOVIAL BIOPSY OF THE KNEE JOINT

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Background:
Ultrasound-guided synovial biopsy is increasingly applied in rheumatology. Usually forceps- or needle-based techniques are used. So far there has been no direct comparison of different devices regarding their suitability in high resolution musculoskeletal ultrasound (hrMSUS)-guided synovial biopsy.
Objectives: To compare different forceps and needle-based instruments in hrMSUS-guided synovial biopsy in a cadaver study.

Methods: A core needle biopsy (A, Quickcore, Cook Medical, Bloomington, IN, USA), a retrograde forceps (B, Retroforce, Karl-Storz GmbH Tuttingen, Germany), an antegrade arthroscopy forceps (C, Karl Storz GmbH, Tuttingen, Germany) and an antegrade shelled and integrated core needle system (D, Synovex, Hipp Medical AG, Kolbingen, Germany) were tested for ultrasound-guided synovial biopsy of the suprapatellar recess in cadaver knee joints. Four senior rheumatologists scored each intervention from 0–5 regarding the following characteristics: visualization, handiness, accuracy, synovial tissue yield, invasiveness and overall suitability. Each intervention was recorded as static images and video clips.

Results: In all devices, enough representative synovial tissue was obtained and the instruments were all well visualized by hrMSUS. Core needle biopsy and the integrated needle system were best visualized due to their horizontally shaped closing mechanism. The core needle obtained a high yield of superficial synovial tissue and was the least invasive procedure. Despite handiness and accuracy were higher in the forceps instruments, overall suitability for hrMSUS-guided synovial biopsy was rated highest for the core needle biopsy.

Conclusions: Technically, all of the tested devices can be used for hrMSUS-guided synovial biopsy. Core needle biopsy seems to be most suitable for this intervention due to a low invasiveness, good visualization and optimal yield of superficial synovial tissue.

References:

Disclosure of Interest: None declared.

**AB1066 DIAGNOSTIC UTILITY OF THE MEDIAN/ULNAR NERVE CROSS-SECTIONAL AREA RATIO IN CARPAL TUNNEL SYNDROME**

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Background: The most commonly used ultrasonographic measurements for the diagnosis of CTS are measurement of the median nerve cross-sectional area (m-CSA) at different levels of the carpal tunnel. The cross-sectional area of a nerve may differ according to biometric characteristics such as age, sex, weight and wrist thickness. 3,4

Objectives: The aim of this study was to assess the diagnostic utility of the ultrasonographic ratio of m-CSA to ulnar nerve cross-sectional area (u-CSA), the m-CSA/u-CSA ratio, in carpal tunnel syndrome (CTS).

Methods: Patients (n=50) with positive symptoms and electromyography results of CTS and control subjects (n=50) with negative electromyography results of CTS were evaluated. The most symptomatic hand of each participant were included in the assessment. Ultrasonographic m-CSA and u-CSA measurements were made at the level of the pisiform bone, and m-CSA/u-CSA ratio was calculated.

Results: Using the m-CSA cut-off value of 9.95 mm² showed a sensitivity of 92% and a specificity of 42%. Conversely, the cut-off value 13.90 mm² showed a sensitivity of 52% and a specificity of 90% in the diagnosis of CTS.

Conclusions: The ratio of m-CSA/u-CSA at the level of the pisiform bone did not provide an additional benefit for the diagnosis of CTS. Ultrasonographic m-CSA measured at the same level was found to be more sensitive and specific method.

References:

Disclosure of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5933

**AB1067 SUITABILITY OF CADAVER MODELS IN ULTRASOUND DIAGNOSTICS AND INTERVENTIONS IN RHEUMATOLOGY: FOOT AND ANKLE**

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Background: Employment of cadaver specimens in ultrasonography provides a unique and safe model for education and enhances the anatomical knowledge of sonographers and may help determine the accuracy of ultrasound-guided interventions.

Objectives: In this systemic literature review we assessed the role and use of cadaver specimens in sonographic studies of the foot and ankle in the field of rheumatology.

Methods: For our literature review we utilized the MEDLINE database, which were supplemented by searches in Google Scholar and Science Direct when the articles were not available through PubMed. Original studies in English language were included in the full paper review with an exception of three German language studies with English abstracts were also included. In the full paper review studies were selected for each feature that used the cadaver specimens of the foot and ankle. Data were extracted on study characteristics and interventions.

Results: The search yielded 1241 articles, of which 130 were selected for detailed review. In the end, 23 full papers met inclusion criteria. The studies could be grouped as follows: description of detailed ultrasound anatomy (9), testing of accuracy of ultrasonic guided interventional procedures (8), examination of artificial tears and lesions (4), foreign bodies (1) and joint effusions (1). The results that were obtained in the studies of the fully reviewed papers utilized a total of 294 cadaveric specimens, with an average of 12.78 (range: 1–48) cadaveric specimens included in each study.

Conclusions: The use of cadaver specimens of the foot and ankle may facilitate the validation of new sonographic methods which assess these joint regions, however the major disadvantage of these studies was the low number of cadaveric specimens.

Disclosure of Interest: None declared.


**AB1068 ULTRASOUND DIAGNOSTICS AND INTERVENTIONS IN RHEUMATOLOGY: WHICH SEMI-QUANTITATIVE SCORING SYSTEM IS THE BEST?**

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Background: Sjogren Syndrome (SS) affects mainly exocrine glands. The latest diagnostic criteria designed for clinical studies are also used as guidance in clinical practice [1].

Objectives: To apply and compare 9 US semi-quantitative scoring systems in B mode scanning of salivary glands in Sjogren Syndrome.

Methods: A research using keywords “salivary glands”, “ultrasonography”, “Sjogren Syndrome”, “semi-quantitative scoring” 2,3,4,5 in Medline/Pubmed was performed. There was a selection of most relevant articles. There were not considered relevant publications with impact factor <1. We performed the examination on SG in B mode US and applied these scores (De Vita, Niemela, Hoevar, Salaffi, Yukinori, Cornecl,Theander) to our patients (primary and secondary SS).

Results: Eighty four SG in patients diagnosed with primary and secondary (57.15%) SS were assessed. In the group of patients with SSA/SSB presence (57.15%), mean score was De Vita 1.78±1.21, Niemela 2.56±2.17, Hoevar and Wernicke 2.39±2.14, Salaffi 2.83±2.52, Yukinori 2.39±2.14, Milic 3.39±2.14, Cornecl 1.78±2.15, Theander 1.28±0.75, Schirmer test was critical and the need for using the artificial tears was correlated to SS alterations in scoring systems proposed by Niemela (r=0.465, p<0.05) and Salaffi (r=0.469, p<0.02). All scoring systems were strongly correlated between them (r=0.8, p<0.01).

Conclusions: Inhomogeneity of parenchyma was considered in all scoring systems. Others considered relevant glandular dimension and margins regularly [2.3,4]. There was no difference in relation to the scoring systems. Xerostomia validated through Schirmer test is correlated to SG parenchymal alterations. Our data is an update about semi-quantitative scoring systems in US of SG in SS.

References:
SHOULDER ULTRASONOGRAPHY IN DIABETIC PATIENTS – IS THERE DAMAGE WITH NO CLINICAL SIGN?

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Background: Degenerative lesions in shoulder rises exponentially with age and diabetes was found to be associated with shoulder pain [1,2].

Objectives: To evaluate the prevalence and type of lesions shoulder in diabetic patients with no pain using ultrasound (US).

Methods: We included consecutive patients with diabetes with no pain or clinical tumeefaction in shoulder. US was performed in both shoulders using the standard scanning planes and dynamic maneuvers. Clinical data as fasting glyceremia, BMI, treatment were recorded.

Results: Forty two shoulders were examined in 21 consecutive patients (mean age 67.92 +/-7.35 years, weight 81.75 +/- 13.57 kg, BMI 25 +/-2 kg/m2, fasting glyceremia 151.85 +/-37.22mg/dl) with diabetes mean 5.33 years +/- 5.99. Majority of patients were under treatment with oral antidiabetics (58.3%). Degenerative lesions were found in subcapular (SSC) 33.3% and supraspinatus (SPS) 8.3% tendons as well as intratendinous micro ruptures with calcifications (33.3% bilateral calcifications in SSC, SPS). Impingement syndrome was objectified in 16.6% of examinations. Minimal inflammatory signs as: sub-acromion sub deltoid bursitis in 50% (minimum in 33.3%, 8.3% bilateral) and long head biceps tenosynovitis in 58.3% (8.3% minimal Doppler signal). 63.3% showed humeral irregularities and also erosions were found (8.3%).

Conclusions: Degenerative and minimal inflammatory lesions in shoulder of diabetic patients exist with no clinical sign (pain, tumeefaction). Ultrasonography might be an useful technique to confirm these alterations before the appearance of symptoms.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5469

UNRELLAVING AUTOIMMUNE DISEASES THROUGH NAILFOLD CAPILLAROSCOPY

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Background: Nailfold capillaroscopy is a non-invasive diagnostic technique designed to evaluate small vessels of the microcirculation. The most important indication for capillaroscopy is Raynaud’s phenomenon. The complexity and meticulous evaluation of the eight fingers is difficult to apply in daily practice given the limited availability of time to perform. For this reason it is necessary to develop simple and abbreviated techniques, to achieve an optimal and rapid evaluation of the patient.

Objectives: Determine the performance of the method of the 4 th finger for the diagnosis of SD pattern in patients with Raynaud’s Phenomenon taking the eight finger pattern as a gold standard.

Methods: Cross-sectional study with blinded and independent measurements. Nailfold Capillaroscopy was performed on the four fingers of each hand, except thumbs. Another observer evaluated the 4 th finger of the hands. The interobserver agreement was made before carrying out the study and was 100%. The 8-finger method (gold standard) was considered positive when at least one finger had SD pattern and the 4-finger method was considered positive when at least one of them presents the SD pattern. We included patients older than 18 years with a diagnosis of Raynaud Phenomenon. Patients with thickening of the skin in the nailfold, digital lesion that made it difficult to assess (trauma, amputation, burns, etc.) and patients who did not consent to the procedure were excluded.

Results: We included 78 patients, 78% was female. The mean age was 53 years (DS +/- 13.5). Sixty-three patients had a score of eight fingers positive (cases) and 15 had a score of eight fingers negative (controls). The sensitivity of the 4 th finger evaluation method was 89% (95% CI: 82–96%) and 93% specificity (95% CI: 89–97%). The positive predictive value of this method was 98% (95% CI: 95–100%) and the negative predictive value was 67% (95% CI: 56–77%). The positive likelihood ratio was 13 (95% CI: 2–89).

Conclusions: The simplified method of the 4 th finger showed good performance for the diagnosis of SD pattern compared to the standard method of evaluation of the 8 fingers.

References:

SIMPPLIFIED ASSESSMENT IN NAILFOLD CAPILLAROSCOPY IN RHEUMATOLOGY


Background: Nailfold Capillaroscopy is a non-invasive diagnostic technique designed to evaluate small vessels of the microcirculation. The most important indication for capillaroscopy is Raynaud’s phenomenon. The complexity and meticulous evaluation of the eight fingers is difficult to apply in daily practice given the limited availability of time to perform. For this reason it is necessary to develop simple and abbreviated techniques, to achieve an optimal and rapid evaluation of the patient.

Objectives: Characterize the utility of NC assessment for diagnosis of AID and to evaluate main differences in NC pattern, according to the presence of RP.

Results: We included n=641 patients with no prior diagnosis of AID, most frequently Systemic Lupus Erythematosus (SLE) (21%, n=123), Sjögren’s Syndrome (SS) (10%, n=62), Mixed Connective Tissue Disease (MCTD) (9%, n=52) and Antiphospholipid Syndrome (APS) (8%, n=48). NC patterns allowed for the classification of RP+ subjects into primary (3%) and secondary (81%); in 4% of subjects NC findings were abnormal but inconclusive. From secondary RP, most patients (77%) and non-scleroderma pattern (62%) were further separated; the former was later classified according to scleroderma-like (15,02%), early (33%), active (38%) and late (15%) scleroderma patterns.29% of RP+ patients did not have AID diagnosed; NC disclosed the diagnosis of SSc (n=24), APS (n=5), SS (n=4), SLE (n=2), MCTD (n=1), overlapping syndrome (n=1) and dermatomyositis syndrome (n=1).

Conclusions: NC findings in RP+ were more pathological than in RP-subjects, probably due to pre-existing AID and more frequent positivity. Secondary non scleroderma pattern was more prevalent in RP+ patients. In RP- group, almost a quarter of NC assessments were normal, but capillary abnormalities were also revealed, suggesting this diagnostic approach can help to disclose microvascular disease, even if RP is absent. NC further disclosed important leads to diagnose SSc, APS and MCTD in our population.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1242
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3815

AB1072
THE DEVELOPMENT OF ULTRASOUND SEMIOTICS OF DEFEATS OF THE JOINTS IN RHEUMATOID ARTHRITIS

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Background: Differential diagnosis of rheumatoid arthritis today is challenging in cases of atypical clinical and laboratory picture arthritis [1]. Often the use of standard x-ray is not informative for the first two years of the disease. Erosive joint damage detected by the standard x-ray only after 2 years from the onset of the disease and only 36% of cases (M. Bukhan et al., 2001), while the degree of articular destruction progresses with time and is correlated with a decrease in joint function.


Methods: We studied 113 patients with RA and 30 with no articular pathology – arthritis using ultrasonic method of investigation of the joints.

Results: The diagnosis of RA was established according to modified ACR criteria of 1987. The activity of the inflammatory process of the I degree was 19 (27,5%) patients, II – 36 (52,2%), III in 14 (20,3%).

Conclusions: The activity of the inflammatory process of the I degree is 19 (27,5%) patients, II – 36 (52,2%), III in 14 (20,3%).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3045

AB1074
THE TYPES OFEROSE LESIONS OF JOINTS IN RHEUMATOID ARTHRITIS

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Background: Early diagnosis of erosive lesions in rheumatoid arthritis (RA) remains today an important task, especially in the absence of specific laboratory markers. Promising research aimed at studying the informative instrumental diagnostic methods (ultrasound, Rg, MRI) to identify the characteristics of erosive joint damage in patients with RA and control.

Objectives: To study diagnostic possibilities of instrumental methods to identify the species of erosive joint damage in patients with RA.

Methods: We examined 104 patients with RA. Among patients of the 1st group were women 81 (77.9%), men - 23 (22.1%), average age was 58±12.1 years. Diagnosis of rheumatoid arthritis was exhibited with the EULAR diagnostic criteria [2] and the ACR [3]. All patients were Rg-graphy, ultrasound and MRI of the hands. Statistical processing of the information package.

Results: Erosive lesion of joints at RA is presented by the proliferation-caused pannus with vascularization and inflammatory-destructive erosion (true erosion inflammation) outside the pannus (image 1). In the study the true erosion of the articular surface of the bone ultrasound method identified at 87.9% of the joints in RA, significantly higher (p<0,0001) than 24.3% of the joints in the Rg-study. So erosion from the focal invasive growth of pannus, associated erosion, erosion, acute and chronic inflammation of the articular surface (erosion of the pannus) in combination with the development of the focal pannus with vascularization and inflammatory-destructive erosion (true erosion inflammation) outside the pannus (image 1). In the study the true erosion of the articular surface of the bone ultrasound method identified at 87.9% of the joints in RA, significantly higher (p<0,0001) than 24.3% of the joints in the Rg-study. 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Conclusions: When comparing the results of a comprehensive study of joints in patients with RA despite the fact that Rg and MRI allow us to visualize and measure bone structure and pathology, ultrasound is only allowed to identify two types of erosive lesions of the joints: true erosion inflammation and erosion of the pannus.

References:
[2] 2010 Rheumatoid Arthritis Classification Criteria: an American College of

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2068

AB1073
D-DIMER AS AN EARLY MARKER IN PATIENTS WITH LUPUS MESENTERIC VASCULITIS

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Background: Gastrointestinal manifestations are common in systemic lupus erythematosus (SLE) patients. Lupus mesenteric vasculitis (LMV) is a major cause of acute abdominal pain in SLE patients. No early serum marker contributes to the diagnosis of lupus mesenteric vasculitis.

Objectives: The aim of this study was to investigate clinical significance of serum D-dimer level as an early diagnosis marker of LMV patients.

Methods: The 57 systemic lupus erythematosus patients were retrospectively analyzed and classified into LMV group (n=19) and Non-LMV group (n=38) between May 2010 and January 2016. The serum D-dimer level was measured on the first day after SLE patients presented acute abdomen as well as imaging, other laboratory-testing parameters, and SLEDAI during the same period. The maximum and mean D-dimer values were analyzed and compared with other potential markers for diagnosis of LMV. The correlation of D-dimer level with other potential severity markers and inflammation parameters were also studied.

Results: Both maximum and mean D-dimer level on the first day of presentation of acute abdomen were significantly higher in LMV patients. The D-dimer level was correlated well with L-lactate and SLEDIAI. In addition, D-dimer level was detected poor correlation with white blood cell count and C-reactive protein level.

Conclusions: D-dimer level could be an effective and early serum diagnosis marker of LMV.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3815

Scientific Abstracts


Acknowledgements: Gratitude my supervisor professor, PhD. Litvyakov A., for the help in conducting studies head of the Department of ultrasonic diagnosis PhD. Shilenok V. and my family (Sirotko and Sviaryn) for their support and understanding.

Disclosure of Interest: None declared


Public health, health services research and health economics

**AB1075** PHYSICIAN POSTGRADUATE EXPERIENCE HAS A PREDICTIVE ROLE FOR PHYSICIAN EFFICIENCY INDEX REGARDING PATIENTS WITH RHEUMATOID ARTHRITIS: A COHORT, EXPLORATORY STUDY

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Background: Much effort has been made to improve the efficiency of health care system by delivering cost-effective, high-quality care. Nurse staffing’s contribution to daily practice plays a significant role to reach this goal.[1]

Objectives: To elucidate the differences between ratios of nurse/physician consultation as well as physician efficiency index (PEI) of senior rheumatologists and junior physicians in rheumatology residency training regarding patients with Rheumatoid Arthritis (RA). In addition, to delineate the correlation of physician postgraduate experience and PEI.

Methods: The mean intervals between standard consultation by a physician or nurse for all senior rheumatologists and junior physicians as well as nurse/physician visits ratio and PEI (= nurse/physician visits ratio * mean interval), regarding RA patients seen during Nov 2013–2015, were calculated. Multiple linear regression analysis was performed to delineate the relationship between physician postgraduate experience and PEI. To monitor treatment outcome, Disease Activity Score in 28 joints-C-reactive Protein (DAS28-CRP) and Health Assessment Questionnaire (HAQ) were consecutively measured three times: first at physician consultation, second at following nurse consultation and third either at a nurse or physician consultation.

Results: 3699 visits, belonged to 672 RA patients (64.1% female, the mean of age 64.9±14.1 and DAS28 at baseline 4.5±1.2), were included. There was a significant difference between the nurse/physician visits ratios of senior rheumatologists and junior physicians (P=0.01). Additionally, the mean PEI of senior rheumatologists was significantly higher than of junior physicians (P=0.04) (Table 1). A positive correlation was found between physician postgraduate experience and PEI adjusted for DAS28 at baseline and number of patients for each physician (Regression coefficient (95% Confidence Interval): 5.427 (1.068–9.878), P=0.022). DAS28 and HAQ score were significantly decreased if physician visits were followed by nurse visits (P=0.004 for DAS28 and P=0.025 for HAQ) (Fig.1), indicating a good treatment outcome at nurse consultations.

Conclusions: Junior physicians should be supervised to delegate responsibilities to nurse staffing. So, entire department operates more efficient, leading to prevent extra expenses (due to the differences in yearly salary of physicians and nurses). Quality of care should be monitored continuously by markers of disease activity and CRP.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2100

**AB1076** LOW BACK PAIN IN TURKISH BUS DRIVERS: PILOT STUDY

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Background: Low back pain is a common problem which increases financial burden of government (1). The incidence of back pain that can be seen in every part of society is also high in drivers (2). We haven’t seen any investigation about low back pain of Turkish drivers in literature. We thought that it should be researched because of changeable ethnic differences.

Objectives: The aim of our study was to determine the rate of low back pain and its relationship between quality of life in drivers.

Methods: Intercity and municipality drivers of Istanbul and Yalova, participated in our study. They were selected according to being at least 18 years of age, working at least 8 hours per day, being a driver for at least three years. Those with congenital deformities, having an accident history and doing an additional job were excluded from this study. After getting drivers’ demographic data, “Oswestry Low Back Disability Questionnaire” for low back pain and “Nottingham Health Profile” for health quality of life were surveyed to face. Chi-square and Spearman’s correlation-parametric test in the SPSS statistics program were used for statistical analysis in this study.

Results: All of the 261 people who participated in this study were male. Their mean of age, weekly working hours and working year were 43±9.28, 50±13.09 and 18±1.04, respectively. %50 of participants had low back pain and those of 43% reported that job satisfaction was affected due to pain. It was determined that 10% of participants, whose job satisfaction was affected, didn’t apply the medical doctor. While there was a significant relationship between low back pain and quality of life (p=0.000); there was no relationship between these two parameters and age and working year (p>0.05). It was determined that applying to medical doctor (p=0.02) and drug use rate (p=0.015) increased if the painful period lasted longer.

Conclusions: Low back pain affects quality of life related to health status. In this study, it was seen that the incidence of low back pain was high in long-distance drivers and affected job satisfaction in a great way. We think that the rates of drug use and medication usage can be reduced by increasing leisure time activity before increasing the severity of back pain and lengthening painful period. In addition, half of this occupation group is influenced by low back pain and once again it has been shown that waist schools should be expanded in our country.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5931
DOES PRECONSULT ELECTRONIC EXCHANGE AFFECT POSTCONSULT DIAGNOSIS?

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Background: Harbor UCLA is an urban safety-net hospital in Los Angeles for underserved patients. In 2014, LA County Department of Health Services adopted an electronic consultation (E-consult) referral and dialogue system to improve access to subspecialists in the ambulatory care setting. The E-Consult system provides a platform for primary care providers to ask questions or engage in dialogue with specialists, request consultation, and track submitted requests. Back and forth messaging prior to acceptance for face-to-face consultation is termed a “preconsult exchange”.

Prior studies of E-Consult systems have suggested benefits which include a reduction in wait times compared to paper referrals1 and a perceived improvement in patient care2. We sought to further clarify the effect of a preconsult exchange versus immediate booking on a patient’s diagnosis and wait time in an effort to provide some guidance on whether E-Consult should be used as a screening tool to reduce unnecessary visits or as a communication method to clarify details before a face-to-face visit.

Objectives: To determine whether preconsult exchange:
1. Influences the odds of arriving at a different diagnosis after face-to-face consultation compared to the requesting provider’s original diagnosis.
2. Influences the odds of arriving at a diagnosis of a different autoimmune condition versus a non-autoimmune condition (fibromyalgia, primary osteoarthritis, chronic pain, or other non-rheumatologic condition)
3. Results in a significant delay in face-to-face evaluation

Methods: We performed a retrospective chart review of all 238 new patient referrals between 11/2014 and 5/2016 to the Harbor UCLA Rheumatology clinic generated through the E-Consult system, reviewed by BC or GM, deemed appropriate, and seen for face-to-face evaluation. These patients were grouped by exposure (Preconsult exchange or not), Odds of change in diagnosis and confidence interval were calculated using 2x2 contingency tables and Chi-Square tests. A student’s T test was used to compare mean number of days between E-Consult initiation and face-to-face appointment.

Conclusions: There was a trend towards a change in diagnosis overall among patients for whom there was a preconsult exchange, but a statistically significant increase in odds for change to non-immunologic diagnoses. This suggests that preconsult exchange highlights those patients for whom there is a higher likelihood of a non-immunologic diagnosis.

However, preconsult exchange was associated with a significant time cost - an additional 26 day delay for a face-to-face visit (due to the time needed for both submitter and reviewer to complete their dialogue) in comparison to an immediately booked patient.

References:

Disclosure of Interest: None declared

FOLLOW UP OF PATIENTS WITH RHEUMATIC DISEASES BY MEANS OF A SMARTPHONE APPLICATION: SATISFACTION INDEX BASED ON A SURVEY AMONG USERS AND CARE PROVIDERS

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Background: Therapeutic adherence is the main variable in order to assess success or failure of any treatment. It is matter of interest to any clinician to get information enough about treatment response along time to reach a better understanding of any factor that conditions adherence failure or treatment interruptions. However, this kind of information is quite difficult to obtain in real scenarios due to lack of time or memory issues.

Objectives: The aim of present study is to assess the opinion of users of a smartphone application developed to improve the follow up of patients with different rheumatic diseases.

Methods: We conducted a survey to the users of REUMapp, an electronic form based on Google Form® software. REUMapp is an electronic interactive form developed for four different clinical scenarios: REUMapp-Esp (spondyloarthritides), REUMapp-Cristal (gout and other microcrystalline arthropathies), REUMapp-AR (Rheumatoid arthritis) and REUMapp-MSK (soft tissues). All forms were developed over the basis of paper forms previously used for the same purposes and to be checked on follow up consultation. Forms were designed to gather information about daily treatment adherence (binomial), daily modifications (categorical), adverse effects (categorical) and therapeutic response in terms of visual analogical scale. REUMapp-Esp and REUMapp-AR include also specific joint recounts and indexes. All the forms could be completed in less than 3 minutes by the patient or his/her care provider. Every form contents became part of a database easily accessible during the follow up visit in a summarized way. Between 2014–2016, 419 apps were installed in patients or care provider’s smartphones from two non public rheumatology clinics of Madrid with fully consentent of them. A survey was send to every user at the third to twelfth month after installation who have had one follow up consultation at least and who previously used the paper forms. Survey was developed using a multiple answer scheme using visual 7-level horizontal Likert scales. Topics of the survey were as follows: simplicity, time consumption and usefulness. Surveyed patients also were asked for the usefulness of the paper-based form.

Results: 205 Patients or care providers answered the survey. From them, 36 patients had diagnosed by rheumatoid arthritis, 23 by spondyloarthritides, 68 by gout or other microcrystalline arthritis and the rest by any other soft tissue rheumatisms. Following table shows the results of the survey. In the non parametric analysis of usefulness, the app was considered more useful than the paper format with a wilcoxon coefficient of contrast for paired data of : -6.658 (p = 0.001).

Conclusions: The smartphone applications described in this study have a good acceptance among patients of care providers in terms of usefulness, time consumption and simplicity and they are considered more useful than the printed models.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6893

IMPACT OF PRE-SCREENING ON RHEUMATOLOGY OUTPATIENT CLINIC PRACTICE

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Background: Chronic rheumatological diseases are predominantly managed in an outpatient setting, and these out patient clinics constitute a significant workload for rheumatology clinicians. When unnecessary outpatient visits occur, service provision to those most in need of rheumatology review, both new referrals and those with established diagnoses in need of urgent review, is compromised. There is an evidence base for such screening in secondary care centres from other internal medicine disciplines (1).

Objectives: To determine the impact of introducing pre-clinic screening, and exploring the potential for follow up using telephone, by a physician extender (PE), on attendances at a rheumatology outpatient department.

Methods: A retrospective analysis of all patients attending a rheumatology outpatient clinic was performed over a 4-week period, 15/08/2016- 09/09/2016. Patients were categorized into new or follow-up attendees and the follow-up patients were further subcategorized into 1 of 4 groups:
A) Attending to receive results of investigations requiring no further treatment;
B) Attending with a chronic rheumatological disease requiring no active change in management;
C) Attending to receive results of investigations requiring further treatment;
D) Attending with a chronic rheumatological disease requiring active change in management.

Patients in categories A and B, may be safely managed by a phone call from a physician, or PE. Those in C and D would need to be reviewed in clinic, following triage by phone using a PE.

Results: 232 subjects were included (5 category A, 118 category B, 4 category C, 105 category D). 123 (53.0%) could be managed by phone utilizing a PE, thus obviating the need for review in clinic. The remaining patients could be triaged by telephone by a PE, and the schedule for review adjusted to prioritise those most in need of review. It is likely that such a strategy for reviewing patients would be more resource efficient, have a greater impact on patient well-being, and be cost-saving.

Conclusions: Routine pre-screening for patients attending rheumatology clinics should be considered to improve effectiveness of the commodity rheumatology expertise.

References:

Disclosure of Interest: None declared

FOLLOW UP OF PATIENTS WITH RHEUMATIC DISEASES BY MEANS OF A SMARTPHONE APPLICATION: SATISFACTION INDEX BASED ON A SURVEY AMONG USERS AND CARE PROVIDERS

C.A. Guillen-Astete1, J.L. Alba-Barton2, 1 Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain; 2 Informatics, Surveys and Sta, Lima, Peru

Background: Therapeutic adherence is the main variable in order to assess success or failure of any treatment. It is matter of interest to any clinician to get information enough about treatment response along time to reach a better understanding of any factor that conditions adherence failure or treatment interruptions. However, this kind of information is quite difficult to obtain in real scenarios due to lack of time or memory issues.

Objectives: The aim of present study is to assess the opinion of users of a smartphone application developed to improve the follow up of patients with different rheumatic diseases.

Methods: We conducted a survey to the users of REUMapp, an electronic form based on Google Form® software. REUMapp is an electronic interactive form developed for four different clinical scenarios: REUMapp-Esp (spondyloarthritides), REUMapp-Cristal (gout and other microcrystalline arthropathies), REUMapp-AR (Rheumatoid arthritis) and REUMapp-MSK (soft tissues). All forms were developed over the basis of paper forms previously used for the same purposes and to be checked on follow up consultation. Forms were designed to gather information about daily treatment adherence (binomial), daily modifications (categorical), adverse effects (categorical) and therapeutic response in terms of visual analogical scale. REUMapp-Esp and REUMapp-AR include also specific joint recounts and indexes. All the forms could be completed in less than 3 minutes by the patient or his/her care provider. Every form contents became part of a database easily accessible during the follow up visit in a summarized way. Between 2014–2016, 419 apps were installed in patients or care provider’s smartphones from two non public rheumatology clinics of Madrid with fully consentent of them. A survey was send to every user at the third to twelfth month after installation who have had one follow up consultation at least and who previously used the paper forms. Survey was developed using a multiple answer scheme using visual 7-level horizontal Likert scales. Topics of the survey were as follows: simplicity, time consumption and usefulness. Surveyed patients also were asked for the usefulness of the paper-based form.

Results: 205 Patients or care providers answered the survey. From them, 36 patients had diagnosed by rheumatoid arthritis, 23 by spondyloarthritides, 68 by gout or other microcrystalline arthritis and the rest by any other soft tissue rheumatisms. Following table shows the results of the survey. In the non parametric analysis of usefulness, the app was considered more useful than the paper format with a wilcoxon coefficient of contrast for paired data of : -6.658 (p = 0.001).

Conclusions: The smartphone applications described in this study have a good acceptance among patients of care providers in terms of usefulness, time consumption and simplicity and they are considered more useful than the printed models.
RESULTS IN THE FOLLOW-UP OF THE NURSING INTEGRATING CASE FINDING AND INITIAL MANAGEMENT FOR IMPACT OF ANKYLOSING SPONDYLITIS VERSUS C. Alcañiz Escandell1, K. Arévalo Ruales 1, I. Chalmeta Verdejo1, C.M. Feced practice nurse (PN)-led LTC review consultations.

To test the feasibility and acceptability of integrating case-finding and outcomes of other long-term conditions (LTCs).

Background: Trials Unit, Keele University, Keele, United Kingdom

CONCLUSIONS: The NCIT has performed the follow-up of more than 500 patients for it provides patient monitoring before treatment administration and prior to rheumatologist consultation.

Disclosure of Interest: None declared


AB1082 RESULTS IN THE FOLLOW-UP OF THE NURSING CONSULTATION FOR THE MONITORING OF RHEUMATOLOGIC PATIENTS TREATED WITH INTRAVERSAL THERAPIES C. Nájera Herranz 1, I. Cánovas Olmos 1, J. Ivorra Cortés 1, E. Grau García 1, C. Alcántara Escarcha 1, K. Arevalo Ruales 1, I. Chalmeta Verdejo 1, C. M. Feced Olmos 1, J.J. Frago Gil 1, R. González Mazarío 1, L. Gonzalez Puig 1, E. Labrador Sánchez 1, I. Martínez Cordellat 1, R. Negueroles Albuixech 1, J.E. Oller Rodríguez 1, F.M. Ortiz-Sanjuán 1, E. Vicens Bernabeu 1, D. Hervás Marín 1, J.A. Román Ivorra 1, Rheumatology Department, HUP la Fe, Biostatistics Unit, IIS La Fe, Valencia, Spain

Background: In the management of rheumatologic patients treated with intravenous therapies, its regular monitoring is recommended in order to ensure its safety. The Nursing Consultation for monitoring rheumatologic patients treated with Intraversal Therapies (NCIT) represents a major support to patient caring for it provides patient monitoring before treatment administration and prior to rheumatologist consultation.

Objectives: To analyze number and types of incidents detected in the NCIT.

Methods: A cross-sectional longitudinal, observational study of data from patients followed-up in the NCIT (which was initiated in 2012) was performed. We have collected data of gender, diagnosis, drug administered, incidents detected previously to the drug administration, and if the incident was detected by telephone (one day before drug administration) or by personal interview. Biostatistical analysis with R (3.3.2.) was performed.

Results: We analyzed 7809 drug infusions corresponding to 545 patients (73% women). 48.25% of patients were diagnosed with osteoporosis (OP), 30.1% rheumatoid arthritis (RA), 5.7% ankylosing spondylitis (AS), 4.2% systemic lupus erythematosus (SLE), 2.9% psoriatic arthritis (PsA) and 8.3% had other diagnosis. The intravenous therapies were antieporeptic drug (7.6%) and biological and immunosuppressive treatment, being the most common drugs tocilizumab (38.89%), infliximab (31.9%) and abatacept (18.05%). In the 7809 treatment infusions, 477 incidents (4.1%) were registered, 33 of them related to the antieporeptic therapies and the other 444 incidents (93%) occurred in the biological therapies. The 63.7% of the incidents were detected by telephone one day before drug infusion. Statistical analysis showed that SLE patients exhibit higher tendency to incidents (4.8% of incidents in the 392 treatments for SLE patients; P=0.026) than other autoimmune diseases. On the other hand, RA and AS patients have incidents detected mainly by telephone (P=0.047 and P=0.029 respectively). We also observed a high number of incidents in the intravenous administration of TCZ (P=0.009).

Conclusions: The NCIT has performed the follow-up of more than 500 patients with only 6% of incidents, contributing to an improvement in the patients' health and in its caring. Moreover, the fact of identifying the incidents helps to reduce the number of personal consultations, avoids drug preparation in those cases where this suspension is induced, and in summary it improves management of hospital resources.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5702

AB1081 INTEGRATING CASE FINDING AND INITIAL MANAGEMENT FOR OSTEARTHROPATHY, ANXIETY AND DEPRESSION INTO ROUTINE PRIMARY CARE NURSE-LED LONG-TERM CONDITION REVIEWS: RESULTS FROM THE ENHANCE PILOT TRAI C. Jinks 1, E. Nichols 1, J. Liddle 1, E.L. Healey 1, A.L. Evans 1, C.A. Chew-Graham 1, K.S. Dziedzic 1, V.A. Tan 1, A.G. Finney 1, M. Porcheret 1, S. Lawton 1, V. Cooper 1, M. Lewis 1, C.D. Mallen 1 on behalf of ENHANCE team, 1Research Institute for Primary Care & Health Sciences; 2Keele Clinical Trials Unit, Keele University, Keele, United Kingdom

Background: Co-morbide osteoarthrosis (OA), anxiety and depression are undermanaged in primary care yet have significant impact on pain, disability and outcomes of other long-term conditions (LTCs).

Objectives: To test the feasibility and acceptability of integrating case-finding and initial management for OA, anxiety and depression within extended primary care practice nurse (PN)-led LTC review consultations.

Methods: A stepped wedge pilot trial with process evaluation. PNs gave a study pack to patients age >45 years attending routine LTC reviews (asthma, COPD, hypertension, ischaemic heart disease, diabetes). The intervention included case finding questions (Generalized Anxiety Disorder (GAD2), Whooley 2-item depression, diagnosing OA clinically (hands, hips, knees or feet)) followed by further assessments (anxiety (GAD), depression (PHQ9), joint examination). PNs completed an electronic patient record and initiated management. Pre-determined success criteria were to recruit 4 practices; deliver training to 2 PNs per practice, recruit 50% of those invited, ensure 75% follow up (6 week, 6 month), and the satisfaction (GPAQ) of intervention patients to be at least as acceptable as that of control patients. 24 audio recorded consultations provided insight into fidelity of intervention delivery.

Results: Four practices were recruited. PNs were sequentially trained in practice prior to switching to intervention. Of the 474 people invited, 319 responded (207 control, 112 intervention) (67% response). 83% and 79% of patients returned week 6 and 6 month questionnaires respectively. Demographic characteristics, general health, pain intensity, anxiety and depression scores were similar across arms. Overall, self-reported health (EQ5DSL) was high (median 0.84; IQR 0.72, 0.94). 14% of participants reported moderate to severe depression (PHQ9). Median GPAQ scores were similar (control 1.00 (IQR: 1.00, 1.29), intervention 1.00 (IQR: 1.00, 1.14)). 96% of those in the intervention arm reported being asked about joint pain, 93% reported being asked about mood. Audio recordings revealed that case finding questions were used as intended in most consultations (joint pain 20/24 consultations, anxiety 15/24, depression 6/24). One referral to physiotherapy and none to primary care mental health services were recorded by the PNs.

Conclusions: Recruitment and follow up were good. However, to target those who may benefit from the intervention, changes to the target population and eligibility criteria are required. There was reasonable delivery of the case finding questions, but limited referral and signposting, highlighting areas to optimise ahead of a main trial.

Disclosure of Interest: ELH, CJ, CCG, ALE and CDM are part funded by NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands. CDM is funded by NIHR School for Primary Care Research, NIHR Research Professorship in General Practice (NIHR-RP-2014–04–026). KSD is part-funded by an NIHR Knowledge Mobilisation Research Fellowship (KMF-2014–03–002). Views expressed in this paper are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2473

AB1082 IMPACT OF ANKYLOSING SPONDYLITIS VERSUS NON-RADIOMIC SPONDYLOARTHRITIS ON EARLY RETIREMENT C. Cobilinschi, R. Ionescu, D. Opris-Belinski, Stanta Maria Clinical Hospital, Bucharest, Romania

Background: Axial spondyloarthritis include non-radiographic Spa (nrSpa) and ankylosing spondylitis (AS), suggesting the extent of sacroiliac involvement on imaging techniques (1). The influence of the two conditions on patients' physical condition and their impact on work capacity should be regularly assessed so that we can better establish integral and effective therapy. In fact, as an SpA (2), early intervention and optimal management may contribute to patient’s quality of life and working capacity.

Objectives: The present study aims to assess the differences between AS and nrSpa patients under anti-TNF therapy regarding disease related retirement (DR) and its contributing factors.

Methods: Over a period of eleven months 136 patients diagnosed with AS or nrSpa on current biological therapy were included. Demographic data and working status were assessed. Statistical analysis was performed with SPSS 20.0.

Results: In the study cohort 69% of patients were males. The predominant age group was situated between 30 to 40 years old (29.8%), while 20.2% were over 50. Of the study group, 66% confirm they are active in their work field with a minimum of seven hours per day, whereas 4.3% reached their retirement age. 29.8% of patients were granted a disability retirement and the majority (42.9%) belonged to the 40–50 age group. Surprisingly, 6.8% of early retired patients were under 30. Out of the DR category, 92.9% were diagnosed with AS, while the rest of 7.1% had nrSpa. The interval from diagnosis to the initiation of biological therapy was 72±85.1 months for AS patients and 64±71.2 for nrSpa. 23.2% of patients applied for early retirement before biological therapy and only 3.1% resumed work after anti-TNF introduction. Patient gender did not influence the working capacity. At the time of study inclusion, 12% of patients with AS and 4% of patients with nrSpa still exhibited signs of highly active disease, according to ASAS/CRP assessment.

Conclusions: Almost a third of patients in the study group were offered early retirement due to axial SpA. The vast majority of disease related retirement patients were known with AS, thus emphasizing the extent of disability brought on by this entity. However, a significant percentage of patients suffered from nrSpa, raising doubts as to whether clinicians can promptly diagnose this entity and offer early, appropriate treatment so that inability no longer occurs.

References:

Disclosure of Interest: None declared
WORK IMPAIRMENT IN PATIENTS EXPERIENCING MUSCULOSKELETAL PAIN

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Background: Many individuals with musculoskeletal disorders (MSD) continue to have pain and limitation despite adequate treatment. Little is known about those who remain occupationally active relative to those who are on sick leave, despite the clear potential for reduced productivity or work ability, and associated downstream effects.

Objectives: To assess self-reported work impairment and its associations with psychosocial risk factors amongst workers seeking care for musculoskeletal pain.

Methods: Recruitment took place in five Irish hospitals. Self-report questionnaires were used to assess risk of progressing to long-term sick leave and work disability (Órebro Musculoskeletal Pain Screening Questionnaire; ÖMPSQ), work ability, work impairment (WPA) and work performance (WRFQ).

Results: 155 patients (53.5% females; mean age 46.50 years; range 20 to 71) completed the questionnaire. 25.2% (n=39) were at high risk of progressing to long-term sick leave and work disability according to the ÖMPSQ. 62.6% (n=97) were classified as functioning poorly according to the WRFQ; 52.3% reported having poor work ability (n=81). Higher work role functioning was associated with higher pain self-efficacy (β = -0.385). Presenteeism was associated with higher pain self-efficacy (OR =0.650) and higher return to work expectancy (OR =1.179). Presenteeism was associated with higher pain intensity (β =0.295) and lower pain self-efficacy (β = -0.385).

Conclusions: MSDs affect many individuals ability to work effectively. While all participants have managed to stay at work despite increased levels of work ability and functioning, approximately a quarter are at high risk of progressing to long-term sickness absence. Interventions that attempt to improve mutable factors, such as pain self-efficacy, may help reduce the likelihood of work disability.

Disclosure of Interest: None declared.

Discourse of Interest: None declared.

DOI: 10.1136/annrheumdis-2017-eular.5981

AB1084 CONTRIBUTION OF CLINICAL TRIALS TO THE EFFICIENCY OF ARTHRITIS RHEUMATOID MANAGEMENT


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Background: Treatment and management of Rheumatoid Arthritis (RA) results in a high cost to the Health system such as the Spanish Health System. During the last 5 years a total of 31 clinical trials (CT) the sponsor is the one that pays for the direct healthcare costs of the patients, which leads to savings to the National Health System (NHS).

Objectives: To estimate the economic impact of conducting clinical trials (CT) for the NHS terms of avoided costs.

Methods: A retrospective observational study was conducted using information from the clinical trials performed at the Clinical Research Rheumatology Department in the HUP la Fe from 2011 to 2015. Also a Cost-analysis was performed according Health System perspective. We calculated the length of stay in the CT for each patient included in the RA diagnosis. Afterwards, we also calculated the total number of weeks of treatment for the total number of patients. In order to evaluate the economic impact in terms of avoided costs, economic evaluation included direct healthcare costs (rheumatologist visits, nurse care, laboratory tests and pharmaceutical treatment), and it was compared to the cost of the best alternative treatment in the market.

Results: A total of 35 CT were analyzed in this period, 14 of them focused on RA. Two observational studies and one CT (premature closure by the sponsor) were discarded. Therefore, 11 were considered in this study and a total of 76 patients with RA were analysed which add together 2609 weeks of treatment.

Distribution of biological drugs: 49 (49%) adalimumab, 20 (20%) ustekinumab, 18 (18%) etanercept, 6 (6%) golimumab, 3 (3%) tocilizumab, 2 (2%) secukinumab, 1 (1%) certolizumab. The treatment was self-administered in 61 patients. Only 30 (30%) patients had undergone previous biological treatment. At present, 43 patients had some additional treatment, 36 with methotrexate and 5 with lefunomide.

SAFETY ASSESSMENT OF THE BIOLOGIC TREATMENTS TO MANAGE RHEUMATOID ARTHRITIS


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Background: Today, the immunosuppressive treatment agents became important for the therapy of rheumatoid diseases. Theoretically, the use of these agents may result in complications in patients that infected with Hepatitis B (HBV) and Hepatitis C (HCV) virus.

Objectives: To aimed the studies the reactions during treatment and prevalence of HBV and HCV infections in rheumatology patients who are using immunosuppressive treatment.

Methods: The records of a total of 1146 patients who were taking an immunosuppressive treatment for a rheumatoid disease were reviewed retrospectively. The hepatitis serology, type of immunosuppressive treatment, the duration of treatment, liver function tests, complete blood count, HBV – DNA and HCV – DNA and antiviral agents and time of use (if patient is infected) were recorded.

Results: There were 682 (59.5%) women and 464 (40.5%) men, the mean age was 45.0±13.13. Arkylosing spondylitis (AS) was diagnosed in 453, rheumatoid arthritis (RA) in 365, psoriatic arthritis in 151, systemic lupus erythematosus in 13, vasculitis in 39, Behcet disease in 28, sarcoidosis in 9, juvenile rheumatoid arthritis in 7, SJogren Syndrome in 7, Still Disease in 3, familial mediterranean fever in 6, retroperitoneal fibrosis in 1 and mixed connective tissue disease in 1 patient. The rate of HbsAg positivity was 1.8% in AS and 2.2% in RA; the rate of HCV positivity was 0.7% and 1.9% respectively.

Discourse of Interest: None declared.

POVERTY, POOR NEIGHBORHOODS, AND SLE OUTCOMES: THE PATIENT’S PERSPECTIVE

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Background: Studies have shown that persons in poverty experience worse outcomes of SLE and that the effect of poverty on outcomes is exacerbated for those living in neighborhoods with a high proportion of households in poverty. We report the results of a project to explore the viewpoint of SLE patients on how income and neighborhood affect disease outcomes.

Objectives: To explore the perspective of SLE patients with SLE on the effect of income, neighborhood, and stress on outcomes: 1) How does presence or absence of money affect care for SLE and in dealing with disease? 2) What role, positive or negative, does neighborhood play in SLE care and outcomes? 3) What are specific stresses that make dealing with SLE difficult?

Methods: We recruited SLE patients for qualitative interviews from a national longitudinal study of SLE conducted between 2003 and 2015. Subjects were selected to highlight the effects of income (those in the highest and lowest income quintiles), neighborhoods (living in neighborhoods with a high proportion of households in poverty), and geographic diversity (four regions of the U.S.: urban, suburban, and rural residents), and range of SLE outcomes. An ethnographically informed conducted hour-long semi-structured interviews were recorded, transcribed, and analyzed using grounded theory methods.

Results: 28 qualitative interviews were completed; 11 from the highest income group and 17 from the lowest (11 from poor neighborhoods). 3 were men, 20 members of racial/ethnic minorities, and mean age was 49, range 22–70. Among the poor, none cited lack of money as limiting their access to care, but all stated that it necessitated choosing which pressing needs to focus on, with food and housing a higher priority than dealing with their SLE. Among the more affluent, financial resources were used to provide help in daily chores or to withdraw from work to reduce stress, and allow for more time to manage their disease. Among the poor, none cited a positive benefit of neighborhood in finding health care resources or in mitigating how they dealt with disease but all stated that they did not need it since starting the biologic.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3237

USE OF NATURAL LANGUAGE PROCESSING TO ENHANCE RETRIEVAL OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY OUTCOMES MEASURES IN US VETERANS

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Background: Rheumatoid arthritis (RA) disease activity measures in the Veterans Affairs RA (VARA) registry are extracted automatically through natural language processing (NLP). While this system is very effective at extracting data when templated notes are properly used, it lacked an error detection and feedback mechanism. Accuracy of the registry is essential for credible epidemiological research and patient care. We report a new automated approach with an active error monitoring and reporting system to alert providers of missing or potentially erroneous elements that can be easily corrected using standardized addendums available in the electronic medical record. The automated NLP system was revised to identify, extract, and integrate these updates to support the calculation of DAS28 and other composite outcome measures for the VARA database.

Objectives: 1. To describe the systems to identify needed corrections of VARA data.
2. To outline the procedures that allow providers to easily use addendums to enter corrections into the medical record to be automatically captured and loaded into the VARA database.

Methods: Procedures were developed and tested at a single pilot VARA site using data available in the Corporate Data Warehouse (CDW) from 01/01/2016 to 12/31/2016. A Java program was designed to retrieve Rheumatology notes, and correspond to an “local” addendum. These addendums were then processed to extract defined elements of RA disease activity listed in the table below. After each scheduled NLP run the system generates a log file that provides a summary, and patient-level report of completed and missing data elements. Providers receive the report and are asked to review the clinical notes of patients with missing elements and follow simple procedures that correct or add missing data elements when template violations occur. Addendums are used to flag and request for review when the items are not available in the notes. Updating the VARA database from addendums occurs during the next NLP run.
Results: During the pilot testing phase the automated system processed 516 notes and identified 489/516 (94.8%) as successful loads, and 27/516 (5.2%) were flagged as problematic since one or more data elements were missing. Misapplication of the template occurred in 21/27 (77.8%) of notes flagged by the monitoring system and corrected with addendums. An additional NLP run produced 510/516 (98.8%) completed assessments with calculated DAS28 scores. Specific elements recovered using this process are presented in table below.

<table>
<thead>
<tr>
<th>Total notes processed (n = 516)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elements Investigated</td>
<td></td>
</tr>
<tr>
<td>Missing data elements</td>
<td>1/516 (0.2%)</td>
</tr>
<tr>
<td>Elements Corrected</td>
<td>1/516 (0.2%)</td>
</tr>
<tr>
<td>Tender Joint Count</td>
<td></td>
</tr>
<tr>
<td>2/516 (0.4%)</td>
<td>2/516 (0.4%)</td>
</tr>
<tr>
<td>Swollen Joint Count</td>
<td></td>
</tr>
<tr>
<td>2/516 (0.4%)</td>
<td>2/516 (0.4%)</td>
</tr>
<tr>
<td>Patient Global Assessment</td>
<td></td>
</tr>
<tr>
<td>11/516 (2.2%)</td>
<td>8/11 (72.7%)</td>
</tr>
<tr>
<td>Physician Global Assessment</td>
<td></td>
</tr>
<tr>
<td>9/516 (1.8%)</td>
<td>9/11 (81.8%)</td>
</tr>
<tr>
<td>Modified Health Assessment Questionnaire</td>
<td>15/516 (2.9%)</td>
</tr>
<tr>
<td>Pain Score</td>
<td></td>
</tr>
<tr>
<td>11/516 (2.2%)</td>
<td>9/11 (81.8%)</td>
</tr>
</tbody>
</table>

Conclusions: The addition of this error monitoring system provides an efficient data correction system and is expected to motivate and reinforce the use of RA templates. The implications of which may be profound as we transition from traditional epidemiological research to a more active learning healthcare enterprise. This pilot study established “proof of concept” and the next challenge is to adapt the technology to other VARA and non-VARA sites. This technology and framework could enable collaborative clinical research networks that are committed to large-scale pragmatic and observational effectiveness studies.

Acknowledgements: Work Sponsored by VA Specialty Care Centers of Innovation, VA Health Services Research and Development.

Disclosure of Interest: G. Cannon Grant/research support from: Amsgen, S. Mehrorta Grant/research support from: Amsgen, B. Sauer Grant/research support from: Amsgen

DOI: 10.1136/annrheumdis-2017-eular.5620

AB1090

IS THERE AN ETHNIC VARIATION IN ACCEPTANCE OF BIOLOGIC THERAPY? A UNIVERSITY HOSPITAL EXPERIENCE

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Background: Ethnic variation in drug adherence & preference is well documented (1). While usually a reflection of patient autonomy, the issue takes significance if it impedes the provision of effective evidence based care. Indeed, race affects rheumatological disease outcomes (2), likely for both biological & psychosocial reasons. Studies from United States of America found ethnic minorities were less likely to be on a biologic for a rheumatological disease compared to Caucasians, even after adjustment for education & insurance (3). Studies in the United Kingdom found similar results (4), although few investigated the disparity in the acceptance of biologics between ethnicities. Leicester, a midland UK city has an ethnically diverse population, where identifying and addressing such disparities is crucial in delivering effective & equal care.

Objectives: To determine any disparity in acceptance of biologic therapy, when offered in person, in a healthcare system free at the point of access, between White British and other ethnicities.

Methods: Data was collected from nurse led Biologics therapy clinics, from October 2016 to December 2016. All patients referred were deemed suitable for a biologic as per NICE guidelines by a Rheumatologist, and were attending the clinic for counselling, assessment & consenting. Proformas were piloted, and improved proformas with information including demographic, disease & treatment details, as well the outcome of the consultation (biologic accepted or rejected) was used to collect data. The collated data were then analysed using EXCEL spread sheet.

Results: Data was collected from 55 patients. Interestingly, sex distribution was nearly equal (54%, female). 57% of the total sample was White British (WB). The remaining 43% included; Indian, Bangladeshi, Pakistani, White Other, Asian, African Caribbean & Any other mixed race. The most common disease necessitating referral for a biologic was rheumatoid arthritis (53%). 16% of patients rejected a biologic drug, of which 66% were ethnic minorities. The rejection rate among ethnic minorities was thus 24% compared to 10% in the WB cohort. The highest rejection rate was within the Any Other Mixed Ethnicity cohort (100%), followed by the Bangladeshi cohort (50%). Of note, all patients who rejected biologic therapy from an ethnic minority background did not speak English as their first language. Rejection rates were highest in the Spondyloarthropathies (21%).

Conclusions: Our results demonstrate a disparity between the White British population and other ethnicities in the acceptance of biologics, despite one to one counselling. This can have detrimental impacts on treat to target concept and disease progression, and thus will be further investigated & addressed.

References:

Disclosure of Interest: Administrators & Rheumatology Nurses of University Hospitals of Leicester.

DOI: 10.1136/annrheumdis-2017-eular.2944

AB1091

HIGH ACCEPTANCE RATE IN RA, AS AND PSA PATIENTS WHEN BEING STARTED ON BIOSIMILAR TNF OR BEING SWITCHED FROM THE ORIGINAL TNF MAB (REMICADE, ENBREL) - A SINGLE CENTER EXPERIENCE

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Background: Biosimilar TNF Mab (BioTNF) have become available in most of the European countries in the last few years. They are labeled to be used in the most common rheumatic diseases, like RA, AS and PsA. Controlled studies have shown comparable efficacy and safety of BioTNF and original TNF (Remicade, Enbrel). BioTNF are allowed to be used in TNF naive patients as well as in TNF pretreated patients (switchers). Prescriptions in different countries may vary due to local most often cost driven restrictions.

So far, little is known about the awareness, acceptance and possible obstacles which may influence patients willingness to accept therapy with BioTNF instead using the original compounds.

Objectives: The study was conducted and designed to get a deeper insight in what may influence patients decision making and willingness to accept treatment with BioTNF firsthand or accept switching.

Methods: Between February 2015 and December 2016 41 patients (BioINF n=29, BioETA n=12) were introduced to BioTNF therapy. 9 Patients (Bio-INF n=3, Bio-ETA n=6) received TNF therapy the first time, in 32 patients (Remicade n=23, ETA n=8) were switched from the originator TNF compound to BioTNF. All patients received comprehensive information on BioTNF in verbal and written form.

A standardised questionnaire was used to ask patients on their awareness, acceptance and about possible obstacles for the usage of BioTNF Mab.

Results: 6 out of 9 TNF naive patients agreed after their first information on BioTNF to start therapy with BioINF (n=3) or BioETA (n=3). Another 2 patients accepted BioETA therapy on their second visit. Only one patients asked to be started on the originator TNF Remicade. In patients being ask to switch from Remicade to BioINF 19 patients accepted promptly to be switch in and patients with Enbrel therapy 6 out of 9. Finally only 1 patient on Remicade TNF therapy denied even after a third visit to be switched. Mayor concern to deny the use of BioTNF were possible lack of efficacy (30%), safety (32%) and missing longterm experience (35%).

The main motivation to switch was patients believe to save money and that they were asked to switch to BioTNF Mab on short notice from their health care insurance company.

Conclusions: There is a high acceptance rate in patients with chronic inflammatory rheumatic disease to be started on or switched to BioTNF (~90%). There are little concerns in patients accepting BioTNF with regard to safety or efficacy of BioTNF. Patients are aware of BioTNF as a less costly way to treat their rheumatic condition. Physicians should be aware of this willingness and offer BioTNF therapy if it is appropriate. Using BioTNF is a cost saving way to use biologics in rheumatic therapy with equal efficacy and safety compared to the originator compounds.

Disclosure of Interest: None declared
SATISFACTION AND BELIEF REGARDING TREATMENT WITH INTERSTITIAL LUNG DISEASE AND RHEUMATIC DISEASES IN MULTIDISCIPLINARY OUTPATIENT CLINIC

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Background: Among rheumatic disease-related lung disease, interstitial lung disease (ILD) is the most prevalent and contributing to the mortality and morbidity. Increasing numbers of reports dealing with ILD with rheumatoid arthritis (RA). Sjögren's syndrome (pSS) and systemic sclerosis (SSc), multidisciplinary discussions (MDDs) have been growing interest for diagnostic accuracy with dedicated service. There was little evidence indicating that multidisciplinary outpatient clinic resulted in improvements in clinical outcomes including satisfaction and belief.

Objectives: We have designed validated a scale of evaluating coping strategies about satisfaction and belief in patient of ILD and rheumatic disease with multidisciplinary approach.

Methods: From December 2015 to September 2016, we evaluated 20 patients of rheumatoid disease with ILD and 20 patients of idiopathic pulmonary fibrosis. Patient perceptions of illness, treatment beliefs, and moods were measured via the multiple choice questionnaires presenting brief illness perception questionnaire, beliefs about medicines questionnaire, and patient health questionnaire for comparing the effectiveness of MDDs and routine ILD management.

Results: Univariate analysis, beliefs in necessity of treatment and adherence differed significantly in high multidisciplinary outpatient clinic for people with ILD (intentional or unintentional). When controlling for other factors that may impact medication nonadherence, more belief in necessity of medication and higher MRCI (OR 1.1, p<0.019) were associated with high adherence. Table 1 shows significant univariate associations with MDD status for the treatment of ILD patients.

Conclusions: The treatment of ILD was quite successful with achievement of the therapeutic target in 66% of cases and ‘unhappy’ in only 15%.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4179

ASSOCIATION BETWEEN USE OF TRADITIONAL CHINESE MEDICINE AND MEDICATION ADHERENCE AMONG CHINESE-AMERICAN RHEUMATOLOGY PATIENTS

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Background: Chinese-Americans (CA) are a fast-growing US immigrant group with high utilization of Traditional Chinese Medicine (TCM) and worse SLE and RA outcomes than Caucasians (1,2). The effect of TCM use on adherence to prescribed western medications for systemic rheumatic diseases is unknown.

Objectives: To evaluate whether TCM use is associated with adherence to western medicines prescribed for systemic rheumatic diseases among CA patients.

Methods: Patients with systemic rheumatic diseases were recruited from 2 rheumatology clinics that serve a predominantly CA immigrant population. Inclusion criteria were speaking Mandarin or English and having medication(s) prescribed by the rheumatologist. TCM use, adherence, Patient-Reported Outcomes Measurement Information System (PROMIS) domains, and other variables were assessed using validated instruments available in English and Chinese. Adherence was classified as high or medium/low based on the 8-item Morisky Medication Adherence Scale (3). Medication complexity was assessed using the Medication Regimen Complexity Index (MRCI) (4); higher score indicates more complexity.

Results: 177 enrolled, mean age 54 (range 20–97), 62% female, 73% high school education, 75% Medicaid (subsidized insurance), and only 18% spoke English. Diagnoses were RA (43%), SLE (17%), SjS (10%), pSS (8%), gout/CPPD (6%), and other (10%). 49% reported TCM use in the past year, most commonly turina massage (48%), acupuncture (47%), and herbs (39%). 27% reported low adherence. Table 1 shows significant univariate associations with high adherence. In multivariate analysis adjusting for all variables in Table 1, only TCM use (OR 2.6, p=0.027) and higher MRCI (OR 1.1, p=0.019) were associated with high adherence.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>High adherence, %</th>
<th>Low/Moderate adherence, %</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td>63 (11)</td>
<td>52 (17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Employed, %</td>
<td>59</td>
<td>48</td>
<td>0.044</td>
</tr>
<tr>
<td>≥20 years US, %</td>
<td>58</td>
<td>39</td>
<td>0.02</td>
</tr>
<tr>
<td>Age at immigration, years (SD)</td>
<td>44 (14)</td>
<td>35 (12)</td>
<td>0.002</td>
</tr>
<tr>
<td>RA, %</td>
<td>56</td>
<td>38</td>
<td>0.029</td>
</tr>
<tr>
<td>MRCI, mean (SD)</td>
<td>15 (7)</td>
<td>11 (6)</td>
<td>0.001</td>
</tr>
<tr>
<td>TCM use, %</td>
<td>63</td>
<td>44</td>
<td>0.03</td>
</tr>
<tr>
<td>PROMIS Sleep disturbance, T-score (SD)*</td>
<td>47 (10)</td>
<td>52 (9)</td>
<td>0.005</td>
</tr>
<tr>
<td>PROMIS Anxiety, T-score (SD)</td>
<td>46 (11)</td>
<td>49 (10)</td>
<td>0.04</td>
</tr>
<tr>
<td>PROMIS Fatigue, T-score (SD)*</td>
<td>49 (11)</td>
<td>52 (10)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Lower score is better.

Conclusions: Among poorly integrated and low socioeconomic status CA rheumatology patients, TCM use was statistically significantly associated with high adherence to western medication, as was higher MRCI. TCM use does not appear to represent an alternate but rather complementary approach to disease management in these patients. Future studies should evaluate whether TCM use is associated with disease activity and outcomes over time.

References:
AB1095 EARLY DIAGNOSIS AND TREATMENT OF CHRONIC DISEASES: NATIONAL REVIEW AND GUIDELINES - RA AS AN EXAMPLE

L. Euler Ziegler on behalf of the High Council for Public Health (HCSP), Rheumatology Department, Academic Hospital and University of Nice, Nice, France

Background: Managing the increasing burden of chronic diseases is a major public health problem. Are early diagnosis and management a key point for their optimal care and outcomes?

Objectives: Assessing early diagnosis and management of chronic diseases was the aim of a study carried out by the High Council for Public Health (HCSP), independent national body gathering experts nominated by the Minister of Health, to provide health authorities with expertise on development of national public health goals, assessment of achievement and contribute to their monitoring.

Methods: A multidisciplinary working party run within the HCSP a review of scientific data supporting early intervention benefits, as well as frequency, impact and mechanisms of delayed management on individuals and society, in order to produce national guidelines. A huge amount of data were analyzed and considered contributions from national Professional organizations and Patient Professional organizations and Patient associations, literature analysis, audition of national agencies representatives.

Results: Early stages of chronic diseases are less studied than later ones. Nevertheless, there is a strong evidence that delayed diagnosis and management are frequent and often adversely affect patients and society. The frequency, length and burden of delayed care were analyzed, varying with each disease, availability of efficient treatments and guidelines, socio-economic context. Optimal time for adequate management from symptom onset was reviewed, as well as medico-economic studies.

Rheumatologic disorders appeared as models, notably Rheumatoid Arthritis (well-established window of opportunity, international guidelines for early diagnosis and management, including T2T and patient active implication). Evidence for early treatment benefit was also found for spondyloarthritids, osteoporosis, obstructive sleep apnea syndrome, chronic obstructive pulmonary disease, renal insufficiency, autism spectrum disorders, bipolar disorders, ... Ethical considerations may arise: in Alzheimer’s disease, a diagnosis source of marked anxiety, there is no effective pharmacological treatment but non pharmacological treatments are quite helpful for patients and family and therefore recommended by health authorities.

Obviously, the benefit of early intervention must be strongly assessed. When this benefit is proven, too many patients are facing delays, often long, with adverse consequences and increased burden for society. The mechanisms of such delayed management are multiple and often intricate: we analyzed the barriers to optimal care linked with professionals, patients, family, health system and society, in order to identify the ways to optimize the outcomes and therefore improve the global health status of the population.

Finally the HCSP established a set of guidelines, in 3 axis

- disseminate widely the available knowledge among professionals, patients, the general public, taking into account the social poor perception of chronic diseases
- implement effectively change in practice toward early intervention, when appropriate: timely coordination between professionals and patient, fair diagnosis announcement, early patient implication, fight against social health inequalities
- develop research on early stages of chronic diseases, diagnosis, management and outcomes.

Conclusions: From a national public health perspective, early diagnosis and management, in the chronic diseases where their benefit is proven, should be better known and effectively implemented.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1819

AB1096 TIMED UP AND GO TEST (TUG) FOR SARCOPENIA SCREENING

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Background: Sarcopenia is a multifactorial syndrome characterized by a decrease of muscle mass and force with functional performance impairment. Sarcopenia has been described as an independent predictor of health adverse outcomes such as falls, decreased quality of life, enhanced risk of death and higher treatment costs. However, there are just a few screening tools of low cost and easy applicability to detect sarcopenia. In this context, a standard mobility assessment such as the TUG test has recently been described as a predictor of sarcopenia.

Objectives: To evaluate the performance of timed up and go test (TUG) as a screening tool for sarcopenia in the elderly.

Methods: This is a cross-sectional home study with 211 elderly participants in the South Region of Brazil. Sarcopenia diagnosis criteria was based on the European Working Group on Sarcopenia in Older People (EWGSOP). Individuals that presented low muscle mass (women: ≤ 6.37kg/m2 and men: ≤ 8.90kg/m2) added to decreased handgrip strength (women: ≤ 20kgf and men: ≤ 30kgf) and/or walking speed (≤ 0.8m/s) were considered sarcopenic. TUG test quantifies functional mobility through the task of getting up from a chair, walking 3m and come back to sit on the chair.

Results: Based on EWGSOP criteria for sarcopenia, 17.1% (n=36) received the sarcopenia diagnosis. A ROC curve was constructed to evaluate the discriminatory power of TUG (AUC: 0.73 [IC 0.67 – 0.78; p=0.0001]). TUG test presented high sensitivity (88.9%) and negative predictive values (93.2%), with a cutoff point of 7.5 seconds (figure 1).

Conclusions: Detecting the beginning of sarcopenia could allow for early interventions and slow the syndrome process, preventing further hospitalizations and economic burden. In this context, TUG is an easy, fast and low-cost test with high sensitiveness for sarcopenia detection that could be used as screening tool for this syndrome.

References:

Acknowledgements: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2385

AB1097 PATIENTS’ EXPERIENCES OF REMOTE MONITORING OF RHEUMATOID ARTHRITIS USING A SMARTPHONE APP

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Background: The care of patients with Rheumatoid Arthritis (RA) is guided by monitoring changes in disease activity. However, whilst a number of patient-related outcome measures (PROMS) exist 1, they are not collected on an on-going basis. Consequently, there are few objective measurements of disease activity, between clinic visits, to inform treatment decisions. In response to this, the REMORA study (REMOTE Monitoring of Rheumatoid Arthritis) is developing a smartphone app, to capture data on disease activity and integrate it directly into the electronic patient record. The project explores whether on-going collection of electronic patient-reported outcomes (ePROMS) between clinic visits can enhance clinical care, support patient self-management, and provide a sustainable source of data for research.

Objectives: To describe patients’ experiences of remote monitoring of their disease activity, and the perceived value in relation to clinical consultations and self-management.

Methods: A diverse sample of 20 patients with RA entered data into the app over...
a three month period in response to daily, weekly and monthly question sets (table 1). An optional diary component was included, but not integrated into the EPR. The ePROs had been determined during earlier interviews with rheumatology patients, practitioners and researchers. Qualitative interviews were conducted with patients at the end of the three month period. Two previously expressed patients’ views on the components of the app, and perceived implications for self-management and clinical care. Interviews were transcribed and analysed thematically.

Results: Qualitative analysis of the data identified a number of themes including; the benefits and limitations of using scales to reflect changes in symptoms experienced, the value of the diary for providing contextual information and an “outlet” for feelings, and the impact the data made to their clinical consultation and self-management. Overall, the collection of longitudinal data was seen as useful by patients. Successful integration with the EPR allowed data to be displayed graphically during clinical consultations. Reviewing remote monitoring data detected changes which may otherwise have been missed such as flares in disease, or gradual improvements in response to new treatments. Data therefore facilitated “a shared conversation” and decision making around treatment plans.

Additionally, being able to self-reflect on data recorded enabled patients to identify triggers and alleviators in relation to their disease activity and take steps to self-manage their RA; for example, by recognising when they needed to rest as opposed to “just carrying on” when their symptoms were more severe.

Table 1. ePROs

<table>
<thead>
<tr>
<th>Daily</th>
<th>Pain, difficulty with physical activities, fatigue, sleep difficulties, physical wellbeing, emotional wellbeing, coping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly</td>
<td>Number of tender &amp; swollen joints</td>
</tr>
<tr>
<td></td>
<td>Global assessment of wellbeing</td>
</tr>
<tr>
<td></td>
<td>Employment status</td>
</tr>
<tr>
<td></td>
<td>Impact on number of hours worked</td>
</tr>
<tr>
<td></td>
<td>Experienced a flare</td>
</tr>
<tr>
<td></td>
<td>Description of flare</td>
</tr>
<tr>
<td>Monthly</td>
<td>Health Assessment Questionnaire (HAQ) impact of disease on daily activities.</td>
</tr>
</tbody>
</table>

Conclusions: The app was well received by patients and feedback suggests that the ePROs recorded can capture changes in disease activity in a manner that is meaningful to patients and facilitates both clinical consultations and self-management.


Acknowledgments: Disclosure of Interest: None declared

AB1098 | TEMPORARY WORK DISABILITY CAUSED BY MUSCULOSKELETAL DISEASES AT THE HOSPITAL CLINICO UNIVERSITARIO DE VALLADOLID: 6 MONTHS EXPERIENCE

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Background: Musculoskeletal diseases are the leading cause of disability in the world and have a huge impact on direct (health) and indirect (labor) costs. Labor casualties in Spain, when temporary, are known as temporary work disability (TWD). Since 2013, follow-up of patients with TWD (when the origin of the disease is a musculoskeletal condition) is being carried out in a monographic consultation within the external consultations of the Rheumatology Service of the Hospital Clínico Universitario de Valladolid.

Objectives: To describe the experience of the last 6 months in the consultation of temporary musculoskeletal incapacies (TWDMSDs) of the Hospital Clínico Universitario de Valladolid.

Methods: The TWDMSDs consultation is operational 2 days a week. The referral system is direct from Medical Inspection via email (1st part confirmatory work leave). The patients come from 7 Health Centers (population 82,000 people). The agenda is configured daily according to the emails sent, contacting the patients by telephone, excluding those with trauma, surgeries, pregnancies, non-localized, rejection or discharge. The assessment of the patients in consultation, corresponds to usual clinical practice. A medical report is issued (medical history, physical examination, completed or requested tests, recommendations and treatment).

The data are collected in SPSS, proceeding to its subsequent analysis.

Results: During the last six months of follow-up, 354 emails have been received. A total of 106 patients were evaluated, with the following characteristics: 54.3% women and 45.7% men, mean age 43.4 years, 95% performed physical work. Axial pathology was observed in 67.8% of cases and peripheral in 32.2%. The patients evaluated with some rheumatic pathology reached 96%. The average delay from the start of the work leave to the email was 12.2 days, and from the start of the work leave to the first consultation of 6.7 days (including weekends). 65.4% of the patients were discharged from the TWDMSDs agenda in the 1st consultation, without requiring interconsultations or requests for diagnostic tests, with an infiltration of 8% of the patients, arthrocentesis at 2%, ultrasonat at 28% and Exercise guidelines were given to 76% of patients. The mean number of consultations up to discharge was 1.3. The mean time from onset of discharge to discharge was 21.1 days and from the first consultation until discharge by Rheumatology was 6.6 days.

Conclusions: The TWDMSDs consultation makes possible the early detection of rheumatologic musculoskeletal pathology, allowing an early action that minimizes the number of requested tests and interconsultations generated and achieves an early diagnosis and treatment of patients, with the consequent benefits that this entails. The patients evaluated in consultation are mainly of average age, with physical work, mechanical pathology, resolution of the problem that causes the TWD and reintegration to the working life of early form. In the discharge report, recommendations are included to minimize future casualties (work refocus, orthotics, exercises, treatment regimens in the event of a recurrence of symptoms) and explain the importance of being actively involved in their pathology to prevent progression.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6552
Conclusions: This survey suggested that CTD have a major impact on FP and family size, possibly mediated by the increased rate of miscarriages as compared to CA. Concerns about reproductive issues could be positively overcome by adequate counselling. Rheumatologists should implement the discussion about FP and the compatibility of pregnancy in the management of young women with RD, especially those with CTD for whom contraception and pregnancy have particular implications.

Acknowledgements: Statistical analysis supported by an unrestricted grant from UCB Pharma and Colloidal Waxes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2268

AB1100  PATIENT SELF-MANAGEMENT APPS AS ONE MODULE OF AN INTEGRATED TIGHT-CONTROL CONCEPT BASED ON THE EXAMPLES OF THE DIGITAL APPLICATIONS RHEUMALIVE UND AXSPALIVE

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Background: Medical Applications have the potential to support physicians and patients to document the course of the disease and optimize therapies. We describe the linkage and integration of patient reported outcomes (PROs) into existing medical office software and rheumatologic documentation systems by means of the digital applications RheumaLive and AxSpaLive. RheumaLive is certified as medical product class I, and certification for AxSpaLive is in preparation.

Methods: RheumaLive and AxSpaLive are applications that can be downloaded free of charge from the common app-stores (Android, Apple) and installed on mobile devices (smartphones, tablets). A freeware version for PCs is also available (Windows- and Mac OS X-Version). A diary functionality allows to document the medication uptake (partially filed, memory-functionality for medication uptake available), validated scores like VAS, SJC, morning stiffness, FFBh (comparable to HAQ), BASDAI, RADAI, etc. and days of sick leave (+/− related to the rheumatic disease). All App-versions are password-protected, which is provided by the treating rheumatologist (relationship patient-physician).

The patient reported outcomes are stored locally on the respective device. For the subsequent visit, they can be printed or sent encrypted to the treating physician via internet in a prespecified interval. A specific software allows to integrate the data into the existing medical office software.

In daily practise, data entered by patients into RheumaLive can be screened and compared with collected clinical data and laboratory measures, because of it’s certification as medical product. In case of an increasing disease activity the patient can be rapidly contacted and medication can be modified, if necessary. Regular F2F-appointments remain integral part of the medical care, even in case of good controlled disease activity. But in case of F2F-appointments, PROs can be delivered by patients, saving time and resources.

The PROs can be made available to rheumatologic documentation systems like RheuDoc via predefined interfaces.

Results: In a first pilot phase 54 patients in 4 rheumatologic specialised practices were documented. In the next phase the number of patients and participating practices/centres should be increased.

Further studies are necessary to show if the integration of PROs which are collected via electronic application can lead to an improvement of rheumatologic diseases.

Conclusions: The integration of PROs collected with RheumaLive and AxSpaLive into existing rheumatologic documentation systems allows a close monitoring of disease courses and therapies according to the “tight control” principle. RheumaLive and AxSpaLive were developed by Starhealth GmbH on behalf of UCB Pharma GmbH.


DOI: 10.1136/annrheumdis-2017-eular.5782

AB1102  LOW BONE MINERAL DENSITY IS A MAJOR CONTRIBUTOR IN THE EUROPEAN HEALTH BURDEN DUE TO ROAD TRAFFIC ACCIDENTS IN PEOPLE AGED 50 YEARS AND ABOVE

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Background: Road traffic accidents (RTAs) are the second leading injury health burden and cause of death in Europe, after falls (1). A significant but as yet unmeasured proportion of such burden is potentially due to low bone mineral density (BMD), especially among older people, through its relationship with fractures.

Objectives: To measure the percentage of deaths, years lived with disability (YLDs) and years lived with disability (YLDs) due to RTA in people aged 50 years and above attributable to low BMD in the European population for the year 2015.

Methods: The estimates followed the Counterfactual Risk Assessment Methodology used in the GBD study (1). Systematic review was performed seeking population-based studies with femoral neck BMD (FNBM) measured by Dual-X-Ray-Absorptiometry in people 50 years and over. Age- and sex-specific prevalence of low BMD (T-score <−2.5SD) was extracted from eligible studies, and this was used as the exposure variable. The age and sex-specific 99th percentile from non-Hispanic whites in National Health and Nutrition Examination Survey (NHANES) 2009–2010 was used as the population-level-risk to estimate the potential impact fraction (PIF) of FNBM for fractures. Relative risks of low BMD for fractures were obtained from a previous meta-analysis (2). Attributional deaths due to RTA-related fractures were obtained through coded hospital data. Disability levels were established by applying disability weights to each type of fracture. Then, PIFs were applied to obtain attributable deaths and disability due to low BMD.

Results: In the European population aged 50–69 and 70 years and above, 10.8% (95% CI: 8.9–12.4%) and 30.9% (29.1–32.4%) of RTA-related deaths, respectively, were attributable to low BMD. In the age group 50–69 this was the second most important risk factor following alcohol use and in those 70 years and above became the most important risk factor, with double the weight of alcohol use. This represents 2,537 and 5,460 absolute deaths in those aged 50–69 and 70 years and above, respectively. The percentage of health burden and disability caused by RTAs attributable to low BMD grow steadily from the ages of 50 and onwards.

Conclusions: This data shows the previously-reported important role of low BMD as a preventable risk factor for European RTAs' health burden in population 50 years and over, which requires urgent attention.
AB1103
THE IMPORTANCE OF ADEQUATE SCREENING TO AVOID FALSE-POSITIVES IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

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Background: The lack of expertise and skills in the diagnosis of in rheumatoid arthritis (RA) in primary level of Colombian medical centers can cause misdiagnosis of rheumatic diseases. Due to this issue in a specialized center in RA we established a multidisciplinary model and a strict disease management algorithm to diagnose properly our patients; as a consequence we have achieved the accurate diagnosis of great proportion of patients that were false positives diagnosed initially as RA.

Objectives: The aim of this study was to show effectiveness and accuracy of a screening method to avoid false-positive diagnosis of RA in a cohort of patients with supposed diagnosis of RA.

Methods: During two years we evaluated patients with presumptive diagnosis of RA. We conducted a cross-sectional study; we included patients who were referred from primary care centers to a RA specialized center in a 24 month period with presumptive diagnosis of (RA). Each patient was evaluated to confirm or rule-out diagnosis of RA as follows: a rheumatologist fulfilled a complete medical record, including joint counts; it was assessed rheumatoid factor and anti-CCP antibodies, as well as other laboratory tests. Then, if the diagnosis was corroborated, the patient was referred to rheumatology; if not, the patient was referred back to primary care center.

Results: Between 2015 and 2016 6813 patients were evaluated in our specialized center, in 76% of cases RA was confirmed, the remaining 1933 patients (24%) had a wrong diagnosis of RA; of these misdiagnosed patients, (87%) were female, and 205 (13%) male, with an average age of 62±12 years. Between differential diagnosis which were found in this cohort of misdiagnosed patients: osteoarthritis in 849 patients (63.3%), Sjögren syndrome (7%) Systemic lupus erythematosus (6%) the remaining 30% of patients had conditions such as gout, psoriasis, osteoporosis, myalgia, soft tissue diseases among others. The majority of patients with wrong diagnosis took DMARDs (23%), calcium (11%), biologics (10%) acetaminophen (9%), neuropathy medications (7%), acetaminophen plus ibuprofen (5%), antidiabetes medications (5%), antibiotics (4%), glucosamine (4%), diacerein (3%), the remaining patients took medications such as NSAID, glucosamine, antigout agents, gastritis drugs, among others.

Conclusions: The results of this program show that almost 25% patients with presumptive RA diagnosis are misdiagnosed; this is evidence that can be extrapolated to primary care centers in Colombia. The most important confounding diagnosis was osteoarthritis and many patients were receiving DMARDs for treatment. For this reason there is an urgent need of education strategies for primary care physicians and the implementation of centers of excellence in RA, in order to conduct a proper diagnosis and avoid clinical and health economics consequences of misdiagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5294

AB1104
COST-EFFECTIVENESS ANALYSIS OF TNF INHIBITORS USE COMPARED TO DMARDS IN THE FATAL AND NONFATAL ACUTE CORONARY ISCHEMIC EVENT

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Background: Epidemiological studies have established that rheumatoid arthritis is associated with an increase in cardiovascular disease. The evaluation of tumour necrosis factor inhibitors (TNFi) on the reduction of the risk of acute myocardial infarction and death due to cardiovascular causes has shown promising results. The economic evaluation for these outcomes are not established yet.

Objectives: To evaluate the cost-effectiveness of TNFi versus disease-modifying antirheumatic drugs (DMards) to avoid a new case of acute ischemic heart disease and death in rheumatoid arthritis patients.

Methods: A cost-effectiveness analysis (CEA) was performed using a Markov model 6-month transition cycle, with time horizon of 30 years, under the Brazilian public healthcare system perspective. Costs are expressed in 2015 Reais and effectiveness measures are new cases of acute ischemic coronary disease and cardiovascular death.

Results: The average cost in 30 years of DMards and TNFi was 14,291,105.28 and 96,151,873.86 Reais, respectively. The incremental effectiveness was 2.69 cases of coronary artery disease and consequent incremental cost-effectiveness ratio (ICER) of 30,527,502.27 Reais per new cases avoided, while for cardiovascular death, incremental effectiveness was 1.33 and an ICER of 61,634,231.69 Reais per new cases avoided. The univariate analysis identified that the most relevant parameter in the ICER on both outcomes was the TNFi drug. The sensitivity analysis established that, in order to reach the amount of willingness to pay (WTP) per semester to avoid an acute myocardial infarction, the average cost of TNFi should be 1,337.47 Reais per case avoided and the average cost for the cardiovascular death avoidance would be 954.22 Reais. All the analyzes performed evidenced an unfavorable relationship of the drug treatment strategy with TNFi.

Conclusions: The findings of the CEA among patients with rheumatoid arthritis for cardiovascular outcomes when compared to the strategy of TNFi drug treatment with the dominant strategy DMards after the first 6 months of exposure point out an unfavorable relationship, surpassing the amount of expenses recommended by the Ministry of Health of Brazil in the year 2015.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2124

Table 1. Patient characteristics by race

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-Hispanic White</th>
<th>Non-Hispanic Black</th>
<th>Hispanic</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>34.1 (7.2)</td>
<td>35.2 (8.4)</td>
<td>32.8 (8.6)</td>
<td>0.1</td>
</tr>
<tr>
<td>Poor self-reported health (%)</td>
<td>12</td>
<td>14</td>
<td>12</td>
<td>0.9</td>
</tr>
<tr>
<td>Some college education (%)</td>
<td>75</td>
<td>61</td>
<td>43</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Income &lt;12,000/year (%)</td>
<td>23</td>
<td>33</td>
<td>34</td>
<td>0.2</td>
</tr>
<tr>
<td>Difficulty paying for meds (%)</td>
<td>68</td>
<td>59</td>
<td>69</td>
<td>0.3</td>
</tr>
<tr>
<td>Medicated (mean, SD)</td>
<td>20.6 (4.6)</td>
<td>21.6 (4.4)</td>
<td>22.3 (4.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>Trust (mean, SD)</td>
<td>27.9 (5.5)</td>
<td>28.6 (5.7)</td>
<td>29.1 (5.5)</td>
<td>0.3</td>
</tr>
<tr>
<td>Hopsful (mean, SD)</td>
<td>3.4 (1.7)</td>
<td>3.5 (1.7)</td>
<td>3.6 (1.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Worried (mean, SD)</td>
<td>4.6 (1.6)</td>
<td>4.8 (1.8)</td>
<td>5.1 (1.6)</td>
<td>0.2</td>
</tr>
<tr>
<td>Important (mean, SD)</td>
<td>5.3</td>
<td>5.6</td>
<td>5.5</td>
<td>0.3</td>
</tr>
</tbody>
</table>

<
Table 2. Association of subject characteristics with perceived importance by race

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-Hispanic Whites</th>
<th>Non-Hispanic Blacks</th>
<th>Hispanics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication beliefs</td>
<td>0.56 (&lt;0.01)</td>
<td>-0.24 (0.01)</td>
<td>-0.28 (0.04)</td>
</tr>
<tr>
<td>Hopeful</td>
<td>0.54 (&lt;0.01)</td>
<td>0.16 (0.09)</td>
<td>0.37 (&lt;0.01)</td>
</tr>
<tr>
<td>Worried1</td>
<td>-0.27 (0.01)</td>
<td>-0.02 (0.07)</td>
<td>0.05 (0.56)</td>
</tr>
<tr>
<td>Trust</td>
<td>0.22 (0.02)</td>
<td>0.33 (0.01)</td>
<td>0.17 (0.11)</td>
</tr>
<tr>
<td>Poor self-reported health2</td>
<td>1.66 (0.10)</td>
<td>1.19 (0.25)</td>
<td>-1.4 (0.16)</td>
</tr>
<tr>
<td>Some college education2</td>
<td>-1.16 (0.25)</td>
<td>1.9 (0.06)</td>
<td>0.65 (0.52)</td>
</tr>
<tr>
<td>Income &lt;12,000/year</td>
<td>0.38 (0.71)</td>
<td>1.65 (0.11)</td>
<td>0.06 (0.06)</td>
</tr>
<tr>
<td>Difficulty paying for meds</td>
<td>0.00 (0.09)</td>
<td>-2.05 (0.04)</td>
<td>-0.42 (0.26)</td>
</tr>
</tbody>
</table>

1Correlation coefficient (p value); 2F-test (p value).

subjects had lower levels of hope compared to Non-Hispanic White subjects (difference between means -0.05). Associations between subject characteristics and their experience of taking the verbal education were measured in the multivariable regression model (including education, difficulty paying for medications, medication beliefs, trust, hope and worry), hope was associated with perceived importance of taking the medication in all three ethnic groups. Additional findings differed by race, with medication beliefs in Non-Hispanic White subjects; difficulty paying for medications in Non-Hispanic Black subjects, and worry in Hispanic subjects being associated with perceived importance of taking the medication.

Conclusions: Our findings confirm the important influence of emotion on decision making, and suggest that while hope is universally associated with perceived importance of taking a medication, other factors differed, highlighting differences in the decision making process across ethnic groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2369

AB1106 VERBAL PATIENT EDUCATION ON VACCINATION IN ADULTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: IS IT ENOUGH TO IMPROVE VACCINATION RATES?

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Background: Patients suffering from autoimmune inflammatory rheumatic diseases (AIIRD) are at increased risk of infections, due to the underlying condition and its treatment. A study on vaccination in AIIRD carried out at Mater Dei Hospital, Malta in 2015 showed that 37.9% of the patients received the influenza vaccine in the previous year and 8.3% had received the pneumococcal vaccine ever. Only 38.3% knew that they had an increased risk of infection because of their condition.

Objectives: The aim of the current study was to establish whether verbal education on vaccination, influenced patients’ vaccination rates in the following year. A further aim was to determine whether the patients had a better understanding of their increased infection risk following verbal education.

Methods: The initial study carried out in 2015 consisted of a short face-to-face interview with 60 patients who suffered from autoimmune inflammatory rheumatic diseases. Following the interview, verbal information was given to the patients on their increased risk of infection, and the importance of vaccination, in particular the influenza and pneumococcal vaccine. After 1 year, the patients were contacted by means of a telephone call. They were interviewed with regards to their vaccination history and knowledge of their infection risk. Of the 60 patients, 2 had passed away. Therefore 58 patients were included in the study.

Results: The study included patients with a variety of AIIRD including rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. 60.3% were females and the mean age was 63.1 years (range 25 to 82 years). Influenza vaccination rates in the previous year improved from 37.9% in 2015 to 41.4% in 2016 (p=0.704). Pneumococcal vaccination rates improved from 6.9% to 17.2% (p=0.086). On questioning the patients regarding their knowledge of increased infection risk, there was no improvement following the verbal education. In fact 37.9% of patients questioned in 2015, and 34.5% in 2016 knew that they were at increased risk of infection because of their condition. 33% of patients studied in 2016 could recall that they had been advised to take vaccination because of their underlying condition or treatment. This improved from 7% in 2015, and 34.5% in 2016 knew that they were at increased risk of infection because of their condition. 33% of patients studied in 2016 could recall that they had been advised to take vaccination because of their underlying condition.

Conclusions: Compared to the initial study, there was no improvement following the verbal education. In fact 37.9% of patients that had complete data on all required variables. A list of Read Codes relating to inflammatory arthritis, compiled by a rheumatologist and a GP, were searched for in primary care medical records of consenting respondents. Period of enrolment was from date of first ever PMR diagnosis in the medical records until survey mail-out.

Results: 704 eligible patients were identified and sent a questionnaire, with 550 (78%) responding. Responders and non-responders did not differ significantly by age or gender. Medical records could be obtained for 385 patients, of whom 310 completed the questionnnaire fully and were included in the analysis. IA score ranged from -8.4 to 2.5, with 21 (7%) patients being classed as having a positive IA score. 8 out of 310 patients had at least one inflammatory arthritis Read code recorded from date of first diagnosis of PMR in their medical record, although only 2 of those were predictive of IA. IA score was calculated in these patients that had complete data on all required variables. A list of Read Codes relating to inflammatory arthritis, compiled by a rheumatologist and a GP, were searched for in primary care medical records of consenting respondents. Period of enrolment was from date of first ever PMR diagnosis in the medical records until survey mail-out.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5271

AB1108 HANDLING OF DE NOVO ARTHRITIS IN ADULTS BY GENERAL PRACTITIONERS: A SURVEY IN A FRENCH COHORT

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Background: A guide of good clinical practice regarding de novo arthritis in adults has been edited.

Objectives: The aim of this work is to identify whether the diagnostic and therapeutic tools proposed by general practitioners (GPs) to adults with a de novo arthritis is in line with the corresponding recommendations.

Methods: A questionnaire regarding the characteristics and the handling of de novo arthritis in adults has been submitted to 300 GPs chosen randomly from a French cohort database. The study period was from February 2015 to February 2016. Fifty seven GPs participated in the study (19%).

Results: No particular specificity was identified in the GP group. The age of patients ranged between 40 and 75 yo. The prevalence of arthritis was less than 5% among the GPs patients. The relative number of each category of arthritis was distributed as follows: Osteoarthritis (22%), Rheumatoid arthritis (22%), Psoriatic arthritis (14%), PPR (8%), other kinds of microcrystalline arthritis: chondrocalcinosis, (38.4%), gout (11.6%). Joints with mechanic degenerative effusion related to osteo-arthritis might be misdiagnosed as an inflammatory arthritis.

The knee was the most frequently involved joint in arthritis. The initial paraclinical
ABSTRACT

DOSE DESCALATION IN A SPECIALIZED OUTPATIENT CLINIC ON BIOLOGICAL THERAPY: COST MINIMIZATION OBSERVATIONAL STUDY


Background: To estimate the annual cost in the use of biological therapy (BT) in patients with different rheumatic diseases when dose modifications are undertaken in daily clinical practice in a specialized outpatient clinic during 2016 and to compare the results with data obtained in 2013.

Methods: Design: Cost minimization observational study under conditions of clinical practice. Patients: Patients with different rheumatic diseases who come to a specialized outpatient clinic on BT in the Rheumatologic department at a tertiary Spanish hospital (with tight follow-up) that was treated with BT under reduced doses during 2016 were collected. Protocol: Reductions in treatment dose or dose frequency were established empirically and were carried out by their rheumatologist in those patients who were in remission (DAS 28 ≤ 2.6) for at least 6 months without steroids. Main outcome: Reduction of annual average cost in euros/annum in BT used patients who are in dose reduction in clinical practice in 2016. Secondary outcome: Differences in annual costs reduction in 2016 compared with 2013. The cost reduction was calculated by comparing the actual expenditure (after modifying treatment dose in clinical practice) with the theoretical costs (official price) in case you had not made the adjustment. Statistical analysis: Sample descriptive analysis. Reducing annual absolute costs and by treatment after tapering down doses in clinical practice in 2016 and the differences found between 2013 were calculated.

Results: During 2016, the dose of the BT of 168 patients (94 Subcutaneous BT and 74 intravenous BT) were modified in clinical practice after reaching clinical remission: mean of DAS 28 (mean±SD)=2.31±0.76 or BASDAI (mean±SD)=2.15±1.39 without radiographic progression. Most patients were women (n=113;67%) and had rheumatoid arthritis (n=103;62%) and the rest were distributed among: spondyloarthritides (n=26;17%), psoriatic arthritis (n=22;13%), juvenile idiopathic arthritis (n=10;5.5%) and Systemic Lupus Ermethematosis (n=5;3%). No patients treated with certolizumab or anakinra was modified treatment doses. During this period, 5 patients discontinued BT (3 remissions and 2 minor adverse events). Table 1 shows the number of patients by type of BT and costs. The BT dose reduction in clinical practice during 2016 represented a saving of 676,501.67€ and a greater efficiency of treatments while in 2013, only 86 patients (30 etanercept, 15 adalimumab, 16 Infliximab (Remicade), 15 Tocilizumab IV and 55 Rituximab) had a modified dose of BT in clinical practice assuming a saving of 396,995.46€. The difference in the annual cost reductions in 2016 compared to 2013 meant a saving of 279,506.21€ more in the last year. Table 1.

Conclusions: In rheumatic diseases we may do a dose de-escalation of BT in patients who go into remission and therefore we could reduce the associated costs of BT and being more efficient with the treatments. We believe that it is important to create specialized outpatient clinics on BT where a tight-control management of these patients and an individualized treatment are carried out.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5251
AB1111  A PROSPECTIVE COHORT STUDY MEASURING COST-BENEFIT ANALYSIS OF THE OTAGO EXERCISE PROGRAMME IN COMMUNITY DWELLING ADULTS WITH RHEUMATOID ARTHRITIS


1School of Nursing, Midwifery and Social Work and MAHSC; 2School of Medical Sciences; 3School of Nursing, University of Manchester, Manchester; 4University of Glasgow; 5University of Manchester, Manchester, United Kingdom

Background: Falls are one of the major health problems in adults with Rheumatoid Arthritis (RA). Interventions, such as the Otago Exercise Programme (OEP), can reduce falls in community dwelling adults by up to 35%. The cost-benefits of such a programme in adults with RA have not been studied.

Objectives: To determine healthcare cost of falls in adults with RA, and estimate whether it may be cost efficient to roll out the OEP to improve function and prevent falls in adults living with RA.

Methods: Patients with Rheumatoid Arthritis aged ≥ 18 years were recruited from four rheumatology clinics across the Northwest of England. Participants were followed up for 1 year with monthly fall calendars, telephone calls and self-report questionnaires. Estimated medical cost of a fall-related injury incurred per-person were calculated and compared with OEP implementation costs to establish potential economic benefits.

Results: 535 patients were recruited and 598 falls were reported by 195 patients. Cumulative medical costs resulting from all injury leading to hospital services is £374,354 (US$540,485). Average estimated cost per fall is £1,120 (US$1,617). Estimated cost of implementing the OEP for 535 people is £116,479 (US$168,504) or £217.72 (US$314.34) per-person. Based on effectiveness of the OEP it can be estimated that out of the 598 falls, 209 falls would be prevented. This suggests that £234,583 (US$338,116) savings could be made, a net benefit of £118,104 (US$170,623).

Conclusions: Implementation of the OEP programme for patients with RA has potentially significant economic benefits and should be considered for patients with the disease.

References:

Acknowledgements: Special thanks to all the participants involved in the research and also the nursing staff who supported the data collection phase of the study at Manchester Academic Health Science Centre (MAHSC).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1439

AB1112 DATANETWORK RHEUMA 4.0 – REAL WORLD DATA FROM PRIVATE PRACTICE

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Background: The datanetwork Rheuma 4.0 (DNR_4.0) is a consortium of 5 internistic-rheumatologic specialized practices. Patient data that were collected routinely will be pooled pseudoonymized (e.g. via RheumaDock) and will be made available to answer numerous healthcare- and scientific research questions.

Methods: The participating centres document the following data in specific management data documentation systems (RheumaDock, Emily, DokuMed.ru). These data will be routed automatically to the data base of the DNR_4.0 via a prespecified interface and can be used for certain research areas: Diagnosis (by rheumatologist (R), anamnesis (R), medication (R), morning stiffness (R, patient (P)), scores like RADI (R, P), DAS28 (R), BASDAI (P), BASFI (P), quality of life (R, P). Also prespecified laboratory measures (R) like ESR, CRP etc. can be collected automatically.

Patient reported Outcomes (PROs) that were entered via mobile applications like RheumaLive and AxSpALive can be collected in certain intervals and be sent encrypted onto the medical data base. The data entered by patients will be screened by the rheumatologist or nurse and will be stored in the underlying data base. Clinical data that are collected during regular P2F-appointments will be stored together with the PROs according to a specific period of time.

Results: The datanetwork Rheuma 4.0 (DNR_4.0) is an association of 5 internistic-rheumatologic specialized practices.

Conclusions: The german biologic registry Rabbit and the “Core documentation” data base deliver valid data about the safety and efficacy of rheumatologic medication. The datanetwork Rheuma 4.0 will make a valuable contribution – especially in conjunction with apps of patient’s self management like RheumaLive and AxSpALive – to health care research, therapeutic strategies and clinical questions from daily practice.

Acknowledgements: RheumaLive and AxSpALive were developed by Starthealth GmbH on behalf of UCB Pharma GmbH.


AB1113 PATIENT PARTICIPATION IS CRUCIAL WHEN INTRODUCING NEW DEVICE TECHNOLOGIES IN THE MANAGEMENT OF CHRONIC ARTHRITIS: APPLYING THE PARKER MODEL, A QUALITATIVE 3-STEP APPROACH

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Background: Patients’ participation in design, development, and implementation of new device technologies is essential to ensure added value in patients’ disease management.

Methods: To explore the applicability and relevance of ava® , an electromechanical device (e-Device), as an alternative method for subcutaneous administration of certolizumab pegol.

Results: The Parker Model is an innovative 3-step qualitative research approach, which combined concept mapping (CM), participatory design (PD), and stakeholder evaluation (SE) to evaluate the development and implementation of a new device technology (ava® , Figure). CM was applied through workshops, with the participation of patients, using a structured group process focusing on relevant themes to identify issues and concerns with the e-Device. Patients used this information in a series of iterative PD sessions; patients participated in 3 interactive sessions to create a personal e-Device prototype in
cooperation with a designer and a medical expert. This was followed by a common group session. Finally, SE was performed based on semi-structured group and individual interviews with patients and disease-management stakeholders.

Results: The study included 9 rheumatoid arthritis (RA) patients, 4 psoriatic arthritis (PsA) patients, 1 ankylosing spondylitis (AS) patient, 2 doctors, 2 nurses, 1 medical rheumatologist, and 4 key public servants involved in the disease management of the selected rheumatic diseases. Saturation was reached after 3 CM patient workshops, generating 121 statements, which were organized by the participants into themes. Through content analysis of the results from the 3 workshops, 4 concepts were generated: technical usability, physical design, concerns, and enthusiasm. These data were used in the iterative PD sessions, resulting in 4 new prototypes. Finally, SE demonstrated that the identified concepts were pivotal for both facilitating and hampering device implementation, thus creating value when introducing the new e-Device.

Conclusion: Patient participation in the 3-step qualitative Parker Model identified important aspects to consider when designing and implementing an innovative device for the treatment and management of RA, PsA, and AS. This is the first time a composite, qualitative research model has been applied when introducing a new device to support these disease areas. The responses from patients and disease-management stakeholders indicated that it is key to include patient input in the design and adaptation of devices alongside education and communication with stakeholders. These resources can help ensure added value when developing devices for the management of RA, PsA, and AS using biologic medicines.

Acknowledgements: This study was funded by UCB Pharma and the Oak Foundation. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: T. Jørgensen Speakers bureau: Abbvie, Biogen, Novartis, Roche, UCB Pharma, L. Klokke: None declared, M. Skougaard: None declared, H. Mountian Employee of: UCB Pharma, H. Gudberg: None declared, L. Kristensen Speakers bureau: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1770

AB1114 PATIENT’S SELF-MONITORING OF DISEASE ACTIVITY OF RHEUMATIC DISEASES VIA WEBAPP – STUDY DESIGN, PATIENT’S PERSPECTIVE AND RECRUITMENT IN THE FIRST 11 MONTHS OF THE SWISS MULTICENTRE, LONGITUDINAL COMPASS II STUDY

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Background: The management of patients with rheumatic diseases is guided in part by asking patients about their medical history at each clinic visit. Patients often find it difficult to accurately remember the course of their symptoms between these appointments as they are often months apart. Regular app-based patients’ self-monitoring of disease activity (with our without feedback to the rheumatologist) between clinic visits might provide a possible solution for this. The COMPASS II study [1] demonstrated that RA patients’ self-assessments of disease activity via App correlate strongly with rheumatologists’ assessments. Following up on this, the Swiss based COMPASS II study is embedded in the Swiss rheumatology registry (SCQM) and hence allows the linkage of data obtained via the COMPASS II App from the patients with routine clinical data collected in the registry. The main aims of the COMPASS II study are to assess if continuous self-monitoring of the disease by patients optimises disease management and outcome in rheumatic diseases, and to assess the fluctuation of disease activity between clinic visits.

Objectives: The objectives of this abstract are to describe the set-up and the recruitment of the COMPASS II study in the first 11 months.

Methods: The COMPASS II App questionnaire consists of the RAPID3 score, a validated, commonly used PRO to self-assess disease activity. Additionally, patients are asked about their therapy compliance and cortisone dose. At inclusion, interested patients with RA, axSpA and PsA are electronically randomized into 3 study arms (Figure 1). In arm 1 patients and rheumatologist are displayed the self-assessed disease activity over time, the patient directly via the App and the rheumatologist via the SCQM registry. In arm 2 only the patients are displayed their disease activity chart and in study arm 3 neither sees the recorded data. Patients are encouraged to fill in the App weekly.

Results: The COMPASS II App went online on the 15/02/2016. In the first 11 months of COMPASS II, 272 patients were enrolled by their rheumatologist. 64% of patients used the WebApp (32% in arm 1, 38% in arm 2 and 30% in arm 3); 82% of patients filled in the questionnaires for longer than a months, the longest follow-up was 11 months. On average patients use the App every 2 weeks. Patients found the App easy to use “The COMPASS II WebApp is so easy to use, it doesn’t even take me 2 min.” and received feedback included “Now my rheumatologist sees how I was since the last appointment instead of me trying to remember how I was half a year ago.”.

Conclusion: The COMPASS II study will validate the utility of app-based patients’ self-assessments in enhancing disease control in a treat to target approach and deliver numerous additional scientific data.

References:

Acknowledgements: COMPASS II is supported by an unrestricted grant from AbbVie.

Disclosure of Interest: None declared


AB1115 THE FEASIBILITY OF UTILIZATION OF MOBILE DEVICES TO ENHANCE PATIENT REPORTED OUTCOMES MEASURES (PROMS) IN RHEUMATOLOGY PRACTICE

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Background: Patient reported outcome measures (PROMs) are accepted modalities of gathering patient-reported health status such as physical, mental and social well-being. In addition to research applications, in some countries such as the United States, some of these measures are being considered as metrics for quality of care. The advent and wide spread use of the electronic medical record (EMR) in the United States has enabled providers (and patients) to collect PROMs electronically via patient portals (1). At the University of Michigan, the patient medical record is maintained by MiChart- an EPIC® software which interfaces with the Patient Reported Outcomes Measures System – PROMIS (2) - an NIH funded project for development of assessment tools for collecting and analyzing patient health status. Our initial effort focused on integrating the PROMIS questionnaires into the patient EMR for two domains: Adult Physical Function and Pain Intensity Scores into patient portals (electronic patient-physician communication tool), thus enabling patient to complete questionnaires from home computers. Our collection rate of completed PROMs questionnaires via patient portals was about 5-10%.

Objectives: The aim of our project was to examine/enhance collection rate of PROMs with the utilization of portable devices/tablet based PROMs at the time of check-in the clinic by the patient.
Epidemiology, risk factors for disease or disease progression

**AB1116 PREVALENCE OF POLIAUTOIMMUNITY AND FAMILY AUTOIMMUNITY IN MEXICO**

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**Background:** Autoimmune diseases share pathophysiological mechanisms, genetic factors and certain environmental triggers. Its frequency is reported up to 24% in the United States for the 10 most frequent autoimmune diseases. Familial autoimmune diseases account for 30% to 50% of cases of autoimmune diseases. It is unknown in our population.

**Objectives:** To identify the prevalence of polyautoimmunity and family autoimmunity in a Rheumatology Service of a third level hospital in Mexico.

**Methods:** Observational, descriptive, cross-sectional study. Consecutive outpatients who attended the Rheumatology Service of the Hospital Civil de Guadalajara “Fray Antonio Alcalde” during the 2 months were entered in a questionnaire to obtain demographic data, autoimmunity and risk factors. Descriptive statistical analysis was done.

**Results:** Of 1,208 patients, 484 (40%) had autoimmunity, of these 58 (12%) had polyautoimmunity and 6 (1%) with Multiple Autoimmune Syndrome (MAS). In the Mas group of 35 autoimmune diseases registered were: RA 42%; SLE 17%; AS 6%; SSc 5%; SS 4%; PsA 3%; JIA 3%; autoimmune hypothyroidism 3%; APS 2%; Dermatomyositis 2% and Psoriasis 1%. In the group with polyautoimmunity SLE was present in 26 (45%) patients, SS in 13 (22%) and autoimmune thyroid disease in 14 (24%). In the MAS group autoimmune thyroid disease in 5 patients. Patients with polyautoimmunity developed first: SLE (14%) and RA (14%). In the patient with MAS autoimmune thyroid disease in 33%. Of the 58 patients with polyautoimmunity 31 (53%) have familial autoimmunity, of which SLE is the most frequent in (22%), followed by autoimmune thyroid disease (17%) and RA (10%). All 6 MAS patients had familial autoimmunity. Referent to risk factors: 154/484 reported active smoking. Of the 58 patients with polyautoimmunity, only 23 (40%) had or are current smokers. Of the 6 patients with MAS 50% presented this risk factor:158/484 (33%) patients had periodontal disease. In patients with autoimmune disease 54% were overweight (28%) or obese (26%). Of the 58 patients with polyautoimmunity 48% were overweight and 21% obese; of patients with MAS 50% were overweight or obese. Only one patient had ASIA syndrome with GCA diagnosed.

**Conclusions:** The search of polyautoimmunity is required in all patients with autoimmune disease and convenient to consider that these patients will have a higher frequency for familial autoimmunity. Smoking and periodontal disease are widely known risk factors that are not taken seriously by patients.

**References:**


**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.6300

**AB1117 LATENT TUBERCULOSIS INFECTION AND TUBERCULOSIS IN PATIENTS WITH RHEUMATIC DISEASES UNDER TREATMENT WITH ANTI-TUMOR NECROSIS FACTOR DRUGS**

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**Background:** The introduction of biological agents, especially the tumor necrosis factor inhibitors (anti-TNF) for the treatment of rheumatic diseases increased the risk of developing tuberculosis (TB). Screening for latent TB infection (LTBI) is strongly recommended before starting therapy with anti-TNF agents.

**Objectives:** This study aimed to identify the prevalence of LTBI and TB among patients with rheumatic diseases on anti-TNF drugs.

**Methods:** In a cross-sectional study, the electronic medical records of all adult patients (>18 years old) undergoing anti-TNF treatment at Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil, were reviewed. Every patient underwent Tuberculin Skin Test (TST) before starting anti-TNF therapy.

**Results:** In total, 176 patients were included. The mean age was 51.9±12.4 years, 34.7% were males, and 90.9% were white. The underlying diseases were rheumatoid arthritis (RA) in 50.6% (N=89), ankylosing spondylitis (AS) in 27.8% (N=49) and psoriatic arthritis (PsA) in 17.6% (N=31). Anti-TNF agents started after TST were: infliximab (22.7%, N=40), adalimumab (48.9%, N=86), etanercept (23.7%, N=43), and golimumab (1.1%, N=2). The prevalence of positive TST was 29.5%. Household contact with TB was significantly associated with a positive TST (p<0.02). RA patients had lower TST reactions than AS patients (p=0.022).

There were six cases of TB (3.4%) diagnosed during anti-TNF therapy.

**Conclusions:** We demonstrated a high prevalence of positive TST (29.5%) among patients with rheumatic diseases in a region with high TB prevalence. Our data corroborates the ACR's recommendation that patients who live in high risk TB incidence settings should be tested annually for LTBI.

**References:**


**Disclosure of Interest:** None declared.

**DOI:** 10.1136/annrheumdis-2017-eular.6952

**AB1118 REVIEW OF METHODS FOR ASSESSING THE RELATIONSHIP BETWEEN WEATHER AND CHRONIC MUSCULOSKELETAL PAIN**

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**Background:** People with chronic pain commonly believe that their pain is affected by the weather. Despite a century’s worth of research, there is no scientific consensus on the existence of a relationship between weather and chronic pain.

**Objectives:** A systematic literature review to (1) gain an overview of existing research on the weather-pain relationship, and (2) summarise the methodologies, methodological rigour and risk of bias in published studies of patients with musculoskeletal conditions.
Methods: Systematic search strategies were developed for 5 databases (Medline, Embase, Psycinfo, Scopus, Web of Science) to retrieve studies that investigated the relationship between weather conditions and chronic pain. Original articles describing observational studies that related chronic pain (primary outcome) to weather conditions (exposure), were included. Study characteristics, methodology (e.g., sample size, and weather variables) aspects of statistical analysis, and data on risk of bias (validation of participants’ exposure and diagnosis, coverage of weather variation, correction for confounders) was extracted. Methodological rigour was summarised by mapping the methodological variability among studies and ranking these from least to most rigorous.

Results: The search yielded 16,081 articles. After removing 3090 duplicates and excluding 12726 articles during title screening, 265 abstracts were assessed for eligibility. Of 64 observational studies that met the inclusion criteria, 30 (47%) investigated pain associated with musculoskeletal conditions, 24 (38%) investigated headache and 10 (16%) investigated pain associated with other conditions such as sickle cell disease and dental pain. After full text assessment, 10 of 30 papers on musculoskeletal conditions were excluded because they investigated risk of acute pain episodes rather than chronic pain symptoms (n=6), or investigated multiple conditions (n=4). The 20 included studies investigated rheumatoid arthritis (6, 30%), osteoarthritis (6, 30%), fibromyalgia (6, 30%) and low back pain (2, 10%). A total of 15 studies (75%) reported some effect of weather on chronic pain, and this was clinically significant (consistent and sufficient size of effect) in 6. Participant numbers varied from 19 to 2491. 1 study was cross-sectional and 19 longitudinal follow ups ranging from 1 week to 3.5 years, with participants scoring their pain daily or weekly for 1 to 12 months. Pain was measured with a Visual Analog Scale or Numerical Rating Scale in 17 (85%). Weather conditions were retrieved from local weather stations, with most studies assuming that participants stayed in the area/city (65%) or postcode area (20%) where they lived.

In 12 (60%) studies, participants were blinded to the study hypothesis. Methods for correcting for confounders were highly variable, with 7 studies not addressing any, and the remaining addressing one or more of 32 confounding variables.

Conclusions: Methodological variability of studies investigating the relationship between weather and chronic musculoskeletal pain is high. This methodological review will inform best research practice for those investigating the relationship between the weather and chronic pain.

Acknowledgements: Mary Ingram, librarian

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6571

AB1119 A DESCRIPTIVE STUDY OF GOUT PATIENTS IN A MULTI-ETHNIC SOCIETY

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Background: Gout is a common inflammatory arthritis with rising global prevalence and health burden, especially in the Asia-pacific regions. Ethnicity may play a significant role suggesting lifestyle and/or genetic predisposition, but such data are limited in Asia-pacific region.

Objectives: Our study sought to assess the demographic and clinical factors of gout in the multi-ethnic Singapore and describe the burden and treatment pattern in our patients.

Methods: 282 adults with rheumatologist-diagnosed gout were recruited from rheumatology clinics of an academic medical centre in Singapore. Data on demographic and lifestyle features, medical conditions, gout severity and treatment were obtained.

Results: 282 subjects were recruited and 92.6% were men. There were 77% Chinese, 18.6% Malays and 2.5% Indians, compared to Singapore’s population median of 73%, 13% and 9% respectively. Mean age at recruitment was 52.6 years (SD 16.1) while age at gout onset was 42.5 years (SD 16.7). 34.4% received primary or no education; 67.0% were employed and 20.7% retired. 22.7% were current alcohol drinkers while 50.7% were teetotallers. 23.4% were current smokers. Mean body mass index (BMI) was 28.1±6.0kg/m2 while 69.9% had BMI ≥30kg/m2. Prevalence of hypertension was 56.7%, diabetes mellitus 18.8%, dyslipidemia 48.2% and chronic kidney disease (CKD, defined as glomerular filtration rate <60ml/min/1.73m2) 32.4%. Malays had significantly less alcohol intake (1.9%) but higher proportions of diabetes (32.1%), CKD (50.9%) and obesity (52.4%), compared with Chinese subjects (26.3%, 16.1%, 28.6% and 19.8% respectively, all P<0.05). Gout severity was rated moderate by 30.9% and severe in 50.4%; 69.3% suffered ≥3 attacks in 6 months. Mean SU was 477.8μmol/L (SD 130.8). 80.1% were on allopurinol. Subjects (32.3%) who achieved serum urate (SU) <360μmol/L, when compared to those with SU >360μmol/L, were more likely to be on urate lowering therapy (82.5% vs. 60.7%, P=0.001), on higher mean allopurinol dose [337 mg/d (SD 166) vs 233 mg/d (SD 140), P<0.001] and statin [54.8% vs 33.3%, P=0.003]. There were no significant differences among ethnicities for SU levels, gout severity and number of attacks.

Conclusions: Gout has substantial health burden in Singapore. Hypertension, dyslipidemia and obesity are more prevalent in our gout subjects compared to our population. Despite notably less alcohol intake compared with other cohorts4,5, Singapore Malays seemed to suffer higher prevalence and comorbidities of gout.

Majority of patients had moderate to severe disease but less than 25% achieved target SU levels highlighting suboptimal management of gout locally.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5350

AB1120 COMPARISON OF NON-RADIOGRAPHIC SPONDYLOARTHRITIS VERSUS ANKYLOSING SPONDYLITIS PATIENTS UNDERGOING BIOLOGICAL THERAPY

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Background: Axial spondyloarthritis include non-radiographic spondyloarthritis (nr-SPA) and ankylosing spondylitis (AS); they reveal the extent of sacroiliitis assessed by conventional x-ray or MRI (1). The natural history of nr-SPA follows various evolution patterns; smoking, male gender, high levels of inflammatory markers, initial radiographic lesions are among predictor factors of progression to AS (2).

Objectives: The objective of the present study was to compare features related to progression of nr-SPA patients versus AS patients undergoing biological therapy with an anti-TNF agent.

Methods: This was an observational, cross-sectional study including 94 patients with nr-SPA and AS under continuous anti-TNF therapy for at least six months. SPSS 20.0 was used to analyze data with a P value of 0.05.

Results: Out of the selected study group, 69 patients were diagnosed with AS having a mean age of 44.8±10.8, while 25 patients had nr-SPA. Patients with nr-SPA were aged 32.1±6.6 years old and 40% of them were women, a rate significantly than in the AS group (P=0.05). Mean age at disease onset was 30.7 years for the AS subgroup versus only 23.8 years for patients with nr-SPA (P=0.001). AS patients presented a significantly higher value of the BMI compared to nr-SPA (27 versus 24.7 kg/m², P<0.001). 91% of patients had positive HLA B27 and 7.4% had a positive family history of SpA, with no significant differences between the two subgroups. A higher level of CRP was noticed in AS patients (P=0.038).In the study cohort the time interval from symptom onset to establishing a diagnosis was of 39±55.6 months, with a mean delay interval of 2.32 years for patients with nr-SPA and higher, of 3.5 for patients with AS (P<0.01).

Conclusions: The nr-SPA group had a considerably higher percentage of females compared to the AS subgroup. AS patients presented higher values of CRP at follow-up visits as opposed to nr-SPA patients. There were no significant differences between nr-SPA and AS patients regarding BASDAI or PIGA scores, smoking status or frequency of uvette. The presence of HLA B27 did not differ between the two subgroups, thus it might not be a reliable predictive factor of progression.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5344

AB1121 TRABECULAR BONE SCORE COMBINED WITH CLINICAL RISK FACTORS CAN PREDICT INCIDENT FRACTURE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Fracture is one of the most common and important comorbidities associated with rheumatoid arthritis (RA) patients, especially patients who use glucocorticoids (GC). However, bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) which is the gold standard of diagnosing and monitoring osteoporosis is not a useful tool for predicting new fracture in RA patients. Previous studies suggested the possibility of trabecular bone score (TBS) as a useful predictor for incident fractures.

Objectives: We aimed to evaluate the accuracy of TBS combined with clinical risk factors or BMD for prediction of new fracture in patients with RA.

Methods: A total of 100 female RA patients were enrolled with assessment of TBS, BMD, and clinical risk factors for fracture. During follow-up period, we...
AB1122 ALL-CAUSE OF HOSPITAL MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND LUPUS ERYTHEMATOSUS IN A UNIVERSITY HOSPITAL DURING 1998 TO 2014

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Background: All-cause and cause-specific mortality is increased in patients with systemic lupus erythematosus (SLE) and Rheumatoid Arthritis (RA) when compared to the general population. Mortality can be attributed to the disease per se, side effects of drugs and effect of comorbidities. The survival of patients has improved over the past years when compared to historical controls.

Objectives: The objective is to describe all-case of mortality in patients with SLE and RA in a university hospital.

Methods: This is an observational, descriptive, and cross-sectional study. We included all patients with SLE and RA hospitalized during 1998 to 2014. The cause of death was obtained from medical records and classified according to International Classification of Diseases (ICD)-10. We made a descriptive analysis of all-causes of mortality in both diseases.

Results: We analyzed 1,330 medical records, of which 215 died in hospital. The respiratory insufficiency was the most common mortality diagnosis in both diseases (RA 29%, SLE 24.1%), followed by sepsis (RA 25%, SLE 20.4%). The all-cause mortality of SLE and RA are shown in Table 1. Of the 467 RA hospital admissions, the 5.1% died, and of the 863 SLE hospital admissions, the 22.1% died.

Table 1. Mortality of RA and SLE

<table>
<thead>
<tr>
<th>Year</th>
<th>RA</th>
<th>SLE</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n=467</td>
<td>n=24</td>
</tr>
<tr>
<td>1998–99</td>
<td>18 (3.9)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>2000</td>
<td>22 (4.7)</td>
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<td>0 (0)</td>
</tr>
</tbody>
</table>

RA: Rheumatoid arthritis, SLE: Systemic Lupus Erythematosus.

Conclusions: Advances in the diagnosis and treatment of SLE and RA, have decreased the morbidity and mortality of the two diseases. Infectious and cardiovascular pathologies were the most frequent causes of death.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3316

AB1123 POOR ASSESSMENT OF RISK OF OSTEOPOROSIS AFTER A FOREARM FRACTURE IN WOMEN: A HEALTH INSURANCE DATABASE STUDY IN THE LOIRE VALLEY REGION (FRANCE)

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Background: Bone Mineral density (BMD) assessment is a useful tool to evaluate bone fragility and is largely recommended in patients at risk of osteoporosis. We have previously reported in 250 women aged 50-year-old or more that only 10% of them had a BMD assessment after a forearm fracture.

Objectives: Herein, we evaluated BMD assessment and prescription of anti-osteoporotic drugs after a forearm fracture in women after 50-year-old in a large population database.

Methods: We identified all forearm fractures in women aged 50 years old or more in the “Centre-Val de Loire, France” area between 01/01/2011 and 31/12/2012, using the National Health Insurance database which cover both private and public sectors of the whole population. We analyzed the reimbursement and determinants of BMD assessment such as age, consumption of drugs inducing osteoporosis, anti-osteoporotics drugs and long term illness.

Results: We identified 414 patients with a forearm fracture during the study period. Among them, 546 (13.25%) had a BMD assessment performed at a median time of 4 months after the fracture. Women who had had a BMD were significantly younger than those who had not (67.44 years versus 74.63 years: OR: 0.941 CI95% (0.902–0.98)). Anti-osteoporotic treatment was positively associated with BMD assessment (OR: 3.233 (CI95%; 1.976–5.290)) while corticosterone was not (OR: 0.866 (CI95%; 0.601–1.247)). Among the women who had a BMD assessment, 168/546 (30.77%) had an anti-osteoporotic drug initiated after the forearm fracture, versus 231/3574 (6.46%) in those who had no BMD performed (Fisher test p.<0.05).

Conclusion: In this large population database, more than 15% of women over 50 year-old have a BMD assessment after a forearm fracture. BMD assessment was associated with anti-osteoporotic drugs initiation.


Disclosure of Interest: None declared


AB1124 EFFECT OF SARCOPENIA, SUBCUTANEOUS ADIPOSE TISSUE AND ABDOMINAL VISCERAL FAT ON MORTALITY RISK OF COMMUNITY-DEWLLING OLDER ADULTS: A POPULATION-BASED PROSPECTIVE COHORT STUDY IN BRAZIL

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Background: Body composition changes resulting from ageing (decreased muscle mass and increased fat tissue) are frequently not accompanied by bone fragility and is largely recommended in patients at risk of osteoporosis. We sought to investigate the relationship between body composition and risk of all-cause of mortality among community-dwelling older adults in Brazil.

Objectives: The current study was designed to describe the association between body composition (skeletal muscle mass, subcutaneous fat mass, visceral fat mass) and all-cause of mortality risk in a large population-based prospective cohort study in Brazil.

Methods: In a large population-based prospective cohort study in Brazil, we identified 839 community-dwelling subjects (516 women, 323 men), ≥65 years, who were assessed by questionnaire on clinical data, laboratory exams and body composition (DXA) at the baseline and followed for 4 years. The mortality was recorded during 4 year-follow-up. Multivariate logistic regression analysis was used to compute odds ratios for all-cause and cardiovascular mortality.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.33982
Results: Over a mean 4.06±1.07 years of follow-up, there were 132 (15.7%) deaths. In men, after adjustment for age, BMI, smoking, physical activity, alcohol, diabetes, dyslipidemia, cardiovascular event, recurrent falls, 25(OH)D and PTH, the presence of sarcopenia (OR 11.36, 95% CI: 2.11–61.83, p<0.004) and visceral fat mass (OR 1.99 95% CI: 1.38–2.87, p<0.001, for each 100g-increase) significantly increased cardiovascular mortality risk while FMI was associated with decreased mortality risk (OR 0.48, 95% CI: 0.33–0.71, p<0.001). Similar results were observed for cardiovascular mortality in men: sarcopenia (OR 14.84, 95% CI: 5.15–47.72, p<0.001), visceral fat mass (OR 1.66, 95% CI: 1.31–2.10, p<0.001) and FMI (OR 0.57, 95% CI: 0.43–0.76, p<0.001). In women, only sarcopenia was a predictor for cardiovascular mortality risk, while FMI was associated with cardiovascular mortality (OR 74.54, 95% CI: 9.72–571.46, p<0.001).

Conclusions: Sarcopenia and fat distribution are associated with all cause and cardiovascular mortality risk in elderly, and they are different according to sex. Visceral fat and subcutaneous fat have opposite roles on mortality risk in elderly men, and this is distinct from what is observed in young adults. These findings point to the risk of encouraging weight loss in the elderly aiming young adult goals. Furthermore, DXA seems to be a promising tool for evaluation risk of mortality in elderly, since it is easily applicable in clinical practice.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2224

AB1125 PREDICTION OF CHRONIC DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS BY USING MACHINE-LEARNING MODELS
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Background: The increased survival in Systemic Lupus Erythematosus (SLE) patients implies the development of chronic damage, occurring in up to 50% of cases after a follow-up of 10 years. Its prevention is a major goal in the SLE management. During the last years, it has been suggested that Artificial Neural Networks (ANNs) could be a useful prediction tool in medical scenarios, by using patients’ data as inputs and the specific outcomes as outputs. The International Conference on Advanced Computing and Communication Systems in 2015 underlined the possible application of sophisticated data analysis tools, such as machine learning methods, in SLE patients, in the light of their potential application to diagnostic and prediction purposes.

Objectives: In the present study, we aimed at predicting chronic damage in a large monocentric SLE cohort by using neural networks.

Methods: For the present analysis, we used data from 413 SLE patients (1997 ACR criteria; M/F 20:393; mean age ± SD 48±11.9 years; mean disease duration ± SD 174±112.4 months; mean follow-up period ± SD 63±30.7 months). At each visit, the patients underwent a complete physical examination and clinical and laboratory data were collected in a standardized, computerized, and electronically filled form. All the patients were evaluated at least twice per year. Autoantibodies and complement serum levels were also registered. Chronic damage was assessed by the SLICC/ACR Damage Index (SDI). We applied Recurrent Neural Networks (RNNs) as a machine-learning model to predict the risk of chronic damage. The clinical data sequences registered for each patient during the follow-up were used for building and testing the RNNs. We used 27 clinical and laboratory items as inputs for the mathematical model.

Results: At the first visit, 35.8% of patients had an SDI>0, with a mean±SD value of 1.7±1.1. For the RNN model, two groups of patients were analyzed: patients with SDI=0 at the baseline, developing damage during the follow-up (N=38), and patients without damage (SDI=0), in whom no damage occurred. We used all the visits before the development of damage, and in the second group, we considered patients with at least 5 visits and a follow-up of 2 years. We created a mathematical model with an AUC value of 0.77, able to predict damage development. A threshold value of 0.35 (sensitivity 0.74, specificity 0.76) seems able to identify patients at risk to develop damage.

Conclusions: We applied RNNs to identify a prediction model for SLE chronic damage. By using longitudinal data, including laboratory and clinical items, we created a mathematical model able to identify patients at higher risk to develop chronic damage.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5331

AB1127 HEALTH LOCUS OF CONTROL IN SYSTEMIC LUPUS ERYTHEMATOSUS – A CROSS-SECTIONAL ANALYSIS OF THE LULA-COHORT IN GERMANY 2013
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Background: Health Locus of Control (HLC) is the degree to which individuals believe that their health is controlled by internal (self-responsibility) or external (fate-luck) factors. This condition might affect different disease aspects, especially in chronic diseases.

Objectives: Our objective was to assess the influence of HLC on different disease aspects in a representative sample of German systemic lupus erythematosus (SLE) patients.

Methods: The LuLa-Study is a longitudinal study on a multitude of SLE associated factors that is being conducted annually by means of a self-reported questionnaire among members of the German LE self-help community since 2001 and is ongoing. Inclusion criteria are a diagnosis of SLE and returning the self-reported paper questionnaire by the LE via the internet. The questionnaire takes place in several normal cellular processes, including introducing the failure of the plant cell wall, degradation processes in the cytoplasm, and the vital role of autophagy, and is being conducted annually by means of a self-reported paper questionnaire by the LE via the internet. The questionnaire takes place in several normal cellular processes, including introducing the failure of the plant cell wall, degradation processes in the cytoplasm, and the vital role of autophagy.

Results: There were 50 patients in the sub-group with ACPA positivity and RF negativity, 5 of them were smokers (39%, n=13). There were 97 patients in the sub-group with ACPA negativity and RF positivity, 28 of them were smokers (29%, n=97). There were 130 patients in the sub-group with ACPA negativity and RF negativity, 28 of them were smokers (21%, n=130). The highest prevalence of smokers was in the sub-group of patients with ACPA and RF positive rheumatoid arthritis (39%) and ACPA positive and RF negative rheumatoid arthritis (38%). The prevalence of smokers in ACPA negative sub-groups of patients with rheumatoid arthritis is significantly lower.

Conclusions: We confirmed that prevalence of smokers is significantly higher in the sub-group of patients with ACPA positive rheumatoid arthritis than in the sub-group with ACPA negative rheumatoid arthritis. Quitting smoking is highly recommended especially to these patients in order to achieve a favorable effect on the course of the disease.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5405

AB1128 CITRULLINATION OF PROTEINS, SMOKING AND RHEUMATOID ARTHRITIS
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Background: Rheumatoid arthritis (RA) is an inflammatory disease characterized by chronic synovitis and erosive destruction of articular cartilage and bone ultimately leading to joint deformities, disability, loss of quality of life and work loss. There are multiple risk factors, both environmental and genetic, that may predispose an individual to RA. Cigarette smoking is the most important risk factor. Citrulline contained within proteins is created post-translationally by the action of the enzyme peptidyl arginine deiminase on the aminoacid arginine. Citrullination takes place in several normal cellular processes, including introducing the failure of the plant cell wall, degradation processes in the cytoplasm, and the vital role of autophagy, and is being conducted annually by means of a self-reported paper questionnaire by the LE via the internet. The questionnaire takes place in several normal cellular processes, including introducing the failure of the plant cell wall, degradation processes in the cytoplasm, and the vital role of autophagy.
Results: Patients with a high internal health locus of control (HLCint 13.1 vs. 9.1) had less pain (numeric rating scale 0–10), less flares, a better mental and physical health related quality of life, lower disease activity and less fatigue. Patients with a high internal ‘doctor’-related health locus of control (HLCdoc 10.7 vs. 7.2) were older, had more co-morbidities, more disease damage and received more frequently an immunomodulatory therapy. No significant differences were found between the patients with a high external ‘doctor’-related HLC compared to the lower scoring patients (HLCcha 11.1 vs. 6.3). Participants with a high external ‘doctor’-related HLC had a more threatening view on their illness and a better adherence to medication (high adherence in 78.6% vs. 59.4%). Participants with a high internal HLC perceived their disease significantly less threatening. Higher education levels (school education, further education) went along with a decrease of external ‘doctor’-related HLC (HLCdoc).

Conclusions: Health locus of control has a significant impact in patients with SLE. The different disease characteristics, treatments, levels of medication adherence and illness perception were noticed. Holistic care needs to consider the impact different HLCs may have. The direction of causality cannot be proved beyond reasonable doubt in this cross-sectional analysis. Hence additional longitudinal studies are necessary.

Acknowledgements: The LuLa-study is supported by unrestricted grants from GlaxoSmithKline and UCB Pharma.

Disclosure of Interest: G. Chehab Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study. J. Richter Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study. R. Brinks: None declared. R. Fischer-Betz Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study. B. Winkler-Rohlfing: None declared. M. Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study

DOI: 10.1136/annrheumdis-2017-eular.3720

**AB1128 HELICOBACTER PYLORI IN SYSTEMIC LUPUS ERYTHEMATOSUS AS ITS ASSOCIATION WITH ENDOCOPIC AND HISTOPATHOLOGICAL FINDINGS**

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Background: Helicobacter pylori (Hp) is a Gram-negative bacteria and cause of most of the chronic gastric infections and its prevalence is above 50% worldwide. This infection is a well-known risk factor to gastric MALT lymphoma but also could be the trigger of several autoimmune diseases such as immune thrombocytopenic purpura and systemic lupus erythematosus

Objectives: To determine the frequency of H pylori in systemic lupus erythematosus patients (SLE).

Methods: A cross-sectional study was done in patients who fulfilled the 2012 SLICC criteria for SLE and were willing to sign the informed consent to be subjected to endoscopic procedure. The sample size was analyzed by pathologist. We used mean and standard deviation to describe the data, to compare both groups Student t test was done and for continuous variables we used chi-square; the correlation analysis was performed with Spearman correlation. The frequency of Hp infection was determined by histopathological evaluation of the endoscopic samples.

Results: Twenty two SLE patients were included and we chose a control group from database of endoscopic clinic with diagnosis of functional dyspepsia. The age range was 21–78 years and 14/22 were female. Two patients were excluded due to Hp infection and the control group was 12/20. We performed 27 endoscopic biopsies in SLE patients and 9 in control group. We found a high frequency of H pylori infection in patients with SLE. Metaplasic and dysplastic changes were also more prevalent in the SLE group. Our data support that Hp infection took place in early stages of disease.

Conclusions: Hp is an immune reactive agent in patients with SLE. It may play a role in SLE pathogenesis. Further research is needed to determine the real role of Hp in SLE.

References:

Disclosure of Interest: None declared

Disclosuer of Interest: None declared

**AB1130 RELAPSE RISK ASSESSMENT IN YOUNG APS PATIENTS WITH AN AUTOIMMUNE DISEASE: AN EXPLORATORY STUDY TO DETERMINE THE PREVALENCE OF SLE IN A YOUNG POPULATION**

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Background: Seropositive Antiphospholipid Syndrome (APS) is crucial in young adults (less than 50 years old) [1]. Young adults affected by APS are at increased risk of thrombotic events. The most frequent manifestation of arterial thrombosis in patients affected by APS is ischaemic stroke, especially in young adults (less than 50 years old) [1]. Young adults affected by APS are at increased risk of thrombotic events.

Objective: To determine, through a systematic review and meta-analysis, the prevalence of back pain (BP) and spondylarthritis (SpA) in the adult general population and explore the heterogeneity between studies in and out Latin America (LATAM).

Methods: MEDLINE, Embase, BIREME, LILACS and Web of Science were searched using a strategy combining key words and related database-specific subject terms to identify relevant cross-sectional studies based on COPCORD methodology published since 2006. Included articles were assessed for risk of bias and quality based on the STROBE statement. Prevalence figures for BP and SpA (European Spondyloarthropathy Study Group criteria) were analyzed according to female percentage of sampled individuals, mean age and sample size. A mixed effect model was used to obtain the combined prevalence and a meta-regression to estimate the effects of these variables. Prevalence stratified values were obtained according to its geographical location.

Results: 44 out of 127 papers in English, Spanish or Portuguese were selected. Of them, 16 contained BP or SpA prevalence data. Estimates for any SpA prevalence ranged from 0.1% to 2%, with an average of 0.3% (95% CI: 0.01%–0.05%). The random-effects pooled prevalence was 0.18% (0.06%–0.36%). The prevalence of BP was 6.54% (3.8%–9.2%) with a pooled value of 5.24% (2.6%–8.7%). In both cases the heterogeneity was significant (P<0.01). No effect was associated to SpA heterogeneity, but an increase in the prevalence of BP was associated to sample size (random effect coefficient: 0.045, p=0.04). The stratified analysis did not show differences in terms of heterogeneity or prevalence for BP (Pooled prevalence for BP: 5.4%; 2.9%–8.5%, p=0.9); on the contrary, for SpA, for non-LATAM studies, the pooled proportion was significantly bigger (prevalence in LATAM 0.05%, 0.01%–0.012%; non-LATAM: 0.35%, 0.09%–0.78%, p=0.02).

Conclusions: We found significant variations in prevalence across this review. In particular, they related to sample size of BP studies. Similarly, there was a significant variation between LATAM versus other latitudes respect to the prevalence of SpA. The limited number of studies included in this meta-analysis however, prevents clear explanations of the mechanisms underlying these results.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3916

**AB1139 A SYSTEMATIC REVIEW ON PREVALENCE OF BACK PAIN AND SPONDYLOARTHRITIS BASED ON COPCORD STUDIES**

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Objectives: To determine, through a systematic review and meta-analysis, the prevalence of back pain (BP) and spondylarthritis (SpA) in the adult general population and explore the heterogeneity between studies in and out Latin America (LATAM).

Methods: MEDLINE, Embase, BIREME, LILACS and Web of Science were searched using a strategy combining key words and related database-specific subject terms to identify relevant cross-sectional studies based on COPCORD methodology published since 2006. Included articles were assessed for risk of bias and quality based on the STROBE statement. Prevalence figures for BP and SpA (European Spondyloarthropathy Study Group criteria) were analyzed according to female percentage of sampled individuals, mean age and sample size. A mixed effect model was used to obtain the combined prevalence and a meta-regression to estimate the effects of these variables. Prevalence stratified values were obtained according to its geographical location.

Results: 44 out of 127 papers in English, Spanish or Portuguese were selected. Of them, 16 contained BP or SpA prevalence data. Estimates for any SpA prevalence ranged from 0.1% to 2%, with an average of 0.3% (95% CI: 0.01%–0.05%). The random-effects pooled prevalence was 0.18% (0.06%–0.36%). The prevalence of BP was 6.54% (3.8%–9.2%) with a pooled value of 5.24% (2.6%–8.7%). In both cases the heterogeneity was significant (P<0.01). No effect was associated to SpA heterogeneity, but an increase in the prevalence of BP was associated to sample size (random effect coefficient: 0.045, p=0.04). The stratified analysis did not show differences in terms of heterogeneity or prevalence for BP (Pooled prevalence for BP: 5.4%; 2.9%–8.5%, p=0.9); on the contrary, for SpA, for non-LATAM studies, the pooled proportion was significantly bigger (prevalence in LATAM 0.05%, 0.01%–0.012%; non-LATAM: 0.35%, 0.09%–0.78%, p=0.02).

Conclusions: We found significant variations in prevalence across this review. In particular, they related to sample size of BP studies. Similarly, there was a significant variation between LATAM versus other latitudes respect to the prevalence of SpA. The limited number of studies included in this meta-analysis however, prevents clear explanations of the mechanisms underlying these results.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4186
Methods: The analysis included 80 APS patients (≤50 years old) who presented a previous stroke event (patients who experienced cerebral venous sinus thrombosis were not included in the analysis). Clinical and laboratory data were retrospectively collected. Treatment was based on physician’s opinion according to the current guidelines. The aGAPSS was calculated for each patient by adding the points corresponding to the risk factors, based on a linear transformation derived from the β regression coefficient as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for aCL IgG/IgM, 4 for anti-β2glycoprotein I IgG/IgM and 4 for LA. Relapse was defined as the recurrence of thrombotic event and/or progression of known ischaemic lesions detected with MRI.

Results: Results pointed out that patients with relapse of thrombotic events and/or progression of known ischaemic lesions were 39 out of 80 (48.7%) and patients without relapse were 41 out of 80 (51.3%). Significantly higher aGAPSS values were observed in relapse group when compared to the non-relapse group [mean aGAPSS 9.08 (S.D. 4.7) Vs. mean aGAPSS 7.22 (S.D. 3.3); T test; p=0.05]. Distribution of aGAPSS values among the two groups is illustrated in Graph 1.

Conclusions: Our analysis suggests that aGAPSS could represent an effective tool to stratify the risk of relapse of thrombosis and/or progression of ischaemic lesions in young APS patients with clinical history of stroke. This data could also aid developing different therapeutic approaches, especially for patients at higher risk of relapse.

References:

Disclosure of Interest: None.

Acknowledgements: None.

AB1131 HIGHER RATES OF OBESITY AND ASSOCIATIONS WITH POORER CLINICAL STATUS IN PATIENTS WITH RA, OA AND SLE: A CROSS-SECTIONAL STUDY FROM ROUTINE CARE

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Background: Obesity is a risk factor for many chronic rheumatic diseases. In rheumatoid arthritis (RA), obesity is associated with increased comorbidities, higher medical costs, disease activity, and poorer physical function.1 In OA, obesity is a risk factor for both incidence and progression, and has a negative impact on outcomes2. In systemic lupus erythematosus (SLE), obesity is associated with more severe renal involvement, lower quality of life, and increased cardiovascular risk3.

Objectives: To assess associations of obesity with patient self-report multidimensional health assessment questionnaire (MDHAQ) scores and physician global assessment scores in patients with RA, OA, and SLE seen in routine care.

Methods: All patients at one academic center complete a MDHAQ, which includes a 0–10 scale for physical function (PF), 0–10 visual analogue scales (VAS) for pain (PN) and patient global assessment (PATGL), compiled into a composite score (MDHAQ). Patients complete a VAS for patient global (PATGL). Body Mass Index (BMI) was calculated from the medical record as weight (kg)/ height (meters)2. Patients were classified by BMI as normal (18.5–25), overweight (25–30), or obese (>30) according to the WHO guidelines. Demographic and clinical MDHAQ data were compared in the 3 diagnostic groups according to BMI groups using ANOVA and chi-square tests.

Results: 396 patients with RA, 425 with OA, and 306 with SLE were studied. Obesity was reported by 40% of RA and SLE patients, and 59% of OA patients. More than 10% were higher than matched individuals in the general population in the same region (30.8%). Obesity was higher in African-American patients (48% in RA, 70% in OA, and 53% in SLE). Education level, gender, and age did not differ significantly across the groups. Obesity was associated with poorer physical function, poorer patient global and higher pain in all 3 diagnostic groups, with higher depression scores in OA and SLE (Table). DOCGl was significantly higher only in OA (data not shown).

Table 1. MDHAQ scores and physician global assessment according to BMI groups

<table>
<thead>
<tr>
<th>MDHAQ scores</th>
<th>Normal (BMI=18.5–25)</th>
<th>Overweight (BMI=25–30)</th>
<th>Obesity (BMI&gt;30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA (N=381)</td>
<td>110 (29%)</td>
<td>112 (30%)</td>
<td>154 (40%)</td>
</tr>
<tr>
<td>Function (0–10)</td>
<td>2.1 (2.2)</td>
<td>2.4 (2.2)</td>
<td>2.9 (2.0)*</td>
</tr>
<tr>
<td>Pain (0–10)</td>
<td>4.4 (2.8)</td>
<td>4.6 (3.0)</td>
<td>5.1 (3.1)*</td>
</tr>
<tr>
<td>Fatigue (0–10)</td>
<td>3.4 (3.1)</td>
<td>3.6 (3.1)</td>
<td>4.5 (3.1)*</td>
</tr>
<tr>
<td>PATGL (0–10)</td>
<td>3.8 (2.7)</td>
<td>4.1 (3.1)</td>
<td>4.8 (2.8)*</td>
</tr>
<tr>
<td>Depression (0–3)</td>
<td>0.5 (0.7)</td>
<td>0.5 (0.7)</td>
<td>0.6 (0.8)</td>
</tr>
<tr>
<td>OA (N=420)</td>
<td>60 (14%)</td>
<td>102 (24%)</td>
<td>247 (59%)</td>
</tr>
<tr>
<td>Function (0–10)</td>
<td>1.7 (1.5)</td>
<td>2.6 (1.8)</td>
<td>3.2 (2.0)*</td>
</tr>
<tr>
<td>Pain (0–10)</td>
<td>5.1 (2.9)</td>
<td>6.7 (2.5)</td>
<td>6.6 (2.6)*</td>
</tr>
<tr>
<td>Fatigue (0–10)</td>
<td>3.4 (2.9)</td>
<td>4.3 (2.9)</td>
<td>5.3 (3.1)*</td>
</tr>
<tr>
<td>PATGL (0–10)</td>
<td>4.5 (3.1)</td>
<td>5.7 (2.5)</td>
<td>5.9 (2.7)*</td>
</tr>
<tr>
<td>Depression (0–3)</td>
<td>0.4 (0.6)</td>
<td>0.6 (0.8)</td>
<td>0.7 (0.8)*</td>
</tr>
<tr>
<td>SLE (N=299)</td>
<td>84 (28%)</td>
<td>85 (28%)</td>
<td>121 (40%)</td>
</tr>
<tr>
<td>Function (0–10)</td>
<td>1.4 (1.5)</td>
<td>1.2 (1.6)</td>
<td>2.3 (2.1)*</td>
</tr>
<tr>
<td>Pain (0–10)</td>
<td>3.5 (3.2)</td>
<td>3.9 (3.1)</td>
<td>5.2 (3.3)*</td>
</tr>
<tr>
<td>Fatigue (0–10)</td>
<td>4.2 (3.3)</td>
<td>4.2 (3.4)</td>
<td>5.1 (3.2)</td>
</tr>
<tr>
<td>PATGL (0–10)</td>
<td>3.6 (2.9)</td>
<td>3.9 (3.1)</td>
<td>4.5 (3.2)*</td>
</tr>
<tr>
<td>Depression (0–3)</td>
<td>0.4 (0.6)</td>
<td>0.4 (0.6)</td>
<td>0.7 (0.8)*</td>
</tr>
</tbody>
</table>

Conclusions: Obesity is more prevalent in patients with rheumatic diseases compared with the general population. Obese patients had poorer status on most MDHAQ scores, particularly physical function and pain. Obesity is an important comorbidity in patients with rheumatic diseases.

References:

Disclosure of Interest: I. Castrejon: None declared, N. Shakoor: None declared, J.A. Block: None declared, T. Finchus Shareholder of: Health Report Services, Inc
DOI: 10.1136/annrheumdis-2017-eular.3812
HIGH CONSUMPTION OF SEAFOODS OR VEGETABLES NEGATIVELY CORRELATES WITH DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS


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Background: Food intake is one of the important environmental factors of various diseases, and possibly influences the pathogenesis of RA. However, we have little knowledge about the impact of food intake on the pathogenesis of RA. Because each country has its own food culture, the study focused on the dietary habit in Japan is essential in order to clarify the clinical impact of food intake in Japanese RA patients.

Objectives: The aim of this study is to clarify the relationship between the dietary habit of RA patients and their disease status.

Methods: We took the questionnaire survey about dietary habit in 2015, in KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort as an essential dietary status was also examined in this cohort. These data were combined and statistically analyzed.

Results: 563 RA patients were enrolled from KURAMA cohort; female: male 4:1, age 63 years old, disease duration 15.5 years, DAS28-ESR 2.8 on average. Multivariate analysis showed that the intake frequency of vegetables had statistically significant negative correlation with DAS28-ESR (β=-0.17, p<0.01), SDAI (β=-0.15, p<0.01) and MMP-3 (β=-0.13, p<0.01). The intake frequency of frozen foods had positive correlation with MMP-3 (β=0.12, p<0.01). The intake frequency of juice had positive correlation with DAS28-ESR (β=0.11, p<0.01) and SDAI (β=0.11, p<0.01) and MMP-3 (β=0.11, p<0.01). The "vegetables and fruits", "meat and fried foods", "vegetables and fruits", "meats and processed foods", and "processed foods" were associated with the development of ILD. There are many patients who are not diagnosed as definite connective tissue disease (CTD) patients. These patients may have undifferentiated connective tissue disease (UCTD).

Conclusions: This study implicates that the disease activity of RA may be alleviated by high consumption of vegetables and fruits, or seafoods. Disclosure of Interest: None declared


CHARACTERISTICS OF AUTOIMMUNE FEATURED INTERSTITIAL LUNG DISEASE IN KOREAN PATIENTS

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Background: Interstitial lung disease (ILD) includes a heterogeneous group of disorders that result in diffuse parenchymal lung disease, with overlapping clinical, radiographic, and physiologic manifestations. Several rheumatologic conditions are associated with ILD. Interstitial lung disease is increasingly recognized in many patients who are not diagnosed as definite connective tissue disease (CTD). These patients may have an undifferentiated connective tissue disease (UCTD).

Objectives: The aim of this study was to compare the prevalence and characteristics of patients with CTD-ILD, UCTD-ILD and idiopathic pulmonary fibrosis (IPF) in Korean patients.

Methods: We studied the prevalence and characteristics of patients with connective tissue disease-associated interstitial lung disease (CTD-ILD), undifferentiated connective tissue disease-associated interstitial lung disease (UCTD-ILD), or idiopathic pulmonary fibrosis (IPF) between January 2016 and June 2016 in Korea university guro hospital. Clinical characteristics, laboratory tests, and high-resolution CT images were analyzed and compared among three groups.

Results: CTD-ILD was identified in 13.0%, UCTD-ILD in 18.2%, and IPF in 68.7% among 307 patients. Female and younger age patients were dominant in CTD-ILD group. Pulmonary symptoms were more common in IFP, while extra-pulmonary symptoms were more common in CTD-ILD and UCTD-ILD group. Patients with CTD-ILD had more abnormal antibody tests than those of UCTD-ILD and IFP. Usual interstitial pneumonia pattern was dominant in HRCT images among three groups.

Conclusions: CTD-ILD is not able to be diagnosed accurately in ILD patients. A systematic evaluation of extra-pulmonary symptoms and serologic tests in patients with ILD can identify CTD-ILD, UCTD-ILD, and IFP.

Disclosure of Interest: None declared

AB1135 ALLOPURINOL AND THE RISK OF INCIDENT PERIPHERAL ARTERIAL DISEASE IN THE ELDERLY AMERICANS: A U.S. MEDICARE CLAIMS DATA STUDY

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Background: Recently we found that use of allopurinol, the most commonly used xanthine-oxidase inhibitor therapy, was associated with a reduction of the risk of myocardial infarction and stroke, acute manifestations of CAD. Given that both PAD and CAD are manifestations of atherosclerosis and a similarity of disease pathophysiology between them, an obvious question was whether allopurinol use would reduce PAD. To our knowledge, no previous studies have examined whether allopurinol use reduces the risk of PAD.

Objectives: To examine whether new allopurinol use is independently associated with a reduction of the risk of incident peripheral arterial disease (PAD) in the U.S. elderly.

Methods: We used the 5% random Medicare sample from 2006–2012 to examine the association of allopurinol use and its duration with risk/hazard of incident PAD, in a retrospective cohort study. Multivariable Cox regression models were adjusted for demographics, comorbidity, cardiac medications and cardiac conditions. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated

Results: A total of 25,282 incident allopurinol use in 3,167 beneficial, of which 3,167 allopurinol use episodes (12%) ended in incident PAD. In multivariable-adjusted analyses, allopurinol use was associated with HR of 0.89 (95% CI, 0.81, 0.95) for incident PAD, as was female gender, 0.84 (95% CI, 0.78, 0.90). In a separate multivariable-adjusted model, compared no allopurinol use, durations of incident allopurinol use were associated support from: HR: PAD; 181 days to 2 years, 0.88 (95% CI, 0.79, 0.97) and >2 years, 0.75 (95% CI, 0.63, 0.89). Other factors significantly associated with a higher hazard of PAD were age 75–85 and >85, female gender, higher Charlson index score, and black race. Sensitivity analyses adjusting for cardiac conditions and medications, confirmed these findings with minimal to no attenuation of hazard ratios.

Conclusions: New allopurinol use was independently associated with a lower risk of PAD in the elderly. Longer allopurinol use durations seemed more protective. Mechanisms of protective effect need to be studied in future studies.

 Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6848

THE AGE OF ONSET OF RHEUMATOID ARTHRITIS CORRELATES WITH AIR POLLUTION AND HEART EXPENDITURE: RESULTS FROM MULTINATIONAL DATABASES

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Background: Environmental variables contribute up to half of the variation in the rheumatoid arthritis (RA) susceptibility. We have recently reported that the age of RA onset (RAo) varies across latitudes around the world, starting younger around the Tropic of Cancer (1). Latitude gradients have been used as a surrogate for studying the influence of the environment on the risks of disease in order to generate regionalization. The development of the GEO-RA database between January 2016 and June 2016 in 41 countries.

Objectives: This is an exploratory study to assess whether the age of RAo correlates with tropospheric pollutants (2), electromagnetic fields, Inequality-adjusted Human Development Index (I-HDI) and Health Expenditures as per national census of participating countries.

Methods: The age of RAo was obtained from the GEO-RA group database that involves 2,481 patients from 41 countries. Information of the tropospheric pollutant PM10 (particulate matter 10µm), the I-HDI, and Health Expenditures per capita was obtained from the World Health Organization’s reports. The average of each country’s electromagnetic fields (nanotesla, nT) from the past 50 years was calculated using geographic coordinates per country through the magnetic field calculator of The National Centers of Environmental Information. Pearson’s correlation and linear regression were used to evaluate the correlation of these environmental variables with the age of RAo by country.

Results: Complete data sets were available in 35 of the 41 countries. Overall, the mean age of RAo was 44±4.8 years, the annual average of PM10 of 57.5±39.3 (µg/m³), the Health Expenditure per capita of US $22,127±2,742, and the electromagnetic fields of 41,900±8,720 nT. The age of RAo was younger in countries with high PM10 levels (r=-0.81, p<0.01), high inequality (I-HDI, r=0.59, 2010;188(2):143–9.

Disclosure of Interest: None declared

The role of social determinants on the prevalence of rheumatic diseases in Latin America. A multilevel copcord study


AB1137
THE ROLE OF SOCIAL DETERMINANTS ON THE PREVALENCE OF RHEUMATIC DISEASES IN LATIN AMERICA: A MULTILEVEL COPCORD STUDY

To determine the impact of individual and regional variables on the geographic distribution of RD across six Latin American countries.

Methods: This is a secondary multilevel analysis of the cross-sectional data of COPCORD studies that investigated the prevalence of RD in Argentina, Ecuador, Colombia, Mexico, Peru, and Venezuela. Individual factors were sex, age, comorbidities, job status, and Health Assessment Questionnaire (HAQ) score. Contextual level variables were country and subject's identification as indigenous. RD predictors, including individual and regional variables, particularly indigenous status were identified with logistic regression models. The effect of contextual variables was estimated with median odds ratio’s (OR) estimation.

Results: Most individuals included in this analysis came from urban areas (62.40%); their mean age was 43.12 years (95% CI 43.01–43.35); and 56.0% of COPCORD studies that investigated the prevalence of RD in Argentina, Ecuador, Colombia, Mexico, Peru, and Venezuela. Individual factors were sex, age, comorbidities, job status, and Health Assessment Questionnaire (HAQ) score. Contextual level variables were country and subject's identification as indigenous. RD predictors, including individual and regional variables, particularly indigenous status were identified with logistic regression models. The effect of contextual variables was estimated with median odds ratio’s (OR) estimation.

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Conclusions: The most common diagnosis was arthritis (40% type unspecified, 19% rheumatoid arthritis), followed by fibromyalgia/chronic widespread pain (24%) and ‘other pain diagnosis’ (23%). We identified four clusters of engagement: high (14%), moderate (22%), low (39%) and tourists (25%). Median days of data entry ranged from 1–175 (IQR: 0–175) for the tourist and high engagement clusters, respectively. Those in the high and moderate clusters (n=2249, 35%) engaged on at least 50% of days in the study (high: 79%; moderate: 50%). Highly engaged participants were older (median 56 [47–63]) when compared to those who were low engagers (47 [39–57]) or tourists (49 [40–58]). A lower proportion of tourists were women (76% [95% CI: 74–78]), than in any other cluster (high: 82% [80–85], moderate: 84% [82–86], low: 81% [79–82]).

Conclusions: There are common factors associated to the prevalence of RD in the region, however, the estimation of its impact varies in significant way across countries and related to the fact of belong to an indigenous group indicating an increase in the estimated ORs.

Acknowledgements: National Council for Science and Technology (CONACyT); Collegio Mexicano de Reumatología (Mexico). EsSalud (Perú), Universidad de Cuenca (Ecuador), ASOREUMA (Colombia), Fedrico Wilhelm Agriola Foundation (Argentina), PDVSA East, SUELOPETROL and Bristol-Myers Laboratory (Venezuela)

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5509

AB1138
ENGAGEMENT IN A UK SMARTPHONE STUDY EXAMINING THE ASSOCIATION BETWEEN WEATHER AND PAIN: PRELIMINARY RESULTS FROM CLOUDY WITH A CHANCE OF PAIN


AB1138
ENGAGEMENT IN A UK SMARTPHONE STUDY EXAMINING THE ASSOCIATION BETWEEN WEATHER AND PAIN: PRELIMINARY RESULTS FROM CLOUDY WITH A CHANCE OF PAIN

K. Druce, J. McBeth, S.N. van der Veer, D.A. Selby, B. Wijdenes, K. Georgatzis, A.M. Chowdry, L. Rakhsmimaranayana, D.M. Schultz, C. Sanders, J.C. Sergeant, W.G. Dixon. 1Arthritis Research UK Centre for Epidemiology, University of Manchester; 2NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester; 3Department of Statistics, University of Warwick, Coventry; 4Oxford Internet Institute, University of Oxford, Oxford; 5School of Informatics, University of Edinburgh, Edinburgh; 6uMotif, London; 7Centre for Atmospheric Science, School of Earth and Environmental Sciences; 8Medical Sociology, Division of Population Health, Health Services Research and Primary Care, University of Manchester, Manchester, United Kingdom

Background: Smartphones can facilitate collection of temporally-rich self-reported data and have proven to enable large recruitment. However, their viability to support epidemiological research is uncertain due to concerns about selection bias and unsustained engagement.

Objectives: To examine the characteristics and engagement of participants in the first six months of Cloudy with a Chance of Pain, a UK smartphone-based study investigating the link between the weather and chronic pain.

Methods: Between 20th of January and 29th of February 2016, we recruited UK residents 17 years or older with chronic pain (>3 months) who owned a smartphone. Participants received prompts from an app developed by uMotif, which they needed to daily report the severity of ten pain-related symptoms (5) for at least 50% of days in the study (high: 79%; moderate: 50%). Highly engaged participants were older (median 56 [47–63]) when compared to those who were low engagers (47 [39–57]) or tourists (49 [40–58]). A lower proportion of tourists were women (76% [95% CI: 74–78]), than in any other cluster (high: 82% [80–85], moderate: 84% [82–86], low: 81% [79–82]).

Conclusions: Smartphones can facilitate collection of temporally-rich self-reported data and have proven to enable large recruitment. However, their viability to support epidemiological research is uncertain due to concerns about selection bias and unsustained engagement.

Methods: Between 20th of January and 29th of February 2016, we recruited UK residents 17 years or older with chronic pain (>3 months) who owned a smartphone. Participants received prompts from an app developed by uMotif, which they needed to daily report the severity of ten pain-related symptoms (5) for at least 50% of days in the study (high: 79%; moderate: 50%). Highly engaged participants were older (median 56 [47–63]) when compared to those who were low engagers (47 [39–57]) or tourists (49 [40–58]). A lower proportion of tourists were women (76% [95% CI: 74–78]), than in any other cluster (high: 82% [80–85], moderate: 84% [82–86], low: 81% [79–82]).

Conclusions: Cloudy with a Chance of Pain recruited a large sample of people with chronic pain, of whom one in three participants engaged in smartphone-based symptom reporting for at least 50% of days in the first six months. Smartphone studies require quick mass participation with sustained daily data entry, providing unprecedented volumes of daily data. While there may be selection bias towards older females in our study, younger men are also less likely to participate in studies using traditional data collection methods. Our study suggests that smartphones could provide a viable alternative to traditional data collection methods.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2692

AB1139
AUTOANTIBODY AGAINST COMPLEMENT COMPONENT 1Q SUBCOMPONENT IS ASSOCIATED WITH THE PATHOGENESIS OF RECURRENT PREGNANCY LOSS


AB1139
AUTOANTIBODY AGAINST COMPLEMENT COMPONENT 1Q SUBCOMPONENT IS ASSOCIATED WITH THE PATHOGENESIS OF RECURRENT PREGNANCY LOSS

K. Ohmura, K. Oku, T. Kitaiotai, M. Kono, S. Tanimura, E. Sugawara, R. Hisada, H. Nakamura, G. Shimamura, Y. Fujieda, M. Kato, T. Bohgaki, O. Amengual, S. Yasuda, M. Sugura-Ogasawara, T. Atsumi. 1Division of Rheumatology, Endocrinology and Nephrology, Hokkaido University Graduate School of Medicine, Sapporo; 2Department of Obstetrics and Gynecology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Background: In recurrent pregnancy loss (RPL), the pathogenesis of the majority of cases remains to be explained. Antiphospholipid syndrome (APS) is one
of the disorder responsible for causing RPL and its overwhemled complement activation recognized as a major pathogenic mechanism. Autoantibodies against complement component 1q subcomponent (aC1q) have been shown to associate with complement activation in primary APS, but the relevance of aC1q in RPL is still unclear. We hypothesized that aC1q would be associated with the pathogenesis of RPL in patients with or without APS, especially in RPL of unknown etiology.

**Objectives:** The aim of this study was to explore the significance of aC1q in RPL.

**Methods:** As a clinical study, we conducted a retrospective cross-sectional study comprising a total of 134 patients with RPL of unknown etiology. 27 with obstetric APS (OAPS), 14 parous patients with connective tissue disease (CTD) without historical obstetric/thrombotic complications and 17 parous healthy controls (HC). Serum levels of aC1q were measured using a solid-phase ELISA (Buhmann Laboratories AG, Switzerland) and defined as positive using cut-off value of more than 15 U/mL according to the manufacturer. In murine model, 8–12 week-old female BALB/c mice were mated with isolated males and the presence of vaginal plug was defined as day 1 of pregnancy. Mice were treated with intravenous injections of anti-mouse C1q monoclonal antibody (JL-1), isotype control IgG2b or PBS. To block C5a receptor (C5aR), mice were intravenously pre-treated with anti-C5aR antibody, 30 minutes before the injection of JL-1 on day 8. Mice were sacrificed on day 16 of pregnancy and fetal resorption ratios, weight of fetuses and placentas, serum levels of C3a and immunohistochemical staining of complement components on placental tissue were compared among each group.

**Results:** Among RPL, OAPS, CTD and HC, 47 (35%), 8 (30%), 3 (21%) and 2 (12%) were positive for aC1q, respectively. In RPL patients, aC1q was more prevalent (p < 0.05) and its titer was significantly higher than in HC (median and interquartile range [IQR] 12 [8–21] vs. 0 [0–4.3], p < 0.001) (Figure 1). In murine model, fetal resorption ratio was higher (p < 0.01), weight of fetuses and placentas lower (p < 0.05), and serum levels of C3a higher (p < 0.01) in mice treated with JL-1 than in control mice. Immunohistochemical findings showed that complement components were more deposited on plaencta in JL-1 treated mice than in control mice. Furthermore, the additional blockade of C5aR cancelled the pathogenic changes in JL-1 treated mice.

**Conclusions:** Clinical findings showed that aC1q could be relevant to RPL. Moreover, we have established aC1q induced pregnancy loss model mouse. Our study indicates that aC1q has a pathophysiologic role in RPL and that anticomplement therapy might be effective for at least some groups of patients with RPL for whom specific treatment remains to be established.

**Disclosure of Interest:** None declared

**AB1140**

WHO DISABILITY ASSESSMENT SCHEDULE 2.0 IS RELATED TO UPPER AND LOWER EXTREMITY SPECIFIC QUALITY OF LIFE

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**Background:** Musculoskeletal complaints influence disability, but the relative contribution of concurrent upper and lower extremity health-related quality of life (HRQOL) on patient perceptions of disability is unclear.

**Objectives:** We evaluated whether two disease specific quality of life instruments (DASH and WOMAC) reflect a patient’s perception of general disability using the WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) and determined whether disability components are explained by upper and lower extremity HRQOL.

**Methods:** We recruited 421 randomly chosen participants 50 years or older without stroke, cancer, or history of surgery for musculoskeletal disease who participated in the Namgang Cohort. Upper extremity HRQOL was determined with the DASH score and lower extremity HRQOL with the WOMAC, as a measure of disability to obtain “HRQOL. Multiple regression analysis was used to assess the relative contributions made by upper and lower extremity HRQOL to disability.

**Results:** Most patients reported knee pain (61.0%), shoulder (17.1%), elbow (28.5%) and hand (56.1%). Mean WHODAS 2.0 total score was 28.06 (SD=14.2), corresponding to mild to moderate disability and WOMAC and DASH scores were 23.2 (SD=22.1) and 22.4 (SD=19.3). When adjusted for age, sex, level of education, spouse, self rated health, hypertension, DM and depression, the DASH total score was correlated with the getting around (r=0.137, p=0.032) and social participation (r=-0.226, p<0.001) and the WOMAC total score was correlated with the getting around (r=0.362, p<0.001) and social participation (r=0.289, p<0.001)

**Conclusions:** We found that in a community-based population, perceived activity limitation and social participation were associated with upper and lower extremity HRQOL. Since the WHODAS 2.0 does not target a specific disease (as oppose to the DASH, WOMAC), it can be used to compare disabilities caused by different diseases.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4589

**AB1141**

PREVALENCE OF LONG-TERM STEROID THERAPY: FRENCH DATA

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**Background:** Corticosteroids are widely used for various diseases, from chronic respiratory conditions to auto-immune disorders. However, there are few epidemiological data about long-term steroid therapy in southern Europe (1, 2, 3).

**Objectives:** To describe chronic glucocorticoid prescriptions in a large cohort.

**Methods:** Information was collected from a national public health-insurance database that covers 4.1 million individuals and 83% of the population, in our geographic area of Provence-Alpes-Côte-d’Azur and Corsica, from September 1, 2009 through August 31, 2011. We identified subjects aged of 15 years and over starting glucocorticoid therapy. Chronic glucocorticoid therapy was defined as ≥7.5mg of prednisone equivalent per day during at least 90 days consecutive. We identified the incident cases of long-term glucocorticoid therapy, defined as those prevalent cases who did not fill glucocorticoid prescriptions during the first 6 months of the 24-month study period.

**Results:** We identified 32,812 patients who were prescribed glucocorticoid therapy, yielding 0.97% prevalence. Of these 32,812 patients, 14,205 (43.3%) met our definition of incident cases, yielding an incidence of 0.42% for 18 months in the overall population aged at least 15 years, corresponding to an incidence of long-term glucocorticoid therapy of 2.8/1000 inhabitants/year. Among the incident cases, the most currently prescribed glucocorticoids were prednisolone (64%) and prednisone (32%). Thirty-six per cent of patients received only one type of glucocorticoid while 33% received two and 5% received 3 or more of them. The average treatment duration was 270.9 days (CI 95% 267.7 – 274).

**Conclusions:** Long-term corticosteroid therapy is frequent in France, its description is close to what is already known in Europe.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6792
AB1142 VITAMIN D LEVELS AND ASSOCIATION WITH DISEASE ACTIVITY IN PARAGUAYAN SLE PATIENTS

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Background: Systemic Lupus Erythematosus (SLE) is a systemic inflammatory disease associated with genetic, environmental, hormonal and immunological factors. Vitamin D levels are nowadays considered as one possible factor associated with disease activity. Therefore, previous studies have analyzed vitamin D to the severity of SLE.

Objectives: To assess the Vitamin D status in paraguayan SLE patients and its association with disease activity.

Methods: An observational Trial has been performed on individuals diagnosed with SLE. Epidemiological, clinical and biochemical data have been recorded for each patient to study the association between vitamin D concentrations, the phospho-calcium metabolism parameters and disease activity. Quantitative determination of Vitamin D was performed using chemoluminescence ARCHITECT assay. Vitamin D status was interpreted as follows: deficiency <20 ng/ml and insufficiency 21–29 ng/ml. The statistical association tests were performed using linear (SLEDAI activity index) and logistic (inactive/Mild vs Moderate/Severe) regressions. The epidemiological, clinical and biochemical variables were used as explanatory variables in these models.

Results: We included 77 SLE patients, of whom 94.8% (73/77) were female. The average age of patients at the time of the study was 30.7±10.3 years. All patients received calcium supplements associated with vitamin D. The average vitamin D concentration was 32.2±12.1 ng/ml. 29.9% (23/77) of patients had vitamin D insufficiency and 13.0% had vitamin D deficiency. 94.8% (73/77) of the population had normal serum calcium and the total population had a normal phosphoraemia. As for the dosage of PTH, it was found that 27.3% (21/77) have high values of PTH. 20.8% (16/77) of the patients had positive anti-DNA. Low C3 complement was observed in 30/77 (39%) and low C4 in 50/77 (64.9%) patients.

The mean value of SLEDAI at the time of the study was 2.32±2.83. When we study the distribution of vitamin D concentration according to the disease activity (SLEDAI) a clear pattern is observed linking lower vitamin D concentrations with higher disease activity. (OR 0.93, 95% CI 0.88–0.99; P=0.001). The prevalence of erosions increased with longer disease duration. Patients who were CCP+ had higher rates of prevalent erosions than those who were CCP– with similar disease duration.

Conclusions: Erosions were common in this cohort of patients, and prevalence of erosions increased with longer disease duration. Patients who were CCP+ had higher rates of prevalent erosions than those who were CCP– with similar disease duration.

AB1143 THE IMPACT OF ANTI-CYCLIC CITRULLINATED PEPTIDE SEROPOSITIVITY ON EROSION PREVALENCE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS OF VARYING DISEASE DURATION

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Background: Little is known regarding the prevalence of erosive disease in a contemporary cohort of patients with RA and whether erosive disease prevalence differs by disease duration and seropositivity to anti-citrullinated protein antibodies (ACPA).

Objectives: To characterize the proportion of patients with RA with erosive disease by disease duration category and stratified by positive and negative serological status (anti-cyclic citrullinated peptide [anti-CCP], a surrogate for ACPA).

Methods: We identified patients with RA aged ≥18 years who were enrolled in the Corrona registry (October 2001–June 2016), with available disease duration, radiographic/MRI/ultrasound studies and serological status based on anti-CCP. Patients were grouped based on RA disease duration (0–2, 3–5, 6–10 and >10 years from diagnosis). Unadjusted prevalence erosion rates were calculated based on the proportion of patients with reports of erosions present on joint radiographs/MRIs/ultrasounds. Seropositivity was based on laboratory results (anti-CCP ≥20 U/mL) at enrolment in the Corrona registry. Chi-squared tests were used to assess differences in prevalence rates.

Results: There were 9759 patients who met inclusion criteria. Most were women (76%), middle-aged (mean [SD] 57 years [14]), with moderate disease activity (mean [SD] CDAI 14.7 [13.4]). Prevalence of at least one biologic or targeted synthetic DMARD had occurred in 41% of patients. Overall, the prevalence of erosive disease was 28.6%, with higher prevalence among CCP+ (35.4%) vs CCP– (20.1%) patients (p<0.001, chi-squared test). The prevalence of erosions increased with increasing disease duration (p<0.001; Table). For each disease duration group, the prevalence of erosions was higher in patients who were CCP+ compared with those who were CCP–.

Table 1. Prevalence of Erosions According to Disease Duration and Serological Status

<table>
<thead>
<tr>
<th>Disease duration (years)</th>
<th>CCP–</th>
<th>CCP+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>19.3 (905/4699)</td>
<td>28.3 (475/1678)</td>
</tr>
<tr>
<td>Serological status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCP–</td>
<td>16.1 (359/2226)</td>
<td>22.7 (169/744)</td>
</tr>
<tr>
<td>CCP+</td>
<td>22.1 (546/2473)</td>
<td>32.8 (306/934)</td>
</tr>
</tbody>
</table>

Data are % (n/N).

Conclusions: Erosions were common in this cohort of patients, and prevalence of erosions increased with longer disease duration. Patients who were CCP+ had higher rates of prevalent erosions than those who were CCP– with similar disease duration.


DOI: 10.1136/annrheumdis-2017-eular.1657

AB1144 GOOD THERAPEUTIC RESPONSE WITH BIOLOGICS: REMISSION IS RELIABILITY. DATA FROM THE AUSTRIAN BIOREGISTRY

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Scientiﬁc Abstracts

1456
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Background: Remission or at last low disease activity is the aim of drug therapy
in patients with chronic inﬂammatory rheumatic diseases. We evaluated disease
activity in patients treated with biologics and using data of the Austrian biologic
registry.
Objectives: The aim of this evaluation was to elucidate disease activity in patients
with rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA)
at baseline and at control-visits every six months after inclusion in BioReg.
Methods: Data were extracted from the Austrian BioReg registry (http://www.
bioreg.at) which was initiated in 2009 to document patients treated with one of
the biologics approved in Austria. Patients with ongoing biologic therapy as well
as biologic-naïve patients starting biologic therapy can be included (baseline,
BL). Further documentation is recommended about every six months (V1,V2 up
to V11). Meanwhile, 1877 patients (rheumatoid arthritis (RA) n=1046, ankylosing
spondylitis (SpA) n=446, psoriatic arthritis (PsA) n=322, other disease n=63) have
been documented. Estimation of disease activity is done using DAS-28 as well as
RADAI-5 in RA, SASPA in PsA, and BASDAI in SpA.
Results: DAS-28 (median values of BL; V1; V2; V9; V10) of patients with RA
are 3,30; 2,51; 2,58; 2,52; 2,49, the respective RADAI-5 values are 3,2; 2,4; 2,2;
2.0; 2,3. BASDAI in patients with SpA were 3,60; 2,61; 2,45; 2,63; 2,20. Median
values of inﬂammation’s laboratory markers (ESR in mm/1st hour and CRP in
mg/l) were always within the normal range (ESR and CRP in RA 15; 12; 12; 12,5;
14 and 2,0; 2,0; 2,0; 2,0; 2,0; in SpA: 8; 6; 7; 8; 8; and 2,0; 1,4; 1,4; 1,1; 1,0 in
PsA 9; 8; 9; 7 (V7); 6 (V8); and 1,6; 1,5; 1,4; 1,9 (V7); 0,8 (V8)).
Conclusions: Our data conﬁrm the efﬁciency of therapy with biologicals. During
5 years of continuous treatment more than half of patients with RA reach and
keep remission with a DAS-28 below 2,6 and normal values of ESR and CRP.
Also patients with SpA and PsA show similar successful therapeutic response.
Acknowledgements: BIOREG is supported by an unlimited industrial grant
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3898

AB1145

GENDER, AGE AND PULMONARY FUNCTION IN DOMINICAN
PATIENTS WITH RHEUMATIC DISEASES

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Background: Interstitial lung disease (ILD) is a frequent entity in patients with
rheumatic diseases, worsening the prognosis of those who suffer it (1). Previous
studies have used the GAP (Gender, Age, Pulmonary function) model stage
system to determine mortality at 1, 2 and 3 years (2). For stage I is 5.6% the
ﬁrst year, 10.9% second and 16.3% the third. GAP II has a mortality of 16.2%,
29.9% y 42.1% for the ﬁrst, second and third year. For stage III, 39.2%, 62.1%
and 76.8% respectively (3)
Objectives: To perform GAP model stage system in Dominican patients with
Interstitial Lung Disease (ILD) related to Rheumatic Diseases (RD).
Methods: This is an observational, cross sectional study, with 42 patients who
presented ILD related to RD. The GAP model stage system was determined by
using demographic variables and pulmonary function tests such as spirometry
and lung diffusion capacity (DLCO).
Results: 36 patients were female; the median age was 45±12 years. The mean
value for Forced Vital Capacity (FVC) was 72%, Forced expiratory volume in 1
second (FEV1) 73%, and the ratio FEV1/FVC 99%. The DLCO mean value was
66±23 ml/min/mmHg. 35 patients (83.3%) were in stage I, 7 patients (16.6%) in
stage II and none in stage III. The statistical signiﬁcant variables were the time
of diagnosis of the RD (p=0.013); with 4.9 years for those in stage I and 10.8
years for stage II; the time of the diagnosis of the ILD (p=0.003) with 2.1 years for
patients in stage I and 4.8 years for stage II and smoking (p=0.063).
Conclusions: These ﬁndings suggest that the GAP model system is an useful
tool to stage patients with interstitial lung disease related to rheumatic diseases. It
can also help us make changes in treatment based on the stage. Special attention
must be paid to those with a longer time of diagnosis of the RD, time of diagnosis
of the ILD and/or smoking.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2152

AB1146

PHARMACOLOGICAL APPROACH OF KNEE OSTEOARTHRITIS
TREATMENT IN PRIMARY CARE IN SPAIN

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Background: Osteoarthritis (OA) is the most prevalent joint disease and the
leading cause of disability from 60 years onwards. In fact, 14,8% of the Spanish
population has OA.
Objectives: This study aimed to analyze the indications and average doses
prescribed in the treatment of knee osteoarthritis in Primary Care in Spain.
Methods: The EMARTRO study was designed as an observational, multicenter,
transversal study to compare probability of suffering a comorbidities based
on presence of symptomatic knee OA visited by GPs. Sociodemographic,
anthropometric, clinical parameters and clinical variables of interest were recorded.
The prescribed medications and doses indicated in syntomatic knee OA were
analyzed in patients included in the EMARTRO study.
Results: A total of 1173 patients were included, of whom 646 had knee OA.
Patients with OA had a mean (SD) BMI of 30.9 (5.1), systolic blood pressure 132.8
(14.5) and diastolic blood pressure 77.9 (9.1) mm Hg. They also had a mean
of 4.3 (1.9) comorbidities, the most frequent were hypertension 358 (62.2%),
dyslipidemia 336 (58.3%), diabetes mellitus II 126 (21.9%), and gastroesophageal
reﬂux 110 (19.1%). As for the symptomatology, the patients presented a mean
(SD) pain in Huskisson’s VAS of 65.18 (15.27) mm and algofunctional Lequesne
score of 11.35 (4.86).
Patients were treated with a mean of 2,2 medications. The 45.5% of osteoarthritic
patients were treated as monotherapy, 35.5% were taking 2 medications for
osteoarthritis, 15.3% 3 and 3.7% 4 or more medications. It should be noted,
taking into account the high levels of pain, that 15% of the patients did not receive
any treatment.
Regarding prescribed medications for knee OA, 378 (58.2%) patients were treated
with paracetamol at a mean daily dose (SD) of 1,150.5 (1,815.5) mg; 232 (35.9%)
received NSAIDs, with metamizole being the most prescribed at doses 1,092
(538) mg, ibuprofen at doses 1,136 (528,8) mg and naproxen at doses 941,8
(238,5) mg. Next, 131 (20.3%) patients were treated with opioids, tramadol being
the most frequent at doses 102.7 (49.7) mg; 87 (13.3%) with SYSADOA being
chondroitin sulphate the most frequent at doses 758.7 (247.7) mg. Finally, 87
(13.3%) of the patients were treated with COX-2, mainly with etoricoxib at doses
of 69.3 (27.1) mg.
Conclusions: Although the patients presented many concomitant pathologies,
it is frequent to approach osteoarthritis in polytherapy. In addition, despite the
high symptomatology, patients are treated primarily with a mild analgesic such as
paracetamol at doses lower than those recommended. It is paradoxical the high
prescription of NSAIDs in a population with a high prevalence of cardiovascular
and gastrointestinal pathologies as well as an increase in the prescription of
opioids.
Disclosure of Interest: M. Herrero Barbero Employee of: Bioiberica, S. Gimenez:
None declared, J. Vergara: None declared, E. Viles I Lladó Employee of:
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J. F. Frias: None declared, A. Castaño: None declared, J. J. Jiménez Díaz:
None declared, Á. Rodríguez de Cossío: None declared, R. Belenguer: None
declared, J. L. Llisterri: None declared, J. Vergés Milano Consultant for: Bioiberica,
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DOI: 10.1136/annrheumdis-2017-eular.3624

AB1147

COMORBIDITY PROFILE IN MEN AND WOMEN AFFECTED BY
SYNTOMATIC KNEE OSTEOARTHRITIS AND IMPACT OF
GENDER IN THE SYMPTOMATOLOGY AND PERCEPTION OF
HEALTH STATUS

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Background: Osteoarthritis (OA) is the most prevalent joint disease and the
leading cause of disability from 60 years onwards. In fact, 14,8% of the Spanish


population has OA. This study aimed to analyze the indications and average doses prescribed in the treatment of knee osteoarthritis in Primary Care in Spain.

Objectives: This study aimed to analyze the comorbidity profile of men and women affected by symptomatic knee OA and the differences between genders in terms of quality of life and mental health.

Methods: The EMARTRO study was designed as an observational, multicenter, transversal study to compare the probability of suffering a comorbidity based on gender with symptomatic knee OA visited by GPs. Sociodemographic, anthropometric, clinical, and laboratory parameters were collected. The probability of suffering a comorbidity based on gender OA was estimated using the Odds Ratio estimation with conditioned logistic regression models. Depending on the variable, comparisons between groups were done using t-Student, Chi-square and Mann-Whitney.

Results: A total of 646 patients were included, 71% were women. Mean (SD) age was 67.9 (6.6) years. Patients were obese without gender differences, with a BMI of 30.4 (4.4) and 31.2 (5.5) (p=0.0651) in men and women, respectively.

Men had a mean (SD) systolic blood pressure higher than women, 134.7 (15.0) vs 132.2 (14.5) mmHg (p=0.0453) and no differences were observed in diastolic pressure (p=0.5930).

As regards to the concomitant pathologies, no increase was detected in the likelihood of suffering comorbidities related to the gender [OR=0.607 (95% CI: 0.268; 1.397)] in men and OA. Men with OA were more likely to have angina pectoris [OR=4.493 (95% CI: 1.299–15.536) p=0.0176] and underwent coronary bypass [OR=3.706 (95% CI: 1.389-9.890) p=0.0089].

Osteoarthritic women elicited more pain in Huskisson’s VAS 62.8 (14.7) vs 56.6 (15.6) mm (p=0.0027) and worse function according to the Lequesne index 10.0 (4.9) vs 12.1 (4.7) (p<0.0001).

In terms of quality of life according to the EuroQol, women presented worse quality of life in dimension of mobility (p=0.0001) and in the dimensions of daily activities, pain/discomfort and anxiety/depression (p<0.0001).

Fatigue symptoms were more common in the Goldberg scale to detect psychological disorders (p<0.0001) and more cases of anxiety and depression according to the HAD scale (p<0.0001).

Conclusions: The results of the present study indicate that women with osteoarthritis of the knee, despite having the same diagnosis and a similar comorbidity profile to men, have a worse perception of health status regarding the symptoms of their osteoarthritis, their quality of life and their mental health.


DOI: 10.1136/annrheumdis-2017-eular.3625

INFODEMIOLOGY AND SEASONALITY OF SYSTEMIC LUPUS ERYTHEMATOUS USING GOOGLE TRENDS
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Background: People affected by chronic rheumatic conditions, such as systemic lupus erythematosus (SLE), frequently rely on Internet and search engines to look for terms related to their disease, and its possible causes, symptoms and treatments. “Infodemiology” and “infoveillance” are two recent terms created to look for terms related to their disease, and its possible causes, symptoms and treatments.

Methods: “Infodemiology” and “infoveillance” are two recent terms created to look for terms related to their disease, and its possible causes, symptoms and treatments. Infodemiology uses the large amount of data generated by Google Trends, a Big Data monitoring approach.

Results: We analyzed the large amount of data generated by Google Trends, considering “lupus”, “relapse” and “fatigue” in a 10-year web-based research. Google Trends automatically normalized data for the overall number of searches and presented them as relative search volumes, in order to compare variations of different search terms across regions and periods. The Mann-Kendall test was used to evaluate the overall seasonal trend of each search term and possible correlation between search terms.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1603

AB1149 THE ABILITY OF THE HEALTH SYSTEM TO IDENTIFY THE BURDEN OF RHEUMATOID ARTHRITIS IN SERBIA: A EULAR SURVEY
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Objectives: to estimate the rheumatoid arthritis (RA) prevalence in two urban regions of Serbia, covering the northern and the southern part, under the European League Against Rheumatism (EULAR) prevalence survey; to assess the ability of the health system to recognize and treat patients with RA.

Methods: The survey was conducted in four Serbian towns: Belgrade in the north and three towns in the south: Cacak (Moravichi region), Užice (Zlatiborski region) and Krusevac (Rasinski region), covering 36.5% of the total Serbian population with more than 99% Caucasians, mostly orthodox Serbs (83%), <4% Hungarian, Roms and Bosnians and a minority of other nationalities. The first-detection phase of the study comprised previously translated and validated telephone Questionnaire usage with 33 items covering signs, symptoms, self-reported diagnosis and classification criteria for RA (CAG 1987) (1). Diagnoses were confirmed by rheumatologists in a second-confirmation phase. Prevalence results were standardized for age and sex with regard to Serbian population (national census 2002). Confirmed RA cases were asked two more questions: “How long had you had symptoms before you were given the diagnosis of RA” and “How had you been treated for that period of time”.

Results: 6213 people were contacted and 63.6% answered the survey; joint pain was reported by 1,799 persons, and joint pain accompanied with joint swelling by 666 persons. A total of 23 RA cases were identified: 2 newly diagnosed. The standardized RA prevalence estimates were 0.30% (95% confidence interval [95% CI] 0.09;0.51) for the north, e.g. 0.09 (95% CI 0.08;0.26) for men and 0.49% (95% CI 0.19;0.79) for women. RA prevalence estimates were 0.42% (0.12;0.72) for the south; 0.28 (0.00;0.56) for men and 0.55% (0.09;1.00) for women, with
the female to male ratio 5.5:1 in the north and 2:1 in the south. Time period from the first symptoms occurrence to the RA diagnosis was 17.7 (13.2) months for the northern part and 25.0 (16.9) for the southern; 20.6 (14.9) for Serbia; in that period patients were mostly treated with NSAIDS (82%) and physical therapy (30%); short-lasting corticosteroids were given to 13%, peroral corticosteroids to 4% and no patients were treated with DMARDs.

Conclusions: RA prevalence in the southern and northern part of Serbia is in line (0.42% [95% CI 0.120.72] vs 0.30% [95% CI 0.090.51]), being more frequently presented in females as compared to males (five times more in the north and two times more in the south). Delay in diagnosis as compared to the first symptoms occurrence was 21 months and during that time no patients were treated with DMARDs.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4899

AB1150 SLEEP HEALTH AND QUALITY OF LIFE IN PATIENTS WITH KNEE OSTEOARTHRITIS BEFORE AND AFTER TOTAL KNEE REPLACEMENT

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Background: Studies report that sleep disturbances are often associated with chronic musculoskeletal disease. There is no agreed definition of sleep health, but some characteristics, such as sleep duration (number of hours daily) and sleep quality or satisfaction (subjective evaluation of good or poor sleep) are used to evaluate sleep health. In a previous study in patients with severe osteoarthritis awaiting total knee replacement (TKR), patients reporting good quality sleep had better health-related quality of life (HRQOL) measured by the specific WOMAC and generic SF-36 questionnaires.

Objectives: To measure sleep health in patients included on a waiting list for TKR and 12 months after TKR.

Methods: Prospective study with a 12-month follow up. Sociodemographic and clinical variables were determined. Sleep health: hours of sleep and reparative sleep (RS) was examined using the question “How well do you usually sleep?” on a Likert scale (1=good [RS], 2=regular, 3=badly, 4=with medication/treatment (non-reparative sleep [NRS]). Function and pain were measured using the WOMAC and SF-36 questionnaires. Comparisons were made using t-tests (paired samples) and McNemar’s test. Linear regression models were used to analyze associations. Dependent variables: WOMAC and SF-36 pain and function dimensions; independent variables: sleep quality, age, sex, BMI, number of comorbidities, depression/anxiety.

Results: 105 patients (79% female, mean age 69.39 years [SD 8.3]) were studied. In statistical studies the main risk factors were defined. Pain, function and sleep duration (WOMAC and SF-36) were measured using the WOMAC and SF-36 questionnaires. In comparisons of patients with RS (p=0.029). Patients with RS had better scores in all quality of life dimensions (<10 points) than those with NRS (p<0.05) at baseline and at 12 months. Multivariate analysis showed RS was independently associated with pain and function (WOMAC and SF-36) (p<0.007).

Conclusions: Sleep health was associated with better HRQOL before and after TKR. Although many patients had RS after TKR, 60% of patients continued not to have sleep health. Although often undervalued clinically, sleep health is closely associated with the health status.

Acknowledgements: This work was funded by project PI/13/00948, integrated in the Plan Nacional I+D+i and cofounded by ISCII-subdirección General de Evaluación and European Regional Development Fund (ERDF).

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1777

AB1151 MONTH OF BIRTH AFFECTS THE RISK OF RHEUMATIC DISEASES: A NATIONWIDE CASE-CONTROL STUDY

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Background: There have been several studies which demonstrated the impact of birth on the risk of certain diseases such as asthma or cardiovascular diseases. However, rheumatic diseases have not yet been thoroughly investigated in terms of association with birth month.

Objectives: In this study, we sought to determine whether birth month or season could affect the risk of rheumatologic diseases.

Methods: The birth month patterns of patients with rheumatic diseases were compared to those of the general population. We utilized the claim data of Health Insurance Review and Assessment Service (HIRA) which covers nearly 90% of total population in Korea. The associations between birth month/season and 32 diseases were investigated using logistic regression.

Results: Our dataset included 17,247,458 (male 9,220,760; female 9,026,708) individuals from HIRA database from January, 1997 to August, 2015. Among 27 rheumatic diseases, 8 diseases including Crohn’s disease (CD), ulcerative colitis (UC), rheumatoid arthritis (RA), systemic lupus erythematosus, polymyalgia rheumatica (PMR), ankyllosing spondylitis (AS), multiple sclerosis, gout, fibromyalgia (FM) were significantly associated with birth month (p<0.05). In terms of seasonality, CD, UC, RA, Sjogren’s syndrome, PMR, AS, Gout, and FM showed significant difference. CD, UC and AS showed higher prevalence in individuals born in winter and lower prevalence in summer. On the other hand, people who were born in summer showed higher possibility to have gout and FM compared to those born in winter. In consistent with previous reports, type 1 diabetes is more prevalent in those born in winter. Angina and myocardial infarction showed higher prevalence in patients born in spring and lower in fall. This consistency reflects the relevance of our dataset and methodology.

Conclusions: We found significant impacts of birth month/year on various rheumatic diseases. Seasonal variation of infectious agent such as exposure or food ingestion during gestation or early infancy may explain the association between birth month/season and certain disease development.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2891

AB1152 THE INCIDENCE OF HYPERSENSITIVITY TO NSAIDS IN THE GROUP OF PATIENTS WITH MUSCULOSKELETAL DISORDERS

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most common cause of drug hypersensitivity reactions (DHR). Recent studies show that the prevalence of hypersensitivity reaction to drug is particularly in Poland.

Objectives: To assess the frequency and the risk.od developing NSAID hypersensitivity in patients with chronic disorders of the musculoskeletal system.

Methods: The study group consisted of 200 patients (age 19–88 years - 54±14, women-161, men-39) hospitalized in the Department of Rheumatology in 2015-2016. All patients filled questionnaire regarding symptoms of DHR after ingestion of non-steroidal anti-inflammatory drugs. The presence of DHR, clinical pattern of the reaction, frequency of NSAIDs administration and comorbidities have been studied. In statistical studies the main risk factors were defined.

Results: Seventy-seven patients from study group (38.5%) reported symptoms that occurred within 24 hours after ingestion of NSAIDs ingestion. Symptoms characteristic for hypersensitivity reaction were reported by 40 patients (20%). Respiratory symptoms like dyspnea and/or cough were reported by 22 patients (11%). Cutaneous symptoms (urticaria/angioedema/dermal flush) were reported also by 29 patients (14.5%). Three patients experienced loss of consciousness. Thirty-seven patients reported isolated stomach cramps. The symptoms developed usually between 2–12 hours after drug intake. In 37 patients oral administration caused DHR reaction, moreover in 14 patients also topical application led to adverse reaction. In most of patients reaction appeared due to COX-1 inhibitor and interestingly in 3 patients reaction was evoked by celecoxib which is perceived to be safe alternative for patients with NSAIDs hypersensitivity. Chronic urticaria, asthma and systemic drug intake occurs the main risk factors of hypersensitivity.

Conclusions: Drug hypersensitivity reactions are reported very frequently in population of patients with chronic musculoskeletal disorders. Our studies suggest that patients taking protractedly NSAIDs are in group with high risk of drug hypersensitivity development.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017.eular.5408

AB1153 OSTEOPOROSIS RISK FACTORS IN PARTICIPANTS OF HEALTHY AGING ACADemy

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Background: Osteoporosis is a major cause of morbidity and mortality in elderly population. It is known that the mortality rate in European population within 1 year of hip fracture is about 30%, and another 30% of patients need long term nursing for the rest of their life. However, the prevalence and associated risk factors in the Polish elderly population have not been well documented. The aim of the
Background: Depression and suicidality are well-described comorbidities in psoriasis (PSO). The prevalence of these comorbidities in psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) is less well described.

Objectives: To assess the prevalence of depression and suicidality in PsA and axSpA in the recent literature, and compare rates to PSO.

Methods: For PsA and axSpA, we evaluated the recent English-language literature identified through a PubMed search; we used a recent review and performed a targeted review of the period since the publication in order to establish the rates for PSO for comparison. 5 Review articles were also examined to identify key publications.

Results: Rates of depression in PSO vary widely, depending on the outcome definition and method of ascertainment. Dowlatshahi et al. reported a pooled rate of 9.0–55.0%, with rates from the literature after the review period ranging from 9.0–39.8%. Rates for suicidality also varied widely, with 2.5–17.3% of patients (pts) reporting suicidal ideation. The limited data available provide ranges for depression in PsA of 3.4–28.6%, and in axSpA of 3.1–44.0%. The single study that differentiated between ankylosing spondylitis (AS) and non-radiographic (nr)-axSpA did not identify a difference between the two groups. 2 Very limited data exist on suicidality in PsA and axSpA. For PsA, the incidence rates (IR) of suicidal ideation, attempts, and suicide per 1000 person-years in the UK were 0.4, 1.3, and <0.001, respectively; 3 no prevalence data were identified. In a study in China, 2.5% of pts with axSpA reported a past suicide attempt, 4 while in Turkey, patients had higher rates of suicidal ideation, attempts, and suicide per 1000 person-years in the UK were 0.4, 1.3, and <0.001, respectively; 5 no prevalence data were identified. In a study in China, 2.5% of pts with axSpA reported a past suicide attempt, 4 while in Turkey, patients had higher rates of suicidal ideation, attempts, and suicide per 1000 person-years in the UK were 0.4, 1.3, and <0.001, respectively; 5 no prevalence data were identified. In a study in China, 2.5% of pts with axSpA reported a past suicide attempt, 4 while in Turkey, patients had higher rates of suicidal ideation, attempts, and suicide per 1000 person-years in the UK were 0.4, 1.3, and <0.001, respectively; 5 no prevalence data were identified. 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Only 13% of patient with fracture and 15% of all patients with osteoporosis and osteopenia were treated by antosteoporotic drugs (ibandronavion/aletromin). Calcium supplementation was received by 30% of patients with fracture and 43% supplemented vitamin D3.

Conclusions: The prevalence of osteoporotic fractures in population of relatively recent received by 30% of patients with fracture and 43% supplemented vitamin D3. Also, about endured fractures, osteoporosis risk factors, screening densitometry, treatment of osteoporosis, supplementation with vitamin D3 and calcium. Also, questions about classical risk factors for osteoporosis (loss of height (5 cm/year), family history, falls, loss of weight, treatment with steroids) were included to questionnaire.

Results: Fractures caused by fall from their own height were reported by 180 (27.9%). Moreover, 96 (14.88%) responders without fracture history declared more than 3cm decrease of height after their forties, what strongly suggest osteoporotic vertebral fractures. Forty three (24%) of the respondents had multiple fractures and single fractures were reported by 137 (76%) responders. The most common localization of fractures was forearm (57%), shin bones (10.4%) and foot bones (9%). Among subjects who underwent densitometry after the fracture 32% had the diagnosis of osteopenia; 19.4% were diagnosed with osteoporosis and in 23.1% bone density was within normal limits. The strongest risk factors for osteoporotic fractures were numerous falls per year (p<0.000) and frequent drinking of alcohol (p<0.008). The risk factors of fractures (sum of risk factors for falls and osteoporosis) among people with previous fractures vs. those without fractures were statistically significant (p=0.037). Only 13% of patient with fracture and 15% of all patients with osteoporosis and osteopenia were treated by antosteoporotic drugs (ibandronavion/aletromin). Calcium supplementation was received by 30% of patients with fracture and 43% supplemented vitamin D3.

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Prevalence of comorbidities in psoriatic arthritis: a cross-sectional study


Background: Psoriatic arthritis (PsA) is associated with important comorbidities: cardiovascular, gastro-intestinal, infectious, malignant, and psychiatric [1, 2]. However, they are less studied in PsA compared to other chronic inflammatory arthritis.

Objectives: The objective of this study was to calculate the prevalence of comorbidities and risk factors in a cohort of PsA patients.

Methods: This was an observational cross-sectional study, including consecutive, untreated PsA outpatients, patients treated with GS or PSL in 8 university hospitals in Romania.

Results: In all, 129 PsA patients were included: 77 (59.7%) women, mean age ± standard deviation 53.5±12.4 years, disease duration 7.7±4.8 years; 53 (41.1%) had peripheral arthritis, 33 (25.6%) dactylitis, 18 (14%) enthesis, and 24 (18.6%) current moderate/severe psoriasis. Most of them had low or moderate disease activity and almost a quarter of them (32; 24.8%) were taking a biologic. The most prevalent comorbidities were: dyslipidaemia 103 patients (79.8%), hypertension 87 (51.9%), obesity 44 (34.1%), diabetes 21 (16.3%) and ischemic heart disease 15 (11.6%). Almost a third of patients (42; 32.6%) suffered a cardiovascular event after their PsA diagnosis, of which heart attack 2 patients, stroke 4, cardiac failure 4 and peripheral arterial disease one patient. Cardiovascular events correlated with smoking (r=0.893, p<0.001) and current moderate/severe psoriasis (r=0.218, p=0.013).

Regarding infectious comorbidities: 11 patients (8.5%) had a history of tuberculosis after being diagnosed with PsA, 7 (5.4%) chronic viral hepatitis, of which 4 with B virus and 3 with C virus, and 5 patients (3.9%) developed severe infections. Five patients (3.9%) were diagnosed with neoplasia, but no correlation was identified with any of the clinical, biological or treatment related included variables. Only 11 patients (8.5%) were diagnosed with depression, but the prevalence is probably underestimated, since not all patients were screened to this end.

Conclusions: PsA is associated with a high prevalence of comorbidities, especially cardiovascular disease. This should be taken into consideration in the therapeutic and the global management of PsA patients.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5838

AB1158 PREVALENCE OF MUSCULOSKELETAL DISORDERS AMONG GARMEN T INDUSTRY WORKERS IN BANGLADESH

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Background: Garment industry is flourishing in many developing countries. Attention is often not paid to ergonomics. It is plausible that the prevalence of musculoskeletal (MSK) pain may be high among garment workers.

Objectives: To estimate the prevalence of symptoms and disorders (MSD) among garment workers in Bangladesh.

Methods: This cross sectional study was carried out among 350 workers in two garment factories by face-to-face interview. The COPCORD (Community Oriented Program for Control of Rheumatic Disorders) methodology was adopted for the survey. The workers were classified into cutting, sewing, finishing and quality operators. Trained interviewers identified subjects with musculoskeletal pain. Trained internists and rheumatologists examined the positive respondents.

Results: The point prevalence of musculoskeletal pain was 61.7%. The parts commonly affected during the preceding 7 days of interview in the whole group were: shoulder (17.9%), lower back (15.2%), neck (13.8%) and knee (10.8%). The cutting operators suffered more from back (15.4%), neck (15.4%) and lower limb (11.5%); sewing operators from lower limb (12.4%), back (8.5%) and upper limb (7.7%); finishing operators from lower limb (50%) and quality control group from back pain (50%). Multiple regional pains were more frequent (n=155) among all operators. The sewing and cutting operators suffered from multiple regional pains more than other operators. The prevalence of Rheumatoid arthritis (RA) 0.9%, spondyloarthropathy (SpA) 1.42%, undifferentiated arthritis (UA) 1.1%, nonspecific low back pain (NSLBP) 4.6%, soft tissue rheumatism (STR) 3.7%, osteoarthritis (OA) 0.9% and lumbar spondylosis 1.1%. Nonspecific pain was the commonest condition (63.7%).

Conclusions: Rheumatic disorders are common causes of morbidity, disability, and work loss among the garment workers of Bangladesh where male and female workers are almost equally affected. Multiple regional involvement are common in this occupational group. Mechanical disorders are the commonest.

Disclosure of Interest: None declared


AB1159 HIGH DOSE GLUCOCORTICOIDS AS A RISK FACTOR OF SIGMOID DIVERTICULITIS PERFORATIONS IN AUTOIMMUNE DISEASES

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Background: It has been reported that glucocorticoids (GCs) and non-steroidal anti-inflammatory drugs (NSAIDs) might increase sigmoid diverticulitis perforations (SDPs) for rheumatoid arthritis patients; however, there are few previous reports referring to the relationship between SDPs and GCs in patients with systemic autoimmune diseases. We investigate relationship between SDPs and GCs in patients with rheumatic diseases.

Objectives: To describe development of SDPs during high dose GC (over 50 mg/kg/day) therapy for systemic autoimmune diseases in our department, additionally reviewing previous reports with regard to the relationship between SDPs and GCs.

Methods: 187 patients hospitalized in our department from April 2015 to December 2016 were retrospectively reviewed.

Results: Among 187 patients, 61 took high dose GCs, 29 took moderate dose GCs (0.5–6.0mg/kg PSL equivalent), 53 took low dose (less than 0.5mg/kg PSL equivalent), and 29 didn’t take GCs. Four patients out of 61 who took high dose GCs developed SDPs (Table). Nobody developed SDPs in moderate, low and
not any dose GCs group. Case 1–3 took NSAIDs. Case 2 received mPSL pulse therapy (mPSL 1 g × 3 days). Case 1 and 2 developed SDPs within 3 months from initiating GCs. Case 1 recurred SDPs at 17 and 63 months from initiating GCs. Case 2 was prescribed Tacrolimus as a concurrent medication. All four patients were operated to remove the perforated segment, and case 2 and 4 were created artificial anus. Although they were clinically diagnosed as SDPs only case 4 clarified perforation in pathological findings.

Conclusions: We should take care of developing SDPs in patients described high dose GCs.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3212

EPIDEMIOLOGY AND CLINICAL PRESENTATION OF OCULAR INOCULATION WITH NON INFECTIOUS UVEITIS

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Background: Uveitis is a sight-threatening inflammation which may involve different anatomical parts inside the eye. The prevalence of uveitis among the population is equal to approximately 0.7% and it may cause irreversible damages to the eye that predominantly affects people in their productive years, being one of the most common extra-articular manifestations in several rheumatic diseases.

Objectives: To describe the clinical features of ocular involvement in a population of patients affected with newly diagnosed Non Infectious Uveitis (NIU).

Methods: A total of 278 patients (mean age 42±18.18 years, range 4-87) from three specialized centres, all affected with uveitides, were enrolled; 158 were female, 120 male, all caucasian but one asiatic. Complete ophtalmologic examination was carried out in all of them, and medications, or any kind of medications were not prescribed. In addition blood tests, serum antibodies level evaluations and HLA haplotype typization were performed. Moreover instrumental tests were performed when a complete symptom complex was suspected. Uveitides were then classified according to the Standardization of Uveitis Nomenclature Working Group Criteria.

Results: 149 (53.6%) patients were affected with Anterior Uveitis (AU), 45 (16.2%) with Panuveitis, 16 (5.8%) with Intermediate Uveitis (IU) and 68 (24.5%) with Posterior Uveitis (PU). None of the patients had a systemic disease at the moment of the uveitis onset. HLA-B27 positivity was found in 15.8% of patients, whereas HLA-B51 positivity was found in 21.9% of patients. Behçet’s Disease (BD) was diagnosed in 39 (14%) patients: in particular AU was found in 9 out of 39 patients (23.1%), while PU in 16 out of 39 patients (41%). Ankylosing Spondylitis (AS) was recognized in 22 (7.2%) patients: AU was diagnosed in 16 out of 22 (72.7%) of them while 4 out of 22 (18.2%) were affected with Panuveitis. The cases of Psoriatic Arthritis (PsA) were found in 9 (3.2%); specifically, AU was recognized in 4 out of 9 (44.4%) of them while PU was found in 5 out of 9 (55.6%) of them. We also defined the most common form of uveitis in patients affected with either Juvenile Idiopathic Arthritis, or Systemic Lupus Erythematosus, or Sarcoidosis, or Vogt-Koyanagi-Harada disease or Inflammatory Bowel Diseases. The idiopathic form of uveitis, was diagnosed in 162 (58.3%) patients. Anti-nuclear antibodies (ANA) levels were assessed in 148 patients of whom 57 (38.5%) have been found ANA positive and 91 (61.5%) ANA negative. Notably 38 (66.7%) ANA positive patients were affected with AU.

Conclusions: Our study provides a depiction of clinical features and epidemiology of ocular involvement in a huge population of patients presenting newly diagnosed NIU. Notably, in our population, idiopathic uveitis was the most commonly diagnosed form; it took shape of AU in 56.6% of cases. The majority of HLA-B27 positive uveitides were also AU (68.2%), while, among HLA-B51 uveitides, PU (59.3%) and AU (37.7%) were recognized as the most common presentations.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2232

PORTUGUESE ADAPTATION AND VALIDATION OF THE ANKYLOSING SPONDYLITIS QUALITY OF LIFE (ASQOL) QUESTIONNAIRE

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Background: Ankylosing Spondylitis (AS) is a chronic rheumatic disease that affects mainly the axial skeleton and entheses. If left untreated, AS evolves with limited spine mobility and irreversible structural changes, with severe repercussions in patients’ quality of life. Throughout the years many instruments have been used in order to evaluate AS impact in patients’ lives, focusing predominantly on symptoms and functioning however, these instruments do not inform on the impact of the condition on quality of life (QoL). The ASQol is a patient reported outcome measure, specifically developed to evaluate QoL AS patients. It has been adapted to several languages worldwide, though a Portuguese version hadn’t been developed yet.

Objectives: Translation of the ASQol questionnaire into Portuguese and ascertain its psychometric properties.

Methods: Translation of the original UK English ASQol into Portuguese was performed by bilingual panel and then assessed by a lay panel. Cognitive debriefing interviews were performed with AS patients to assess face and content validity. Finally, a sample of AS patients were included in a test-retest postal survey, administered on two different occasions, two weeks apart, to investigate the reliability and construct validity of the new Portuguese adaptation of the ASQol. Nottingham Health Profile (NHP) was used as a comparator measure.

Results: The Portuguese version of ASQol proved to be relevant and easy to understand.

Validation of the ASQol included fifty-eight AS patients, with a mean age of 51 years (Range 25.0 – 80.0), with 55.2% males. The Portuguese ASQol had good internal consistency at Time 1 (α=0.90, p<0.001) and Time 2 (α=0.94, p<0.001). Correlation between ASQol scores and NHP was moderately strong with Spearman’s rank correlation coefficients between ASQol and NHP section scores, including the distress scale embedded within, all p<0.01. These results suggest that patient’s quality of life is influenced by many factors in addition to disease severity, including social skills and ability to adapt to physical limitations.

The Portuguese version of ASQol was able to discriminate between patients who differed on their perception of general health and presence of comorbidity, although there were no significant differences according to self-perception of disease severity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2232

Scientific Abstracts

AB1160

Validation of outcome measures and biomarkers
Conclusions: The Portuguese version of the ASQol performed well, demonstrating good psychometric properties for use in clinical studies and trials of patients with AS. The lack of significance in the analysis by self-perceived disease severity may be due to the relatively small sample size.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6807

AB1162
RAPID3 SCORE CAN PREDICT DISEASE ACTIVITY IN PRIMARY SJÖGREN’S SYNDROME

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Background: Sjögren’s syndrome (SS) is a chronic autoimmune disease that causes salivary and lacrimal gland dysfunction, resulting in oral and ocular dryness. The European League Against Rheumatism (EULAR) SS disease activity index (ESSDAI) is a systemic disease activity index measuring disease activity in patients with SS. The ESSDAI includes 12 domains. EULAR SS patient-perceived index (ESSPRI) is used to evaluate dryness, fatigue, and pain symptoms, and their impact on the disease. Routine Assessment of Patient Index Data 3 (RAPID3) is used to evaluate disease activity in patients with rheumatoid arthritis which is another inflammatory disorder.

Objectives: This study aims to evaluate whether RAPID3 is useful in primary SS.

Methods: 30 patients with primary SS were enrolled in the study. ESSDAI, ESSPRI and RAPID3 scores were recorded. Chi-square, Mann Whitney U test and Pearson correlation analysis were performed for the statistical analysis.

Results: Demographically and clinical data were shown in the Table-1. Mean ESSDAI, ESSPRI and RAPID3 scores were 3.8±3.6, 5.8±1.7, and 14.8±5.2, respectively. RAPID3 scores were positively correlated ESSPRI (r=0.669, p<0.001). In addition, when we set the cut-off value to 12 on the RAPID3 score (>12 accepted as active, and ≥12 accepted as inactive), ESSPRI score was significantly higher in active patients (6.4±1.4 vs. 4.1±1.4, p=0.002). However, there was no relationship between RAPID3 and ESSDAI scores. Schirmer test was positively correlated with tear break up time (BUT) (r=0.573, p=0.007). Lissamine green score was negatively correlated with Schirmer test and BUT (r=–0.484, p=0.007, and r=–0.507, p=0.004, respectively). Despite there was high compliance among these three scales evaluating eye involvement, these scales did not appear to correlate with the ESSDAI, ESSPRI, and RAPID3 scores that assess global disease activity. The mean age was significantly higher in patients with Schirmer test ≤5 mm compared to the patients with >5 mm (55.6±6.9 vs. 47.6±8.5 years, p=0.044).

Table 1. Demographics and clinical variables

<table>
<thead>
<tr>
<th>SS (n=30)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>51.0±8.7</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>6.3±4.6</td>
</tr>
<tr>
<td>Sex, % females</td>
<td>100</td>
</tr>
<tr>
<td>WBC, 10³/µl</td>
<td>5.9±1.8</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>13.3±1.8</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>19.5±16.4</td>
</tr>
<tr>
<td>CRP, mg/dl</td>
<td>7.2±13.5</td>
</tr>
<tr>
<td>ANA positivity, %</td>
<td>83.3</td>
</tr>
<tr>
<td>Anti-Ro positivity, %</td>
<td>65.5</td>
</tr>
<tr>
<td>Anti-La positivity, %</td>
<td>46.2</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.2±0.4</td>
</tr>
<tr>
<td>Schirmer test, mm</td>
<td>11.4±6.4</td>
</tr>
<tr>
<td>BUT, sec</td>
<td>3.2±1.8</td>
</tr>
<tr>
<td>Lissamine green score</td>
<td>2.2±1.1</td>
</tr>
</tbody>
</table>

SS: Sjögren’s syndrome; WBC; white blood cell count, ESR, erythrocyte sedimentation rate, CRP; C-reactive protein, ANA; anti-nuclear antibody; HAQ; health assessment questionnaire, BUT; tear break up time.

Conclusions: In SS, it is not simple to detect disease activity. Comorbid psychosomatic diseases affect the set detecting global disease activity. On the other hand, the activity of glandular involvement and global disease activity are not with compliance. Therefore, new and easy tools are necessary in primary SS. In our study, RAPID3 score is correlated with ESSPRI. This result suggests that RAPID3 is useful to detect disease activity in primary SS.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6243

AB1163
ANTIBODIES BINDING SYNTETIC OLIGONUCLEOTIDES DISTINGUISH LUPUS FROM RHEUMATOID ARTHRITIS, SCLERODERMA AND SJÖGREN’S SYNDROME

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Background: The SLE-key® RuleOut iCHIP® antigen microarray-based test rules out a diagnosis of SLE with a sensitivity of 94%1.

Objectives: Here we report the use of the iCHIP® platform and a set of synthetic oligonucleotide antigens to distinguish between SLE subjects and those with a diagnosis of Rheumatoid Arthritis (RA), Scleroderma (SSc), Sjögren’s syndrome (SS), or healthy individuals (HC).

Methods: We examined IgM and IgG antibody binding to 22 synthetic oligonucleotides (44 features) in the sera of HC subjects (N=40); SLE (N=30); SSc (N=40); SS (N=20); or RA (N=30) patients. Univariate analysis (FDR adjusted p-values) was used to determine the ability of each feature to separate between SLE and the different classes of subjects.

Results: Table 1 shows that multiple oligonucleotides successfully distinguished SLE patients from other groups. All significant features were IgG antibodies, except for 1 IgM, Table 2 shows the impact of single nucleotide change on antigen binding. PolyG (G17) separates SLE from all but SS, T1G16 separates SLE from HC subjects, while G16T1 gave no significant separation. The addition of a G to the 5’ and 3’ end of T16 enhanced IgG antibody binding and improved separation between SLE and other autoimmune diseases with at least 10-fold improved significance as compared to T20. PolyG sequence length impacts the ability of the oligonucleotides to separate between SLE and the other groups (Fig. 1A). Unexpectedly, sequences either shorter or longer than G14 were effective in separating SLE from HC, RA, and SSc, while G14 was not effective. Furthermore, none of the polyG homopolymers could separate SLE from SS. Sequences rich in C or T were more effective at separating between SLE and SS patients (Fig. 1B).

Table 1

<table>
<thead>
<tr>
<th>Compared to</th>
<th>SLE</th>
<th>Number of significant oligonucleotides</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>IgM</td>
<td></td>
</tr>
<tr>
<td>HC</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>RA</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>SSc</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
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Table 2

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<th>SSc Vs SLE</th>
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Figure 1

Conclusions: Autoantibody binding to oligonucleotides can be used to differentiate SLE from other autoimmune conditions and healthy subjects.

• The structural basis for the differences in binding of antibodies from disease sera to the various oligonucleotides is not yet understood, but may be due to immunologically unique conformations and secondary structures of oligonucleotides of defined length and sequence.

• SSc can be differentiated from SLE based on particular antibody binding to epitopes of oligonucleotides containing C and T.

• RA can be differentiated from SLE more significantly than the other autoimmune conditions.

Figure 1
The CHIP® microarray technology is being further developed to generate a clinically useful test to rule in a diagnosis of SLE relative to other related autoimmune diseases.

References:
3. Fattal et al., Immunology, 2015.

Disclosure of Interest: Authors wish to acknowledge Cohen-Gindi O, Lerner M, Tarnapolski O, Blumenstein Y, Javaherian A, Pitts J, Barton M and Wong E. and the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115309 EU/VAE.

DOI: 10.1136/annrheumdis-2017-eular.6129

AB1164

RABIOPRED, AN INNOVATIVE THERAGNOSTIC TOOL FOR PRECISION MEDICINE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Anti-TNF alpha biologicals are an important breakthrough in the treatment of Rheumatoid Arthritis (RA) patients. However, 30–40% of RA patients do not respond to these therapies. Therefore, there is an unmet need for a tool to predict treatment response that would help clinicians choose an optimal treatment for RA patients.

Objectives: Under the framework of Horizone2020 SME Instrument of European Commission, Firalis has identified and developed a panel of 2195 mRNA genes which can predict non-response to anti-TNF alpha therapy using the HTG EdgeSeq platform. As a predictive combination of a nuclease protection assay & next generation sequencing (NGS).

Methods: RABIOPRED assay is a proprietary panel of Firalis signatures, which also includes targets selected by the BTCure consortium, to predict treatment response of anti-TNF alpha biologicals. In total 2175 targets were selected for the development and 2159 are successfully included in the panel. Each oligonucleotide is a 100-mer comprising a 25-mer “wing” at the 5’ end and 3’ end, and a 50-mer sequence in between that is complementary to the target mRNA. QC is checked for secondary structure and absence of homology with other sequences. Analytical parameters are assessed and repeatability of the RABIOPRED assay is validated on both Paxgene and purified RNA samples. Sample input is set at 32 μl for Paxgene RNA blood and 25 ng for extracted RNA.

Results: Mean correlation factor for 12 samples on 8 replicates for Paxgene and RNA samples are R²=0.97 and R²=0.99 respectively. First analysis and predictive modelling shows an AUC over 0.95 for the prediction of non-response to anti-TNF alpha. In the present work, we disclose the performance of the CE-IVD RABIOPRED assay based on more than 200 samples obtained from the prospective clinical studies. PRINT and RA-TNF. The algorithm will be further validated within the ongoing RABIOPRED Proof-of-Performance study (ClinicalTrials.gov Identifier: NCT030216260) in 720 patients treated by anti-TNF alpha biologicals (5 originators and 3 biosimilars) launched in December 2016. First version of the CE-IVD RABIOPRED assay will be available during Q2 2017 and open for testing.

Conclusions: We are showing that we can accurately measure mRNA expression with RABIOPRED assay using HTG-EdgeSeq NGS platform. Preliminary performance of the assay shows that it can efficiently predict treatment response to anti-TNF alpha biologicals. The algorithm will be later on validated in a multi-centric proof-of-performance clinical study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6180

AB1165

THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE (MCID) RAISES THE SIGNIFICANCE OF OUTCOME EFFECTS ABOVE THE STATISTICAL LEVEL

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Background: In measurement of outcome effects, the patient's subjective perception to feel a change in health defines clinical effectiveness irrespective of statistical significance. Nevertheless, many – especially pharmacological – studies argue with statistical effects alone.

Objectives: To review, develop, illustrate, and discuss current and proposed new concepts of effect quantification and significance.

Methods: First, for determining minimal clinically important differences (MCIDs) were reviewed and further developed focusing on their characteristics and (dis)advantages. The concepts were illustrated by empirical rehabilitation effects (evaluation study) and a randomized controlled trial (investigative study) in knee osteoarthrosis.

Results: In controlled studies, empirical score differences between verum and placebo become statistically significant if sample sizes are sufficiently large. For example, a score difference of 5 points (scale 0–100) between the verum and the placebo effect becomes statistically significant, if the sample sizes are n=33 for each of both groups at a standard deviation=10 of the score differences (baseline to follow-up). MCIDs by contrast, are defined by patients' subjective score, which led to “anchoring” of effects by the “transision” item, where patients rate their change of health between baseline and follow-up in an evaluation study. The MCID for improvement by the “mean change method” is the difference of the mean change experienced by the “slightly better” group minus that of the “almost equal” group. The MCID can be expressed as absolute or relative score, as effects size (ES), standardized response mean (SRM) and standardized mean difference (SMD) (bivariate). It can further be adjusted by multivariate regression modeling. In our example of knee osteoarthritists, the MCID for pain relief was 8.74 (scale 0–100) and for baseline score by patient, SMD=0.469. This is consistent to the range of 0.30–0.50 for MCIDs reviewed in literature. After adjusting for potential confounders, the MCID was 7.09 score points or an increase of 2.9% per score point to feel better obtained by logistic regression.

Conclusions: Absolute and relative MCIDs are easy to interpret and apply to data of investigative studies. MCIDs expressed as ES/SRM/SMD reduce bias, which mainly results from dependency on the baseline score. Multivariate linear and logistic regression modeling further reduces bias by adjustment for possible confounders and increased precision. Anchor-based methods should use clinical/subjective perception to define MCIDs and should be clearly differentiated from distribution-based methods that provide statistical significance only.

References:
1. Angst F, Aeschlimann A, Angst J. The minimal clinically important difference (MCID) raised the significance of outcome effects above the statistical level, with methodological implications for future studies. J Clin Epidemiol 2016;epub 13/12/2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6417

AB1166

QUANTUM BLUE® ADALIMUMAB: EVALUATION OF A POINT OF CARE RAPID TEST FOR THERAPEUTIC DRUG MONITORING OF SERUM ADALIMUMAB LEVELS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting approximately 1% of the population [1]. The pathogenesis of RA involves the overexpression of tumor necrosis factor alpha (TNF-α) and other cytokines [2]. Adalimumab (ADA) is a human monoclonal antibody directed against TNF-α and is highly effective in the treatment of RA. For efficient treatment trough levels of ADA need to be adjusted within a therapeutic window which is 5 to 10 μg/mL [3]. A rapid test allows faster reporting of trough levels, providing a great advantage over test formats that need samples to be sent to a central or service laboratory. Here we report on the technical performance evaluation of the Quantum Blue® Adalimumab test. RF showed no influence on correct measurement of ADA at all levels, with the lower limit of quantification between 0.1 μg/mL and 1000 μg/mL.

Methods: The sandwich lateral flow immunoassay uses a TNF-α coated gold label and a highly specific monoclonal antibody immobilized on the test membrane to detect ADA in diluted human serum samples. Sensitivity of the assay was determined by calculating limit of detection (LoD) and limit of quantification (LoQ) according to CLSI EP17-A2 guideline. Moreover, the assay was evaluated regarding cross-reactivity with other therapeutic antibodies targeting TNF-α, influence of rheumatoid factors (RF) and high dose hook effect. A method comparison was performed against a commercially available ELISA (RIDASCREEN® ADM Monitoring, R-Biopharm, Germany) to compare the trough level results of 40 patients treated with ADA. All statistical analyses were performed with Analyse-it for Excel.

Results: The Quantum Blue® Adalimumab test allowed analysis of serum samples within 15 minutes. The samples were diluted 1:20 in chase buffer before application onto a test cassette (volume 80 μL). The readout was performed with the Quantum Blue® Reader resulting in adalimumab concentration levels in the lower μg/mL range. The test exhibited a LoD of 0.2 μg/mL and a LoQ of 0.69 μg/mL. No high dose hook effect was detected for samples containing up to 1000 μg/mL ADA. The latter two data sets allowed a measuring range of 1 to 35 μg/mL of ADA in patient samples. Other therapeutic TNF-α blockers, like infliximab and golimumab, showed no cross-reactivity with the Quantum Blue® Adalimumab test. RF showed no influence on correct measurement of ADA at all tested concentrations. The method comparison to a well-established commercial ELISA method revealed a slope of 1.12 and a regression coefficient (R²) of 0.90 (by Passing-Bablok). A Bland-Altman analysis showed a bias of 1.9% confirming the overall excellent correlation of the two methods as well as the accuracy of our new developed rapid test.

Conclusions: The BÜHLMANN Quantum Blue® Adalimumab assay enables the quantitative determination of ADA trough levels over the clinically relevant range in serum with a time to result of only 15 minutes. The assay exhibits an excellent accuracy and correlation to a well-established laboratory reference
method. Hence, it represents a valuable tool for the clinician to assess the trough levels during ADA treatment follow up at the point of care.

References:

Disclosure of Interest: None declared

**AB1167 AUTOACTIVE T CELLS TO CITRULLINATED HSP90 IN INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS**

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**Objectives:** To address this issue we investigated the spontaneous T cell responses to the putative autoantigen citrullinated HSP90 (citHSP90) in different stages of RA-ILD.

**Methods:** In RA-no ILD (n=19), indetermine ILD (ILA1) (n=24), subclinical RA-ILD (ILA2) (n=20), clinical RA-ILD (ILA3) (n=4) and other connective tissue disease associated ILD (CTD-ILD) (n=14) patients. Cultures derived from whole blood or peripheral blood mononuclear cells isolated from patients with RA-ILD, clinical RA-ILD, ILA 2, ILA 3, and CTD-ILD were stimulated with citHSP90, citrullinated BSA, or no antigen. The concentration of 13 cytokines and chemokines in the plasma supernatant were then measured using Luminex xMAP technology.

**Results:** CitHSP90 induced significantly higher levels of IFN-γ levels in RA-ILD (ILA=2+3) groups compared to the RA-no ILD group (p=0.002), but did not stimulate the production of other cytokines (p>0.05). Furthermore, citHSP90 did not stimulate the production of IFN-γ or other cytokines stimulated those individuals with non-RA CTD-ILD (p=0.1039, IFN-γ).

**Conclusions:** The production of IFN-γ by T cells stimulated with citHSP90 during the activation of B cells may be involved in the pathogenesis of RA-ILD. The presence of autoreactive Th1-like cells in RA patients in conjunction with citrullinated autoantigens may indicate the involvement of this autoantigen in the pathogenesis of RA-ILD. Early targeting of the immune reactions in the lung might therefore be a new approach to modulate disease.

**References:**

**AB1169 COMPENSATORY INCREASE IN FCERIIB EXPRESSION ON B CELLS IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Objectives:** We aimed to clarify how the abnormal activation of B cells involves inhibition FcεRI on B cells in SSc patients currently remain unknown.

**Methods:** Blood samples were collected from 76 SSc patients (38 limited cutaneous SSc [lcSSc], 38 diffuse cutaneous SSc [dcSSc]) and 59 healthy subjects. FcεRI expression was evaluated on FcεRIIB. Inhibition of immune responses, FcεRIIB is the only FcεRI that has an inhibitory function. Previous studies revealed that a decrease in the expression of FcεRIIB on B cells induced excessive immune responses and resulted in the development of autoimmunity. However, the expression levels of FcεRIIB on B cells in SSc currently remain unknown.

**Methods:** Blood samples were collected from 76 SSc patients (38 limited cutaneous SSc [lcSSc], 38 diffuse cutaneous SSc [dcSSc]) and 59 healthy subjects. FcεRI expression was evaluated on FcεRIIB.

**Results:** The expression of FcεRIIB on B cells was significantly stronger than that on the B cells of healthy subjects (Figure 1) (p<0.05 and p<0.001, respectively).

**Conclusions:** FcεRIIB mRNA expression on SSc B cells was also significantly stronger than that on the B cells of healthy subjects (p<0.01).

**Methods:** The expression of FcεRIIB on SSc naïve B cells and DN memory B cells was significantly stronger than that on the B cells of healthy subjects (p<0.01). The expression of CD80, CD86, and CD95, activation markers on B cells, was stronger in all B cell subsets, except for CD80 in switched memory B cells (CD19+IgD+CD27+). The mRNA expression of FcεRIIB was measured using real-time PCR. We examined the relationship between FcεRIIB expression and clinical features.

**Results:** The expression of FcεRIIB on SSc naïve B cells and DN memory B cells was significantly stronger than that on the B cells of healthy subjects (Figure 1) (p<0.05 and p<0.001, respectively). FcεRIIB mRNA expression on SSc B cells was also significantly stronger than that on the B cells of healthy subjects (p<0.01). The expression of CD80, CD86, and CD95, activation markers on B cells, was stronger in all B cell subsets, except for CD80 in switched memory B cells and plasmablasts. Patients with the stronger expression of FcεRIIB on DN memory B cells more frequently had interstitial lung disease than those with normal levels (p<0.05). Cyclophosphamide pulse therapy significantly reduced the expression of FcεRIIB on preswitched memory B cells and switched memory B cells (p<0.05 and p<0.05, respectively).

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6897

**AB1168 TOUCH STUDY: TECHNOLOGY AND OUTCOMES USED IN CLINIC IN A DAY HOSPITAL**

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**Background:** Patient reported outcomes PRO are a key element in the global evaluation of patient care, especially those followed in day hospital. The use of touchscreen computers is one of the new features in the day hospital of Instituto Português de Reumatologia.

**Objectives:** To evaluate the transition from paper to touchscreen computer technology of the PRO in use in Reuma.pt
Conclusions: Our results suggest that SSc B cells exhibit compensatory increases in the expression of FcγRIIB in order to suppress the abnormal activation of B cells, and the expression of FcγRIIB may be an indicator of the clinical severity of SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2064

AB1170

PREVALENCE OF ANTI-CARP ANTIBODIES IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME: ASSOCIATION WITH CLINICAL, SEROLOGICAL AND HISTOLOGICAL ASPECTS

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1Dipartimento di medicina interna e specialità mediche; 2Dipartimento di radiologia, Oncologia e Scienze Patologiche, Sapienza University of Rome, Rome, Italy.

Background: The presence of antibodies against carbamylated peptides (anti-CarP) has been associated with increased disease activity and severe joint damage in rheumatoid arthritis. Our group has demonstrated their prevalence in 27% of cases and an association with the presence of germinal centres (GCs). Thus, these antibodies have been proposed as a new tool for identifying SS patients with a more aggressive disease.

Objectives: To confirm the presence of anti-CarP antibodies in a large monocentric cohort of patients with SS and investigate their association with clinical, serological and histological features.

Methods: Serum samples from consecutive patients with SS (AECG criteria) were collected and stored at -20°C. Anti-CarP antibodies were detected by a modified ELISA. The mean ±3 times SD was used as cut-off. Minor paraffin embedded salivary glands were stained by H&E and IHC using lymphocytes T and B markers [anti-CD3, anti-CD20 (DAKO)]. GCs presence was defined by H&E and confirmed by identification of follicular dendritic cells [anti-CD21, DAKO]. Images were analysed as follows: focus score (FS) calculation, mean foci area, percentage of segregation, foci, GCs and lymphoepithelial lesions.

Results: Clinical and laboratory features of SS patients are shown in table. Serum anti-CarP were detected in 30/104 patients (28.8%) without association with any clinical or serological feature (Fisher’s exact test). Positive patients were more likely to present SF (P=0.024). No association was found with the presence of GCs or LELs. Anti-CarP titre correlated with the FS (P=0.045, r=0.304), the number of foci (P=0.008, r=0.347), mean foci area (P=0.028, r=0.331) and the percentage of SF (P=0.046, r=0.331) (Spearman’s test). Prevalence of anti-CarP was higher in patients with arthritis [7/15 (46.6%)] than those without [23/89 (25.8%)].

Conclusion: Anti-CarP titre was higher in patients with arthritis compared to those without (322.3±173.8 au/ml vs 279.5±171.1, P=0.004, respectively).

Conclusions: This is the largest cohort of SS patients screened for anti-CarP so far. Our results show a prevalence of anti-Carp antibodies in agreement with the literature; however, no association was found with any clinical or serological aspect. Anti-CarP do not seem to be associated with histological features predictive of lymphoma, i.e. GCs and LELs. Nonetheless, considering the titre correlation with the FS, mean foci area and percentage of segregation, higher serum levels of anti-Carp may reflect a severe tissue inflammation more prone to form organized infiltrates. This finding, in association with the evidence of higher levels in patients with arthritis, may support the idea that these antibodies are useful to measure the severity of systemic inflammation.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5774

AB1171

ARTIFICIAL AND EXTRA-ARTICULAR DAMAGE INDEX ASSESSMENT IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Juvenile Idiopathic Arthritis is a broad term used to describe several different forms of chronic arthritis in children. Variable assessment tools can be used for assessment of JIA disease activity. JADI is composed of 2 parts (Viola et al., 2005).

Objectives: Assessment of the articular and extraarticular damage index in juvenile idiopathic arthritis patients.

Methods: This study was carried out on 60 JIA patients. Patients who had inflamed synovia related to trauma or malignant disease, septic arthritis, bone diseases, as dysplasia or osteomyelitis were excluded. Clinical assessment: sex, age at disease onset, JIA category, educational level, loss of school years and previous use of systemic corticosteroid and second-line drug therapies. Local examination: number of swollen joints, joints with pain on movement/tenderness, joints with limited range of motion, joints with active arthritis were recorded for every patient. Disease activity: was measured by using the (JADAS-27).

Functional ability: was assessed by (CHAQ). Laboratory assessment: included ESR and CRP. Radiographic assessment: scored according to the adapted Sharp/van der Heijde score. Damage assessment: was assessed using the Juvenile Arthritis Damage Index. The (JADI-A) and (JADI-E).

Results: Patient characteristics: 6 had systemic onset, 29 had polyarthritis, 14 extended oligoarthritis, 11 had persistent oligoarthritis and none of them had psoriatic arthritis. 38 females and 22 males (56.7%) percent of patients lost some years of education ranging from 0–3 years. Patients in remission were very few 5 patients only. According to the C-HAQ score (13.3%) of patients had no disability (11.7%) mild disability (41.6%) moderate disability and (33.3%) severe disability. 60% patients had articular damage and 35% patients had extraarticular damage. The wrist was the most frequently damaged joint. The growth failure, pubertal delay and leg length discrepancy were the most frequently reported extraarticular items. Correlation of JADI with other disease variables: showed that JADI-A is correlated with physician’s global assessment, CHAQ, radiological damage.

Conclusions: Ours is the first study that has used JADI to assess outcome in patients with JIA in Egypt. JADI has a good correlation with traditional outcome measures in JIA and may be a good tool to be used in clinical practice and is likely to increase current understanding of the natural history of the disease.

References:

Acknowledgements: First of all, thanks to Gracious Allah. I would like to express my profound gratitude and appreciation to Prof. Dr. Enass Abdel Kader Elewa and to Prof. Dr. Mahmoud Moustafa Ashour for support and supervision.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6707
Background: The Leeds Assessment of Neuropathic Symptoms (LANSS) and the painDETECT questionnaire (PDQ) are two validated screening tools for neuropathic pain (NP). Recent evidence reported a low level of agreement between these tests in knee Osteoarthritis. Several studies have recently applied the PDQ in Rheumatoid Arthritis (RA), suggesting a NP component in these patients, although the application and performance comparison with LANSS is yet to be studied.

Objectives: Evaluate PDQ and LANSS performance for NP classification and investigate its optimal cutoff points in a RA cohort.

Methods: Observational, cross-sectional study was designed including RA patients followed at our Rheumatology department. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit where LANSS and PDQ were applied. Agreement between the two questionnaires was evaluated using kappa coefficient analysis. Receiver operating characteristic (ROC) analysis was performed using each tool as gold-standard and cutoff points to optimize agreement were investigated. Non-concordant patients were compared with concordant patients using parametric and non-parametric analysis for significance level in NP classification.

Results: 112 RA patients were included, 86 (77%) were females, with a mean (SD) age of 55.1 (10.8) years and median disease duration of 13 years (range: 2–41), 102 (91%) were treated with DMARDs and 42% with a biologic DMARD. 48% patients had NP applying the LANSS (≥13) and 28% had NP in the PDQ (19 possible and 12 likely) and no demographic or clinical significant differences were found between these two groups. 82 (73%) patients had concordant NP classification (59 negative, 23 positive) by the two tests. Concordant group showed significantly higher mean score on PDQ than non-concordant group (14 vs 12 years and 8 vs 13, respectively, p < 0.05) with no other significant differences found. A moderate agreement ($\kappa = 0.41$) and linear correlation (r=0.58, p<0.001) were observed between the two tests. In the ROC curve analysis, PDQ (≥13) showed an area under the curve (AUC) of 0.80, 95% CI [0.71–0.90] with a specificity and sensitivity of 74% and 73%, respectively, using LANSS as gold standard. LANSS ($\geq$12) had an AUC of 0.80, 95% CI [0.71–0.90] and a sensitivity and specificity of 74% and 73%, respectively, using PDQ as gold standard. After ROC curve analysis, optimal cutoff for PDQ was 10, showing greater sensitivity (69%) but lower specificity (51%) with a slight increase in the agreement between the tests ($\kappa$=0.48). For the LANSS, the optimal cutoffs were the previous value or 13 (sensitivity 68% and specificity 78%) with a modest gain in the agreement ($\kappa$=0.42). Correction for both cutoff points resulted in a more substantial increase in agreement level ($\kappa$=0.51).

Conclusions: In this study, LANSS and PDQ had a moderate level of agreement, possibly because they capture different dimensions of NP. New possible cutoffs were studied to increase agreement between the tests. Further studies with other conditions and a validated gold-standard for NP are needed to confirm this data.

References:

Disclosure of Interest: T. Martins Rocha: None declared, S. Pimenta: None declared, M. Bernardes: None declared, A. Bernardo: None declared, M. Barbosa: None declared, R. Lucas: None declared, L. Costa: None declared DOI: 10.1136/annrheumdis-2017-eular.5127

AB1174
ORM2 AND APA2 SERUM LEVELS CAN PREDICT OA PATIENT RESPONSE TO CHONDROITIN SULFATE/GLUCOSAMINE HYDROCHLORIDE: RESULTS FROM THE MOVES STUDY

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Background: A shotgun proteomic analysis performed on sera from patients enrolled in the Multicentre Osteoarthritis interVention trial with Sysadona (MOVES) led to the discovery of a panel of putative protein biomarkers useful to stratify osteoarthritis (OA) patients into responders and non-responders, either to Chondroitin sulfate/Glucosamine hydrochloride (Droglican®), Bioiberica S.A., Barcelona, Spain or Celecoxib.

Objectives: To validate the sensitivity and specificity of a panel of six serum proteins useful to predict the patient response to Droglican treatment, in order to optimize therapeutic outcomes in OA.

Methods: We analyzed the serum levels of a panel of six putative predictive protein biomarkers by enzyme-linked immunosorbent assays (ELISAs): APAO2, APA2, APA1, APA4, CA4BP, ORM2. All the subject studied belonged to the MOVES cohort at baseline (Droglican sub-cohort, n=260). Non-parametric and multivariate analysis were performed to test the effects of the clinical variables, including gender, age, BMI, radiologic Kelgren/Lawrence (KL) grade and WOMAC score at baseline, as well as the serum levels of each of the six mentioned proteins, on the response to Droglican treatment according to the OMERACT-OARSI criteria and the WOMAC pain score (20%, 30%, 50% and 70% reduction) recorded at the end of the trial (after 6 months of treatment).

Results: Non parametric analysis showed decreased serum levels of ORM2 and APA2 in responders compared to non-responders, both for KL grade (ORM2, APA2; p<0.001), WOMAC (ORM2, APA2; p<0.001), and serum levels of the panel of protein biomarkers in responders. The best protein panels were obtained by the combination of APA2 and ORM2.

References:


AB1173
PHYSICIAN VISUAL ANALOG SCALE ESTIMATES FOR OVERALL GLOBAL ASSESSMENT, INFLAMMATION, DAMAGE, AND DISTRESS TO ASSESS PATIENTS AND SUPPORT DECISION-MAKING IN RHEUMATOLOGY CARE: ANALYSIS OF INTER-RATER RELIABILITY

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Background: A physician global estimate of patient status (DOGCL) was developed to quantify inflammatory activity in rheumatoid arthritis (RA) clinical trials. However, DOGCL may be affected by joint damage and/or distress (in fibromyalgia, depression, etc.). One approach to document the possible impact of these problems on DOGCL is to add 3 physician visual analog subscale (VAS) estimates for inflammation, damage, and distress. These subscales have been shown to be useful in patients with diagnoses other than RA (1) but inter-rater reliability has not been analyzed.

Objectives: To analyze inter-rater reliability between senior rheumatologists and trainees on 4 VAS estimates for overall DOGCL, inflammation (DOGINF), damage (DOCDAM) and distress (DOCSTR), in patients with various rheumatic diagnoses.

Methods: Patients seen in routine care were assigned 4 physician VAS estimates for overall DOGCL, and levels of inflammation or reversible symptoms (DOGINF), organ damage or irreversible symptoms (DOCDAM), and distress or symptoms not explained by inflammation or damage (DOCSTR). VAS estimates were assigned independently by a senior rheumatologist and a rheumatology trainee for the same patient at the same visit. Mean differences, correlations, and possible discordance of ≥2 units/10 between estimates of the senior rheumatologist and the trainee were analyzed.

Results: VAS estimates by the 2 physicians were analyzed in 64 patients with different rheumatic diseases, including osteoarthritis (16%), RA (14%), fibromyalgia (14%), and systemic lupus erythematosus (13%). Mean differences of scores assigned by the senior rheumatologists versus trainees were <0.43/10, less than 5% of the total scales, slightly lower for DOGINF, and slightly higher for the 3 other subscales (p<0.001) (Table). Mean estimates of both physicians for damage and distress were higher than for inflammation by 1.1 to 1.6 units (Table). Concordions of all 4 VAS between rheumatologists and trainees were significant (p<0.001) (Table). More than 70% of the estimates were concordant for DOGINF (75%), DOCDAM (78%), and DOCDAM (70%), while concordance was somewhat lower for DOCSTR (57%) (Table).

Conclusions: Good inter-rater agreement between two physicians is seen for VAS estimates, inflammation, damage, and distress. Mean scores for damage and distress were higher than for inflammation, indicating the complexity of rheumatology care. Quantitative scores can add to documentation of patient status and to support of clinical decisions for doctors, patients, and payers.


DECREASED AUTOPHAGIC ACTIVITY IN T LYMPHOCYTES
FROM PATIENTS WITH NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS

X. Luo 1, Y. Liu 2, M. Yang 2, 1Department of Rheumatology; 2West China Hospital, Sichuan University, Chengdu, China

Background: Alterations in T-lymphocyte homeostasis have been suggested to play a key role in the pathogenesis of SLE. Autophagy is now emerging as a core player in the development and the functioning of the immune system.

Objectives: We investigated the autophagic behavior of T-cells from patients with SLE.

Methods: Thirty patients with SLE and twenty-five healthy subjects matched for gender and age were recruited. The levels of mRNA encoding ATG5, ATG7, Beclin-1 and LC3 were determined by quantitative real-time polymerase chain reaction (qPCR), and evaluated by flow cytometry. The number of autophagic structures was examined by TEM in T-cells from SLE patients and healthy controls.

Results: We documented a decreased level of mRNA expression of LC3 and Atg7 in T-cells from patients with SLE (t=2.282, P<0.027, t=3.573, P<0.001). A decreased percentage of autophagic cells was confirmed in T-cells from patients with SLE, as compared to healthy donors by flow cytometry (t=2.034, P<0.047). No significant correlations between autophagy levels in T-cells and the disease activity of patients were observed (P>0.05).

Conclusions: Our results indicate that autophagy activity in T-cells from SLE patients is decreased, which may contribute to the development of SLE, and thus that resetting autophagy activity may be an important therapeutic goal in this autoimmune disease.

Disclosure of Interest: None declared.


Rehabilitation

THE COMBINATION OF PHYSIOTHERAPY AND BIOLOGICAL THERAPY FOR THE MANAGEMENT OF ANKYLOSING SPONDYLITIS

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Background: The management of the ankylosing spondylitis (AS) aims at relieving patient’s pain, restoring their joint mobility and preventing structural damage which results in progressive deformity, in order to improve the functional status and quality of life of these patients, using various pharmacological and non-pharmacological means. The importance of the physiotherapy in patients with AS under biological treatment was reported in some studies, but the literature on this topic is still scarce.

Objectives: Report the experience of our department of Physical and Rehabilitation Medicine, in the management of the AS, especially the effect of the combination of physiotherapy and biological therapy on pain, disease activity, spinal mobility, functional capacity and quality of life.

Methods: Prospective study on 20 patients diagnosed with AS, treated with tumor necrosis factor alpha inhibitors (TNFa inhibitors) and placed under physiotherapy for 3 months. At baseline and at the end of 3 months, we evaluated Bath AS Disease Activity Index (BASDAI), occupant-wall distance, Hertz index, Schober index, Bath AS Functional Index (BASI) and Visual Analog Scale (VAS) of patient’s quality of life.

Results: For the 20 patients (9 females), aged 38.4 years±10.24 [range 19–55], treated with TNFa inhibitors (Etanercept in 35% and Adalimumab in 65%) and included in a physiotherapy program of 3 months (3 sessions/week), comprising muscle relaxation, flexibility exercises for cervical, thoracic and lumbar spine, range of motion exercises of coxofemoral joints, muscular strengthening, straight posture and respiratory exercises.

After 3 months, all outcome parameters showed statistically significant improvements (P<0.05), as shown in the following table.

<table>
<thead>
<tr>
<th>Paired Differences</th>
<th>Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Par 1 BASDAIbaseline – BASDAImonth3</td>
<td>3.44615</td>
<td>0.000</td>
</tr>
<tr>
<td>Par 2 BASFiBaseline – BASFiMonth3</td>
<td>2.9654</td>
<td>0.000</td>
</tr>
<tr>
<td>Par 3 OWIbaseline – OWImonth3</td>
<td>1.7125</td>
<td>0.023</td>
</tr>
<tr>
<td>Par 4 SCHOBerBaseline – SCHOBerMonth3</td>
<td>-1.5667</td>
<td>0.000</td>
</tr>
<tr>
<td>Par 5 HIRTZbaseline – HIRTZmonth3</td>
<td>-0.7273</td>
<td>0.001</td>
</tr>
<tr>
<td>Par 6 VASpatient_baseline – VASpatient_month3</td>
<td>4.0833</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Conclusions: According to our results, the combination of physiotherapy and
biological therapy is an effective mean in increasing functional capacity and joint mobility, decreasing disease activity, improving quality of life for AS patients. Currently available data do not adequately address what role physiotherapy may have on patients with AS receiving biological drugs [1]. There are a few studies evaluating the effects of exercises in patients with AS receiving TNF inhibitors [2,3].

Results:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5453

AB1178
A PROSPECTIVE STUDY ON THE EFFECTS OF 3-MONTH COURSES OF TRADITIONAL PHYSIOTHERAPY AND YOGA IN PATIENTS WITH CHRONIC ARTHRITIS AND PRIMARY FIBROMYALGIA

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Background: Physical activity is of fundamental importance for people with rheumatic diseases (RD). The traditional approach of Physiotherapy (PT) has been placed side by side with other physical programs, such as Yoga (Y), aimed at reducing chronic pain and improving the quality of life.

Objectives: To evaluate the effects of PT and Y on patients with inflammatory and non-inflammatory RD: Chronic Arthritis (CA) and Primary Fibromyalgia (FM).

Methods: Patients were enrolled in a prospective study including 3 months of PT and 3 months of Y (with a specific focus on the control of breathing - Ai-jutsu). Each activity was performed bi-weekly in a dedicated facility. Patients were randomly allocated to either the group starting with PT or that starting with Y. After 3 months they switched to the other activity. At the beginning and at the end of each activity patients underwent a medical assessment of their physical status and were proposed questionnaires: 1) HAQ for disability in everyday life; 2) ZUNG self-rating depression scale; 3) Tampa scale for Kinesiophobia assessing the fear and avoidance of movement. Patients with FM compiled also the FIQ for the impact of FM in everyday life. All patients rated their physical pain by VAS (Visual Analogic Scale) from 0 to 10.

Results: Thirteen patients with CA (77% female, median age 62 years, median disease duration 19 years) and 8 with FM (100% female, 56 years, 9 years) participated in the study. At baseline, there were no differences between CA and FM patients in terms of ZUNG, HAQ and Tampa scores. After 3 and 6 months of activity, all items had a tendency toward improvement, with a statistically significant reduction for VAS in both groups (nearly 30%). By intra-group comparison, between the beginning and the end of each activity, we observed that patients with CA had a significant reduction of ZUNG and HAQ scores (50 vs 40.5 and 0.600 vs 0.475, respectively) during PT activity, while FM patients had a trend toward the increase of Tampa score (24.5 vs 34.5). During Y activity, significant reductions were observed in VAS score for CA patients (5 vs 2.5) and in Tampa score for FM patients (34.5 vs 23.5). Overall, all items had a tendency toward improvement for FM patients during Y activity.

Conclusions: This pilot study involving both patients with inflammatory and non-inflammatory RD demonstrated benefit from an integrated program of sequential PT and Y and highlighted differences in patients’ needs according to their disease type. Particularly, PT seemed to bring more benefit to CA patients, probably because of the individualized work on joint movement range and muscular strengthening, while FM patients may have had a negative impact by this approach. A negative correlation between the beginning and the end of each activity, we observed that patients with CA had a significant reduction of ZUNG and HAQ scores (50 vs 40.5 and 0.600 vs 0.475, respectively) during PT activity, while FM patients had a trend toward the increase of Tampa score (24.5 vs 34.5). During Y activity, significant reductions were observed in VAS score for CA patients (5 vs 2.5) and in Tampa score for FM patients (34.5 vs 23.5). Overall, all items had a tendency toward improvement for FM patients during Y activity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6397

AB1190
THE INTENSIVE EXERCISE PROGRAMME FOR NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND FOR ANKYLOSING SPONDYLITIS MAY IMPROVED QUALITY OF LIFE AND DISEASE ACTIVITY

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Background: The therapy for axial spondyloarthritis (axSpA) is complex. Although anti-inflammatory medication is necessary for axSpA treatment, the exercise therapy is required to maintain mobility. The limited data are available to evaluate the effect of exercise therapy on quality of life in axSpA, particularly in patients with the non-radiographic form of the disease (nr-axSpA).

Objectives: To investigated the quality of life in axSpA subgroups, nr-axSpA and Ankylosing spondylitis (AS) in response to intensive rehabilitation programme

Methods: 46 patients with axSpA characterised according to criteria of Assessment of SpondyloArthritis国际社会 (ASAS) as nr-axSpA (n=23) and AS (n=23) by the increase disease and treatment underwent 24 weeks long intervention. The intervention consisted in twice a week outpatient group physiotherapy as exercise units of 60 minutes and a daily home-based exercise programme. All outcomes, disease activity (Bath AS Disease Activity Index, BASDAI and AS Disease Activity Index, ASDAS-CRP) and quality of life (AS quality of life, ASQoL and European quality of life, EuroQoL) as well as patients self-reported outcomes such as “patients global assessment” and “pain assessment” were measured at baseline and at the end of exercise programme.

Results: Altogether, 41 axSpA patients (AS, n=22 and nr-axSpA, n=19) finished complete six months programme. The disease activity was improved in all axSpA patients (ASDAS-CRP 2.08±0.12 to 1.83±0.11, p<0.01), particularly in nr-axSpA subgroup, ASDAS-CRP (1.98±0.19 to 1.71±0.15, p<0.05). There were no differences in the changes in ASDAS-CRP and BASDAI over the exercise training between groups (data not shown). After exercise therapy, positive changes of “Patients global assessment”, were evaluated by patients of both subgroups, nr-axSpA (33.42±5.13 to 23.68±4.11, p<0.01) and AS (35.22±3.94 to 25.22±2.92, p<0.01). The “assessment of pain during the last 7 days”, however, was improved only by patients in the nr-axSpA subgroup (34.7±4.58 vs. 21.05±4.71, p<0.05).

The quality of life, ASQoL was not changed after rehabilitation programme.
The EurQol was changed in all axSpA (0.74±0.21 to 0.77±0.18, p<0.05), but significantly was improved only in nr-axSpA subgroup (0.72±0.23 to 0.78±0.18, p<0.01), not AS. Similarly, the improvement of the assessment of “hodiernal health status” was found after an intervention only in the nr-axSpA subgroup (65.81±21.80 to 78.00±13.77, p<0.01).

Conclusions: Our study demonstrated beneficial effect of intensive exercise programme on disease activity and patients self-reported outcomes in nr-axSpA and AS patients. The patients suffering from nr-axSpA can profit at least similarly from the rehabilitation care as those with radiographie form. The exercise programme should be recommended for both subtypes of axSpA.

References:

AB1181 LOCAL STEIOD AND INSULIN INJECTION IN MANAGEMENT OF CARPAL TUNNEL SYNDROME: A COMPARATIVE STUDY
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Background: Carpal tunnel syndrome (CTS) is the most common focal nerve entrapment. Local corticosteroid (CS) injection has been widely used to treat CTS. Recently; Local insulin Injection in CTS has been studied as insulin has anti-inflammatory anti-edematous effects.

Objectives: To compare the effectiveness of local steroid and insulin injections in management of CTS.

Methods: Forty patients complaining of mild or moderate idiopathic CTS (diagnosed clinically & electrophysiologically and classified according to American association of neuromuscular diagnostic medicine monograph) divided into 2 equal groups.

Group I received two local injections of 10 IU NPH insulin into the affected carpal tunnel 2 weeks intervals. Group II: received single injection of triamcinolone acetonide (20 mg/0.5 ml) all procedures done after informed consent. Patient with severe or secondary type of CTS were excluded from this study. Evaluation of the patients was done at baseline, 2 and 4 months later clinically by measuring visual analogue scale (VAS), Phallen and compression tests and electrophysiologically by measuring motor and sensory nerve conduction studies of median and ulnar nerves using a standardized technique.

Results: There was significant improvement in all clinical parameters in both groups after 2 and 4 months from injection (p<0.01) including VAS, Phallen and compression tests with more improvement was noticed in group I. However the improvement was more in group I but the difference between results in both groups were statistically nonsignificant.

Conclusions: Local insulin injection is as effective as (or even better than) local steroid injection in management of CTS.

References:

Acknowledgements: Thanks a lot to Dr. Samar Abd Alhamed for her great efforts in completing statistical analysis in this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5898

Education

AB1183 PATIENT’S EDUCATION IN THE ADMINISTRATION OF SUBCUTANEOUS DRUGS IN THE RHEUMATOLOGY DAY-CARE HOSPITAL UNITS
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Background: Rheumatology Day-Care Hospital Unit (DHU) is defined as a hospital unit for a few hours with the objective to do diagnostic clinical trials and/or multiple test, patient education and treatments that cannot be done in the outpatient clinic, but which do not justify the complete stay in the hospital.

Objectives: Analyze the number of visits that one patient needs in the Rheumatology-DHU to learn the self-administration of a subcutaneous drug.

Methods: All patients who were prescribed a subcutaneous drug (except monoclonal) during the period January 2015 - December 2016 were referred to Rheumatology-DHU. The nurse gave instructions, she supervised the patient’s learning and she decided if the patients needed a new control in Rheumatology-DHU.

Results: The following data were recorded: sex, age, diagnosis, drug, number of visits each patient needed in Rheumatology-DHU. In patients who had already been discharged and adherence to treatment. None declared.

References:
The patient's education by nurse in Rheumatology-DHU is necessary for the right visits or more new referrals to Rheumatology-DHU. Therefore, age is not a limiting factor. In 9% of the patients, the education was done to a reference person and not to the patient himself. We analyzed PTH and MTX groups (because they had the highest number of patients) and we observed that in the PTH group 82% required education of the relative. This percentage was 77% in the MTX group. The number of visits in the Rheumatology-DHU were: 1 in 26 patients (MS of 66 +/- 19.6 years), 2 in 59 patients (MS 65 +/- 18); 3 in 13 patients (MS 64 +/- 13); 4 in 6 patients (MS 67 +/- 14); 5 in 2 patients (MS 68 +/- 17), 6 in 2 patients (MS 70 +/- 22), and in 9 in 1 patient (47 years). Adherence to treatment was 98.2%. A total of 238 visits were made in Rheumatology-DHU.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>MTX</th>
<th>PHT</th>
<th>GOL</th>
<th>ETA</th>
<th>ADA</th>
<th>CER</th>
<th>ABA</th>
<th>SECU</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>62/16</td>
<td>30</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>52/17</td>
<td>9</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Angulosing spondylitis</td>
<td>48/12</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Osteoporosi Total (%) 40 (37%) 40 (37%) 9 (8%) 7 (6%) 6 (6%) 4 (3%) 2 (2%) 1 (1%) 109


Individual semi-directed interviews, have been performed and their thematic content analysed with the QDA Miner program. A guide had been achieved by rheumatologists, psychologists and patient association representatives. The project has been approved by the ethical committee of the University of Katowice, Poland.

AB1184 - EDUCATIONAL NEEDS OF PATIENTS WITH RHEUMATIC DISEASES RECEIVING BIOLOGICS


Background: Biologics are still a challenge in patients receiving biologics. Most of the patients represent their experience with biologics as a new and partially enigmatic tool for management of rheumatic diseases.

Objectives: The study was designed to evaluate educational needs and sources of education in patients with rheumatic diseases treated with biologics.

Methods: Anonymous questionnaires were distributed in 23 Polish rheumatological centers involved in the treatment, 1231 questionnaires were used for analysis. Responses were received from 806 patients with rheumatoid arthritis, 427 with ankylosing spondylitis, 117 psoriatic arthritis, and 62 adult patients with juvenile idiopathic arthritis (in whom administration of the drugs had been introduced before they were 18-year-old), as well as 19 ones receiving the drugs due to other musculoskeletal disorders. The investigated group constituted one fifth of all rheumatological patients on biologics in Poland.

Results: Almost all the patients had learnt for the first time on biologics from the rheumatologist (93%). Few patients only had got such data from internet or from other patients. Likewise, most of the patients got majority of educational data on treatment with biologics from rheumatologist who was supervising the therapy (82%). Remaining sources included internet (8%) and other patients (5%). Relative low number of patients was educated by nurses (2%). Most of the patients (87%) were looking for more details on biological treatment. The patients with rheumatic disease lasting less than 10 years, were more interested in the management than those suffering longer. Most of the patients (94%) considered their rheumatologist as the main person responsible for their education on biologics. There was no difference between patients with various rheumatic diseases as well as no difference was found between female and male patients. Biological treatment attracted more interest in younger than older patients.

Conclusions: Education is still a challenge in patients receiving biologics. Most of the patients represented traditional attitude to health education, expecting almost all educational data to be provided by their physician. We were surprised that role of the nurses was found to be rather low. An increase in role of nurses seems to be the future aim of the educational efforts in Polish rheumatology.


AB1185 - REAL-LIFE EXPERIENCE AND MUTUAL EXPECTATIONS OF PATIENTS AFFECTED WITH CHRONICAL INFLAMMATORY RHEUMATIC DISEASES AND THEIR RELATIVES: CONSEQUENCES IN PATIENT EDUCATION: A QUALITATIVE STUDY BY THE PROXYRIC GROUP OF THE PATIENT EDUCATION DIVISION OF FRENCH RHEUMATIC DISEASE SOCIETY

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Background: Interaction with relatives has a significant role on patients’ health, and can also impair relatives’ health. Education processes need codification to enrol relatives in the programs.

Objectives: To create a patient education program for relatives and patient affected by rheumatic inflammatory diseases.

Methods: Individual semi-directed by 2 psychologists interviews, have been performed and their thematic content analysed with the QDA Miner program. A guide had been achieved by rheumatologists, psychologists et patient association representatives. The (patient/relative) dyad, has been first questioned together, and then individually.

Results: 20 patients, average age 59 years (27–79) affected with Rheumatic Arthritis (n=13), Spondyloarthrits (n=9) with an average disease duration of 12,8 years (1–39) and one of their relatives (being their spouse in 18 cases) have been recruited in 7 rheumatology departments in France. Common life duration was 27,5 years as an average (1,5–57). About 2/3 of patients and relatives have a common view on: relative’s role in bringing an emotional support but needs a knowledge on disease and treatments; emotional distress experienced by both patient and relative; the worries and relative’s feelings of not knowing how to do; the help brought by the relative in everyday’s life and his participation to care management. Only a few relatives talked about concerns, regrets of past life, and burden feeling of patient. Relatives also express unfairness feelings. 2/3 of patients and relatives report will of independence of the patient, who wants to manage alone, and does not express his difficulties. 50% of relatives think they anticipate patient’s needs, they are also directly requested by the patient. On the other side, the patients often report that they watch over relative’s health. 50% of patients and relatives mention the idea of complementarity and a “team”, but also tensions or conflicts. Patient Education contribution would be sharing and exchanging biological and medical information and patient’s data and relatives, who therefore would prefer group education (12/20). Relatives however more often mention a common education with patient, and patients prefer a separate education of relative. The main limit to this study is that participation to study has favored harmoniously functioning dyads, what may explain the weak rate of abandonment feeling.

Conclusions: Expectations on relatives’ role seem to be common in terms of practical and emotional support. Relatives sometimes mention the “positivation” of their role, but also emotional distress and helplessness feeling. Patients fear they are a burden and want to be independent. A specific educational management of relatives is more often suggested by patients than by relatives.


AB1186 - OPTIMISATION OF RHEUMATOLOGY UNDERGRADUATE TEACHING: SELF-DIRECTED DEVELOPMENT OF POWERPOINT PRESENTATIONS BASED ON THEORETICAL CLINICAL CASES

F.A.H. Coolens1, 2, R.L. Batten1, J. Stewart1, D. Cosny1, 1City Hospitals Sunderland NHS Foundation Trust, Sunderland, 2NIHR Newcastle Biomedical Research Centre based at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle upon Tyne, United Kingdom

Background: One element of rheumatology undergraduate teaching in City Hospital Sunderland, UK traditionally involves “paper cases” delivered via small group learning and discussion. Although popular it has had poor feedback from both the students and the tutors at times especially when the tutor to student ratio is high (1:16). With limited numbers of tutors (Consultant Rheumatologists), this issue was becoming more frequent.

Objectives: We wished to explore alternative yet still interactive methods to highlight key learning points relating to common rheumatological conditions in a 60 minute teaching session and to make this fun and engaging.

Methods: 30 undergraduate medical students (January 2017) were given modified teaching material for a 60 minute teaching session a week later. This material involved a partially populated Microsoft Powerpoint slideshow including prompts about a theoretical patient’s clinical case in the notes section. This guided development of a clinical case presentation which covered diverse aspects of clinical care, including its effect on side effects and hand activity scores. Clinical cases addressed systemic lupus erythematosus, early rheumatoid arthritis (RA), ankylosing spondylitis and established RA. Students (groups of 2-3) received one case each were encouraged to use images and online teaching repositories to enhance their presentation. This provided the framework for a 20 minute teaching presentation which was given to their students peers at a formal teaching day 1 week later. A tutor was also present during these sessions (with a ratio of 1:10) to ensure adequate understanding of topics had been achieved and to answer any questions. Feedback was sought from the students and compared with previous “paper case” (non-modified) sessions.

Results: Feedback obtained (n=9) showed 55% of students rated the modified teaching session as “excellent” with the remainder rating it as “good”. Free-text comments included “good to have students do to the presentations so they cover relevant points” “very useful to have a quick 20 minute overview of different conditions & preparation was useful” and “lots of learning, interactive”. Additional comments included the wish for more time to cover the points in even more depth. Informal feedback from the tutors of these events was also favourable with tutors believing students had a developed a greater depth of understanding. These findings compared favourably with the previous years “paper-case” feedback (March 2016). Note only 23% (n=11) of students had rated the session as “excellent” as well as free text comments emphasising wishes for more time to read through cases and smaller group discussion.

Conclusions: Current “paper based” modalities can easily be utilized and “re-purposed” to optimize both self-directed and formal teaching components of undergraduate teaching. This can promote the understanding of complex rheumatological learning points in a relatively short period of time and allow students exposure to modalities, such as imaging, which may previously be excluded in a traditional “paper case” format.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6451

AB1187 SURVEY ON GENERIC DRUGS (GE) AND BIO-SIMILAR DRUGS (BIO-S) OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND THEIR DOCTORS - COHORT STUDY OF THE JAPANESE CLINICIAN BIOLOGICS RESEARCH GROUP

K. Funahashi1, T. Yoshitama2, T. Tetsu Oyama3, A. Sagawa3, K. Katayama3, “GO TRANS”: OUTCOME OF THE PROGRAM OF WORKSHOPS

Methods: 30 research group member facilities. It was an anonymous written survey. After informed consent document was signed, participants were asked to complete a survey back. The group was 78% female, the majority of whom were in their 60’s, and had most had disease history of more than 10 years. Those with a good impression of a GE, who prescribed them, and conducted a comparative study of patient’s and doctor’s awareness regarding these drugs.

Methods: The survey was carried out amongst 4151 patients being treated at 20 research group member facilities. It was an anonymous written survey. After the section on patient background (age, gender, disease history) was completed, participants were asked to fill in the answers of generic drugs, their attitudes towards changing to a generic, whether or not they had ever experienced an adverse effect with a generic drug, what knowledge they had regarding bio-similar drugs, and if they had any interest in or experience with using bio-similar drugs. We also asked 32% of patients if they trusted bio-similar drugs became possible in Japan in 2015, but the degree of knowledge that patients have regarding them is unknown.

Objectives: Therefore we carried out a patient survey about generic and bio-similar drugs, and at the same time, we also conducted a questionnaire for doctors, who prescribed them, and conducted a comparative study of patient’s and doctor’s awareness regarding these drugs.

Results: The survey was carried out amongst 4151 patients being treated at 20 research group member facilities. It was an anonymous written survey. After the section on patient background (age, gender, disease history) was completed, participants were asked to fill in the answers of generic drugs, their attitudes towards changing to a generic, whether or not they had ever experienced an adverse effect with a generic drug, what knowledge they had regarding bio-similar drugs, and if they had any interest in or experience with using bio-similar drugs. We also asked 32% of patients if they trusted bio-similar drugs became possible in Japan in 2015, but the degree of knowledge that patients have regarding them is unknown.

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Methods: The survey was carried out amongst 4151 patients being treated at 20 research group member facilities. It was an anonymous written survey. After the section on patient background (age, gender, disease history) was completed, participants were asked to fill in the answers of generic drugs, their attitudes towards changing to a generic, whether or not they had ever experienced an adverse effect with a generic drug, what knowledge they had regarding bio-similar drugs, and if they had any interest in or experience with using bio-similar drugs. We also asked 32% of patients if they trusted bio-similar drugs became possible in Japan in 2015, but the degree of knowledge that patients have regarding them is unknown.

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were under immunosuppressive therapy and 60% of them received biological treatment. 20% of patients had clinical activity data. The average of global VAS was 12 (0–100) and the average of VAS pain was 0.9 (0–100). The average of initial PEDSQL 4.0 was 80.7 (0–100) and the PEDSQL 4.0 at three months was 74.4. At the end of the workshops, 100% of parents and patients would recommend other patients to attend it, more than 50% of patients think that they would be able to go to medical visits without their parents and 90% of them would take responsibility for their treatments. A 90% of patients think that workshops have helped to improve their relationship with their rheumatologist and 60% of them have improved their knowledge about the disease. Regarding to physical activity levels, 30% of age have increased it compared to baseline. More than 50% of parents have observed a positive attitude change towards the disease after the program.

Conclusions: Transition programs are important for the transfer to be effective throughout the involvement of adolescent, who takes responsibility for his/her disease and also to ensure their psychosocial needs are met. Rheumatologists must be ready to cover these needs with the support of other specialists. Our experience with the program was very positive since most of the patients improved their knowledge about the disease and its autonomy concerning their medical consultations and treatments, being very satisfied with the contents of the workshops.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6525

AB1190 BEHAVIOR AND TRENDS IN COLOMBIAN PATIENTS WITH RHEUMATIC DISEASES RELATED TO THE TECHNICAL TOOLS IN CONSULTATION OF RHEUMATOLOGY

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Background: In the last decades the internet has changed the way of communication with patients using email, social media and other technological tools, as a complement to the consultation. The development of websites and electronic history are part of these tools that have come to change communication with the patient.

Objectives: To analyze the behavior and trends of Colombian patients with rheumatic diseases related to use electronic tools.

Methods: We analyzed 425 patients between September 2015 and December 2016, who attended to consultation at Country Medical Center. Everyone was provided the website http://www.dra-mc stomchangalorrequemologica.com/. This website was developed by Oceotsft (http://www.oceotsft.com/), company specialized in development of websites and software. In this website we have general information the clinic, access, schedules, glossary, news, medical information and can request online appointment.

Results: We included 425 patients with rheumatic diseases, 85.5% female, with an average age of 52.5 years old. 95% lived in urban areas. 92% had internet access. 80% had smartphone. They were stratified by educational level, finding that 70% had college level. And by age groups it was found that patients between 30 and 50 years old in 72% of cases used the electronic way to request the appointment or ask questions. Patients between 18 to 29 years prefer social media. Patients over 60 years old preferred to use the telephone. The reasons for using the online appointment were: easy access at any time 84% tool speed 10%. Difficulty for the use of the telephone at work 2%. Others 4%. When patients communicate via email 90% of the questions are related to requesting an appointment or ask questions. Patients between 18 to 29 years old prefer social media. Patients between 30–40 or –40–50 years had a higher score than those aged 30–40 or 40–50 years (5.8 vs 5.2 vs 5.1 respectively) but were similar in the 2nd test (6.5 vs 6.3 vs 6.8). By nationality, Spaniards had higher initial scores than foreigners (5.78 vs 4.91, p < 0.001). Men showed higher scorings than women in their 1st test (5.92 vs 5.56), but the difference was lost in the 2nd test (6.79 vs 6.47). Younger residents (ages 20–30 years) had a 1st higher score than those aged 30–40 or 40–50 years (5.8 vs 5.2 vs 5.1 respectively) but were similar in the 2nd test (6.55 vs 6.3 vs 6.4). For specialties, dermatology, internal medicine and RHB had initial scores higher than MFC (7.3 - 6.1 - 6.3 vs. 5.4), but in the second test there were no significant differences. Conclusions: The level of knowledge of rheumatology of the residents who start a training rotation in this specialty is moderate, with an average of 5.59 points out of 10 possible. At the end of the rotation their scores increased an average of 22%, which shows a significant improvement but still not very high. Several factors were related to basic knowledge scores but lost significance in the final test, reflecting appropriate improvements in knowledge in all subgroups.

Acknowledgements: To Fundacion Valenciana de Reumatologia and to MSD laboratories for an unrestricted grant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4498

AB1192 NATIONAL BAROMETER TO ASSESS THE EMOTIONAL ASPECTS OF PATIENTS WITH RHEUMATOID ARTHRITIS. OPINAR PROJECT

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Background: The WHO defines health as the state of physical, psychic and social well-being. In contrast, patients with rheumatoid arthritis (RA) frequently report that treatment is directed mainly at combating physical affection and hardly anything to emotional and social aspects.

Objectives: To assess the emotional impact and degree of satisfaction with the medical care received in the patient with poor prognosis RA.

Methods: National, structured, anonymous survey of 26 questions conducted between March and July 2016. Responses were counted as percentages or as means/medians of the score given on a Likert scale from 1 to 10 (minimum and maximum, respectively). Analyses were performed using Microsoft 2012: mean (m), standard deviation (SD), median (M), interquartile range (IQR) and statistical significance of differences (Student t test).

Results: The survey was completed by 100 of 122 enrollees, 75 by telephone and 25 via email; 83 women and 17 men, with a mean age of 49.4 years (SD 12.1); from all the Spanish Autonomous Communities. 52% were considered of poor
prognosis (participant’s own perception). 66.7% of self-perceived high-activity RA by patients exceeded the physician’s impression; and 31.03% of the intermediate-activity. The degree of knowledge and the importance given to certain aspects of the disease in relation to the poor prognosis ranged from 8 to 9/10 in the different items analyzed. The awareness of their seropositivity against FR and ACPA was 77% and 17%, respectively. 63% consider the physical aspects more disabling, but 52% gave more value to feeling good emotionally. The mean treatment score for physical aspects was 7.07 (SD 2.52), whereas for emotional aspects was 3.39 (SD 2.57). 51.9% of self-considered poor prognosis patients believed that biological treatment was delayed and 50% related that to poorer outcome. 97% wished to participate in the doctor’s decision and 95% declared they had no choice. There were no statistically significant differences between the prognostic groups.

Conclusions: More than half of the patients self-reported poor prognosis. Two-thirds estimated poorer health status than physicians if their RA was of high activity; 1/3 if it was intermediate. Patients considered all assessed aspects as determinants of poor prognosis (m = 8). The degree of knowledge of their condition was high, being lower for joint damage and activity and prognostic markers. The beginning of treatment with biologicals was perceived as delayed in more than half of those who declared themselves with poor prognosis and half of them related it to a worse evolution. A high percentage of patients showed low satisfaction with the emotional attention received. Most claim to be more involved in medical decisions, although more than 1/3 does not seem to be able to do so.

Acknowledgements: Coordinadora Nacional de Artritis (ConArtritis)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5336

AB1193 DEVELOPING THE KOREAN EDUCATIONAL NEEDS ASSESSMENT TOOL (KOREAN-ENAT) IN RHEUMATOID ARTHRITIS: A CROSS-CULTURAL VALIDATION USING RASCH ANALYSIS

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Background: The Educational Needs Assessment Tool (ENAT) is a 39-item patient-completed questionnaire designed to help patients identify and prioritize their educational needs. It was originally developed in the UK and validated in 7 rheumatic diseases including rheumatoid arthritis (RA).1

Objectives: This study aimed to undertake cross-cultural adaptation and validation of the ENAT in RA for use in Korea.

Methods: The study involved two main phases: (1) Cross-cultural adaptation of the ENAT from English into Korean and (2) validation of the Korean-ENAT. The first phase followed an established process of cross-cultural adaptation of self-report measures.2 For the second phase, patients with RA completed the Korean-ENAT at the outpatient clinic of a university hospital and Rasch measurement computer program, WINSTEPs, was used to analyze the data. Fit to the model was determined by the observed data Infit and Outfit statistics (≥0.50 and <1.50); where a value of 1.00 suggests a perfect fit to the model expectations. The unidimensionality of the scale was determined by item (and person) separation index ≥1.50 and reliability ≥0.80.

Results: An adequate conceptual equivalence was achieved following the adaptation process. A total of 123 patients completed the Korean-ENAT. Their mean ± SD age was 46.7±12.3, disease duration 53.7±71.2 months and the self-report measures.3

Table 1. Fit statistics for the Korean ENAT subscales

<table>
<thead>
<tr>
<th>Subscales</th>
<th>MNSQ</th>
<th>ZSTD</th>
<th>MNSQ</th>
<th>ZSTD</th>
<th>PTMEA CORR.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>1.31</td>
<td>2.30</td>
<td>1.40</td>
<td>2.80</td>
<td>0.75</td>
</tr>
<tr>
<td>Movement</td>
<td>1.06</td>
<td>0.10</td>
<td>1.01</td>
<td>0.10</td>
<td>0.85</td>
</tr>
<tr>
<td>Feelings</td>
<td>0.77</td>
<td>-1.90</td>
<td>0.80</td>
<td>-1.60</td>
<td>0.84</td>
</tr>
<tr>
<td>Disease</td>
<td>1.27</td>
<td>2.00</td>
<td>1.15</td>
<td>1.00</td>
<td>0.84</td>
</tr>
<tr>
<td>Treatments</td>
<td>1.78</td>
<td>2.80</td>
<td>1.40</td>
<td>2.40</td>
<td>0.85</td>
</tr>
<tr>
<td>Self-help</td>
<td>1.05</td>
<td>0.50</td>
<td>1.08</td>
<td>0.70</td>
<td>0.84</td>
</tr>
<tr>
<td>Support</td>
<td>0.75</td>
<td>-2.10</td>
<td>0.75</td>
<td>-2.10</td>
<td>0.83</td>
</tr>
</tbody>
</table>

MNSQ = mean-square; ZSTD = z-standardized; MNSQ between >0.50 and ≤1.50 for model fit.
PHYSICAL ACTIVITY IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES


Background: Inflammatory arthropathies are a group of diseases that have common characteristics, like unknown etiology, autoimmune or autoinflammatory pathogenesis, genetic predisposition and chronicity. These affect people of all ages and can cause physical, psychic, and social disability. Physical activity is essential to decrease symptoms of pain, fatigue and weakness, improving joint mobility, increasing muscle mass, flexibility and psychosocial health.

Objectives: To describe the physical activity in patients with inflammatory arthropathies.

Methods: In this transversal, observational study we evaluated all patients with inflammatory arthropathies treated with intravenous biologic therapy in a Day Hospital Unit (DHU) of a tertiary hospital. We collected the following data: demographics, indexes of disease activity according to each disease, fatigue questionnaire (FACIT), health questionnaire SF–12, physical activity questionnaire (PAQ), and fibromyalgia questionnaire (FIQ*F). This represents a cohort of patients that initiate an educational program on the importance of physical activity in the management of the disease.

Results: We included 222 patients (60.8% female), with a median age (SD; range) of 56.19 (12.89; 25–82) and a median disease duration (SD) of 16.54 (9.6). Of all included patients, 54.1% had rheumatoid arthritis, 39.2% had spondyloarthritis and 6.8% has psoriatic arthritis; 26.8% were in remission, 43% practice more than one sport. According to the IPAQ questionnaire, 19.8% performed high physical activity, 44.1% middle, 36% low physical activity, and 5.1% sedentary. Fortye five (20.3%) patients had fibromyalgia according to FIRST questionnaire. According to the IQPA questionnaire, 73% of patients considered that their diseases affect the performance of physical activity. 67% of the patients had none or very low daily physical activity, 80% would like to do more exercise. Among sports or physical activities performed by the patients, the most common was walking (65%), then swimming (12%), cycling and gym (8%) and running (6%). Of the patients who perform physical activity, 43% practice more than one sport.

In a multivariate regression logistic, only the gender and the age related with the physical activity, and not the disease; males (p = 0.024; Exp(B) 2.389; CI 95%: 1.124–5.059) and younger persons (p = 0.004; Exp (B) 0.959; IC 95%: 0.943–0.987) performed more physical activity.

Conclusions: Patients with inflammatory joint diseases perform low physical activity. The nurse plays a very important role in educating and informing the patients about their illness, and helping them in changing their lifestyle, encouraging increased physical activity with appropriate programs depending on the alterations that produce each disease, in order to improve their quality of life.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4938

THE EFFECTS OF KINESIO TAPING ON PAIN, JOINT RANGE OF MOTION, MUSCLE STRENGTH AND DISABILITY IN IMPINGEMENT SYNDROME

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Background: The impingement syndrome is common cause of shoulder pain. Physical therapy includes manual therapy techniques, electrotherapy modalities and exercises in this problem. The Kinesio Taping application is a definitive rehabilitative taping technique that is designed to facilitate body’s natural healing process while providing support and stability to muscles and joints without restricting the body’s range of motion.

Objectives: The purpose of this study was to determine the efficacy of kinesio taping (KT) on subjects’ pain, joint range of motion, muscle strength and level of disability in treatment of impingement syndrome (IS).

Methods: The study was conducted patients with IS. The subjects were divided into two random groups as general physical therapy applications group (GPTG) and kinesio taping group (KTG). GPTG was treated transcutaneous electrical nerve stimulation (TENS), hotpack and ultrasound for ten session. KTG’s therapy was contained shoulder kinesio taping application in addition to TENS, hotpack and ultrasound. KT was applied as “Y strip” to deltoid and supraspinatus muscles and was “I strip” to muscle of teres minor. The groups were evaluated before and after treatment in terms of pain, range of motion (ROM), muscle strength and scores of shoulder disability. Visual analog scale was used to assess of pain (night pain, rest pain, pain with motion and general pain), goniometer measurements was used to assess of shoulder ROM. Shoulder Disability Questionnaire and Disabilities of the Arm Shoulder and Hand were used to assess of shoulder disability.

Results: 54 patients with IS aged 18 to 65 years were recruited to the study. Demographic data were similar in the groups. When compared before and after treatment, the level of pain, night pain, rest pain, pain with motion and pain in functional use) was significantly decreased in both groups (p<0.05) (Table 1), also an improvement was seen in muscle strength (p<0.05), ROM (p<0.05) and in the scores of disability of shoulder (p<0.05) in both groups. In terms of overall pain relief the KTG scores better than GPTG. Internal and external rotation muscle
Active internal and external rotation ROM increased in KTG (p < 0.05). Functionality and disability scores improved in two groups. It was detected that there was no difference between the groups in terms of the values of muscle strength, functionality and disability scores.

**Conclusions:** The kinesiologic band can be used as a supportive therapy method in the early shoulder treatment program because it provides painless shoulder motion to clinicians. We consider that KT applications in addition to general physical therapy applications may have positive effects in the treatment of impingement syndrome.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3799

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**THU0723-HPR**

**A PHYSIOTHERAPY-LED IN-PATIENT INTENSIVE REHABILITATION PROGRAMME FOR ANKYLOSING SPONDYLITIS: FOLLOW-UP OUTCOMES**

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**Background:** Physiotherapy and exercise are highly important in the management of Ankylosing Spondylitis (AS). Physiotherapy is delivered to patients with AS in either in-patient or out-patient settings. Knowledge of the effectiveness of an in-patient delivered programme is useful for physiotherapists in assisting patients to achieve their goals.

**Objectives:** To assess the short-term effectiveness of an intensive rehabilitation programme using BASMI and EASI-QOL outcomes, and long-term patient satisfaction and physical activity behaviour and adherence to exercise plan.

**Methods:** Thirty-two AS patients (25 males and 7 females) admitted to an in-patient rheumatology ward underwent a 1 to 2-week physiotherapy-led intensive rehabilitation programme and were then discharged with a home exercise programme. Pre/post rehabilitation BASMI scores were available for 26 patients. The primary outcome measure was the proportion of patients achieving an improvement on BASMI scores at discharge. Secondary outcome measures included improvements in physical activity levels and adherence to home exercise programme for longer than 3 months which was obtained via a postal patient satisfaction and physical activity questionnaire achieving a response rate of 50% (n=16).

**Results:** Improvements in BASMI scores was achieved in 69% of patients (n=18) at the end of the in-patient rehabilitation period. Improvements in EASI-QOL were achieved in 83% of patients (n=15) at the end of the in-patient rehabilitation period. Ninety-four percent of patients (n=15) increased their physical activity levels after discharge, with 81% (n=13) of patients maintaining their home exercise programme for 3 months more. Thirty percent (n=7) of patients carry out at least 150 minutes of physical activity per week (National Recommended Physical Activity Guidelines is 150 minutes/week of moderate intensity).

**Conclusions:** This recent audit shows the effectiveness of an intensive physiotherapy-led in-patient rehabilitation programme for Ankylosing Spondylitis improving BASMI scores in 18 patients and improving physical activity behaviour over the long-term. Future work will aim to compare demographics and medical treatment differences between improvers and non-improvers.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3799

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**THU0724-HPR**

**SELF-MANAGEMENT EXERCISE PROGRAM ASSOCIATED TO SPA THERAPY INCREASED THE PHYSICAL ACTIVITY LEVEL OF PEOPLE WITH SYMPTOMATIC KNEE OSTEOARTHRITIS: A QUASI-RANDOMIZED CONTROLLED TRIAL**

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**Background:** Treating knee osteoarthritis (OA) in the medical phase is today well standardized. Guideline oriented approaches aiming at increasing physical activity (PA), improving pain and disability.

**Objectives:** To assess effectiveness of self-management exercise program associated to spa therapy at 3 month on the improvement of physical activity (PA) level, disability, pain, anxiety, fears and believes in symptomatic knee osteoarthritides (OA).

**Methods:** Prospective, multicentric, quasi-randomized controlled trial with alternate month design method (one month periods). People with symptomatic knee OA people (stage I-V, Kelgren and Lawrence scale) with low and moderate PA level were included in 3 spa therapy resorts. Intervention group (IG) received 5 self-management exercise sessions (1h30; education, aerobic, strength training, range of motion) + information booklet + 18 sessions (1h) of conventional spa therapy (STC). Control group (CG) received information booklet + 18 sessions of STC. The primary outcome was changes at 3 months in PA level (IPAQ short form) and secondary outcomes were WOMAC function, pain (VAS), HAD anxiety/depression, KOFBeQ fears and believes changes.

**Results:** 131 subjects were included. The mean age was 65.6 years [±6.7]. WOMAC function score was 22.1±6 [±11.3] and pain was 4.6/10 [±1.9] in inclusion. Both groups significantly increased PA level measured with continuous IPAQ total score (ME±minutes/weeks), with superiority for IG (+77.8%; p=0.0062) than CG (+50.7%; p=0.0099). There was no change in setting time. Disability (-11.3%; p=0.0370) and pain (-15.2%; p=0.0032) also decreased significantly for both groups. Anxiety (-11.6%; p=0.0195) and fears and believes (-18.2%; p=0.0146) decreased significantly only in intervention group. Other data will be presented later.

**Conclusions:** This study confirms the impact of STC on disability and pain and gives news data’s on physical activity level. Self-management exercise program improve anxiety, fear and believes. Complex educational strategies comprising information booklet with or without self-management exercise program can be proposed and adapted to OA phenotypes.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1929

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**THU0725-HPR**

**COST EFFECTIVENESS ANALYSIS OF ABATCEPT COMPARED WITH TNF INHIBITORS IN PATIENTS WHO ARE POSITIVE FOR ANTI-CITRULLINATED PROTEIN ANTIBODIES BASED ON RESULTS FROM AN OBSERVATIONAL TRIAL**

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**Background:** Anti-citrullinated protein antibodies (ACPA) are highly specific to RA and patients (pts) who are ACPA positive (+) tend to develop more severe, erosive disease than ACPA-negative pts. In an observational study exploring the clinical value of ACPA in RA, pts with ACPA+ response to abatacept (ABA) or a TNF inhibitor (TNFi), mean (SE) changes from baseline in CDAI at 6 months was –8.6 for ABA and –5.6 for TNFi initiators.2

**Objectives:** To evaluate the costs and benefits of treating pts with RA who are ACPA+ with ABA vs TNFi on background MTX.

**Methods:** An economic analysis was carried out estimating lifetime direct costs and quality-adjusted life years (QALYs) of ACPA+ pts with RA treated with ABA or TNFi from a UK National Health Service (NHS) perspective. QALYs are a measure of quality burden, adjusted to reflect quality of life lived. As data for the economic analysis were derived from a real-world study, an “average” pt was modelled, whose baseline characteristics were based on the observational study. CDAI changes at 6 months for each treatment were converted to HAQ changes, and disease progression was based on HAQ score changes over a lifetime. Continuation of therapy was based on rates from the real-world study. Mean long-term survival on treatment with ABA or TNFi was derived from the literature.3 In the base case, pts discontinuing ABA or TNFi moved to palliative care (MTX). Direct medical costs and quality of life scores were correlated to HAQ scores.4,5 Costs included hospitalizations, joint replacements and treatment costs. Estimates of different direct costs and QALYs between ABA and TNFi initiators were used to calculate an incremental cost-effectiveness ratio (ICER; cost per QALY gained). The annual cost of TNFi was calculated as an average of TNFi drugs in the UK (£ 9113). For ABA, an average cost of five biologics was used (£ 9244) to reflect a realistic cost to NHS UK. A sensitivity analysis examined the effect of varying the input parameters of efficacy, cost and utilities on costs and outcomes.

**Results:** Based on an “average” pt from the observational study, the total estimated QALYs for ABA and TNFi initiators were 6.4 and 6.27, respectively. Total lifetime costs were £ 41,378 and £ 40,627, respectively. The lifetime cost for
Caribbean metacarpal osteoarthritis (CMC-OA) is a common joint condition, with a prevalence of 13% in people aged 41 to 50 years, increasing to 68% in people between 71 and 80 years. In the absence of disease-modifying interventions, non-pharmacological approaches are considered as core treatments for hand OA, while surgical treatment is recommended for those with severe CMC-OA.

Objectives: To describe function and previous treatment in patients referred for surgical consultation due to CMC-OA.

Methods: Individually referred for surgical consultation due to their CMC-OA at three Norwegian departments of rheumatology were invited to participate. Those who agreed attended a clinical assessment and reported their symptoms, disability and functional limitations at the Quick-Dash; 38.6 versus 30.4, (p=0.006) and MAPHand; 2.0 versus 1.7 (p<0.001), for women and men, respectively. However, for finger range of motion, men had slightly more flexion deficit and less palmar abduction in their left hand compared to women.

Conclusions: Among patients referred for surgical consultation due to CMC-OA, women self-reported lower hand function and scored poorer than men in observer-based assessments. Even if conservative treatment is recommended before referral for surgery, only a few participants had received such treatment for their hand OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3662

THU0728-HPR

OBJECTIVES: To explore the attitudes and needs concerning blended care of two Health Professionals like to go? self-management: Is this the way patients and professionals like to go? C. Bode 1, E. Taal 1, H. Vonkeman 2, F. Ben Allouch 1, K. Hohl 1, 1 Psychology, Health & Technology, University Twente; 2 Rheumatology, Medisch Spectrum Twente, Enschede, Netherlands

Background: Blended care, the integration of online and face-to-face care, promises to combine the best of two worlds.

Objectives: To explore the attitudes and needs concerning blended care of two key stakeholders: health professionals and patients.

Methods: Rheumatologists (8) and specialized nurses (5) were recruited in a Dutch hospital and patients with an inflammatory rheumatic disease (10) were recruited via flyers in hospitals and patient organizations in Germany. A semi-structured interview schedule was used to explore knowledge, experiences, needs and perceived (dis)advantages of a blended care format for fatigue self-management. Transcribed verbal data were coded with hierarchical coding schemes.

Results: Perspective of professionals: Blended care matches needs for psychosocial interventions in medical settings, has a patient-friendly and flexible format, reflects the active role of patients and can easily be imbedded in standard care. Reported barriers were low education and skills in technology use in patients, the lack of proven and safe interventions and costs for development/implementation. Patient perspective: Patients expected better communication, time saving and improved autonomy in self-management. They were concerned about loss of personal contact and in general, patients were very critical regarding online activities, privacy risks and guaranteed quality of eHealth products.

Conclusions: Health professionals and patients differ in their attitudes towards blended care. Professionals are better informed and have a more positive attitude, whereas patients’ attitudes towards blended care are mainly driven by their reservations towards the reliability and safety of the Internet in general. Results will be discussed on the background of attitudes towards eHealth in different countries.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6838

THU0726-HPR

WHAT CHARACTERISES PATIENTS REFERRED FOR SURGICAL CONSULTATION DUE TO CARPOMETACARPAL OSTEOARTHRITIS? E.M.H. Gravas 1, R. Nossum 2, R.E.M. Eide 3, A. Klokkereide 4, K.H. Matre 3, M. Olsen 3, S. Dane 2, O. Andreassen 1, N. Osteras 1, I. Kjeken 1, 1 Diakonhjemmet Hospital, Oslo; 2 St.Olav’s Hospital, Trondheim; 3Haukeland University Hospital, Bergen; 4 Haugesund Rheumatism Hospital, Haugesund, Norway

Background: Carpometacarpal osteoarthritis (CMC-OA) is a common joint condition, with a prevalence of 13% in people aged 41 to 50 years, increasing to 68% in people between 71 and 80 years. In the absence of disease-modifying interventions, non-pharmacological approaches are considered as core treatments for hand OA, while surgical treatment is recommended for those with severe CMC-OA.

Objectives: To describe function and previous treatment in patients referred for surgical consultation due to CMC-OA.

Methods: Individuals referred for surgical consultation due to their CMC-OA at three Norwegian departments of rheumatology were invited to participate. Those who agreed attended a clinical assessment and reported their symptoms, disability and functional limitations at the Quick-Dash: 38.6 versus 30.4, (p=0.006) and MAPHand: 2.0 versus 1.7 (p<0.001), for women and men, respectively. However, for finger range of motion, men had slightly more flexion deficit and less palmar abduction in their left hand compared to women.

Conclusions: Among patients referred for surgical consultation due to CMC-OA, women self-reported lower hand function and scored poorer than men in observer-based assessments. Even if conservative treatment is recommended before referral for surgery, only a few participants had received such treatment for their hand OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3662

THU0727-HPR

BLENDED INTERVENTIONS FOR FATIGUE SELF-MANAGEMENT: IS THIS THE WAY PATIENTS AND PROFESSIONALS LIKE TO GO? C. Bode 1, E. Taal 1, H. Vonkeman 2, F. Ben Allouch 1, K. Hohl 1, 1 Psychology, Health & Technology, University Twente; 2 Rheumatology, Medisch Spectrum Twente, Enschede, Netherlands

Background: Blended care, the integration of online and face-to-face care, promises to combine the best of two worlds.

Objectives: To explore the attitudes and needs concerning blended care of two key stakeholders: health professionals and patients.

Methods: Rheumatologists (8) and specialized nurses (5) were recruited in a Dutch hospital and patients with an inflammatory rheumatic disease (10) were recruited via flyers in hospitals and patient organizations in Germany. A semi-structured interview schedule was used to explore knowledge, experiences, needs and perceived (dis)advantages of a blended care format for fatigue self-management. Transcribed verbal data were coded with hierarchical coding schemes.

Results: Perspective of professionals: Blended care matches needs for psychosocial interventions in medical settings, has a patient-friendly and flexible format, reflects the active role of patients and can easily be imbedded in standard care. Reported barriers were low education and skills in technology use in patients, the lack of proven and safe interventions and costs for development/implementation. Patient perspective: Patients expected better communication, time saving and improved autonomy in self-management. They were concerned about loss of personal contact and in general, patients were very critical regarding online activities, privacy risks and guaranteed quality of eHealth products.

Conclusions: Health professionals and patients differ in their attitudes towards blended care. Professionals are better informed and have a more positive attitude, whereas patients’ attitudes towards blended care are mainly driven by their reservations towards the reliability and safety of the Internet in general. Results will be discussed on the background of attitudes towards eHealth in different countries.

Disclosures of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6838

Abstract THU0726-HPR – Table 1. Hand function

<table>
<thead>
<tr>
<th></th>
<th>Right hand</th>
<th></th>
<th>p-value</th>
<th>Left hand</th>
<th></th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Women</td>
<td>Men</td>
<td>p-value</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>No. of joints with bony enlargements, mean (SD)</td>
<td>1.9 (2.3)</td>
<td>1.2 (2.9)</td>
<td>0.10</td>
<td>1.6 (2.3)</td>
<td>1.3 (2.8)</td>
<td>0.46</td>
</tr>
<tr>
<td>Proportion with normal max grip strength*, % (SD)</td>
<td>65.7 (27.6)</td>
<td>90.9 (26.1)</td>
<td>&lt;0.001</td>
<td>64.0 (26.3)</td>
<td>83.5 (21.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proportion with normal pinch strength*, % (SD)</td>
<td>66.2 (28.8)</td>
<td>73.6 (28.3)</td>
<td>&lt;0.001</td>
<td>66.8 (25.8)</td>
<td>71.5 (29.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of painful joints, mean (SD)</td>
<td>4.2 (3.3)</td>
<td>2.0 (2.1)</td>
<td>0.001</td>
<td>3.8 (3.0)</td>
<td>3.3 (1.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain at rest*, mean (SD)</td>
<td>2.3 (2.2)</td>
<td>1.7 (1.8)</td>
<td>0.10</td>
<td>2.8 (2.6)</td>
<td>2.3 (2.1)</td>
<td>0.23</td>
</tr>
<tr>
<td>Pain following grip strength assessment*, mean (SD)</td>
<td>2.7 (2.5)</td>
<td>2.4 (2.9)</td>
<td>0.60</td>
<td>2.6 (2.3)</td>
<td>2.5 (2.4)</td>
<td>0.92</td>
</tr>
<tr>
<td>Pain following pinch strength assessment*, mean (SD)</td>
<td>2.9 (2.7)</td>
<td>2.7 (2.4)</td>
<td>0.56</td>
<td>10.4 (27.8)</td>
<td>10.7 (33.6)</td>
<td>0.96</td>
</tr>
<tr>
<td>Total flexion deficit, mm (SD)</td>
<td>11.2 (30.5)</td>
<td>8.0 (24.4)</td>
<td>0.56</td>
<td>50.0 (11.9)</td>
<td>48.5 (10.6)</td>
<td>0.49</td>
</tr>
<tr>
<td>Palmar abduction thumb*, mean degrees (SD)</td>
<td>50.9 (11.7)</td>
<td>51.5 (12.2)</td>
<td>0.77</td>
<td>50.0 (11.9)</td>
<td>48.5 (10.6)</td>
<td>0.49</td>
</tr>
<tr>
<td>Abduction CMC*, mean degrees (SD)</td>
<td>37.9 (8.9)</td>
<td>40.3 (12.0)</td>
<td>0.20</td>
<td>37.9 (8.9)</td>
<td>38.1 (10.6)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

*Measured in Newton using the GripIt. t* Numerical rating scale (NRS): 0–10; t= no pain. * Measured in degrees using the Pollexograph.
as age, gender, disease duration and hand dominance, were homogeneous at the beginning of the study. In both groups there was a reduction in hand pain with time (intragroup analysis). Pain in the functional group, expressed as mean ± standard deviation, was 6.82±1.72 and 4.77±2.45 at the beginning and end of the treatment, respectively, and the corresponding figures for the nighttime group were 7.29±1.63 and 5.12±2.58. The p values for both groups were p<0.001. There were no statistically significant differences in the majority of the parameters assessed between the groups, including the outcome pain. Three measures considered to be occasional, presented a significant difference between the groups: right palmar abduction p=0.023 and right tripod pinch strength p=0.006 with better results for the group that used the night splint; and time execution of the pick-up test with eyes closed to the right hand p=0.048 with more representative results for the functional (daytime) splint use.

Conclusions: There was no statistically significant difference between functional and night splint in terms of pain, function or any of the other parameters assessed in rhizarthrosis patients after one year of treatment.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5590

THU0729-HPR PATIENTS AND CAREGIVERS PREFERENCES RELATED TO THE USE OF INFORMATIC TECHNOLOGY TOOLS FOR EDUCATION IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints affecting more than 1% of global population, it is a long term condition that causes disability and affects the quality of life (1). It has been demonstrated that patient’s involvement with its treatment and disease management can be more effective than information only given by the physician or a health care professional (2).

Objectives: To describe patient’s preferences regarding information technology tools for education and RA management in a specialized center in Bogota Colombia.

Methods: We conducted a descriptive study where a survey was applied to a group of patients or caregivers attending to a patient-focused symposium in Bogota Colombia. Descriptive epidemiology was done, percentages and averages were calculated for qualitative variables.

Results: We included 452 participants, 80% were patients and 20% caregivers, only 25% referred to assist to informative activities regarding disease management, 41% reported to have information regarding RA, also between 29% and 45% of patients acknowledged the role of the health-care team in the disease activity management. Regarding technology information tools patients considered that WhatsApp was the most important tool to received messages to disease management (40%) followed by YouTube and websites. 70% reported to have a computer or a mobile phone with internet connection, 60% reported to use Facebook while only 30% reported to use easily websites and twitter.

Conclusions: It is important to know the preferences and access that patients and caregivers have to informatics technology in order to create self-care programs that really are going to be used in this population. This survey is evidence not only to start an educational program in our specialized center but to the health care professionals and stakeholders in Colombia.

References:

THU0730-HPR CONTENT AND SUPERVISION OF GROUP EXERCISE THERAPY (GET) FOR AXIAL SPONDYLOARTHRITIS (AXS) IN THE NETHERLANDS; A NATION WIDE SURVEY

F. Van Der Giesen1,2, S. Van Weely3, L. Nopuhaa3, T. Vliet Vlieland2. 1Rheumatology, Haga Teaching Hospital, The Hague; 2Orthopedics, Leiden University Medical Center, Leiden; 3Dutch Arthritis Foundation, Amsterdam, Netherlands

Background: For axSpA patients exercise therapy is recommended in (in)ternational treatment guidelines. Apart from mobility exercises, muscle strengthening and cardio vascular training are recommended therapeutic modalities [1,2]. In the Netherlands 45 therapy groups (land based exercises; 1, hydrotherapy; 13, combination groups; 31) are organized by 17 local patient organizations exclusively for AxSpA patients. It is unclear if the treatment recommendations are followed and what the nature of the supervision in these exercise programs is.

Objectives: To describe the therapeutic modalities used and characteristics of the supervision in GET for patients with axSpA in the Netherlands.

Methods: A questionnaire was sent to the coordinating supervisors of GET from the17 local patient organisations involved in GET for axSpA with questions regarding the frequency and duration of group exercise programs and treatment modalities (mobility, strengthening and cardio-vascular exercises) used in land-based and hydrotherapy parts of the programs. In addition the questionnaire included questions regarding the number of supervisors involved in the supervision of GET, their professional background (physical therapist, other), years of experience with GET (<1yr, 1–5 yrs, >5yrs) additional education related to rheumatic diseases (yes/no) and rheumatology network membership (yes/no).

Results: All 17 coordinating supervisors of GET for axSpA returned the questionnaire. All exercise groups were performed once a week with a median (range) duration of 30 minutes (30–60) for the hydrotherapy and 105 minutes (45–180) for the combination therapy groups. Regarding land-based treatment modalities, active joint range of motion exercises and muscle strengthening exercises were used as was stated by 15/17 and 14/16 coordinators respectively. Given the frequency in combination therapy groups showed a wide variety, as did the program composition (water based/land and water based). Identifying considerable practice variation. The majority of the supervisors were physical therapists with long standing experience but only a minority had postgraduate rheumatology education. To ensure the quality of GET for patients with axSpA, reducing practice variation is a future challenge.

Education of GET supervisors might be important aspects and target of priority.

References:

Acknowledgements: This study was funded by the Dutch Arthritis Foundation.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4192

THU0731-HPR CAN A THREE WEEKS PROGRAM IN A REHABILITATION CENTER IMPROVE SYMPTOMS AND EXERCISE-FREQUENCY FOR RHEUMATIC PATIENTS?

G. Jarret, A. Orpina, Skogil Helse- og Rehabiliteringsenter AS, Lillehammer, Norway

Background: Rehabilitation for people with rheumatic disorders (15% of world-wide population) is a long term project (Stoffer et al. 2015). Rheumatic patients do not exercise as often as recommended (Holm et al. 2015). Intensive multidisciplinary interventions in rehabilitation-centers are in some countries an option – of which there is little effect knowledge. Perhaps data from a quality-management perspective can shed some prespective on this subject.

Objectives: Primarily to observe short and long term effects of a three weeks intensive multidisciplinary program for people with rheumatic disorders, and secondary to see if a correlation can be found between level of training frequency and levels of pain, stiffness, and self rated health.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5450
Methods: 738 patients (age 62.0±11.1, 84% women), followed a three weeks multidisciplinary program of individual and group sessions - with physiotherapy as main focus - during the period of August 2010 to September 2016 at Skgolli Health- and Rehabilitation Center, Lillehammer, Norway. 3-month follow-up: N=252 and 12-month follow-up: N=118. Data from self-report questionnaires at T1-T4 was gathered and Pearson product-moment correlation coefficients were used to analyze the data obtained, using IBM SPSS Statistics v.23.

Instruments:
- NRS-11 for pain and stiffness at baseline (T1), at discharge (T2), and at 3- (T3) and 12 months (T4) after discharge.
- Likert scale (1–6) for self-rated level of health at T1, T2, T3 and T4.
- Self-reported level of training frequency at T1, T3 and T4

Results: There was a clear mean improvement (p<0.0001) on all factors at T2 on all scales. At T3 there was a mean improvement (p<0.01) on all factors, except pain, of small/moderate effect size. There was a mean improvement (p<0.05) on self-rated level of health and training frequency at T4 of a small effect size. Worth noting is that the degree of stiffness and pain at T4 is back to T1-level.

There was a correlation (p<0.05) between level of training frequency and self-rated level of health (small at T1/T3, medium at T4), but no correlation between level of training frequency and level of pain or stiffness, at any time. This suggests that a higher training frequency is associated with a higher sense of health - regardless of symptom levels.

Conclusions: People with rheumatic disorders seem to have a very positive short term effect on all aspects after a three week intensive multidisciplinary program, but gradually return to pre-rehab levels during the following year - especially regarding symptoms like stiffness and pain. At the same time there seems to be a much slower decline in self-rated level of health – especially for those who regularly exercise. Properly randomized controlled trials are however needed to be able to draw any clear conclusions.

Implications: There might be a need for intensive multidisciplinary programs for rheumatic patients at intervals of less than a year, to be able to better keep the general health and function gained. Another possible implication is to implement a stronger focus on teaching rheumatic patients the necessity for an active lifestyle – including regular exercises – for them to be able to maintain their sense of general health, regardless of symptom levels.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1258

THU0732-HPR

ENHANCED MANAGEMENT OF ANKYLOSING SPONDYLITIS THROUGH GUANGDONG INTERNET HOSPITAL IN CHINA: A RANDOMIZED, CONTROLLED TRIAL

H. Zhengping 1, L. Tianwang 1, H. Zhixiang 1, P. Xia1, Z. Lihua 2, H. Yukai1, 2, H. Koksvik2, K. Grønning 1, A. Steinsbekk 1.

Background: Ankylosing Spondylitis (AS) is a kind of common chronic disease. Guangdong Internet Hospital is China’s first officially recognized network hospital and the government encourage development of telemedicine in the country. Increasing research evidences support the efficacy of telemedicine in management of chronic diseases. However, there are still few researches about AS management by using telemedicine.

Objectives: We here conducted a 6-month randomized, controlled trial to evaluate the feasibility and efficacy of Guangdong Internet Hospital in AS management.

Methods: A total of 102 AS patients were randomly divided into two groups: standard care (ST) group or standard care with Network-Enhanced Management (ST-NEM) group. NEM enhanced disease management including cognition of the disease, medication management, behavioral management and psychotherapy. Individuals were assessed by using several tools at baseline and 6 months later: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for the disease activity, Ankylosing Spondylitis Functional Index (BASFI) for the functional limitation, the Zung Self-Rating Anxiety Scale (SAS) and the Zung Self-Rating Depression Scale Zung (SDS) for the psychological status. Pittsburgh sleep quality index (PSQI) for the sleep quality, and SF-36 for the general health status.

In addition, we made a satisfaction survey about the network platform in the management of the disease. Both group received the same medications during the period. There were no significant differences in baseline demographic and clinical characteristics between the two groups.

Results: After 6 month, 91 patients completed the trial. BASFI (1.75±0.73 vs. 2.04±0.69, P=0.026), SAS (28.12±1.22 vs. 39.56±6.81, P=0.022), SDS (26.5±1.34 vs. 32.12±3.64, P=0.031), PSQI (3.31±0.46 vs. 4.79±0.54, P=0.019) and SF-36 (SF-36: 54.24±16.66 vs. 61.41±8.56, P=0.014; SF-36: 63.42±11.08 vs. 68.98±10.46, P=0.032) were significantly lower in ST-NEM group than ST group after 6 months. There was no significant difference in BASDAI (2.66±0.91 vs. 2.75±0.75, P=0.068) between the two groups. Individuals assigned to the ST-NEM group reported significantly improved in functional limitation, psychotherapy (daily) and patient education. The control group received treatment as usual. The primary outcome measure was physical function assessed by the “30 second Sit to Stand test” (30sSTS, number of sit and stand during 30 seconds, higher score is better) and self-management/coping measured by the “Effective Musculoskeletal Consumer Scale” (EC17, higher score is better).

Results: Forty patients (mean age 27.5, 65% female) with IRD (intervention/control: 3:2 rheumatoid arthritis, 3:9 juvenile idiopathic arthritis, 4:5 psoriatic arthritis, 8:3 ankylosing spondylitis and 2:1 polyarthritis) were randomized. 19 out of 20 patients completed the intervention. At twelve months follow up there were 3 patients lost to follow up from the intervention group, and 2 in the control group. Patients in the intervention group had a significant improvement in the 30sSTS test 3, 6 and 12 months after completed intervention, compared to the control group (Table 1). The within group analysis showed that both groups improved at 6 and 12 months. The EC17 showed no difference between the two groups at 3, 6 or 12 months.

Conclusions: The results indicate that the intervention group significantly improved their physical function one year after the intervention compared to the control group, but there was no effect on self-management/coping. These results
might reflect that the focus of the intervention was mainly intensive exercise, and less on self-management / coping. This was a small study and the results should be interpreted with caution.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2256

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**THU0734-HPR**

**ASSESSMENT OF LOCAL DISEASE ACTIVITY AFTER AN INTENSIVE HAND EXERCISE PROGRAM IN PATIENTS WITH RHEUMATOID ARTHRITIS MEASURED BY ULTRASOUND IMAGING: AN EXPLORATORY RANDOMIZED CONTROLLED TRIAL**

C. Bartholdy, M. Henriksen, E. Wæhrens, K. Ellegaard.1,1. The Parker Institute, Frederiksberg, Denmark

**Background:** In 90% of patients with rheumatoid arthritis (RA) the joints of the hand are affected, causing impaired hand function. In general, reduced strength and range of motion of the hand are seen in patients with RA. Studies have shown positive effect on pain and function after exercise intervention for the hand in patients with RA. However, it is unclear if the disease activity in the joints of the hand is influenced by an exercise program. Ultrasound imaging (US) is shown to correlate with other markers of disease activity in RA and can be used as a surrogate measure for inflammation in the joint, as US visualizes synovial hypertrophy and increased blood flow.

**Objectives:** To investigate if intensive hand exercise combined with joint protection education for the hand in women with RA can be conducted without a negative effect on the disease activity in the wrist and metacarpal (MCP) joints.

**Methods:** This is a sub-study of a randomised clinical trial investigating hand exercise therapy as add on to education in joint protection during activities of daily living (ADL) performance. The intervention group (IG) had both ADL education and exercise therapy and the control group (CG) had only ADL education. The participants were women with RA involving the hand who had been on stable medication for at least three month.

At baseline all participants were examined by a rheumatologist. The joints were examined, blood samples collected and pain and strength of the hand were measured. Patient's functional ability was assessed using the Assessment of Motor and Process Skills (AMPS). US examination of the wrist and MCP 2–5 joints was performed using a linear probe 10 MHz. The evaluated was made according to a validated scoring system sum. (1)

**Results:**

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>Baseline values</th>
<th>Change from baseline to</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>3 months Mean (95% CI)</td>
</tr>
<tr>
<td>30sSTS Within group</td>
<td>Intervention</td>
<td>12.75 (3.2)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>13.15 (2.7)</td>
</tr>
<tr>
<td></td>
<td>Between groups</td>
<td>7.6 (4.3–10.9)</td>
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<tr>
<td>EC17 Within group</td>
<td>Intervention</td>
<td>64.5 (19.1)</td>
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<tr>
<td></td>
<td>Control</td>
<td>64.4 (10.3)</td>
</tr>
<tr>
<td></td>
<td>Between groups</td>
<td>-1.3 (-7.6–4.9)</td>
</tr>
</tbody>
</table>

Eight withdraw during the study period, six from the IG and two from the CG. Thus, 22 from the IG and 25 in the CG were included in the final analysis. The mean age 63.6 (12.6) years and mean disease duration was 12.7 (11.3) years, baseline mean tender and swollen joint were 4.8 (4.7) and 1.3 (1.7), respectively. No differences in change from baseline in tender joint count, hand pain and strength and functional ability was seen between the two groups (data not shown). The mean score and change from baseline in US score and inflammatory marker (CRP) in the blood are seen in table below.

**Conclusions:** Women with RA of the hand experience no negative effect on the disease activity in the joints of the hand after eight weeks combined hand exercise and joint protection education.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5193

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**THU0735-HPR**

**SHARED CARE OF RHEUMATOLOGIST AND NURSE CONSULTATIONS IN FOLLOW UP OF RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS OUTPATIENTS WITH LOW DISEASE ACTIVITY: A MONOCENTRIC, RANDOMIZED CONTROLLED TRIAL**

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**Background:** Due to national regulations, the role of nurses in the management of arthritis patients differs significantly in all European countries (1). In Belgium, regularized consultations conducted by a rheumatology nurse do not exist.

**Objectives:** The study investigated whether rheumatology nurse consultations alternating with rheumatologist consultations for RA or AS patients with low disease activity is non-inferior compared to the usual care by the rheumatologist. Primary outcomes were safety and disease activity. Secondary outcomes were fatigue, pain, functional index, patient satisfaction, the level of self-management and self-efficacy.

**Methods:** This is a monocentric randomized controlled trial. The intervention group received a consultation conducted by a rheumatologist alternating with a rheumatology nurse every 8 weeks. Patients in the control group received usual care: consultations performed by a rheumatologist every 8 weeks.

**Results:** Mixed method analyses were performed. No statistical significant between-group effects were found nor in the RA group nor in the AS group, although there was a clinical relevance towards disease activity by AS patient in the intervention group. DAS 28 dropped with a mean difference of 0.4 (-1.1 –0.2, SD 0.30). The ASDAS and BASDAI both decreased with 1.1 (-1.4 –1.3, SD 0.1 and -1.7 –1.4, SD 0.1 respectively). No safety signals from biochemical parameters such as SGOT, GOT and creatinine were detected. Inflammatory markers (ESR and CRP) remained stable in both groups. The secondary outcomes showed no significant between-group effects for both diseases. The self-efficacy outcome noticed a positive in-between-group effect by patients with RA in the intervention group.

**Conclusions:** In the follow-up of patients with RA or AS and low disease activity, outcome is not different when rheumatology nurse consultations alternating with rheumatologist consultations are compared to usual care. Implementing nurse consultations can positively influence the disease activity and patient self-efficacy.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2341
Efficacy of different types of exercise programs in osteoporosis with high risk of falls

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Background: While ageing the frequency of osteoporosis increases. The most frequent risk factor is falling and consequently bone fractures which in this population is associated with high mortality. According to WHO data, 28–35% of elderly 65 years falls at least once per year, which increases to 32–47% over 70 years.

Objectives: The purpose of this randomized control study was to investigate the efficacy of a land-based and water-based exercise program specifically targeting balance to reduce fall risk in patients over 65 years with osteoporosis. We assumed that water-based training program would develop balance efficiently even at elderly people with severe degenerative diseases. Coordination in water is possible to be developed efficiently.

Methods: The study was carried out in the National Institute of Rheumatology and Physiotherapy. 61 participants were randomized [n=20 sensorimotor training group, n=20 control group (CG)] in the land-based sensorimotor training program (SMT) and 21 people [n=7 At Chi group (AC), n=7 water adapted sensorimotor training group (WASM), n=7 control group] in the water-based training program (WBT). The control group did not participate in any training program. The exclusion criteria included: neurological, cardiovascular and musculoskeletal diseases, which contraindicated the participation in the training program. Functional Reach Test (FRC), Timed Up and Go Test (TUG), Star Excursion Balance Test (SEBT) and coordination test by stabilometer were used to measure static and dynamic balance. The measurements were performed before and after the training period. The results of the SMT were analysed with two-sample t-test, and the results of the WBT with non-parametrical methods. The results were defined with p<0.05 statistical margin by SPSS program.

Results: After 18-weeks of the SMT program significant improvement was experienced in the SMT group compared to the CG with the following parameters: FRC (p<0.001), TUG (p=0.01). In the Coordination test no significant difference was found between the SMT and the CG (p=0.09). After 8-weeks of the WBT programs significant improvement in the mediolateral direction of SEBT was detected in the WASM (p=0.028) and in the AC group (p=0.043) compared to the CG. FRC test was shown marginal significance (p=0.075) in the WASM group, while in the AC group remarkable improvement (p=0.043) was recognised compared to the CG. In the TUG test significant improvement was found in the CG and the WASM (p=0.026, p=0.043) compared to the CG.

Conclusions: The findings from this study support the efficacy of the land- and water-based exercise programs in improving balance in this sample. Our results pointed out that balance improved efficiently even at degenerative joint diseases. Limitations of our research was the small number of the participants and the short duration of the program. In the light of the promising outcome we will continue our research that would result in an efficient fall prevention in this population with high risk of falling.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3783

Promoting physical activity in rheumatoid arthritis: developing a theory-based behaviour change intervention

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Background: Physical activity has numerous benefits for people who have RA, however interventions targeting physical activity behaviour in people who have RA have had limited efficacy [1].

Objectives: To develop a theory-based behaviour change intervention to promote physical activity in people who have RA.

Methods: Development was guided by the UK’s Medical Research Council Complex Interventions framework [2] and consisted of three components; 1. Narrative review which explored the use of behaviour change theory in previous interventions 2. Systematic review which examined the content and structure of previous interventions 3. Qualitative study which explored the preferences of key stakeholders (people who have RA and health professionals) about the design of the intervention.

Results: Previous interventions lacked consideration of behaviour change theory in design and delivery, and there was a large degree of variance in content, structure and delivery. Lack of knowledge of current physical activity recommendations. NSW Public Health Bulletin, Vol. 22(3–4): 78–83.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3257

Experiences and appreciation of shared medical appointment of young adults with a rheumatic disease, in transition from child to adult care

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Background: Young adults with rheumatic diseases deal with questions and uncertainties since their disease and treatment affect both physical and socio-emotional development. As part of the transition from child to adult care, the UMC Utrecht offers a shared medical appointment (SMA). During a SMA, four to six patients are seen together in the presence of a doctor and nurse specialist. Compared to an individual consultation with a doctor or nurse, a SMA is offering extensive exchange of information and shared experiences focussed on everyday life, as sport, study, work and treatment. During a SMA, patients learn from each other how to support self-management. In practice, the care providers notice that young adults are reluctant to join a SMA, they hesitate to have a consultation in presence of their peers. When invited, most patients, however, do attend a SMA, and it is unknown how these young adults experience and appreciate the SMA.

This evaluation is a first step of a larger project. The results will be deepened and supplemented with the findings on interviews with SMA participants and adults who are not SMA participants, in order to give an advice for further development of the SMA in our clinic.

Objectives: Evaluating experiences and appreciation of SMA in transition patients in order to further develop the SMA in our clinic.

Methods: In the period of January 2014 till December 2016, patients in transition who participated in SMA were asked to fill in an evaluation questionnaire. This questionnaire focussed on expectations, quality of medical care compared to an individual consultation, information about disease and treatment during a SMA and the presence of other young adults. Data was analysed by the researchers and patient partners using SPSS and thematic analysis.

Results: Forty-five patients filled in the evaluation questionnaire, among them 35 women, with an average age of 19.6 years. The majority had a form of juvenile idiopathic arthritis (n=39); with average disease duration of 9.4 years and most were using a DMARD and/or biological (n=35). The results showed that participating patients were just as satisfied with the medical care in a SMA compared to a regular consultation; they indicate that more information was given in a SMA and the presence of peers was experienced as pleasant. Most appreciated were sharing experiences, individual stories and tips. Personal attention and lack of privacy were perceived as less pleasant, moreover young adults expressed to find it difficult to discuss personal issues.

Conclusions: Although it is difficult to motivate the young adults to attend the SMA, whenever they do attend, they appreciate a SMA in positive way, especially on benefits of sharing information and meeting peers, when offered in addition to individual consultations with doctor and nurse.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3257
recommendations for people who have RA was highlighted in the qualitative study, and delivery preferences were identified. Intervention development was mapped to the Behaviour Change Wheel [3] and employed the Theory of Planned Behaviour as it’s theoretical basis. The proposed intervention is outlined in Table 1.

Conclusions: We have developed a theory-based intervention which considers the preferences of key stakeholders. Future research will determine the feasibility and effectiveness of this intervention.

References:

Disclosure of Interest: None declared

THE PHENOMENON OF ALEXITHYMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Alexithymia as a radical in the structure of premorbid personality is attracting the attention of researchers as one of the possible psychological risk factors in the development of psychosomatic disorders in rheumatic diseases. Clinical experience supports the evidence of the relevance of alexithymia as a conception in relation to the many somatic patients, who show a limited ability to describe and differentiate emotion and create fantasies, and hence indicate the role of alexithymia phenomenon in the pathogenesis of psychosomatic disorders in SLE.

Objectives: To study the relationship of the levels of alexithymia with other clinico-psychological characteristics.

Methods: 87 patients with systemic lupus erythematosus (SLE) was surveyed with the Toronto Alexithymia Scale (TAS).

Results: According to the results obtained, SLE patients demonstrated a high level of alexithymia (73.86±2.6 points). The results of the research showed that the level of alexithymia, on one hand, does not depend upon gender, age, character and activity of the pathological process (p>0.05). On the other hand, there was a significant inverse correlation between alexithymia and the level of the patient’s education (r = -0.42 p=0.031). Moreover, internality in interpersonal interaction (r = -0.44 p=0.028), and significant direct correlation with indicators such as, the disease duration (r = -0.46 at p=0.01), the intensity of neurotic disorders (asthenia (r = -0.42 p=0.033), depression (r = -0.52 p=0.006), anxiety (r =-0.43 p=0.028), hypochondriasis (r = -0.48 p=0.01), as well as psychological defense mechanism “Regression” (r =-0.42 p=0.022).

Conclusions: Therefore, between the development of alexithymia in SLE patients and certain clinico-psychological characteristics, a particular association exists which provides a definite step for psychotherapeutic interventions aimed at correcting alexithymia personality traits of SLE patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2615

INFLUENCE OF BIOFEEDBACK THERAPY ON THE MICROCIRCULATION IN SYSTEMIC SCLEROSIS

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Background: Microcirculatory disorders are one of the most important clinical symptoms of systemic sclerosis (SSc), therefore we found it feasible to evaluate the clinical efficacy of biofeedback (BFB) in the complex therapy of patients with SSc based upon analysis of nailfold capillaroscopy.

Objectives: To study the impact of the method of biofeedback therapy on microcirculation disturbances in patients with SSc.

Methods: The study included 40 patients with SSc under observation. Among the patients examined, 95% were women and 5% were men. The average age of the patients - 38±3.3 years, duration of illness - 14±2.6 years. Raynaud’s phenomenon (RP) was observed in all the patients. A severe form of RP was seen in 80% of the patients. The effectiveness of biofeedback therapy was analyzed by comparing the dynamics of the measures from the nailfold capillaroscopy and comparing the data obtained of patients from the main and control groups.

Results: It was found that, patients who were under biofeedback therapy, showed significant positive dynamics in the following signs of capillaroscopic picture: dilation of the capillaries (c2 = 8,643 p=0,026), morphological changes of the capillaries (c2 = 4,619 p=0,032), as well as the level of haemorrhage (c = 2 = 4,514 p=0,034). In the control group of patients, in only one indicator of capillaroscopy that a significant change was noted, particularly by the presence of dilated capillaries (c2 = 5,833 with p=0,016). These findings suggest that treatment results were significantly better in the main study group of patients with SSc.

Conclusions: The implementation of biofeedback therapy favors a decrease in reflex musculo-tonic syndromes, improvement of microcirculation and peripheral blood flow and significantly allows an amelioration in the results of SSc therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2616

PLACEBO AND NOCEBO EFFECTS INDUCED BY CONTEXTUAL FACTORS. A SURVEY ON BELIEFS AND ATTITUDES OF ITALIAN MUSCULOSKELETAL PHYSIO THERAPISTS

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Background: Context effects are well known and were described as integral part of the clinical setting (1). The conscious use of contextual factors (CF) has been recently proposed as an effective modality capable to influence the psychotherapy outcome by faciliation of placebo responses. (2) To date, the knowledge about CF adoption in clinical practice of physical therapists is absent. Objectives: The aim of this study was to investigate frequency of use, beliefs and attitudes about contextual factors among Italian physical therapists specialized in manual therapy (OMTs)

Methods: An invitation to participate in an online survey was sent to 906 OMTs through the database of the Master in Musculoskeletal Rehabilitation (MRDM) of University of Genova. Analysis of the survey was performed with the software SPSS. This likely correspond to more than 85% of the whole OMTs population in Italy. A 17 items questionnaire and two clinical scenarios assessed behaviour, beliefs and attitudes of OMTs about CF adoption in clinical practice and data were analysed by descriptive statistics.

Results: 906 OMTs were invited to participate in the survey and 558 responded (62%). The majority of OMTs uses CF in their practice frequently (52%). They believe that an actual effect of CF can occur in acute pain (57%), chronic pain (78%) and rheumatologic disorders (56%). OMTs consider the use of CF ethically acceptable when it exerts beneficial psychological effects and their effectiveness was shown during clinical experience (31%). They disagree on the adoption of CF when they are based on deception, undermine the trust between OMT and patients, create legal problems or produce side effects (17%). 38% of respondents do not communicate the use of CF to their patients and they adopt CF as addition to other physical therapy interventions with the aim of optimizing clinical responses (20%). Expectation and psychological mechanisms are believed to be the main aspects behind placebo and nocebo effects induced by CF (7%).

Conclusions: The use of CF is quite common among Italian OMTs and they mostly had positive attitudes towards their use and effectiveness.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4361

A NEW AND ALTERNATIVE TREATMENT IN SYSTEMIC SCLERODERMA DIGITAL ULCERS

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Background: Digital ulcers (DUs) are a major clinical problem for patients with systemic sclerosis (SSc). Patients with DUs may suffer from severe pain and often undergo a limitation of daily life activities, thus resulting in a functional impairment with a significant impact on the patient’s health-related quality of life. Prevention of further complications and lesions is possible if the initial evaluation is performed early and correctly and if a treatment is started promptly.

Objectives: The primary objective is to demonstrate the effect of Lecoxen cream (Ekuberg Pharma, Italy) in comparison with another cream (Fitostimolino cream, DAMOR SpA, Italy) on the reduction of the number and size of DUs in patients with systemic sclerosis evaluating in addiction the reduction of pain dealing with ulcer symptoms.

Methods: In this single-blind randomized progressive trial 39 women, with confirmed digital ulcers present for at least 4 weeks with a surface area greater than 0.5 cm² but smaller than 2.5 cm², that follow Iloprost therapy (0,05mg/2 times/month), afferent to the Operative Unit (O.U.) of Rheumatology of the Local Health Unit (U.O.) of San Martino Hospital, Lecce, were randomized to receive the topical application of Lecoxen cream (group I: 20 women) or Fitostimolino cream (group II: 19 women). We took digital photographs to measure ulcer surface area and to draw the periwound area before the first cream application and after 30 days. Then an evaluation of DUs diameter and number was carried out. A
tailored questionnaire was administered as Visual Analogue Scale (VAS) during monitoring visits, to evaluate intensity of pain. Furthermore quality of life was monitored through Short Form (36) Health Survey.

**Results:** Mean age was similar in the two study groups with values of 45.4±5.6 years and 46.1±4.1 respectively. In the patients treated with Lecoxen cream, the reduction of lesion size was significantly higher (70%–75%) (p < 0.001) in comparison with those registered in group II (40–45%) (p < 0.05); a significant improvement was observed in levels of pain in Group I (30 days: p < 0.001), while in group II the results of reduction were not significant. The analysis of SF36 survey showed highly significant reduction (p < 0.001) of indexes in group I. At last visit, 32 ulcers were healed: 17 in the group I, 11 in the Group II (p < 0.01). Two-way analysis of variance (ANOVA) test was used to examine differences. Intragroup changes were evaluated with the paired Student t-test. A p-value of < 0.05 was considered to be significant.

**Conclusions:** Lecoxen cream showed the greatest effect on the mean reduction of the lesion size and pain levels. In the patients treated with Lecoxen cream the reduction of lesion size was 70%–75%; the reduction was smaller in the group II. At last visit, 32 ulcers were healed: 17 in the group I, 11 in the Group II. Data collected from SF36 surveys are very interesting, because they show a clear improvement in quality of life of scleroderma patients, who underwent different three treatments. In particular, a better subjective perception of tactile sensation and minor discomfort in the pathological skin have been reported. On the basis of the results, it could be argued that the medical device Lecoxen cream may be useful in the treatment of DUs in patients suffering from systemic sclerosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6225

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**THU0744-HPR**

**ASSESSMENT OF ADALIMUMAB SUBCUTANEOUS INJECTION RELATED PAIN AND EFFECTIVENESS OF NURSE SUPPORT FOR PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Subcutaneous injection of biologic agents gives more freedom and independence for patients with rheumatoid arthritis (RA) than intravenous injection. Despite this, patients with RA sometimes select intravenous injections due to concerns over self-injection, such as injection anxiety, including pain, and lack of confidence in giving a self-injection [1]. It is reported that one in five people are estimated to experience injection anxiety [2]. Therefore, an understanding of subcutaneous injection pain and anxiety and support for anxiety of patients with RA are important for appropriate usage of subcutaneous biologics.

**Objectives:** The aim is to evaluate pain and anxiety caused by adalimumab (ADA) subcutaneous injection and assess the effectiveness of nurses’ care.

**Methods:** Patients with RA using ADA self-injections were enrolled. In this study, it was assessed in 4 categories: general, needle insertion, drug injection, needle removal. Pain was evaluated using Visual Analogue Scale (VAS) scale. Effectiveness of support by nurses was also assessed using self-questionnaires and free-format comments. Statistical analyses were performed utilizing Wilcoxon’s signed rank test and Spearman’s rank correlation coefficient.

**Results:** Twenty patients (Male: Female, 4: 16) completed the questionnaire. Average age and disease duration were 68 and 12.6 years, respectively. Mean ± SD of Pain VAS were 34.9±28.1 mm (General), 30.3±30.6 mm (needle insert), 42.5±35.8 mm (drug injection) and 11.8±16.4 mm (needle removal). There were no statistically significant differences between general pain and needle insertion (p = 0.631), or general pain and drug injection (p = 0.121). However, statistically significant differences were found between general pain and needle removal (p < 0.001). Moreover, there were statistically significant differences between needle insertion and removal (p = 0.003), and needle injection and needle removal (p = 0.0048). General pain showed statistically significant correlation with needle insertion pain (r = 0.653, p = 0.0018) and drug injection pain (r = 0.615, p = 0.004). However, general pain was not correlated with needle removal pain (r = 0.137, p = 0.565).

Patients with RA answered that support by nurses is effective for relieving pain (30%), reduction of anxiety (35%) and improving treatment motivation (50%). According to the patients, nurses helped raise motivation by explaining that treatment prevents the progression of RA and allows many patients to feel better (30%), reduction of anxiety (35%) and improving treatment motivation (50%).

**Conclusions:** These data indicate that needle insertion and drug injection pain have great influences on general pain. Support by nurses is likely to reduce injection anxiety and pain, resulting in higher motivation toward self-injection treatment.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5000

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**THU0745-HPR**

**A COMPARISON OF THE EFFECTIVENESS OF WHOLEBODY VIBRATION, PROGRESSIVE RESISTIVE EXERCISE AND HOME-BASED EXERCISE IN PATIENTS WITH KNEE OSTEOARTHRITIS**

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**Background:** Knee osteoarthritis (OA) is the most common type of lower extremity OA. Systematic reviews of randomized controlled trials (RCTs) indicate that exercise therapy reduces pain and patient-reported disability in patients with knee osteoarthritis (OA), but to date, type and the optimal exercise regimen has not been identified.

**Objectives:** The aim of our study was to determine the effects of whole body vibration training exercise, progressive resistive exercise, home-based exercise used in osteoarthritis treatment on pain, muscle strength, functional status and quality of life.

**Methods:** Forty-five patients (mean age=53.86±5.33 years, 42 female, 3 male) diagnosed with bilateral knee osteoarthritis (Grade II-III, Kelgren & Lawrence) were included in this study. The assessments were performed at baseline, after three months when they completed the exercise programme and sixth months. Whole body vibration exercise training programme (Group-I), progressive resistive exercise training in Group-2; home-based exercise training in Group-3; were applied for three days per week, three months, totally 36 sessions. All the groups were included patient education programme at baseline. The pain was assessed according to Visual Analog Scale (VAS) and quadriceps muscle strength was evaluated by using handheld dynamometer. The functional status of the patients was evaluated by WOMAC (Western Ontario and McMaster Universities) index and health related quality of life was evaluated by Nottingham Health Profile (NHP).

**Results:** Significant improvement was found after treatment on pain, quadriceps muscle strength, functional status and quality of life in all groups (p < 0.05). When the groups compared by ANOVA it was found that outcome measures were not significantly different between Group-1, Group-2 and Group-3 (p < 0.05).

**Conclusions:** Supervised resistive exercises and whole body vibration exercises were more effective in strengthening lower extremity muscles when compared to home exercise training in patients with knee OA. However, the increase in muscle strength was not observed at long- term follow- up in both groups. Neither whole body vibration exercise training programme nor progressive resistive exercise and home-based exercise programme were found to be superior for the treatment of osteoarthritis. All types of exercises and programmes were beneficial for pain, functional status, quadriceps muscle strength and quality of life. Further studies with long-term follow-up are warranted.

**References:**

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6854

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**THU0746-HPR**

**RHEUMATOLOGY NURSE SPECIALISTS AND DMARD PRESCRIPTION - WHERE ARE WE NOW?**

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**Background:** It is widely acknowledged that a multidisciplinary team approach is the best way to care for rheumatology patient group. The rheumatology nurse specialist (RNS) is an integral part of this multidisciplinary team. EULAR has published recommendations for their role in the management of chronic inflammatory arthritis (van Eijk-Hustings Y et al, 2012). The Department of Health also highlights the need for providing different models of care in a more cost effective way. It recognises that the nurse specialists’ role is the bedrock of an effective care providing team and can contribute to answering the challenge of effectively delivering DMARD education for patients. Methotrexate was accepted as index DMARD for the purpose of the exercise. A questionnaire

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5000
EFFECT OF DIFFERENT PHYSICAL THERAPY RECOMMENDATIONS ON PHYSICAL THERAPY INCREASING PHYSICAL ACTIVITY IN PEOPLE WITH A KNEE OSTEOARTHRITIS

E.O. Günaydın

Results: The between-groups results showed a significant improvement for the (p < 0.05), while there was no difference in 60 degrees/sec isokinetic quadriceps strength test in the Kinesio taping group and TUG test in the ESWT group.

Conclusions: The results of this study showed that; ESWT, Kinesio tape and exercise therapy are all effective in decreasing pain intensity, improving knee strength and functional status levels of patients with knee osteoarthritis (OA). A quarter of the cohort felt unprepared to impart the skills to peers (median experience 1 year).

In conclusion, there is wide variation in the training of rheumatology nurse specialists. This can potentially have a negative impact on a relatively young workforce. There is a need for improving training standards to help deliver good quality rheumatology care.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2783

EFFECT OF DIFFERENT PHYSICAL THERAPY PROGRAMS ON PAIN, STRENGTH AND FUNCTIONAL SITUATIONS ON KNEE OSTEOARTHRITIS

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Background: Knee Osteoarthritis (OA) is one of the most common causes of disability with an increasing prevalence and incidence with age. Although there are studies in the literature that examine the efficacy of ESWT, Kinesio taping and exercise on knee OA, there is no study to compare these methods with each other.

Objectives: The purpose of this study is to compare the effects of Extracorporeal Shockwave Therapy (ESWT), Kinesio taping and exercise therapy on pain, knee strength and functional situations of patients with knee osteoarthritis (OA).

Methods: Forty eight female patients aged between 50–65 and previously diagnosed with a grade 1–3 (Kellgren-Lawrence scale) knee OA included in this study. Patients were assessed before treatment and after treatment at 6 weeks and at 12 weeks. Visual Analog Scale (VAS), (ISO9693/2000 D&R GmbH, Germany) isokinetic device, Timed Up and Go test (TUG) and WOMAC scale were carried out for assessing patients’ pain, knee strength and functional situations. After randomising the patients into 3 different groups, the first group received 1 session of ESWT per week, the second group received 2 sessions of ESWT per week and the third group was prescribed with an exercise program only.

Results: The between-groups results showed a significant improvement for the pain during night, pain during resting and WOMAC test in the exercise group (p < 0.05), while no difference was found for the other measurements (p > 0.05). The inter-groups results showed significant improvements in 3 of the groups (p < 0.05), while there was no difference in 60 degrees/sec isokinetic quadriceps strength test in the Kinesio taping group and TUG test in the ESWT group.

Conclusions: The results of this study showed that; ESWT, Kinesio tape and exercise therapy are all effective in decreasing pain intensity, improving knee strength and functional status levels of patients with knee OA and can be used as alternative approaches to treat symptoms of knee OA.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5437

THU0748-HPR

RECOMMENDATIONS ON PHYSICAL THERAPY PRESCRIPTION FOR AXIAL Spondyloarthritis in the netherlands

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Background: In national and international guidelines physical therapy, comprising exercise interventions and education, is recommended as a required treatment modality for the optimal treatment of axial spondyloarthritis (axSpA) [1-3]. However, specific details regarding referral for physical therapy and optimal content and dose of exercise interventions are lacking. Research showed large variation in the content of exercise therapy in axSpA patients, which reflects a great need for uniform guidelines.

Objectives: To develop practice recommendations on indications for referral, content, dose and safety aspects of exercise therapy for axSpA patients based on scientific evidence, expert opinion and patient values. The ultimate aim is improving the quality of exercise therapy care for people with axSpA.

Methods: The recommendations are based on scientific evidence, expert opinion and patient values and were formulated following a combination of literature review and three expert-group meetings (consisting of patients, rheumatologists, physical and exercise therapists, policy makers, scientists and special interest groups). In three consecutive expert-meetings clinically relevant questions, draft recommendations based on the scientific literature, and final recommendations including level of agreement were generated. Lastly, a field consultation among physical and exercise therapists, rheumatologists, scientists and special interest groups will be scheduled and an implementation strategy, comprising of an information intervention and directives, will be developed.

Results: In the first expert-group meeting 18 clinically relevant questions were formulated, on: indication and referral, assessment, content of treatment, evaluation and safety. In addition to recently published systematic reviews, additional literature reviews concerned assessment, safety and the dosage of exercise therapy. Related to the clinical questions, a framework for the therapeutic process and 12 draft recommendations were developed and discussed in the second meeting. In the third and last meeting the 12 recommendations regarding the delivery of physical therapy and exercise interventions were set and the level of agreement was determined.

Conclusions: The expert-meetings and literature searches led to 12 practice recommendations and a clear starting point for the development of the implementation strategy. Twelve practice recommendations regarding the delivery of physical therapy for patients with axSpA were developed, based on scientific evidence, expert opinion patient values. The field testing and development and execution of a dissemination and implementation strategy will be done in 2017.

References:


Acknowledgements: The Dutch Arthritis Foundation financially supported this project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4432

THU0749-HPR

INCREASING PHYSICAL ACTIVITY IN PEOPLE WITH A CHRONIC DISEASE: EXAMINING THE EFFECTIVENESS OF A MOTIVATIONAL AND A PLANNING INTERVENTION, THEIR INTERACTION AND VARIOUS POTENTIAL MODERATORS AND MEDIATORS

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Background: Physical activity has many health benefits, especially in people with a chronic disease. Behaviour change interventions appear more effective than just advice when increasing physical activity. However, most studies that compare different interventions overlook interaction effects between methods and possible parameters for effective interventions.

Objectives: Present study examined the effectiveness of a motivational and an action planning intervention for increasing physical activity in patients with a chronic disease. Their interaction as well as various potential moderators and mediators were studied in order to identify which intervention is effective in which context.

Methods: In a healthcare centre specialised in the treatment of people with a chronic disease, participants whose physiotherapist would advise them to be more physically active were randomly assigned to one of four interventions in a factorial design: 1) a control condition with only advice, 2) a motivational intervention...
with information about health benefits and selecting personally relevant motives and social support sources regarding physical activity, 3) an action planning intervention in which participants specified which physical activities they would do, when, where and for how long and 4) a combination of these interventions. Prior to the intervention, participants’ leisure time physical activity in the past week was measured with items from the SQUASH. Also behavioural intentions, expected social support and planning behaviour with regard to leisure time physical activity were measured. Directly after the intervention, positive outcome expectations and self-efficacy were measured. After a week, physical activity measures were administered again.

Results: 298 participants (71% female; mean age 62 years; 40% with a rheumatic disease) completed the study. Figure 1 displays the average change in physical activity for each intervention. Multiple regression analyses showed that both the motivational intervention (β=0.22) and action planning (β=0.31) significantly predicted positive physical activity change and that these effects appeared additive as opposed to catalytic. The effects were not moderated by intention, expected social support or planning behaviour, nor mediated by outcome expectations or self-efficacy. The motivational intervention’s effectiveness was weakly correlated with the number of personally relevant exercise motives identified (r=0.22) and the action planning’s effectiveness was weakly related to the number of plans made (r=0.19) and to one’s outcome expectations after the intervention (r=0.21).

Conclusions: These data suggest that using a motivational or action planning intervention seems beneficial for increasing physical activity in patients with a chronic disease, independent of one’s intentions, expected social support and planning behaviour. The data also suggest that action planning is preferable over a motivational intervention and that the added value of a motivational intervention is minimal if action planning is used. This study was limited by only measuring physical activity after a week and by using self-report. Future studies should investigate longer term effects, other potential moderators and mediators and interaction effects between other promising behavioural change methods.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2137

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**THU0751-HPR**

**THE EFFECTIVENESS OF THERAPEUTIC FOOTWEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Therapeutic footwear is recommended in guidelines for the treatment of foot problems in patients with rheumatoid arthritis (RA) and commonly prescribed and frequently used, especially in patients with established RA, foot deformities or erosions in foot joints.

Objectives: The objectives of this study were to summarize the effectiveness of therapeutic footwear on foot function, pain, physical functioning, health-related quality of life, adherence, adverse events and patient satisfaction in patients with RA.

Methods: All randomized controlled trials, randomized controlled cross-over trials, (quasi-experimental) clinical trials, and uncontrolled studies investigating the effect of therapeutic footwear in patients with RA related foot problems were included. Therapeutic footwear consists of custom-made or ready-made shoes. A literature search was conducted in The Cochrane Central Registry for Controlled Trials (CENTRAL), PubMed, EMBASE and PEDro up to January 19, 2017. Selection and inclusion of articles, data extraction (using a standardized template) and assessment of methodological quality (using a checklist for between-group and within-group comparisons) was conducted by two independent reviewers. Quantitative data analyses was conducted, when quantitative data analysis was not possible qualitative data analysis was performed.

Results: Thirteen studies were identified. In five studies, one of which was of high quality, between-group comparisons were reported. In six studies, in which two were of high quality, within-group differences were reported. Qualitative data-syntheses for the within-group differences of custom-made therapeutic footwear resulted in weak evidence for the reduction of foot pain and improvement of physical functioning. Qualitative data-analyses of the within-group differences of ready-made therapeutic footwear resulted in a medium to large effect for the reduction of foot pain (SMD -0.68, 95% CI -1.00 to -0.37; P=0.0001; 162 participants), and a small to medium effect for the improvement of physical functioning (SMD -0.32, 95% CI -0.62 to -0.02; P=0.04; 128 participants). Quantitative data-analyses of the between-group differences of ready-made therapeutic footwear resulted in inconclusive evidence for foot pain and physical functioning.

Conclusions: In within-group designs, there is weak evidence for the reduction of foot pain and improvement of physical functioning after wearing custom-made therapeutic footwear. Furthermore, in within-group designs there is a medium to large effect of ready-made therapeutic footwear on the reduction of foot pain, and a small to medium effect on the improvement of physical function. Controlled, between-group designs resulted in inconclusive evidence. A definite RCT is necessary to investigate the between-group effectiveness of therapeutic footwear in patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5809

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**THU0751-HPR**

**EFFECTIVENESS OF FOOT ORTHOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS RELATED TO QUALITY OF LIFE AND PAIN. A SYSTEMATIC REVIEW AND META-ANALYSIS**


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Background: Foot pain and deformity is almost ubiquitous in RA and results in considerable physical and psychosocial impairment [1]. Epidemiological studies consistently suggest a 90% prevalence of foot pain despite advances in pharmacological therapy [2]. Mechanical and other non-pharmacological interventions such as orthoses and footwear, have an important role in managing foot pathology in patients with their systemic disease controlled [1,3]. The effectiveness of treatment with insoles, especially in early periods, was studied in a randomized controlled trial, which results suggested an immediate clinical improvement, reducing foot pain, disability and limited functionality [1].

Objectives: The aim of this study is the effectiveness of foot orthosis in patients with rheumatoid arthritis in terms of quality of life and pain.

Methods: A systematic review and meta-analysis was conducted of randomized controlled trials.

Participants: Patients with rheumatoid arthritis were included. The criteria of exclusion were Juvenile Rheumatoid Arthritis, analysis of gait.

Intervention: Studies had to compare foot orthosis

Comparison: Other type of treatments, other type of foot orthosis, sham

Outcomes: Evaluation of Pain or Quality of life with any tool that measure this outcome

The search was conducted in Cochrane, CINAHL, PubMed, EMBASE, LILACS, and Cumiden. An independent peer review was carried out. The Mesh term and fields used were foot, ankle, joint, rheumatoid arthritis, foot, orthosis, insole, foot orthosis.

Results: After the analysis of 21 studies, 4 were included for the systematic review. The 4 studies enrolled 285 participants. Follow-up periods varied from 6 to 30 months.

Only two studies were included in the meta-analysis [4,5], both of them with pain (measured with Foot Function Index) as the selected outcome.

A meta-analysis of the two trials showed that use of FO resulted in a non-significant improvement in disability compared with control (MD (95% CI): 4.37 (-6.24, 14.98); N=64) (Figure 1).

Conclusions: Foot orthoses showed improvements in pain and disability/quality of life, but no significant differences between groups were found. Future research needs to increase the number of RCTs in this topic because results are not conclusive.

References:


Disclosure of Interest: None declared

THURSDAY, 15 JUNE 2017
HPR measuring health (development and measurement properties of PROs, tests, devices) —

THU0752-HPR
DEVELOPMENT OF THE “TREATMENT BELIEFS IN KNEE AND HIP OSTEOARTHRITIS (TOA) QUESTIONNAIRE”
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Background: Use of non-surgical treatment modalities in osteoarthritis (OA) is suboptimal1, which might be influenced by patients’ beliefs about treatments. An instrument for measuring treatment beliefs in OA is not available yet.

Objectives: To develop a questionnaire assessing patients’ beliefs about treatment modalities of hip and knee OA; the “Treatment beliefs in OA (TOA) questionnaire” and to evaluate its clinimetric properties.

Methods: The item pool, drawn from two previous qualitative studies, comprised beliefs regarding 5 treatment modalities: physical activity, pain medication, physiotherapy, injections and arthroplasty. A draft questionnaire comprising beliefs on these 5 treatment modalities was developed (200 items, Table 1). Two samples of patients with knee or hip OA (N=840, N=700) were recruited from our hospital to test the clinimetric properties of the TOA questionnaire. Descriptive analyses, exploratory factor analyses (EFA; sample 1) and confirmatory factor analyses (CFA; sample 2) were conducted for each treatment module separately. Internal consistency was assessed with Cronbach’s Alpha (both samples). In order to examine test-retest reliability a subsample of sample 2 (N=67) was asked to fill out the final TOA questionnaire again after two weeks.

Results: 351 patients filled out the draft TOA questionnaire (sample 1), 289 patients filled out the final TOA questionnaire (sample 2), with a subsample (N=50) who filled out the final questionnaire twice. EFA yielded a two factor solution for each treatment modality. The factors were labeled “positive treatment beliefs” and “negative treatment beliefs”. The final TOA questionnaire comprised 60 items; items per treatment modality ranged from 9 to 14. CFA showed adequate fit indices for physical activities and physical therapy, while fit indices for the treatment modalities pain medication, injections and arthroplasty just failed to reach adequate cut-off values. Internal consistency was good to excellent for the subscale positive treatment beliefs (Cronbach’s α between 0.84 and 0.90), and mediocre to acceptable for the subscale negative treatment beliefs (Cronbach’s α between 0.66 and -0.79). Test-retest reliability was satisfactorily good with ICCs from 0.66 to 0.88 and SEMs from 0.17 to 0.52.

Table 1: Example items in the TOA questionnaire

<table>
<thead>
<tr>
<th>Items TOA-questionnaire</th>
<th>Items</th>
<th>Items</th>
<th>Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>I think [doing physical activity] leads to risks</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>My quality of life improves through [using pain medication]</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>I think [physiotherapy] causes pain</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>I can do household chores more easily through [an injection]</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>I think [a joint replacement] is pervasive</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Conclusions: The TOA questionnaire is the first questionnaire assessing positive and negative beliefs regarding five treatment modalities for knee and hip OA. The TOA questionnaire showed moderate structural validity and good internal consistency and test-retest reliability. The TOA questionnaire is useful for a better understanding of patients’ treatment beliefs. Future research will examine how treatment beliefs, in interaction with other variables, influence treatment choices.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4815

THU0753-HPR
PREDICTING THE FUTURE DEVELOPMENT OF SPONDYLOARTHRITIS AMONG PATIENTS WITH IDIOPATHIC ACUTE ANTERIOR UVETITIS USING REAL-WORLD DATA
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Background: Previous studies have suggested an association between idiopathic acute anterior uveitis (AAU) and spondyloarthritis (SpA), including showing that at least 40% of AAU patients have undiagnosed SpA. However, the clinical factors to predict the incident diagnosis or future development of SpA remain poorly recognized.

Objectives: The objectives of this study were: 1) to describe the patient characteristics of AAU patients with and without SpA diagnosis, and 2) to identify the predictive factors of SpA diagnosis among AAU patients using real-world data.

Methods: Adult patients with at least one diagnosis of AAU (ICD-9-CM: 364.01 or 364.02) were selected from a large US insurance claims database (01/01/2008–06/30/2015). The first AAU diagnosis was defined as the index date. Patients were required to have at least 6 months of continuous data availability before the index date. Patients with intraocular surgery, penetrating or blunt eye trauma, or a diagnosis of rheumatoid arthritis or SpA on or prior to the index date were excluded. Potential predictive factors for subsequent diagnosis of SpA included demographic characteristics, type of AAU (primary [first diagnosis] vs. recurrent), SpA-related comorbidities, and healthcare resource utilization prior to the index date. Factors predictive of SpA diagnosis were selected into a multivariable Cox proportional hazards model based on statistical significance and clinical relevance. Hazard ratios (HR) and p-values were estimated for each factor.

Results: A total of 48,822 patients with AAU were included, and among them, 1,032 patients were newly diagnosed with SpA during the follow-up period which was 24 months on average. Patients with SpA were younger (45.7 vs. 50.4 years), more likely to be male (52% vs. 42%), more likely to have recurrent AAU (44% vs. 29%), back pain (21% vs. 13%), SpA-related comorbidities, and healthcare resource utilization prior to the index date. Predictive factors in the final Cox model were: male vs. female (HR=1.55; p-value <0.01), age <45 vs. ≥45 years old (1.65; 0.01), recurrent vs. primary AAU (1.94; 0.01), back pain under age 45 vs. no back pain (1.90; <0.01), back pain above age 45 vs. no back pain (1.46; <0.01), psoriasis (5.16; <0.01), IBD (2.50; 0.01), joint pain (1.14; 0.19), imaging test use (1.03; 0.74), corticosteroids use (1.07; 0.33), and nonsteroidal anti-inflammatory drugs use (1.93; 0.40). Conclusions: There are significant differences among isolated AAU patients and AAU patients that developed SpA later. The most predictive factors of SpA diagnosis were male, age <45 years, recurrent AAU, back pain, and other extra-articular manifestations of SpA such as IBD and psoriasis. Since delayed diagnosis is common among SpA patients, identifying such predictive factors can help inform risk stratification.

DOI: 10.1136/annrheumdis-2017-eular.3028

THU0754-HPR
WORK STATUS IN WOMEN WITH FIBROMYALGIA – A 12-YEAR FOLLOW UP STUDY
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Background: Fibromyalgia (FM) affects approximately 1–3% of the general population in the Western world and about 10% have been found to report Chronic Widespread Pain (CWP). The work ability is often affected in persons with FM and CWP. Previous research has shown a small improvement of symptoms over time in patient with FM and CWP. Sustain in work has been
Dietary protein intake and upper leg muscle mass and strength in older adults. Whether there is an independent association with lower muscle strength in patients with knee OA. To confirm this relationship, future research is needed to test this association in longitudinal and interventional studies in patients with knee OA.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3386

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**THU0757-HPR**

**EUROPEAN QUALITATIVE RESEARCH PROJECT ON PATIENT-PREFERRED OUTCOMES IN EARLY RHEUMATOID ARTHRITIS (EPOERA): RATIONALE, DESIGN AND METHODS OF AN ONGOING MULTI-COUNTRY, MULTI-CENTER, MULTI-LANGUAGE, LONGITUDINAL QUALITATIVE STUDY**

K. Van der Elst 1, A. Bremander 2, A. De Groef 1, I. Larsson 3, E. Mathijssen 4, A. Van de Putte 1, J. Vriezekolk 4, R. Westhovens 1, Y. van Eijk-Hustings 5.

**Background:** Ample studies exist on outcome assessment from the patient perspective in Rheumatoid Arthritis (RA), but little is known about health and quality of life in persons with FM/CWP. There is lack of research about long-term follow-up of work status in FM and CWP. To enable patients with FM or CWP to sustain in work or return to work it is crucial to gain knowledge about which factors that can contribute to work status over time.

**Objectives:** To investigate change in work status and possible predictors of work status after 12 years of a cohort of women with FM and CWP.

**Methods:** In 2004, 166 women with FM and CWP participated in a randomized controlled trial in Sweden investigating effects of patient education and pool exercise. The women were invited to participate in a follow-up study in 2016 in which long-term effects on work status, aspects of health and physical function were investigated. 126 participated in the follow-up study of which 98 were >65 years of age (age of retirement in Sweden) and included in the present study of work status. Data was collected by a standardized interview, a battery of questionnaires and an examination including tests of physical function. Work status refers to percentage of full-time work divided into four categories: 0%/1–49%/50–79%/80–100%. Wilcoxon’s signed-rank test was used for comparisons of work status over time within the group.

**Results:** Multivariable forward stepwise logistic regression was used for analyses of predictors of work status after 12 years. The dependent variable was work status dichotomized into <50%/≥50% work. Independent variables were baseline values of age, work status, symptoms of stress, pain intensity, overall health status, leisure time physical activity, walking capacity, health related quality of life and depression.

**Conclusion:** The results showed a significant increase in work status (p<0.001) at the 12 years follow-up. Proportions of work status in category 1–4 at baseline were 56%/10%/22%/10% and at follow-up it was 36%/15%/23%/28%. The participants age, overall health assessed with Fibromyalgia Impact Questionnaire (FIQ) and health related quality of life assessed with SF-36 Physical component summary (PCS) at baseline predicted work status 10–12 years later. Age (years): OR 0.90 (95% CI 0.84–0.97), p<0.004, FIQ total score (0–100): OR 0.94 (95% CI 0.91–0.97), p<0.001, SF-36 PCS (0–100): OR 1.1 (95% CI 1.0–1.2), p=0.019.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2817

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**THU0755-HPR**

**DIETARY PROTEIN INTAKE AND UPPER LEG MUSCLE STRENGTH IN PATIENTS WITH KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOSTRITIS INITIATIVE**

A.H. de Zwart 1, M. van der Leeden 1,2, L.D. Roorda 1, M. Visser 3, M. van der A.H. de Zwart 1,2, L.D. Roorda 1, M. Visser 3, M. van der 1, H. Guney 1, S. Karahan 2, A. Ates 3, M. Turgay 3, G. Kinikli 3.

**Background:** Protein is an essential building block for muscle tissue. Adequate dietary protein intake is needed to preserve muscle tissue. In a part of the general older population, knee OA is common and is strongly related to more pain and activity limitations. Therefore, optimizing muscle function in patients with knee OA is important.

**Objectives:** To investigate the relationship between protein intake and muscle strength in patients with knee OA.

**Methods:** A total of 88 patients with RA participated to the study. Disease activity was assessed using the Disease Activity Score in 28 joints (DAS28). Functional disability was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI). The Disabilities of the Arm, Shoulder and Hand Score (QuickDASH) was used to assess the upper extremity function. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess the lower extremity function. The Time Scale for the Knee Index (TSK) was used to assess pain-related fear of movement. The multiple stepwise linear regression model with R-square (R²) was used to compare across the models and explain the total variance.

**Results:** Eight independent variables namely, age (r=0.215; p=0.044), QuickDASH (r=0.504; p<0.001), HAQ-DI (r=0.315; p=0.003), WOMAC Pain (r=0.512; p<0.001), WOMAC Stiffness (r=0.419; p<0.001), WOMAC Function (r=0.398; p<0.001), WOMAC Total (r=0.429; p<0.001), WOMAC range (r=0.419; p<0.001), demonstrated significant correlations with TSK. There were correlations between two independent variables (QuickDASH, p=0.013; WOMAC Pain, p=0.034) and TSK (R²=0.293).

**Conclusion:** Health professionals should keep in mind that fear of movement was likely to cause poorer upper extremity functional disability and lower extremity pain levels in spite of varied drug therapies in patients with RA.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4782

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**THU0756-HPR**

**PREDICTORS OF FEAR IN MOVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS**

G.I. Kinki 1, H. Guney 1, S. Karahan 2, A. Ates 3, M. Turgay 3, G. Kinikli 3.

**Results:** After adjusting for age and gender, lower protein intake was still associated with lower muscle strength (B = -1.102, 95% CI -0.680 to -1.524, p<0.001) and was maintained after controlling for other relevant confounders.

**Conclusion:** Lower protein intake is independently associated with lower muscle strength in patients with knee OA. To confirm this relationship, future research is needed to test this association in longitudinal and interventional studies in patients with knee OA.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3386


**THURSDAY, 15 JUNE 2017**

**HPR professional education, training and competencies**

**THU0758-HPR**

**APPLICATION OF THE EULAR RECOMMENDATIONS FOR PATIENT EDUCATION FOR PEOPLE WITH INFLAMMATORY ARTHRITIS IN SWITZERLAND**

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**Background:** The recently published EULAR recommendations for patient education (PE) in people with inflammatory Arthritis (IA) encompass two overarching principles and eight recommendations (1). The average overall agreement of PE experts with the recommendations is fairly high (at least 88% (SD+/-0.5) on a 1–10 Numeric Rating Scale NRS) (1, 2). The recommendations ought to be disseminated and implemented to establish a core standard for delivering PE and training for health professionals (HPs) in delivering PE across Europe.

**Objectives:** The Swiss HPs in rheumatology organisation, hrSwitzerland, aimed to evaluate the current standard of PE as well as the agreement with and application of the EULAR PE recommendations in Switzerland, in order to develop further implementation steps.

**Methods:** An online survey was conducted among HPs and rheumatologists in the major rheumatology clinics (n=28) of the German and French part in Switzerland. The current knowledge and skills in PE and the performance of PE in clinical practice were assessed by multiple choice questions. The agreement with the PE recommendations was assessed on a 1–10 NRS and their application in the rheumatology clinics on a 4-point scale ("applied"/"rather applied"/"rather not applied"/"not applied").

**Results:** A total of 57 HPs, among them 12 rheumatologists, 21 nurses, 15 physiotherapists, 6 occupational therapists, 2 medical assistants from 12 rheumatology clinics participated. Of these HPs, 31 (55%) worked for more than 6 years in rheumatology and 15 (27%) indicated to have a formal training in PE. They perceived that PE formed a substantial part of their work (33.5% on average), the most important element being "providing information" (48%), compared to 27% counselling and 25% behavioural interventions.

The average overall agreement with the PE recommendations was 7.0 (SD+/- 2.25). Recommendations 3 and 7 were well applied (72%) in the rheumatology clinics. Least applied were the recommendations 4 and 6 with 21% and 24% respectively. Recommendations 1, 2, 5 and 8 reached between 40–50% application rates.

Image/graph shows Agreement with and Application of the PE Recommendations in Switzerland

**Conclusions:** The overall agreement with the recommendations was high, although lower than the overall agreement of PE experts (1, 2). The application of most recommendations was found to be moderate to low in Swiss rheumatology institutions; however no comparisons with other countries are available. "Providing information" was reported as the most important PE element. This emphasises the need to implement the PE recommendations as well as to improve HPs' knowledge on delivering and evaluating effective PE, in order to provide beneficial PE interventions for people with IA in Switzerland.

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**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6038

**THURSDAY, 15 JUNE 2017**

**HPR interventions (educational, physical, social and psychological)**

**THU0759-HPR**

**DOES PHYSIOTHERAPY AND REHABILITATION PROGRAM IMPROVE MOBILITY AND DAILY LIVING ACTIVITIES IN ELDERLY INPATIENT WITH OSTEOPOROSIS?**

M. Karapinar, T. Firat, N. Kirdi. 1Department of Physiotherapy and Rehabilitation; 2Hacettepe University, Ankara, Turkey

**Background:** Osteoporosis (OP) is a generalized skeletal disorder characterized by compromised bone strength and deterioration of bone quality, often leading to fragility. Elderly osteoporosis is being public health problem that highly affects people especially above 65 years. Physiotherapy and rehabilitation programs are...
important in the prevention and management of osteoporosis. Exercises improve mobility in elderly inpatient by increasing activity, muscular strength, flexibility, and reducing the risk of falls and length of stay in hospital.

Objectives: The aim of our study was to investigate the effects of physiotherapy and rehabilitation program on mobility, physical activity and quality of life in elderly inpatients.

Methods: A hundred and twenty four patient with OP (mean age: 73.03±5.9) participated in this study. A total of patients who were randomized as study and control group followed by Hacettepe University Faculty of Medicine Department of Internal Medicine, Division of Geriatric Medicine Department of Physiotherapy and Rehabilitation, Geriatric Rehabilitation Unit were, included to the study.

Assessment for cognitive function (Mini Mental State Test), functional mobility (De Morton Mobility Index), activities of daily living (Katz Index of Independence in Activities of Daily Living), quality of life (EuroQol-5D) were used at admission and discharge. Activities of Daily Living were measured by patient, and rehabilitation program including breathing, balance and coordination and strengthening exercises were performed by the intervention group under supervision of physiotherapist during the stay in hospital. Control group did not special exercise, they continued their activities of daily living. Exercise. Length of stay in hospital of all participant was recorded.

Results: Sixty two patients were randomly assigned to the each group. The groups were similar in sociodemographical feature (p>0.05), Improvements in mobility, quality of life and daily physical activity levels were found in the study group (p<0.05). There were no significant differences between control and intervention group in length of stay in hospital (p>0.05).

Conclusions: Our advice line gives patients easy access to specialist advice. Patient satisfaction is high. Responses are timely and fast. Multiple concerns are commonly addressed, such as advice regarding flare of disease and medication queries. This service will be

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2160

THU0761-HPR  BIOLOGICAL THERAPY SURVIVAL: MULTI-CENTRIC ANALYSIS IN REAL CLINICAL PRACTICE CONDITIONS

Background: Biological treatment (BT) has changed the evolution of rheumatic diseases. A way to product label, in clinical practice, in 3 Spanish hospitals.

Methods: Observational retrospective study, based on clinical history (CH) of patients with Rheumatoid arthritis (RA), Psoriatic Arthritis (PA), and Espondiloarthritis (EA) treated with BT.

CH standardization was performed by data collected since 2013 by rheumatologists thought MEDiades® RHEUMA tool.

Variables: age, gender, indication (RA, PA, EA); TB: Etanercept (ETN), adalimumab (ADA), certolizumab (CRT), golimumab (GOL), infliximab (IFX), abatacept (A), tocilizumab (TCZ), rituximab (RTX); Start and end date from 2002 to 2016

Exclusion criteria: Patients and/or treatment lines with incomplete data (lack data or n<15) were also excluded.

Descriptive statistics and Kaplan-Meier survival analysis were performed with r-project.com

Results: From initial 1155 patients, 76 patients were excluded because of incomplete data. Almost half of the patients (42.35%) were diagnosed with RA, 30.03% have EA and 18.07% PA. 10% were excluded because of other indications. 79.48% of patients with RA are women, as 96.36% of EA and 96.96% of PA; Most of the patients are over 55 years. In all indications, the range of 36–54 years is the one that present a higher percentage of patients.

For the Kaplan-Meier survival analysis, the complete set of BT that each patient had received was analyze independently, considering 1206 cases. Table 1 shows average time and percentage survival at 1 year and 5 years showed that the higher survival rates were for IFX in RA (94.4%) and PA (94.7%) and for ETN in EA (89.4%).

Conclusions: Our advice line gives patients easy access to specialist advice. Patient satisfaction is high. Responses are timely and fast. Multiple concerns are commonly addressed, such as advice regarding flare of disease and medication queries. This service will be

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2160

THU0760-HPR  PATIENT ADVICE LINE - THE POTENTIAL CLINICAL AND FINANCIAL BENEFITS TO A RHEUMATOLOGY DEPARTMENT
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Background: EULAR recommendation 3 for the role of the nurse in the management of chronic inflammatory arthritis states that patients should have access to nurse-led telephone services to enhance continuity of care and to provide ongoing support (1). In the UK quality standard 6 of the National Institute for Health and Care Excellence guidelines for the care of rheumatoid arthritis (RA) recommends that people with RA and disease flares, or possible drug related side effects should receive advice within 1 working day of contacting the rheumatology service. In 2016 audit data from England and Wales show that 96% of trusts report being able to provide patients with a telephone advice line but no further detail on these services was available (2).

Objectives: Data from our patient advice line were collected over a 6 month period. The objective was to understand who was using the helpline, the speed of our response, how much of the workload could be managed by nursing staff and the clinical and financial impact.

Methods: All patient calls made to our patient helpline were recorded and data were collected retrospectively on patient demographics, disease, purpose of call, response time and the cost and revenue produced. Patient feedback was collected via a questionnaire. Data were collected from April 2016 to November 2016.

Results: 150 patient calls were responded to. 108 calls were from females and were 42 years. The majority of patients had RA (75%). Other conditions are displayed in the graph below. The majority of calls were regarding a flare of their condition or medication queries (79/180 and 39/180 respectively) with some patients calling for more than one reason. 83% of calls were answered within 24 hours. A clinical nurse specialist is available to respond to calls over weekends. Income generated from responding to calls by the department was £1 900 per month. The expenditure was £1 650 per month. Patient satisfaction was high with 130/150 stating the main reason for the call was answered to their satisfaction (7 stating no, 13 not stated).

Conclusions: Our advice line gives patients easy access to specialist advice. Patient satisfaction is high. Responses are timely and fast. Multiple concerns are commonly addressed, such as advice regarding flare of disease and medication queries. This service will be

References:

Acknowledgements: By their collaboration: Dr Casado; Dr Valls; Dr Martínez; Dr Aguilar; Dr Vergara; Dr Begazo
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5072

STUDY OF MEDICAL ECONOMICS DISEASE MANAGEMENT (SSDM) MOBILE TOOLS: A POSSIBLE NEW AND EFFECTIVE WAY TO INCREASE PATIENT ADHERENCE TO MEDICAL ADVICE

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Background: Lack of Patient adherence to medical advice (PAMA) are recognized as an era of interest for the last decades. There have been several initiatives to improve PAMA such as patient centred care, shared decision-making, introduction of e-health and m-health. Although they are proven better than usual care, neither of these initiatives is proven successful. Outcome of medical interventions depends on complex physiological and sociocultural factors of which many are uncontrolled by health professionals.

Objectives: In the present study we assess beliefs about priorities in public health care, and adherence to medical advice to establish a novel approach to improve PAMA

Methods: The Norwegian Citizen Panel (NCP) is an experimental survey. Respondents are randomized to answer similar questions with slightly different wording. NCP is currently about 5000 respondents based on random selection performed by the Norwegian people register. The present study is based on two question experiments from NCP addressing beliefs about priorities in public health care, and adherence to medical advice. The question on priorities in health care is divided in six groups (two control group, four experimental). The question on adherence is divided in three groups (one control group, two experimental). All questions are answered with a seven point Likert scale.

Table 1

<table>
<thead>
<tr>
<th>Question</th>
<th>Question phrases</th>
<th>Result</th>
<th>Confidence interval</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prioritising waiting lists for surgery</td>
<td>1a</td>
<td>Patients with severe illness are treated first</td>
<td>0.7442</td>
<td>0.7169</td>
</tr>
<tr>
<td>1b</td>
<td>Patients with severe illness are treated first resulting in longer waiting for care in your family</td>
<td>0.7596</td>
<td>0.7239</td>
<td>0.7864</td>
<td>285</td>
</tr>
<tr>
<td>1c</td>
<td>Patients with severe illness are treated first, resulting in longer waiting for yourself</td>
<td>0.7600</td>
<td>0.7351</td>
<td>0.7860</td>
<td>266</td>
</tr>
<tr>
<td>1d</td>
<td>Those who benefit most from treatment are prioritised</td>
<td>0.5326</td>
<td>0.4877</td>
<td>0.5576</td>
<td>265</td>
</tr>
<tr>
<td>1e</td>
<td>Those who benefit most from treatment are prioritised, resulting in longer waiting for one in your family</td>
<td>0.5560</td>
<td>0.5208</td>
<td>0.5912</td>
<td>277</td>
</tr>
<tr>
<td>1f</td>
<td>Those who benefit most from treatment are prioritised, resulting in longer waiting for yourself</td>
<td>0.5818</td>
<td>0.5465</td>
<td>0.6171</td>
<td>273</td>
</tr>
<tr>
<td>2</td>
<td>Treatment rejection</td>
<td>2a</td>
<td>Medical doctor denies treatment</td>
<td>0.5009</td>
<td>0.4774</td>
</tr>
<tr>
<td>2b</td>
<td>Medical expertise does not support the treatment*</td>
<td>0.5361</td>
<td>0.5157</td>
<td>0.5564</td>
<td>564</td>
</tr>
<tr>
<td>2c</td>
<td>Medical expertise and patient organisation agree on not approving the treatment*</td>
<td>0.5730</td>
<td>0.5478</td>
<td>0.5982</td>
<td>523</td>
</tr>
</tbody>
</table>

Question 1-4 is used to assess beliefs on health care systems priorities. Question 2 assesses aspects of potential new ways to increase patient adherence. All questions are answered using a 7-point Likert scale. Result is based on positive attitude regarding wording in the question.

* Question phrases refer to how the physician explains to the patient why the treatment is rejected.
Conclusions: This study is the first to use experimental survey to assess PAMA. The result indicates that healthcare priorities form a base of trust between health care providers and patients. It further indicates that PAMA might increase if the healthcare provider refers to national expertise and patient organisations beliefs of a given treatment. This finding is supported by psychological theories of self-monitoring [2]. Informing the patient about the views of the patient organisations and adherence in the reasoning for a given treatment, may improve patient adherence to medical advice.

References:

Acknowledgements: Siv Markved for the suport and encouragement to do the study.

Disclosure of Interest: None declared


THU0764-HPR WHAT MOVES THE RHEUMATOLOGIST? UNRAVELLING DECISION MAKING IN SSC REFERRAL – A QUALITATIVE STUDY
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Background: Well-coordinated multidisciplinary non-pharmacological care is considered to be a cornerstone in the management of patients with systemic sclerosis (SSc). However, unmet information and healthcare needs are found to be common in patients with SSc [1]. In addition, referrals by rheumatologists do not always correspond with potential treatment goals as identified by health professionals [HP][2].

Objectives: The aim of this study was to gain insight in the perspective of rheumatologists about the referral process of SSc patients to non-pharmacological care and to identify starting points for its optimisation.

Methods: Semi structured in-depth interviews were held with 13 out of 24 rheumatologists, specialised in SSc management, from different Dutch university and regional medical centres. The qualitative data analysis used an inductive thematic analysis by moving through a process of coding in layers of abstraction and interpretation: familiarization with data, generating initial codes, grouping similar codes in categories, discussing categories, searching for themes among categories, reviewing themes, defining and naming themes, and producing the final report.

Results: One major theme was identified as influencing decision making: "beliefs" and its three sub themes: a) beliefs about one's own professional role; b) beliefs about the patients' ability to take an active role in managing the disease and c) beliefs about the added value of non-pharmacological care. We also found an additional theme reflecting the "needs" of the rheumatologists regarding professional multidisciplinary collaboration (Figure 1). Another remarkable finding to be further explored was the discrepancy we found between the reliance of rheumatologists on established routines with regard to when and to whom to refer and the low confidence in HPs competencies on the other hand.

Conclusions: This study gives insight that rheumatologists base their referral decisions on complex reasoning mindlines and beliefs about their own professional role, the patient's role and HP competencies.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5886

THU0768-HPR PATIENT SATISFACTION AND SELF-MONITORING OF CHRONIC INFLAMMATORY ARTHRITIS
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Background: Effective drug treatment for patients with inflammatory arthritides have brought a major proportion of patients in clinical remission. The need for regular follow-up intervals in specialized care is less; patients take greater responsibility for their own care, and patients request access to more flexible health care services. As a result of this development, the University Hospital, St.Olavs Hospital, Department of Rheumatology, has developed a on-demand pathway (PORS) for patients with inflammatory arthritis (RA, PsA and AS) in clinical remission or low disease-activity aiming for increased patient responsibility and flexibility.

Objectives: The aim of this study was to investigate patients' satisfaction with PORS regarding disease status, treatment, knowledge, responsibility, and cooperation with health care professionals.

Methods: We conducted a quest-back survey for patients included in PORS for ≥ 1 year in the period from June 2016 to October 2016. The survey contained 10 questions about the pathway. The response alternatives and scoring were: not at all = 1, to a small extent = 2, to some extent = 3, to a large extent = 4, to a very large extent = 5, and not relevant = 0.

Results: We identified 1048 eligible patients, 10 invitations were returned (unknown address), and 312 responded (30%). The descriptive analyses (see table) showed that the patients in general considered their disease activity to be in a stable phase. The cooperation with their general practitioner was good, they had to some or large extent sufficient knowledge to take responsibility for the blood test controls and adhere to prescribed medication. The patients were to some extent satisfied with the renewals of prescriptions and access to health professionals. The patients were less satisfied with the ‘promise’ of getting outpatient appointments within 14 days if needed. Finally, the patients would largely recommend PORS to other patients.

Conclusions: Patients with inflammatory arthritides in general were satisfied with a management pathway encouraging greater responsibility for managing their own care and the possibility for more flexible contacts with the health care services. However, fulfilling the promise of outpatient appointments within 14 days were not always possible to achieve.

Acknowledgements: We would like to thank the local Rheumatology fund for financing the project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3223

THU0776-HPR REFERRAL TO TELECARE. A NEW MODEL OF RHEUMATIC PATIENT FOLLOW-UP

Objectives: To analyze the medical ramifications that are made to the consultation
of telecare of Rheumatology Nursing (CTCER) of our hospital and health care activity generated by this.

**Methods:** Design: Observational study cross.

Patients: 301 patients for follow-up were derived to CTCER in a hospital of third level of January - November 2016. Our hospital serves a population of 600,000 people.

Protocol: We have a specific document for referral to CTCER where the rheumatologist specifies the reason for referral, the nurse review period and diagnosis. Nurse appoints the patient in its agenda for the telephone follow-up on the date indicated and recorded in the history of the patient efforts made the day of the appointment. The most common medical efforts making the nurse are preset by consensus with rheumatologists. Coming out than expected are reviewed with responsible for the patient's rheumatologist.

Variables analyzed: diagnosis, reason shunt type of FAME, adverse events, appearance of Comorbidities, nurse management, new problems after telephone consultation.

Statistical analysis: descriptive analysis of the main variables.

**Results:** Of the 301 patients, 68.4% were women. The diagnoses were: rheumatoid arthritis (RA) 116 (38.5%), spondyloarthropathy (SpA) 34 (11.3%), psoriatic arthritis (PsA) 45 (15%), systemic lupus erythematosus (SLE) (19.6%), vasculitis 1 (0.3%), arthritis juvenile idiopathic (AJI) 5 (1.7%), Still's disease adult 3 (1%), osteoporosis 4 (1.3%), 4 undifferentiated arthritis (1.3%). Them reasons of referral were: control to the month of home of FAME synthetic 120 (38.4%), control to the home of FAME biological 28 (9.3%), review consultations 110 (36.5%), control toxicity hepatic 17 (5.6%), control alteration hematologic 7 (2.3%), control alteration renal 1 (0.3%), control of security of treatment Mycophenolate 4 (1.3%), control of safety of Teriparatide 2 (0.6%), wish gestational 1 (0.3%), analytical control not performed in consultation 13 (4.3%) (Table1). The most derived synthetic FAME was methotrexate 174 (57.5%) and the most derived biological FAME was etanercept 16 (5.3%) (table2).

Nurse managed bypass autonomously 298 (99%) referrals, need help of the rheumatologist in 2 (0.7%) referrals and having only 1 shunt referred to 2017. 17 (5.6%) leads new problems with the call appeared: intolerance digestive 11 (3.7%), headache 3 (1%), worsening 1 (0.3%), moderate infection 1 (0.3%), poor adhesion 3 (1%), new comorbidity 3 (1%).

**Conclusions:** The inquiry of telecare is a collaborative work rheumatologist-nurse. The nurse can manage leads independently without having to go to your rheumatologist. This type of call nurse brings improvements in patient care, prevents displacement, decreased on-site visits and improves the safety of patients.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1674

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**THU0767-HPR**

ADVANCED PRACTICE MUSCULOSKELETAL PHYSIOTHERAPY SERVICES: A NATIONAL EVALUATION

O. Fennelly, C. Blake, O. Fitzgerald, R. Breen, A. Brennan, J. Ashton, C. Cunningham on behalf of The National Clinical Programmes for Rheumatology and Orthopaedics, School of Public Health, Physiotherapy and Sports Science, University College Dublin; National Clinical Programme for Rheumatology, Royal College of Physicians; Department of Rheumatology, St. Vincent's University Hospital; Health Service Executive, HSE; Physiotherapy, AMNCH; Physiotherapy, Beaumont Hospital, Dublin, Ireland

**Background:** Patients with musculoskeletal (MSK) disorders may remain on lengthy hospital outpatient waiting lists to be reviewed by a consultant doctor, although medical or surgical intervention may not be required (1,2). In 2012, a waiting list initiative saw the introduction of Advanced Practice Physiotherapists (APPs) across 16 hospitals in Ireland. APPs triage and manage patients awaiting a consultant doctor appointment, who are deemed non-urgent or unlikely to require surgery on screening of referral letters. APP scope of practice generally involves some traditionally medical-controlled acts such as: administering injections, ordering investigations/imaging, surgical listing and onward referral to hospital specialties; and depending on consultant doctor availability, their input may be sought on clinical decisions if required.

**Objectives:**

- Profile the national APP patient caseload
- Establish the clinical outcomes of APP consultations

**Methods:** A national database was established with all APPs (n=22) submitting patient data for 2014. These data were analysed using descriptive statistics.

**Results:** Data showed that APPs assessed 13,981 new patients, who presented most commonly with MSK disorders of the knee (n=3,096), lumbar spine (n=2,926) and shoulder (n=1,945) (Fig. 1) and the median wait time was 167 days (IQR 91–316). Including an additional 2,596 return appointments, the most common clinical outcomes were physiotherapy and/or clinical investigations (Table 1), and clinical decisions were made independently by the APP in 77% (n=11,728) of recorded cases (n=15,189).

**Conclusions:** APP services provide a more efficient MSK clinical pathway and reduce demands on the Consultant Doctor services. Collection of National Data enables ongoing service evaluation and monitoring of key performance indicators.

**References:**


**Acknowledgements:** I would like to thank the National Clinical Programmes and Health Service Executive for their funding and support of this project.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4300

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**THU0768-HPR**

PHONE FOLLOW-UP PROGRAM ENHANCES TREATMENT SAFETY AND DRUG CONCORDANCE ON DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS) THERAPY FOR RHEUMATOLOGY PATIENTS

P.F. Lee, Y.S. Cheung, C.K. Lam, M.C. Leung, C.M. Chan, W.L. Ng. United Christian Hospital, Hospital Authority, Hong Kong, Hong Kong

**Background:** DMARDS are beneficial for a number of rheumatic conditions. However, treatment effect may take a few weeks. On the other hand, patients may experience adverse effects (AEs) early on and they may not be able to follow complicated dosage titration regimen. In order to enhance treatment safety and empower self-management, rheumatic disease patients requiring initiation or change of DMARDS were recruited to a rheumatology nurse phone follow-up program.

**Objectives:** (1) To evaluate the service outcomes of Rheumatology Nurse Phone follow-up Program and (2) explore the factors that may influence treatment adherence

**Methods:** Upon initiation of DMARDS therapy at out-patient clinic or before hospital discharge, patients and/or their caregivers will be counseled for the new treatment plan and self-management knowledge by rheumatology nurse. A telephone follow-up by rheumatology nurse will be arranged within 4 weeks to monitor patients’ condition. Treatment responses, AEs, drug concordance of patients and advice given in each phone consultation (PC) were recorded. Retrospective case review was performed.

**Results:** There were 1230 episodes of PC performed by rheumatology nurse in 2015. 180 episodes of PC involved 76 patients (56 female) were randomly selected. The average number of PC was 2.4 times per case. The mean age of patient was 58 (24–85) years. Disease categories mainly involved rheumatoid arthritis (60.5%), systemic lupus erythematosus (7.9%), spondylarthritids (5.3%) and gout (3.9%). The most common DMARDS prescribed were methotrexate (40.8%), hydroxychloroquine (27.6%), sulphasalazine (22.4%) and 39.5% of the study cases have received steroid courses. Among the 76 patients, 8 (10.5%) have taken wrong dosage and another 4 (5.3%) patients have not started therapy due to worries about potential AEs. Altogether 40 patients (52.6%) reported AEs after starting DMARDS. The most common AEs were rash, itchiness, dizziness, alopecia and oral ulcers. For non-adherence behaviour, 8 patients (10.5%) have self-stopped their medication and another 7 patients (9.2%) have self-adjusted the medication respectively. Eventually 90% of the cases were able to continue therapy with or without adjustment of regimes. Only 7 cases (9.2%) required interruption of current treatment or switching to other DMARDS due to AEs within the study period.
THU0770-HPR

COST SAVINGS BY FAVOURING INFliximAB BISIMILARS IN THE EASTERN REGION OF AUSTRIA

B. Reichardt1, G. Reiter1, T. Stamm1, R. Heaton1, P. Heaton1, 1Behandlungsökonomie, BGKK, Eisenstadt; 2Section for Outcomes Research, Care, Maastricht University Medical Centre, Maastricht, Netherlands

Objectives: Since April 2015, the availability of infliximab biosimilars offered a new potential for cost savings in limited financial resources of the healthcare system. In Austria, there is currently no open tendering for drugs dispensed at homecare providers were identified using the trust’s biologic database and clinic records. Information on biologic delivery quantities and schedule were provided by Homecare companies. Data was analysed used Microsoft Excel®; number (and cost in accordance with pharmacy tariffs) of doses “wasted” was calculated by referring the date of treatment cessation with the date and quantity of last biologics deliveries and patient stock levels as reported by the homecare company. Doses obtained from charge were excluded. Baseline delivery frequency was captured over a six month period. Four costs were calculated: (1) Total waste. (2) Wasted supply exceeding two months to assess whether an increase in delivery frequency to two monthly could reduce waste. (3) Waste from unopened deliveries to establish whether waste could be reduced by improved patient education around refusing deliveries in the event of treatment failure or intolerance. (4) Waste from the second biologic prescription issued as a result of stopping biologic at the three month review to assess viability of the proactive phone. A proactive patient phone call was then initiated and waste data captured for a three month period following this intervention.

Results: 27 patients stopped treatment during the 6 months baseline data collection. 23 patients had drug waste totalling £ 32,140.80. The total value of wasted stock exceeding two months supply was £ 5,414.36. Three patients accepted deliveries for further supply and stopped treatment before opening final deliveries, creating a waste total of £ 5,509.09. Four patients stopped treatment at their three month review, £ 4,572.22 of additional biologic was supplied and then wasted as a result. Following the pro-active phone call intervention, 21 patients were contacted before their second supply was due and supply subsequently limited for 8 patients, four of whom stopped treatment at their next consultant review. Limiting supply in the four patients saved £ 6,682.

Conclusions: Initiating a proactive phone call at three months following biologic initiation can reduce drug waste. Other initiatives such as patient education to refuse deliveries and increasing delivery frequency also appear viable waste reduction initiatives.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6333

THU0771-HPR

INCORPORATING SENIOR PHARMACIST INPUT IN TERIPARATIDE PATHWAY ENSURES ADHERENCE TO PRESCRIBING GUIDANCE - AUDIT/QUALITY IMPROVEMENT RESULTS FROM A DISTRICT RHEUMATOLOGY UNIT

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Background: Teriparatide is licensed for up to two years to treat severe osteoporosis. It is the most expensive osteoporosis treatment available (around £ 3500 per year). Hence a locally adapted national NICE guidance is needed for prescribing in our department; but the previous level adherence was uncertain. In 2011, a directory of services was agreed for our metabolic bone clinic. At the time a Rheumatology senior pharmacist review with the prescribing senior clinician was agreed on our teriparatide treatment pathway, including pre-treatment DXA, and a specified bone profile screen before treatment and for repeat prescribing at specified intervals. The agreement also incorporated access for our patients to senior pharmacist advice if needed via the department’s secretarial team.

Objectives: Our objective was to assess the impact of the senior pharmacist input on our adherence to the agreed guidelines in our Teriparatide pathway, including assessing treatment completion and response.

Methods: Patients with osteoporosis who were started on Teriparatide between 2011–2015 were identified from pharmacy prescribing spreadsheets. A retrospective review of case notes of all patients were carried out. Data including age, gender, prior agents tried, pre-treatment bone profile, and pre and post treatment DXA, and treatment completion were collected on a Microsoft Excel 2010 spreadsheet for processing and descriptive analysis.

Results: 33 patients who were started on teriparatide treatment between 2011–2015 were identified (29 female and 4 male). Mean age was 76.2 (range 63–92). All had pre-treatment DXA, and 32 (97%) were compliant with recommendations for initiation of teriparatide treatment with respect to DXA (one patient borderline). All 33 patients had a pre-treatment bone profile within acceptable limits before start of treatment (adjusted Calcium, Serum Parathyroid Hormone, Vitamin D level, e-gfr). 28 (84.8%) patients tried one agent before initiation of Teriparatide treatment and 5 (15.2%) patients tried 2 agents. 24 (72.7%) patients completed the full course of recommended treatment. 11 out of 24 patients who completed Teriparatide treatment have had post-treatment DXA. 3 out of 24 patients who completed Teriparatide treatment had a fragility fracture after treatment.

Conclusions: This audit confirms the benefit of incorporating Rheumatology senior pharmacist review in our pathway from the excellent compliance with guidelines in initiating and managing Teriparatide noted in the results. This is likely to have also contributed to the high completion rate of the treatment course. However, only 11 out of 24 had post treatment DXA, and this needs improvement by the next audit cycle, through input of senior clinicians who are in charge of requesting DXA. We would, therefore, recommend incorporating senior pharmacist input for review in teriparatide treatment pathways routinely.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7031

THU0772-HPR

VARIATION IN RHEUMATOLOGY NURSING CARE IN THE NETHERLANDS: A SURVEY AMONG NURSES

Y. Van Eijk-Hustings on behalf of Working Group Rheumatology Nursing Research. Clinical epidemiology and medical technology assessment/Patient & Care, Maastricht University Medical Centre, Maastricht, Netherlands

Background: EULAR recommendations for the role of nurse aim at guaranteeing a certain standard of care for people with rheumatic musculoskeletal diseases...
Health Professionals in Rheumatology Abstracts

FRIDAY, 16 JUNE 2017

HPR measuring health (development and measurement properties of PROs, tests, devices) —

**FR01073-HPR**

THE EDUCATIONAL NEEDS OF PATIENTS WITH UNDIFFERENTIATED SPONDYLARTHROPATHY

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**Background:** The educational needs of people with undifferentiated spondyloarthropathy (USpA) have not been well studied. The educational needs assessment tool (ENAT) has been translated to Swedish and validated in other rheumatic diseases but not USpA. 1

**Objectives:** To validate the educational needs assessment tool (ENAT) in people with USpA and use it to study their educational needs.

**Methods:** A cross-sectional study recruiting a random sample of patients with USpA from a hospital register. USpA was diagnosed according to the International Classification of Disease, ICD-10 (M46.0, M46.1, M46.8, and M46.9). 1 The study was approved by the Regional Ethics Board and all included patients signed an informed consent. We used a postal survey to collect data on disease activity (BASDAI) and educational needs (Swedish version of the ENAT). 2 The data was then utilized to assess the construct validity, internal consistency, unidimensionality and response bias of the ENAT using Rasch analysis. Given fit to the Rasch model, we transformed the ENAT ordinal scores into interval logit-units and assessed differences between patient subgroups using the student’s t-test.

**Results:** Complete responses were derived from 77 patients (48 women), mean (SD) age 50 (12) years, disease duration was 16 (11) years, BASDAI 4.9 (1.9) and BASFI 3.1 (2.3). When used as a 7-subscale questionnaire, the ENAT satisfied the requirements of Rasch model (c²=11.488; p=0.119) including strict unidimensionality.

In general, the mean (SD) ENAT scores for patients with USpA were 86 (32). Women reported higher needs than men in the domains of pain, mean (SD) 13.1 (6.8) vs. 10.1 (6.0), p<0.05; movement mean (SD) 13.0 (5.5) vs. 9.9 (5.7), p=0.02 and self-help, mean (SD) 17.0 (5.8) vs. 14.1 (5.0), p=0.03. Higher disease activity (BASDAI >4) was associated with higher educational needs, mean (SD) 22.6 (31.9) vs. 17.3 (29.4), p=0.02. There was no significant difference in educational needs between age groups.

**Conclusions:** The Swedish ENAT has been validated in USpA thus enabling an accurate estimation of the educational needs of people with USpA in Sweden.
Our data suggest that women and patients with higher disease activity are likely to have high levels of educational needs and these groups should be targeted in educational interventions for people with USpA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2989

EFFECTS OF VIRTUAL REHABILITATION ON SHOULDER PERIARTHRITIS
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Background: The virtual rehabilitation (Nintendo Wii) program works with a 3-dimensional, computer-assisted, virtual reality creation system. The system creates a mirror effect and provides the smoothness of the movement of the adult. It keeps visual and sensory feedback during exercise. The avatar that appears on the screen detects motion and displays the result thanks to the control commander. The use of virtual reality practice in the exercise program is a new way of improving participation and motivation of participants.

Objectives: The aim of our study is to investigate the effect of virtual rehabilitation on kinesophobia and clinical fragility in patients with shoulder periartthritis.

Methods: Fifteen cases diagnosed with shoulder periartthritis were included in the study. In the study, we used Tama Kinesiophila Scale for kinesiophobia, VAS for pain severity, manual muscle test for muscle strength and goniometer for ROM. In addition to clinical fragility Scale for fragility and 4-item Quality of Life Questionnaire were used to assess quality of life. Finally, Shoulder Pain and Disability Index (SPADI) was used for shoulder disability. Eight of 15 patients were included in the control group (CG) and 7 in the virtual rehabilitation group (VRG). Both groups were treated with Therapeutic US, TENS and Cold Pack. In addition to these, the control group consisted of 15 sessions of active stretching (CG); they were given 10 MWT, 5x SST (sec) as performance tests. Each of the tests was performed twice, with a break between testing.

Results: Statistically significant reductions in Fragility, Kinesiophila, SPADI and VAS values were observed in the VRG analyzes; A statistically significant increase in the 4-item quality of life questionnaire, range of motion and muscle strength values was assessed (p<0.05). In the CG, there was a statistically significant decrease in kinesiophila, VAS and SPADI values; There was a statistically significant increase in joint range of motion and muscle strength evaluations (p<0.05). There was no statistically significant difference in the fragility evaluation of the CG (p>0.05).

Conclusions: Fragility and kinesiophila decreased in both groups after treatment compared to before treatment, but this decrease was found to be higher in VRG (p<0.05).

Methods: The study included 32 OA patients (27 F, 5 M) who undergone TKA surgery 6 months prior to the study. Mean age and BMI of the patients were 64±10.58 and 30.49±5.87, respectively. Participants performed the Timed Up and Go Test (TT), 1 Meter Walk Test (10MWT), Single Leg Stance Test (SLST), Functional Reach Test (FRT), 2 Minute Walk Test (2MWTT), Five Times Sit to Stand Test (5x SST) as performance tests. Each of the tests was performed twice with a

Table 1. Test-Retest Reliability analysis of the performance tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Day 1 Mean (SD)</th>
<th>Day 2 Mean (SD)</th>
<th>ICC (95% CI)</th>
<th>SEM</th>
<th>2 SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUG (sec)</td>
<td>10.67±4.53</td>
<td>10.61±5.05</td>
<td>0.95 (0.90–0.99)</td>
<td>1.01</td>
<td>2.79</td>
</tr>
<tr>
<td>10 MWT (sec)</td>
<td>9.89±3.37</td>
<td>9.72±3.03</td>
<td>0.97 (0.94–0.98)</td>
<td>0.58</td>
<td>1.6</td>
</tr>
<tr>
<td>SLST (sec)</td>
<td>14.96±14.90</td>
<td>18.97±19.15</td>
<td>0.74 (0.48–0.87)</td>
<td>7.59</td>
<td>21.02</td>
</tr>
<tr>
<td>FRT (cm)</td>
<td>26.19±7.33</td>
<td>26.50±6.63</td>
<td>0.84 (0.88–0.97)</td>
<td>1.79</td>
<td>4.95</td>
</tr>
<tr>
<td>2 MWT (sec)</td>
<td>145.25±37.63</td>
<td>145.32±38.06</td>
<td>0.98 (0.96–0.99)</td>
<td>5.32</td>
<td>14.73</td>
</tr>
<tr>
<td>5x SST (sec)</td>
<td>13.54±6.66</td>
<td>13.04±5.03</td>
<td>0.96 (0.91–0.98)</td>
<td>1.25</td>
<td>3.46</td>
</tr>
</tbody>
</table>

Unit: Mean ± SD, ICC: Intraclass Correlation Coefficient (CI): Confidence Interval, SEM: Standard Error of Measurement, MDC: Magnitude of Detectable Change at 95% Confidence Interval, sec: seconds, cm: Centimeters, m: meters, TUG: Timed Up and Go Test, 10 MWT: 10 Meter Walk Test, SLST: Single Leg Stance Test, FRT: Functional Reach Test, 2 MWT: 2 Minute Walk Test, 5x SST: Five Times Sit to Stand Test.

Table 2. Concurrent Validity of Performance Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>r value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUG (sec)</td>
<td>-0.713</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>10 MWT (sec)</td>
<td>-0.776</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>SLST (sec)</td>
<td>-0.754</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>FRT (cm)</td>
<td>0.695</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>5x SST (sec)</td>
<td>-0.766</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

* Spearman Correlation Test; sec: seconds, cm: Centimeters, m: meters, TUG: Timed Up and Go Test, 10 MWT: 10 Meter Walk Test, SLST: Single Leg Stance Test, FRT: Functional Reach Test, 2 MWT: 2 Minute Walk Test, 5x SST: Five Times Sit to Stand Test.

FR0733-HPR
FR0734-HPR
FR0735-HPR
FR0736-HPR

ANALYSIS OF LEFT VENTRICULAR FUNCTION WITH ECHOCARDIOGRAM IN PATIENTS WITH PSORIATIC ARTHRITIS AND NOT DIAGNOSED CARDIOVASCULAR DISEASE
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Background: It is known that some rheumatological disorders may affect the cardiovascular system. In the last years, psoriatic arthritis (PsA) has been pointed out as one of these.

Objectives: The aim of this study was to analyze if there was any subclinical dysfunction sign in patients with PsA of whom no cardiovascular disease had been diagnosed.

Methods: Forty three patients with PsA were studied. A comprehensive echocar-
1-day interval. ICC models were used to determine the test-retest reliability. Berg Balance Scale (BBS) was used as the reference standard to establish concurrent validity.

Results: All tests showed good to excellent reliability (ICC > 0.94) except SLST which showed moderate to good reliability (ICC = 0.74). Three of the tests (SLST, 10 MWT, 5x SSS) found to have moderate to excellent validity (r > 0.75) and three (2 MWT, TUG, FRT) found to have moderate to good reliability (r > 0.69). Results are presented in details at Table 1 and Table 2.

Conclusions: TUG, 10MWT, SLST, FRT, 5x SSS and 2 MWT are reliable and valid outcome measures, and could be used to assess balance and fall risk in patients with TKA. MDC scores presented in this study can be used to evaluate change in performance over time or effectiveness of interventions. 2 MWT and 5x SSS were determined as the most reliable and valid methods among the investigated tests.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.59218

THE SOURCES OF PAIN IN ABDOMEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Systemic diseases of connective tissue associated with the early development of atherosclerosis [1,2]. It is well-known that the main cause of decrease the quality of life patients with rheumatoid arthritis (RA) is a chronic pain syndrome. The cause of pain can be joint inflammatory process, systemic manifestations of RA (vascular disease, pericarditis, pleurisy, perineuropathy) [3], complications of drug therapy, comorbid conditions. Pain in the stomach area may be associated with NSAID-gastroptropy, problems with spinal discs, and perhaps with atherosclerotic lesions of the abdominal aorta.

Objectives: To estimate atherosclerotic changes of arteries in patients with RA and to determine possible sources of pain in the abdomen by ultrasound-control palpation.

Methods: We included 75 patients with RA (age 38.7±7.4, males 93.3%) and 29 healthy subjects, matched for age and gender, without a history of cardiovascular diseases. An ultrasound investigation of the arterial wall with measurement of the intima-media thickness (IMT) of carotids was performed. To determine the source of pain in the abdominal cavity ultrasound-control palpation of duodenal bulb, gallbladder, lumbar discs, and abdominal aorta was done. Seventy of pain was assessed using the VAS.

Results: It has been determined, that in RA group IMT was 0.8 mm (0.7–0.9), compared with 0.6 mm (0.6–0.7) in control group. IMT positively correlate with the age, duration of disease, Ritchie index, C-reactive protein level. In 22 (29.3%) patients with RA we found atherosclerotic plaques lesion in carotids, aorta, and vessels of the lower extremities. Present of atherosclerotic plaques associated with disease duration (12 years (10–15) in group with plaques and 5 years (3–8) in group without plaques). The presence of atherosclerotic plaques is associated with rheumatoid factor (c=1.02, p=0.05), and systemic manifestations of RA (c=1.59, p=0.001).

In RA group 36 (48%) patients had indicated the presence of pain in the abdomen while performing ultrasound control palpation. In 15 (20%) cases was detected pain during palpation of the lumbar spine, VAS 48 (36–59). In 21 (28%) cases, patients indicated pain during palpation of the abdominal aorta, VAS 42 (31–65). In this group of patients we found signs of the atherosclerotic lesions of aorta, change in the contour of the vessel, the heterogeneous structure of the vascular wall. Atherosclerotic plaques in the abdominal aorta are founded in 21 (28%) cases.

Conclusions: Patients with RA had an increase thickness of IMT and atherosclerotic plaques, which appear in various vascular regions. During performing ultrasound-control palpation in 36 (48%) patients was detected pain, associated with vertebral changes 15 (20%), and with atherosclerotic changes of abdominal aorta – 21 (28%).

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1809

THE EXPERT, WE ARE THE SPECIALIST

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Background: Patient participation is known in the field of rheumatology research and is becoming more customary. The patient perspective can improve the care and line specific needs of the patient to the delivered care.Recently, our rheumatology department within the Maasstad Hospital introduced the Value Based Health Care principle in order to optimize the current healthcare system.
We thought to measure the value for patients we should let them participate in the project and asked them about what is of value for them and what are there goals. A good reason to start with a patient panel.

**Objectives:** For this reason we aimed to create a patient panel of rheumatology patients that are well informed and prepared to actively cooperate and participate in research, and co-design novel healthcare strategies.

**Methods:** Staff members (e.g. doctors and nurses) were asked to nominate patients that are expected to actively participate in the panel. Nominated patients were verbally approached and asked to participate. After mutual agreement a contract was signed were patients discretion was warranted, the capacity to handle confidential information was assessed and equality between members of the panel and staff was ensured. Enrollment of the panel is mainly staff-driven, but panel members are also invited to actively recruit other rheumatology patients.

**Results:** The initial enrolment period lasted for six months. Thereafter, meetings were organized were discussion were held on various themes such as goals and value for rheumatology patients. Additionally, a focus group of rheumatoid arthritis (RA) patients was assembled to evaluate a PROMs measurement tool. To date, a number of four panel discussion have been held. Currently, our patient panel consists of 54 patients with all kinds of rheumatic diseases. Their demographic and clinical data are presented in Table 1.

**Disclosure of Interest:** None declared


<table>
<thead>
<tr>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
</tr>
<tr>
<td>Gender (female)</td>
</tr>
<tr>
<td>Age (yrs)</td>
</tr>
<tr>
<td>Disease duration (yrs)</td>
</tr>
<tr>
<td>Diagnosis (%)</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
</tr>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>SpA (including AXPs and AS)</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Our panel has been asked to participate in other (hospital-wide) programmes including the development and evaluation of a patient portal. We organize about three meetings for the whole panel every year and arrange focus group meetings to discuss specific subjects.

**Conclusions:** Panel members are very open and enthusiastic. Some quotes: “I’m happy to do something in return for the good care I receive.” and “I want to promote participation in scientific research.” Deployment of patient participation for co-creating innovations alongside research is an asset these days to connect changes to patients perception.

In real live involving patient as an expert is not an effortless action for both patients and the expert care takers, it leads to satisfaction and an effective treatment.

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**Background:** Since the disease activity of patients with RA tends to fluctuate between visits and disease flares are easily missed during regular visits, patients might benefit from a more closely spaced determination of disease activity, which could be realised by iMonitor. iMonitor is a Software Medical Device developed and funded by Pfizer. This online system allows patients to complete three kinds of patient-reported outcome measures (PROMs): the Health Assessment Questionnaire (HAQ), the Rheumatoid Arthritis Impact of Disease (RAID) and the Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5). More often, PROMs results might contribute to identification of patients who need additional medical attention in between visits and reduction of visits for patients with stable disease activity.

**Objectives:** To determine the degree to which the PROM-scores in iMonitor are associated with DAS28. Moreover, PROM preferences and completion rates were studied.

**Methods:** Patients were recruited at Bernhoven (Uden, the Netherlands) by an announcement on the hospital website, leaflets and meetings. Instruction classes were organised in which researchers assisted patients in using iMonitor. Patients indicated which PROM(s) they want to complete in iMonitor and chose reminder email frequency (weekly, two-, four-, six, and eight-weekly). Descriptive analyses were used to describe characteristics of the study population. Scatter plots with regression equations were performed with DAS28 as dependent and PROM as independent variable to determine the association between DAS28 and PROMs. Moreover, PROM’s correlations were calculated. PROM-score within the fourteen day window before and after DAS28 assessment were included.

**Results:** In total 33 patients with RA were included, seventeen of them were female (52%). Mean (±SD) age was 56±11 years. Seventeen patients (52%) attended the instruction classes. Majority of patients (n=10) chose all three PROMs to complete, nine patients chose RAID+RADAI-5, seven chose HAQ+RAID, three chose RAID, two chose RADAI-5 and two chose HAQ+RADAI-5. From March 2016 until December 2016, 435 PROM-values, 329 DAS28-values and 222 HAQ-values were gathered. When taking PROM-values within the fourteen day window before and after DAS28 assessment, 159 DAS28-values could be coupled to 529 PROM-values. Regression analysis showed the following proportions of explained variance (R²): 0.17 for HAQ, 0.32 for RAID and 0.29 for RADAI-5. Pearson’s correlation coefficients were 0.41 for HAQ, 0.57 for RAID and 0.54 for RADAI-5. Most chosen reminder email frequency was four weeks (n=21). Completion rates (measured until December 31, 2016) were 65% for patients with one week PROM-frequency and for patients with two, four, six and eight week frequency completion rates were 39%, 24%, 30% and 0%, respectively.

**Conclusions:** RAID and RADAI-5 were moderately associated with DAS28 and showed highest proportions of explained variance. The association between HAQ and DAS28 was weaker. Patients receiving a weekly reminder email showed highest completion rates. This pilot study is a first step towards personalised healthcare and patient involvement in online remote monitoring.

**References:**


L.F. Perez, A. Martinez, M. Moreno, L. Silvera, Reumatologia, Instituto Nacional de Cardiologia Ignacio Chavez, Mexico City, Mexico

**Background:** Anxiety and depression are often present in chronic rheumatic diseases. Recognition of these psychological disorders is fundamental for proper patient management. The absence of screening leaves more than 50% of patients with depression unidentified. Patient Help Questionnaire-9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7) are two validated self-applied questionnaires that are appropriate to assess the prevalence of, depression and anxiety, respectively.

**Objectives:** 1) To assess the prevalence of depression and anxiety in a hospital based outpatient Rheumatology clinic and 2) To provide the attending physician with appropriate instruments that allow a rapid orientation on the psychological status of her/his patient.

**Methods:** Consecutive patients that attended our outpatient Rheumatology clinic from March to June 2016 were invited to participate in this cross-sectional study. Participants filled out PHQ-9 and GAD-7 in the waiting room. The prevalence and severity of anxiety and depression were calculated for the most prevalent diagnoses.

**Results:** A total of 410 patients were recruited; 339 (82.8%) were female. Overall, 191 (46.9%) patients reported depressive symptoms (PHQ-9 ≥ 5). Of them, 87 (21.2%) were classified as having moderate depression or higher (PHQ-9 ≥ 10). Prevalence of depression and anxiety among study participants according to each rheumatic disease is depicted in Table 1. Prevalence of moderate or severe depression was significantly different among various rheumatic diseases (p=0.001). Regarding anxiety symptoms, they were reported in 168 (40.7%) and 87 (16.2%) of them had moderate or severe anxiety.

**Conclusions:** This cross-sectional study shows that anxiety and depression are frequent in the Rheumatology clinic. We demonstrated that the use of a self-applied screening tool can help clinicians to properly detect depression and anxiety associated with diverse rheumatic diseases. Specia attention should be paid to patients with fibromyalgia and osteoarthritis.
**Does the Use of Technological Devices Improve the Reliability of Measuring the Active Cervical Range of Motion in Patients With Neck Pain? A Systematic Review with Meta-Regression**

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1Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Savona; 2Department of Health Sciences, University of Genova, Genova, Italy

**Background:** Economic impact of neck pain shows an increasing trend. In order to limit the costs of spine disorders management, it is important to assess clinical efficacy and the cost-worthiness of new technological devices, recently introduced in physical therapist's clinical practice.

**Objectives:** This systematic review compares, in patients with non-specific neck pain, the reliability of measures of Active Cervical Range of Motion (ACROM) detected with technological devices with those assessed with low cost, commonly-used devices. As secondary outcomes, it was investigated if ACROM reliability depends on the plane on which the measured movement is performed.

**Methods:** The literature was carried out in Medline, Scopus, Embase, The Cochrane Library, CINHAL, PEDro, and other available databases until August 2016. Inclusion criteria were: reliability design, population of adults with non-specific neck pain, examiners of any level of experience, measures repeated at least twice and statistics indexes on reliability. Exclusion criteria were: other study designs, asymptomatic population or mixed population, single or none ACROM measure inadequate statistics. The risk of bias was assessed by OAREL. It was considered inexpensive a device that costs at maximum 500 euros. A Univariate, and a Multivariate Analysis, were performed by using the Linear Mixed-Effect Model

**Results:** Searching the databases yielded 35,151 records. Nine studies met all eligibility criteria. The OAREL mean score of the selected studies was 3.7 out of 11. No significant effect of the type of device (inexpensive versus expensive) on ICC was observed for intra-rater (ICC=0.93±0.01; p-value=0.89) and inter-rater reliability (ICC=0.80±0.07; p-value=0.99) [Table 1]. The plane of movement did not affect inter-rater reliability (p-value=0.11) while significantly influenced the intra-rater reliability (p-value=0.0001) assessed with low-cost devices. Intra-rater reliability significantly decreases (p-value=0.0129) in frontal plane movements (side bending) compared with movement on the sagittal plane (flexion-extension).

**Table 1. Comparison of intra and inter-rater reliability between tool types**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ICC Descriptive statistics</th>
<th>Mixed effect model</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>β (95% CI)</td>
<td></td>
</tr>
<tr>
<td><strong>Intra-rater reliability</strong></td>
<td></td>
<td>β</td>
<td></td>
</tr>
<tr>
<td>Tool Type</td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expensive</td>
<td>0.91 (0.07)</td>
<td>0.01 (0.04: 0.06)</td>
<td>0.56</td>
</tr>
<tr>
<td>Inexpensive</td>
<td>0.93 (0.02)</td>
<td>0.01 (0.00: 0.01)</td>
<td>0.56</td>
</tr>
<tr>
<td><strong>Direction</strong></td>
<td></td>
<td>β</td>
<td></td>
</tr>
<tr>
<td>Flexion &amp; Extension</td>
<td>0.91 (0.07)</td>
<td>0.01 (0.00: 0.01)</td>
<td></td>
</tr>
<tr>
<td>Rotation</td>
<td>0.95 (0.02)</td>
<td>0.03 (0.01: 0.07)</td>
<td></td>
</tr>
<tr>
<td>Side Bending</td>
<td>0.92 (0.01)</td>
<td>0.01 (0.02: 0.04)</td>
<td>0.79</td>
</tr>
<tr>
<td>Age</td>
<td>rho = 0.29</td>
<td>0.00 (0.01: 0.01)</td>
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</tr>
<tr>
<td><strong>Inter-rater reliability</strong></td>
<td></td>
<td>β</td>
<td></td>
</tr>
<tr>
<td>Tool Type</td>
<td>0.99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expensive</td>
<td>0.87 (0.09)</td>
<td>0.03 (0.15: 0.21)</td>
<td>0.06</td>
</tr>
<tr>
<td>Inexpensive</td>
<td>0.80 (0.12)</td>
<td>0.03 (0.15: 0.21)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Direction</strong></td>
<td></td>
<td>β</td>
<td></td>
</tr>
<tr>
<td>Flexion &amp; Extension</td>
<td>0.82 (0.09)</td>
<td>0.03 (0.15: 0.21)</td>
<td>0.06</td>
</tr>
<tr>
<td>Rotation</td>
<td>0.96 (0.11)</td>
<td>0.04 (0.02: 0.11)</td>
<td>0.06</td>
</tr>
<tr>
<td>Side Bending</td>
<td>0.77 (0.13)</td>
<td>-0.04 (0.10: 0.01)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>rho = 0.58</td>
<td>0.01 (0.01: 0.03)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

**Conclusions:** The use of expensive devices to measure ACROM in adults with non-specific neck pain problems not seem to improve the reliability of the assessment. The assessment of side bending showed the lowest level of inter-raters reliability. Since the quality of the analysed studies is low, the conclusion of the present study should be taken cautiously.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4801

**FRI0744-HPR**

**The Effectiveness of the Lower Dose of Laser Treatment on Knee Osteoarthritis**

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**Background:** During knee osteoarthritis (OA) therapy; medications, physical therapy modalities, exercises and surgical procedures are used. In previous studies, the benefits of low level laser therapy (LLET) for pain in the low back, shoulder, elbow, and hand have reported.

**Objectives:** In this study we aimed to investigate the effectiveness of LLLT on pain, functional status, and quality of life in patients with knee osteoarthritis.

**Methods:** Patients with Kellgren-Lawrence stage 2–3 knee osteoarthritis were enrolled. It was planned as a prospective, randomized and double-blind study. Group 1 received active laser therapy and group 2 placebo laser therapy. Patients have been provided active/placebo laser therapy for two weeks (5 days a week, a total of 10 sessions). Patients were evaluated before, immediately after and 1 or 3 months after treatment. Outcome measurements included pain intensity at rest and at movement on visual analog scale, knee function using Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scale, active/passive joint range of movement, quality of life using Short form 36 (SF-36), and 15-meter walking distance, painless walking distance.

**Results:** In this study, we observed improvements in knee pain, 15-meter walking distance, WOMAC pain, stiffness and function scores, Lequesne index, and SF-36 physical function and social function (p<0.05) in active LLET group. At all, significant improvements were detected in SF-36 physical role, mental health, vitality, and emotional role function in active laser group (p<0.05).

**Conclusions:** The present study demonstrated that LLET is safe and effective upon pain and functional parameters on knee osteoarthritis. However, we think future long-term studies should be completed to include more patients in order to determine the priority and effectiveness are required.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5187
INVESTIGATION OF ASSOCIATION BETWEEN WRIST PAIN, FUNCTIONAL PERFORMANCE, GRIP AND PINCH STRENGTH IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: CROSS-SECTIONAL STUDY

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Background: Juvenile idiopathic arthritis (JIA), among the most common chronic diseases of childhood, can be associated with pain. reduced range of motion, decreased muscle strength and functionality (1).

Objectives: The aim of this study was to assess the relationships between wrist pain and functional performance, grip and pinch strength in children and adolescents with JIA.

Methods: Cross-sectional study design was included 42 (36 female). 6 male children and adolescents with JIA aged between 8 and 18 years. Patients who have at least one affected wrist included in the study. Sociodemographic data and clinical features were assessed by physical therapists. Hand grip strength was assessed with Jamar dynamometer. Lateral, tip and palmar pinch strengths were assessed with Baseline pinchmeter. Wrist pain during the activity was evaluated with Numeric Rating Scale (NRS). A score of 0 indicated "no pain" and 10 indicated "extreme pain" for NRS. Functional performance of hands was assessed with "Jebson Taylor Hand Functional Test" (JTHFT). JTHFT consists 7 subtests: writing a 24-letter, card turning, picking up small objects and placing them in a container, stacking checkers, stimulated feeding, moving light objects and moving heavy objects. All tests except writing performed on both right and left hand for JTHFT.

Results: The mean age and duration of disease was 13.05±3.04 (age range 8–18) and 6.55±3.78 years. respectively. Patient population consisted of 28 patients with polyarticular arthritis. 14 patients with oligoarticular arthritis. 39 of 42 patient's wrists were affected bilaterally. Significant relationships were found between writing and right palmar pinch strength (r=-0.34 p=0.023), right hand grip strength and right stimulated feeding (r=-0.32 p=0.039), left hand grip strength and left moving heavy objects (r=-0.33 p=0.028). Also, significant relationships were found between right lateral pinch strength and stimulated feeding (r=-0.33 p=0.028) and right stacking checkers (r=-0.31 p=0.039). For right side, significant relationships were found between palmar pinch and moving light objects (r=-0.35 p=0.020), moving heavy objects (r=-0.32 p=0.039), stimulated feeding (r=-0.36 p=0.017), stacking checkers (r=0.36 p=0.017), card turning (r=-0.34 p=0.026) and JTHFT-total score (r=-0.33 p=0.028).

Conclusions: The results of our study showed that hand grip and pinch strengths considerably decreased in children and adolescents with JIA, according to the normal means of the grip strengths of healthy children and adolescents reported in the literature (2). Our study suggested that decreased hand grip and pinch strengths may result impairment daily functions but wrist pain does not effect on. The results of our study showed that hand grip and pinch strengths were associated with JIA. Althought patients with JIA had only one affected knee joint, hip flexion muscle strength was primary predictor of stair climbing performance. We suggested that stair climbing performance should be considered in patients with juvenile idiopathic arthritis. Thus, not only affected joint, but also all lower extremity joints should be assessed multidimensionally.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4937

FEASIBILITY OF FOUR QUESTIONNAIRES TO EVALUATE PATIENT EDUCATION FOR PEOPLE WITH INFLAMMATORY ARTHRITIS

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Background: No core set of outcomes to evaluate patient education (PE) programmes exists. Evaluation of existing outcome measures is recommended (4). A Norwegian expert panel comprising patients and health professionals experienced in patient education (PE) participated in a 3-round Delphi-process. The aim of the process was to obtain consensus about outcome domains that might be influenced by PE for people with inflammatory arthritis (IA). Six domains were identified: Understanding disease and treatment, knowledge about healthy life style, coping strategies, self-efficacy, empowerment and communication with health professionals. Through a systematic literature search and further Delphi-rounds, the expert panel identified four patient-reported outcome measures (PROMs) that might capture these outcome domains.

Objectives: To test the feasibility of four identified PROMs suitable to evaluate patient education programmes.

Methods: Arthritis Self-Efficacy Scales (ASES) for pain and symptoms, Effective Consumer Scale (EC-17), Health Education Questionnaire (heiQ) and Patient Activation Measure (PAM) were tested in 13 PE programmes for people with IA at six rheumatology departments in Norway. The PROMs were divided into two test-sets, set A (ASES, EC-17 and PAM) and set B (ASES and heiQ). Data were collected before, immediately after and 3 months after PE programmes. The instruments were tested for missing values, internal consistency (Cronbach’s α) and ability to detect change. Floor and ceiling effects were considered to be present if more than 15% of the patients achieved the lowest or highest possible score on each item.

Results: 104 patients answered the questionnaires before participation in a PE programme, 63 in group A and 41 in group B, respectively. 96 (92%) answered the questionnaires after intervention and 78 (75%) responded at 3-month follow-up. Missing values were few in all PROMs (range 0–1.7%). Cronbach’s α was acceptable in ASES pain (0.75) and ASES symptoms (0.81), EC-17 (0.91) and PAM (0.78). heiQ comprises eight separate subcategories; seven categories had acceptable Cronbach’s α (0.72–0.86). All PROMs showed statistically significant improvements after the PE programmes. At 3-month follow-up statistically significant changes were found only in EC-17 (p<0.01, SRM 0.4) and in four of eight heiQ subcategories: emotional distress (p=0.01, SRM 0.5), skill and technique acquisition (p=0.02, SRM 0.5) and health service navigation (p=0.02, SRM 0.5). There were ceiling effects in all PROMs at baseline, 10/13 items in PAM, 5/17 in EC-17, 3/11 in ASES and 14/40 in heiQ. No floor effects were detected in any of the PROMs.

Conclusions: Based on this pilot study in patients with IA, EC-17 and three of the heiQ subcategories were the most feasible PROMs in terms of internal consistency and ability to detect change. Although ASES did not exhibit significant changes at 3-month follow-up, it should be considered as an outcome measure, because it is the only instrument to measure self-efficacy.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1706
CROSS-CULTURAL VALIDATION OF THE PORTUGUESE "RHEUMATOID ARTHRITIS IMPACT OF DISEASE" SCORE: CROSS-SECTIONAL STUDY

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Background: The Rheumatoid Arthritis Impact of Disease (RAID) score1 assesses 7 impact domains of interest for people with rheumatoid arthritis (RA). Its use in research and clinical practice has been growing, and it is already translated into over 70 languages2 but the cross-cultural validity of the Portuguese RAID has not been well established.

Objectives: To validate the Portuguese RAID for use in Portugal.

Methods: This was a single centre, cross-sectional validation study involving 2 phases: (i) cognitive debriefing with 38 patients to determine comprehension of the existing2 Portuguese RAID (ii) cross-cultural validation using data from adult patients who were willing and able to complete the Portuguese RAID unaided. Analyses included fit to the Rasch model (implying construct validity, reliability and statistical sufficiency), tests for unidimensionality and invariance across different patient subgroups i.e. age, gender, education background, disease duration, function and culture. To test invariance to culture, the Portugal dataset was compared with datasets from France (n=195) and the UK (n=205).3 RUMM2030 software was used in all analyses.

Results: Phase I led to minor changes in phrasing 3 items to enhance understanding and conceptual equivalence between the original RAID and the Portuguese version. In Phase II, 288 patients were included: mean (SD) age=60 (12) years, 82% females, 76% with disease duration ≥5 years, 30% on biologics.

The Portuguese RAID was shown to have adequate fit to the Rasch model and high internal consistency (Table 1). Unidimensionality and invariance to age, gender, disease duration and function were confirmed (data not shown). The scale was well targeted for patients with different levels of disease impact (Figure 1). Pooling the datasets from Portugal, France and the UK revealed no cultural response bias (Table 1). RAID was then calibrated into logit-based scores to enable parametric analyses and bias-free cross-cultural comparisons if desired (data not shown).

Table 1. Results of Rasch analysis from pooled data

<table>
<thead>
<tr>
<th>Country</th>
<th>N</th>
<th>RAID Fit Residual Person Separation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portugal</td>
<td>288</td>
<td>7</td>
</tr>
<tr>
<td>UK</td>
<td>205</td>
<td>7</td>
</tr>
<tr>
<td>France</td>
<td>195</td>
<td>7</td>
</tr>
<tr>
<td>Pool</td>
<td>688</td>
<td>7</td>
</tr>
</tbody>
</table>

DF: degrees of freedom; *6 items for cross-cultural comparisons (items 2 ‘Function’ and 5 ‘Physical well-being’ combined).

Figure 1. Distribution of items and persons along the same scale (logit score) confirming good targeting of the RAID.

Conclusions: This study confirms the Portuguese RAID as a robust unidimensional tool for use in Portugal. The raw scores of the 7-item RAID can be used with confidence in clinical practice. Conversion charts are available to enable accurate cross-cultural comparisons across Portugal, France and the UK.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2754
evidenced by Spearman correlation coefficients of ≥ .50 were hypothesized between IPAAQ-LF total or its subscales and the armband to conform construct validity (p<.05).

**Results:** IPAAQ-LF total PA (Median [IQR]: 16.71 (5.91–45.15) MET.hrs/day) was associated with Physical Activity Level (r=.434, p<.01), moderate to (very) vigorous PA (MET≥3.6, r=.432, p<.01) and inactive time (MET<1.8, r=.382, p<.05) obtained with the armband. Similar, IPAAQ-LF moderate PA (Median [IQR]: 10.39 (2.41–23.71) MET.hrs/day) was related with PAL (r=.492, p<.01), moderate to (very) vigorous PA (r=.456, p<.01), moderate PA (r=.444, p<.01) and inactive time (r=.491, p<.05). Also, IPAQ-LF sitting (Median [IQR]: 14.91 (10.89–20.80) hrs/day) was correlated to PAL (r=.461, p<.01), moderate to (very) vigorous PA (r=.391, p<.05), moderate PA (r=.386, p<.05) and inactive time (r=.496, p<.01). No relevant nor significant correlations were found for the other IPAAQ-LF subscales. Taken together, no hypothesis could be confirmed.

**Conclusions:** Even at a group level, the convergent construct validity of IPAAQ-LF in axSpA was not confirmed. Self-reported PA outcomes may provide important contextual information on PA, but perform poor at quantifying PA levels in axSpA. Future research on a feasible self-reported PA measurement tool for these patients is required.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6932
# PAIN SPREAD AND PAIN INTENSITY IMPROVE OVER 1, 2, 3, OR 4 YEARS FOLLOWUP IN WOMEN WITH FIBROMYALgia AND CHRONIC WIDESPREAD PAIN. A 12 YEAR FOLLOWUP STUDY

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**Background:** In the Western world, the prevalence of chronic widespread pain (CWP) is about 10–15% while Fibromyalgia (FM) affects approximately 1–3% of the population. The ACR 1990 criteria define CWP as pain >3 months on the right and left side of the body, above and below the waist and axial skeletal pain. The 1990 criteria for FM are CWP in combination with pain in >11 of 18 tender points on manual palpation. Previous studies indicate that some patients with FM or CWP improve over time and the key to improvement is an important question in research and clinical practice.

**Objectives:** The primary objective was to investigate the change of pain intensity and pain distribution after 12 years in 166 women with FM or CWP. The secondary objective was to compare baseline values of health related variables between patients who fulfilled the criteria for FM/CWP at the 12 year follow-up and patients who did not.

**Methods:** In 2004, 166 women with FM or CWP participated in a randomized controlled trial in Sweden aiming to investigate effects of patient education and pool exercise. All 166 were invited to the present study in 2016 and 2012 women (75%) participated. Data was collected by a standardized interview, questionnaires of health related aspects and a physical examination. Primary, within-group changes were calculated for pain distribution (Bergman’s pain drawing 0–18) and the subscale for pain intensity (0–100 mm) included in the Fibromyalgia Impact Questionnaire (FIQ). Secondary, the group who fulfilled criteria for FM or CWP at follow-up were compared with the group who did not fulfill the criteria for FM or CWP, in overall health status (FMQ total), symptoms of stress (Stress and Crisis Inventory – SCI-93), walking capacity (6 min walk test), hand grip force (the Grippit) and self-reported physical activity (Leisure time physical activity instrument).

**Results:** Primary: The 126 women with FM or CWP improved in pain distribution: mean values at baseline 12.9 (SD 3.4) vs follow-up 11.4 (SD 4.7), p < 0.001 and pain intensity: mean values at baseline 69 (SD 18.5) vs follow-up 59 (SD 22), p < 0.001. Secondary: 18% (n=23) of the 126 women did not fulfill the 1990 criteria for FM or CWP at follow-up, and they showed significantly better health status, lower symptoms of stress and higher walking capacity in 2004, than the women who still had FM or CWP at follow-up. Baseline mean values FM/CWP (n=123) vs Not FM/CWP (n=23): FIQ total 66 (SD 16) vs 55 (SD 15), p = 0.006; SCI-93 80 (SD 23) vs 59 (SD 22), p < 0.001; 6 min walk test 502 m (SD 86) vs 542 m (SD 80), p = 0.028. No significant differences were found between the groups for baseline values of hand grip force and level of physical activity.

**Conclusions:** This study showed that distribution and severity of pain improved during 12 years in women with FM or CWP. The group that improved most (18%), reported better health status, lower stress and had better walking capacity 12 years earlier. This knowledge is important for health care professionals to motivate the patients to apply a variety of strategies, including physical activity, to improve their health and symptoms.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1257

# IMPACT OF CORTICOSTEROID UTILIZATION ON BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG INITIATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Treatment guidelines recommend low dose corticosteroids (steroids) as an effective short-term (<3 months) therapy among rheumatoid arthritis (RA) patients to “bridge” patients until benefits of disease modifying anti-rheumatic drugs (DMARDs) are observed and in flare management. 1,2 Physici-

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.1322

# POTENTIAL BENEFITS OF BIOLOGICS ON CARDIOVASCULAR DISEASES AND ORTHOPEDEIC SURGERIES IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONALWIDE POPULATION-BASED COHORT STUDY IN TAIWAN


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**Background:** Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder, precipitating chronic inflammation of the joints, and also affects organs throughout the body, and even results in joint deterioration/disability. RA-related inflammation that is responsible for synovial lesions may be implicated in

**Disclosure of Interest:** Shareholder of: AbbVie, Employee of: AbbVie, C. Kaplan Grant/research support from: AbbVie, J. Griffith Shareholder of: AbbVie, Employee of: AbbVie, C. Kaplan Grant/research support from: AbbVie, A. Ganguli Shareholder of: AbbVie, Employee of: AbbVie, J. Wang Grant/research support from: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.1257
the development of accelerated atherosclerosis, leading to increased risk of cardiovascular disease (CVD), and increased mortality.

Objectives: This study aimed at examining changes in the risk of death, CVD and RA-related orthopedic surgeries between the patients treated with conventional synthetic and biologic disease modifying antirheumatic drugs (csDMARD and bDMARD) for RA during 1997–2011.

Methods: Two cohorts of severe RA patients and their matched controls were identified from National Health Insurance claims database. The csDMARD cohort was patients who had medication claim for cyclosporine >50 mg/day with concomitant use of >2 csDMARDs for >28 days within 56 days after cyclosporine use during 1997–2003 (N=1,569). After csDMARD cohort was determined, the bDMARD cohort was selected if patients had >1 claim for bDMARD during 2003–2011 (N=1,530). Adjusted hazard ratios (aHRs) for the risk of death, myocardial infarction (MI), stroke, and RA-related orthopedic surgeries were assessed between the two primary joint involvement and their controls, respectively, using Kaplan-Meier survival curves and Cox proportional hazards models.

Results: RA patients using bDMARD showed a markedly decreased risk of death (aHR=1.05; 95% CI=0.84–1.33) compared with RA patients using csDMARD (aHR=0.87; CI=0.74–1.03). Also, bDMARD was associated with a reduced risk of stroke (aHR=0.37; CI=0.22–0.62) compared with csDMARD (aHR=0.73; CI=0.51–1.05). For RA-related orthopedic surgeries, risks were slightly lower for bDMARD (aHR=0.41; CI=0.32–0.52) compared with csDMARD (aHR=0.57; CI=0.48–0.69).

Conclusions: The introduction of biologics in the treatment of RA has shown to have beneficial effects on improving clinical outcomes, including decreased risks of death, stroke and RA-related orthopedic surgeries.


Disclosure of Interest: None declared.

FRIO758-HPR EVALUATION OF MUSCULOSKELETAL COMPLAINTS ASSOCIATED WITH SMARTPHONE USE AMONG UNIVERSITY STUDENTS AND RELATED RISK FACTORS

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Background: Smartphone use for long periods in a static and unsupported arm position could bring about abnormal alignment of upper limb and could cause postural problems and musculoskeletal pain. There are very few studies in the literature that examine the effect of smartphone use on musculoskeletal problems and related factors.

Objectives: The primary aim of our study was to determine the musculoskeletal complaint associated with smartphone use among university students. Other purpose of the study was to investigate the relationships with smartphone type, smartphone use frequency, smartphone use posture, smartphone use addiction level and psychological characteristics. 

Methods: 349 university students (240 women, 109 men; mean age 20.79±1.35) were included to our study. We conducted a survey that contains questions about students’ smartphone usage patterns and habits. Nordic musculoskeletal Questionnaire was used to determine the musculoskeletal complaint associated with smartphone use. Working posture while using smartphone were evaluated with Rapid Upper Limb Assessment (RULA). Smartphone addiction level were determined with Smartphone Addiction Scale (SAS). Also we used the Beck Depression Inventory (BDI) to determine the psychological distress. Pearson correlation analysis was used to evaluate the associations between parameters.

Results: Our results showed that university students had a high frequency of smartphone use and that the frequency was related to the level of addiction (r=0.199 p=0.00). %43 of students were use their smartphones extremely more than 12 hours a day and they use smartphones often for messageing with smartphone applications (%66.5). The most frequent symptoms were found in the neck (%59.6), shoulder (%51.82) and upper back (%54.4) regions. Statistically significant relationship was found between daily frequency of smartphone use and RULA neck posture score (r=0.170, p=0.001). Also there were statistically significant relationships found between BDI score and upper limb (r=0.135, p=0.005) and upper back (r=0.152, p=0.004) postures while using smartphone.

Conclusions: Smartphone users complain at least one area (neck, upper extremity, upper back). The frequency of smartphone use and addiction level is associated with abnormal postures while using smartphones which associated with psychological distress. Consequently, musculoskeletal rehabilitation programs should include an analysis of preventive strategies which should be multifactorial with the team work of all health professionals.

References:
Steroid was used by 39.2% of patients with diabetes and hypertension. Cardiovascular events (ischemic heart disease and ischemic stroke) occurred in 2.2% of patients and 45.5% of patients with cardiovascular events were receiving concomitant steroid. Infections requiring hospital visit were recorded in 1.8% of patients; 77.8% of patients with infection were on biologic DMARD and 33.3% were receiving concomitant steroid. Out of Two hundred seventy six patients who underwent DXA scanning for estimation of bone mineral density, 48.6% were having decrease bone density (37% osteopenia, 11.6% osteoporosis).

Steroid use was significantly associated with decrease bone density.

Conclusions: Comorbid conditions are frequently associated with Rheumatoid arthritis as observed in our cohort of patients. Patient care should not be focused only on arthritis care. All RA patients should be screened for comorbidities and treated accordingly in order to avoid their deleterious effect on patient health.

Disclosure of Interest: None declared

FRI0759-HPR COLLABORATION BETWEEN GENERAL PRACTITIONERS AND RHEUMATOLOGISTS TO MANAGE CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS PATIENTS

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Background: To reduce the risk of cardiovascular disease in rheumatoid arthritis (RA) patients, adequate cardiovascular risk management (CVRM) is necessary. CVRM implies assessment, treatment and monitoring of cardiovascular risk factors1. The updated EULAR guideline states that cardiovascular risk assessment should be considered at least once every five years in all patients with RA. A few studies show suboptimal risk management in daily practice in selected groups of patients.

Objectives: This study aims to describe current performance of the CVRM recommendation in a hospital based RA population in the South of the Netherlands. In this region, general practitioners (GPs) and rheumatologists closely collaborate into manage RA patients’ cardiovascular risk.

Methods: Due to the collaboration, CVRM is performed as a part of a transmural care program. The rheumatologist informs the GP when a patient has been diagnosed with RA. The patient is placed on a list for CVRM to be screened by a specialised nurse practitioner. As a part of the collaboration, laboratory results requested by the GPs and rheumatologists are collected in one digital patient record system. This system is used to check whether the RA patient’s lipid profile was determined in the previous five years. If not, a letter with the listed patient is sent to the GP a reminder for screening the patient. In this study, we checked six months later whether lipid testing was ultimately performed.

Results: In 70% (n=475) of all 679 RA patients (mean age 63 (SD 9 years), 68% women and median disease duration of 7 years (IQR 3–11)) a lipid profile was determined in the previous five years.

Of the 204 non-screened RA patients, 98 had been screened after sending the letter to their GP (+48%), see Figure 1. No differences in gender and disease duration were found between the screened and non-screened patients (p=0.46 and p=0.25 respectively). By contrast screened patients were 10 years older compared to the non-screened patients (66 year (SD12) vs 56 (SD 15) year; p=0.0001).

Conclusions: As a result of the collaboration between GPs and rheumatologists, 70% of all RA patients were screened for CVRM. A small intervention, sending a reminding letter to the GP, increased this percentage even further, to 84%. This collaboration can be seen as a good practice to provide care in line with the EULAR guideline.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2423

FRI0760-HPR BIOSIMILAR USE AMONG EUROPEAN RHEUMATOID ARTHRITIS PATIENTS AND IMPACT ON PATIENT OUTCOMES

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Background: Biologic agents have been shown to help control disease progression in rheumatoid arthritis (RA) and significant reduce joint damage. However, their considerable cost has limited their widespread use.

Objectives: Biosimilars offers the opportunity for significant cost savings for national health services and the aim of this research is to better understand their use among European rheumatologists and their potential impact on patient outcomes.

Methods: We used data collected as part of an online treatment survey conducted among a panel of 261 rheumatologists between January and December 2016 across 5 European markets (France, Germany, Italy, Spain and the UK). Physicians were sampled to provide a representative mix of practice types and regions. Our record form sample included 9,650 patient currently treated with a bDMARD, 297 of which received a biosimilar. We split the sample into 2 groups, biosimilar patients = those treated with Benevapi (etanercept), Remsima (infliximab), Inflectra (infliximab) and Flixbax (infliximab) and originator patients = those treated with Enbrel (etanercept) or Remicade (infliximab). We analysed patient demographic data along with current DAS, joint count, HAQ score and perceived disease severity to assess response to therapy over time.

Results: A total of 2.4% of our logistic sample with the greatest uptake of these agents reported in the UK (3.8%) and the lowest in France (1.6%). Use of biosimilars increased in patients who started their current biologic in 2016 (8.1%), with a marginally higher use seen in patients on their 2nd or higher line of bDMARD therapy vs. those on their 1st bDMARD (8.4% vs. 7.5%, respectively).

We saw no significant difference in the distribution of biosimilar and originator patients by age and gender although biosimilar patients appeared to have more severe disease. While a smaller proportion of biosimilar patients were perceived to have moderate/severe RA at diagnosis (73.1% vs. 88.4%) a greater proportion were thought to have moderate/severe disease at their latest visit (64.3% vs. 44.2%). The average DAS28 of biosimilar patients was higher at a directional level but their average HAQ score and tender/swollen joint count were non-significantly lower. Biosimilar patients were more likely to suffer from a comorbid condition (87.2% vs. 74.1%) and a autoimmune condition beyond their RA (17.2% vs. 11.6%). There were no significant differences in the proportion of patients unable to work due to their disease (4.3% on average from the total sample).

We analysed the data focusing solely on 1st line patients to reduce any bias introduced by previous lines of therapy but observed similar trends. A higher proportion of biosimilar patients were considered to have moderate to severe RA at their latest visit (67.9% vs. 43.0%) and a greater proportion of patients had a DAS28 ≥5.1 (23.3% vs.3.0%).

Conclusions: Our research suggests that biosimilar uptake remains limited amongst European rheumatologists with a directional trend towards 2nd line use. Our data did not clearly show any significant differences in the profile of biosimilar patient’s or outcomes. Increased governance from healthcare regulators and additional clinical data may be needed to further establish the efficacy and safety of these agents and drive their wider use, ensuring greater cost efficiency and the potential for wider access to biologic therapies for RA patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6598

FRI0761-HPR CHRONIC WIDESPREAD PAIN PREVALENCE IN THE GENERAL POPULATION: A SYSTEMATIC REVIEW & META-ANALYSIS

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Background: Chronic widespread pain (CWP) is a worldwide health problem and a significant contributor to disability. Understanding the impact of individual-dependent (e.g., gender) and contextual-dependent (e.g., survey method, latitude) factors have on CWP prevalence may provide a foundation population-based strategy for addressing CWP.

Objectives: To determine a general population worldwide estimate of CWP prevalence and to examine the individual and contextual-dependent factors related to CWP prevalence.

Methods: A systematic review was undertaken using seven databases. Along with data extracted from the manuscripts, additional contextual data including WHO development status and region, human development index (HDI); measure

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6598
of socioeconomic position), Gini coefficient (measure of inequality), and latitude were added. Methodological reporting quality was assessed using meta-
regression analyses.

Results: Thirty studies across 20 countries (630,654 participants) met the inclusion criteria. Studies varied in CWP diagnostic criteria, survey method, and reporting quality. Study CWP sample prevalence ranged from 1·4–24·0%, with CWP in men ranging from 1·1–15·3%, while in women it ranged from 1·7–22·1%. Estimated overall CWP prevalence was 9·4% (7·6–11·3%). By gender, the global CWP prevalence estimate in women was significantly higher than for men (10·9% [8·1–13·7%] v 6·7% [4·5–8·8%], p<0·01; Table 1). A meta-regression of the contextual factors showed the HDI was related to CWP prevalence (p=0·002), while other measures such as survey type, methodological reporting quality and Country induced showed no significant effect.

Conclusions: Globally CWP affects one in ten individuals within the general population, with women more likely to experience CWP than men. HDI was noted to be the socioeconomic factor related to CWP prevalence, with those in more developed countries having a lower CWP prevalence than those in less developed countries. There was a lack of data from countries with a lower socioeconomic position, and further CWP data in these areas can help determine if there are socioeconomic effects associated with CWP prevalence and can refine the CWP prevalence estimate.

References:

Acknowledgements: The author also wants to thanks, Mr Himanshu Negi (Data Entry help).

Disclosure of Interest: S. Baghel: None declared, R. Rawat: None declared, R. Thakran: None declared, C. Messi: None declared, S. Kapoor Consultant for: Advisory board of Novartis,Pfizer, S. Garg Consultant for: Advisory board of Intas, V. Kashyap: None declared, Q. Zaheer: None declared, A. Malaviya Consultant for: Advisory board of IPCA, Janssen, Pfizer, Roche, BMS,Dr. Reddy’s, Zydus

DOI: 10.1136/annrheumdis-2017-eular.2089
Conclusions: Despite treatment, patients with PSS still experience a high disease burden. Here we have provided novel insights into the higher treatment cost and increased healthcare utilisation burden of PSS compared with the sicca-free cohort, in particular for patients with extra-glandular disease manifestations.

Acknowledgements: Funded by GSK. Jennie Frain, PhD, Fishawack Indica Ltd, UK, provided medical assistance funded by GSK


FR10764-HPR MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND END STAGE RENAL DISEASE

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Background: Cardiovascular related mortality is higher in patients with rheumatoid arthritis (RA) compared to the general population, and accounts for more than half of all deaths in end stage renal disease (ESRD). The prevalence of ESRD is increasing and there are an increasing number of older patients with RA. Our recent study demonstrated approximately 1% of patients with ESRD have RA. The implications of ESRD on RA relative to the burdens of cardiovascular diseases, cardiovascular and all-cause mortality are not known.

Objectives: To determine whether patients with RA who have ESRD are at increased risk for cardiovascular disease (CVD) events, cardiovascular mortality and all-cause mortality compared to the general population of patients with ESRD.

Methods: Retrospective cohort study of adult patients (age 18 and older) with ESRD receiving renal replacement therapy (hemodialysis or peritoneal dialysis) in the United States Renal Data System (USRDS) who initiated dialysis between 2003 and 2008 looked for up to five years. Patients with an ICD-9 diagnostic code for RA on or before the start of dialysis and a 5% random sample of those without RA were included. Incident cardiovascular events, cardiovascular related mortality and all-cause mortality was determined in those with RA compared to those without RA.

Results: There were 2,824 subjects including 407 with RA and 2,417 without RA included in the analyses. There was no significant difference in the total number of incident CVD events by RA status (n=311 (76.4%) vs. n=1936 (80.1%) without RA) (p=0.09). 76 patients with RA (18.7%) died from a CVD related cause compared to 403 without RA (16.7%) (p=0.32). Overall mortality was significantly higher in those with RA (n=226 (55.5%)) vs. n=970 (40.1%) (p<0.01). Compared to those without RA, those with RA had a significantly shorter mean time in months from start of dialysis to any incident CVD event (17.5 (12.4) vs. 21.2 (14.1) (p<0.01), CVD death, (34.2 (12.5) vs.37.9 (12.6) p=0.02), or all-cause mortality (33.1 (13.0) vs. 37.8 (12.6) (p=0.01). In final adjusted models, RA was associated with an increased risk for both CVD related mortality (aHR=1.23 (95% CI 1.05–1.43)) and all-cause mortality (aHR=1.22 (1.05 – 1.42) within five years. Risk factors for CVD and overall mortality included older age, a higher Charlson comorbidity index, black race, needing assistance with ADLs and living in a nursing home. Black race and Hispanic ethnicity was associated with significantly less CVD and all cause-related mortality.

Conclusions: Physicians treating patients with RA and ESRD should be aware that patients with RA are at increased risk for cardiovascular related mortality and all-cause mortality compared with the general population of ESRD patients. Patients with ESRD and RA at higher risk for mortality can be identified by both demographic risk factors as well as overall health status.

Acknowledgements: Funding for this work was supported by the Translational Research Program (TRP) at the Medical College of Georgia and the Medical and Graduate Student Preceptorship award from the Rheumatology Research Foundation, Atlanta, Georgia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1152

FR10765-HPR PREVALENCE OF SARCOPENIA IN ELDERLY WITH OSTEARTHRITIS OF LARGE JOINTS

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Background: Lean muscle mass and strength decline starting approximately at 40 years of age to become 25% of body weight at 75–80 years old [1]. Within the existing literature, sarcopenia is a highly prevalent condition in older people. The prevalence of sarcopenia increases considerably with age ranging from 5% to 15% in persons aged 60–70 years and 11% to 50% in persons aged 80 years and older. In older persons, sarcopenia is related to falls and physical disability leading to reduced quality of life [2]. The prevalence of osteoarthritis increases with age so that 30 to 50% of adults over the age of 65 years suffer from this condition [3]. Age-related factor that contributes includes to the development of OA include a decline in muscle strength. People with lower extremity OA had a two to five times increased incidence of falls than age-matched healthy controls [4].

Objectives: Conduct analysis of condition of muscle strength and muscle functioning in older persons with osteoarthritis.

Methods: Prospective study of 159 patients aged 74±13.3 years was held. Controls, normal 11% to 50% to LBM in accordance with criteria of sarcopenia EWGSP. Muscle strength was estimated by a hand dynamometer and muscle functioning was estimated on the basis of SPPB tests. Amount of pain was estimated by VAS.

Results: Sarcopenia was revealed in 31,45% of older persons with osteoarthritis. Cases of OA were observed in 28.30% (95% CI 21.5 - 36.0) in patients with osteoarthritis with sarcopenia (average number of falls – 1,93) and in 16,98% of patients without sarcopenia (95% CI 11.5 – 23.7) (average number of falls – 0.48). Level of pain in patients with osteoarthritis with sarcopenia amounted 3.16 times higher in patients without sarcopenia – 3.49 points (p<0.05). Muscle strength in patients with sarcopenia was 14.36 kg, in patients without sarcopenia was significantly higher – 18.53 kg (p<0.05). Common point of SPPB tests in patients with sarcopenia was 6.9, in patients without sarcopenia significantly higher – 7.85 (p<0.05).

Conclusions: Patients with sarcopenia in the presence of osteoarthritis were observed to have significant decrease of muscle strength and muscle functioning, increase of frequency of falls which raises risk of repeated falls and their frequency, and consequently, deteriorates condition of musculoskeletal system in older persons.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3097

FR10766-HPR DOWNS ARTHROPATHY - CLINICAL AND RADIOLOGICAL FEATURES OF ARTHRITIS IN CHILDREN WITH TRISOMY 21

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Background: Down’s Arthropathy (DA) was first reported in the literature in 1984. Crudie estimates suggest higher incidence and prevalence rates of DA compared with Juvenile Idiopathic Arthritis (JIA), (JIA prevalence 1/1000, estimated DA prevalence 8.7/1000). Despite this fact, there remains a paucity of data on this condition. DA is rarely recognised at onset, & remains under-diagnosed. As a direct consequence children with DA are presenting with significant joint damage and disability at diagnosis.

Objectives: Perform a musculoskeletal examination on children with Trisomy 21 (T21) aged 0–20 years

Methods: Children with T21 were invited to attend a screening clinic. Screening involved completion of a health questionnaire & a comprehensive musculoskeletal examination. DA cases detected were investigated & managed as per normal clinical practice. Data on a convenience sample of 33 newly diagnosed children with JIA was collected to create a comparison group.

Results: 503 children with Trisomy 21 were included for DA, 22 new cases have been diagnosed. All of these children had poor language skills or were non-verbal. Only 11% of the parents suspected that their child may have arthritis prior to attending our screening clinics, and this was only after reading our recruitment literature. In total, we now have 33 children attending our centre with DA (combining cases attending pre-dating the start date of the study). This suggests the prevalence of DA in Ireland is 18–21/1000.

The majority of children presented with a polyarticular pattern of disease. No cases of uveitis have been observed to date. 88% of the DA cohort had small joint involvement of the hands, significantly higher than that observed in the JIA comparison group. Erosive changes were reported on X-Ray in 29.2% of the DA cohort (9.5% in the JIA Cohort). Methotrexate-associated nausea was a significant barrier to treatment with this DMARD in DA. There was a significant delay in diagnosis of DA, 1.7 years v 0.7 years in the JIA cohort.

Conclusions: Children with T21 are at increased risk of developing arthritis. There is a lack of awareness of this risk among health care professionals & the general public at large. This almost certainly contributes to poor recognition of the disease and a delay in diagnosis. The predominant pattern of disease is polyarticular small joint arthritis. Treatment with standard protocols used in JIA
is complicated by drug-associated side effects in children with T21. However, a good response to treatment with steroid intra-articular joint injections has been observed. Our study has raised a number of questions. Future research to accurately define this disease & identify best practice with regards to treatment would be invaluable. We advocate that all children with T21 should have annual musculoskeletal examination as part of their health surveillance programme.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7020

FR0767-HPR

PARTICIPATING IN A MUSCULOSKELETAL RANDOMISED CONTROLLED TRIAL: IDENTIFICATION OF EDUCATION TRAINING NEEDS BY OCCUPATIONAL THERAPISTS AND PHYSIOTHERAPISTS IN THE UK

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Background: There is an association between clinical teams engaging with research and impacts in the delivery of health services. Randomised controlled trials (RCTs) provide strong evidence to influence practice in musculoskeletal services. For occupational therapists (OTs) and physiotherapists (PTs) implementing RCTs is not yet commonplace. As part of a multi-centred clinical effectiveness and efficacy RCT of splints for thumb base osteoarthritis (OTTER II Trial) we established an education training programme to support clinical therapists deliver the trial across 15 UK hospitals.

Objectives: To evaluate the content of trial training to educate and support OTTER II Trial clinicians in undertaking clinical research roles.

Methods: Two trial training days were run in the North and South of England. Therapists provided details of their clinical trial experience. They were asked to identify one area in which they felt confident and one in which they were not confident in participating in a RCT. These perceived facilitators and barriers were summarised using descriptive statistics and content analysis.

Results: Thirty five clinicians (20 OTs,15 PTs) attended a training day, 13 (37%) had no previous experience with clinical trials; 19 (54%) had been involved with at least one previous clinical trial. Clinicians considered they were already confident in; delivering the trial standardised assessment and treatment to patients n=21 (60%); trusting the OTTER II trial team and their own hospital research departments to support their research role n=13 (37%); understanding the trial protocol and what needed to be delivered n=6 (17%) and, being convinced that the trial asked a relevant question 3 (9%). Areas in which clinicians considered they did not have confidence included; the logistics and time management of delivering a RCT in their own hospital n=18 (51%); the associated trial paperwork to be completed n=8 (23%); NHS computer access/win access for randomisation procedure n=7 (20%); recruiting participants to time and target n=6 (17%) and staff capacity to deliver a RCT in the NHS alongside clinical commitments n=5 (14%).

Conclusions: Well documented trial protocols and support from a trusted research team and local hospital research departments were identified as key areas that help clinicians become confident to engage with a national clinical RCT. Clinicians are less confident about managing the practical logistics, staff time and trial paperwork involved in delivering a national RCT. Clinicians identify that they perceive their confidence in clinical assessment and treatment skills that already equip them to recruit and treat patients as part of a national trial. The logistics of delivering a trial requires ongoing negotiation and support from clinical service managers and the clinical trial teams to ensure clinicians are supported to deliver the RCT to time and target.

References:

Acknowledgements: The OTTER II Trial is funded by Arthritis Research UK (Grant Ref number 21019).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1095

FR0768-HPR

MUSCLE WASTING IN OSTEOARTHRITIS MODEL INDUCED BY ANTERIOR CRUCIATE LIGAMENT TRANSECTION


Background: Osteoarthritis (OA) is a chronic joint disease characterized by progressive loss of articular cartilage and abnormal bone formation. Furthermore, there are changes in periaricular muscles, such as loss of muscle mass, strength and function. These features may contribute to functional impairment among patients.

Objectives: This study aimed to investigate the molecular pathways involved in muscle wasting in an animal model of OA induced by anterior cruciate ligament (ACL) transection in rats.

Methods: Female Wistar rats were allocated into two groups: OA (submitted to the ACL transection; n=9) and SHAM (submitted to surgical procedures without ACL transection; n=8) [1]. Spontaneous exploratory locomotion, nociception and body weight of animals were evaluated weekly. Twelve weeks after the disease induction, animals were euthanized and the right knee joints were collected for morphometric and histological analyses by histopathology, according to OARSI histologic scoring system [2]. Gastrocnemius muscle from the right hind paw were dissected and weighed. Gastrocnemius was used for evaluation of muscle atrophy [3] and protein expression of myostatin, MuRF-1, MyoD and myogenin. Data were compared by Student’s t test or ANOVA followed by Tukey’s test or ANOVA following Bonferroni–Winer’s U-test. The results are expressed as mean values ± standard deviation (SD) for symmetric variables and as medians with interquartile range for asymmetric variables. Significance was accepted at P<0.05.

Results: Histopathology of the right knee joints confirmed the development of the disease in animals from OA group. Gastrocnemius area of animals from OA group had a reduction of about 10% compared to animals from SHAM group. Protein expression of myostatin was increased in OA group, while myogenin expression was decreased. MuRF-1 and MyoD expression was similar in both OA and SHAM groups. Spontaneous exploratory locomotion, nociception, body weight and weight of gastrocnemius showed no difference between OA and SHAM groups.

Conclusions: Gastrocnemius atrophy in OA induced by ACL transection involves increased protein expression of myostatin and decreased protein expression of myogenin. In this model, muscle wasting may be linked to myostatin-induced deficits in satellite-cell differentiation due to decreased expression of myogenin.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4856

FR0769-HPR

EVALUATION OF THE EFFECTIVENESS OF DEEP WATER RUNNING FOR THE TREATMENT OF CHRONIC NONSPECIFIC LOW BACK PAIN

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Background: Low back pain (LBP) is one of the most common musculoskeletal conditions and can lead to disability. Aerobic exercises have recently been suggested as important in the management of pain and physical disability of LBP patients, and there are studies that prove the efficiency of this type of exercise in the treatment of LBP. One proposed modality is Deep Water Running (DWR) which are aquatic conditioning exercises that simulate normal running on soil.


Methods: It was a randomized controlled trial with a duration of 16 weeks with evaluations performed before the intervention and 8 and 16 weeks after the beginning of the training. The population was composed of 60 patients aged over 18 years with diagnosis of chronic nonspecific low back pain. The intervention group performed 3 times a week aerobic exercises in a heated pool. The sessions had duration of 50 minutes and frequency of 3 times a week for 16 weeks and with 70% of the maximum heart rate, with 10 bpm less for the difference in the behavior of HR in aquatic environment. The control group underwent aerobic conditioning by treadmill exercise for 50 minutes, 3 times a week for 16 weeks, and also with 70% of maximal heart rate. Evaluation instruments: Visual analog pain scale (EVA) in cm; Likert Scale of pain improvement and worsening according to the patient and according to the evaluator; Functional capacity through the Roland-Morris questionnaire and 6-minute walk test; SF-36 for general quality of life; And absenteeism and anti-inflammatories used during the study period. Evaluations were performed by an evaluator who was unaware of the patient allocation group.

Results: The two groups were homogeneous regarding most clinical demographic characteristics, in the initial evaluation. The two groups showed statistically significant improvement in the variables Roland Morris, EVA for pain and Time up and go, but no statistically significant differences were found between groups. At the Likert scale, the 6-minute walk test and the amount of anti-inflammatories used during the study, no significant differences were found, the two groups remained unchanged. No adverse events were observed in either group during the exercise program.

Conclusions: Deep water running aerobic exercise is as effective as treadmill running in improving pain and functional capacity in patients with chronic nonspecific low back pain.
A BETTER WAY TO DECREASE KNEE SWELLING IN PATIENTS WITH KNEE OSTEOARTHRITIS: INTERMITTENT PNEUMATIC COMPRESSION – A RANDOMIZED CONTROLLED CLINICAL TRIAL

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Background: One of the most common symptoms of knee OA is swelling. Knee swelling negatively affects knee mechanics and muscle activity in patients with OA. Thus, knee swelling should be eliminated in the early period of rehabilitation. The utility of cold therapy for musculoskeletal injuries has been clearly established (1). It was shown that cold therapy may not be a statistically effective modality in improving range of motion, decreasing knee swelling (2), and improving clinical outcomes in patients with knee OA rather than cold therapy. Intermittent pneumatic compression (IPC), which has been used to treat limb edema, is a common option for patients with lymphedema and venous leg ulcers. Currently, IPC is primarily used in the prevention of deep venous thrombosis. It is also used for venous insufficiency, arterial occlusive disease, prevention of hematoma, etc (3). However, despite its widespread use, the literature on IPC in musculoskeletal injuries is limited. In particular, there is no report on whether IPC, which is known to have positive effects on circulatory problems, affects the knee swelling in OA.

Objectives: In this study, we hypothesized that IPC may have better outcomes on knee swelling. We also investigated whether IPC may contribute to better short-term patient outcomes in patients with knee OA rather than cold therapy.

Methods: This was a randomized, prospective, comparative clinical study. The study included 81 patients aged 18–65, who were admitted to the Cr – Ahşap Balat Hospital. The patients were randomly divided into two groups. One group (n=36) received ultrasound, transcutaneous electrical nerve stimulation, electrical stimulation, exercise, and cold packs. The second group (n=45) received ultrasound, transcutaneous electrical nerve stimulation, electrical stimulation, exercise, and IPC. The primary outcome was pre- and post- treatment follow-up was knee swelling. Secondary outcome measures included range of motion, muscle strength, pain intensity and disability. Results: Intermittent pneumatic compression significantly decreased knee swelling in patients with osteoarthritis (p<0.001). A significant difference between the groups was found in knee swelling in favour of the intermittent pneumatic compression group (p=0.028). We also found significant improvements in range of motion, muscle strength, pain intensity and disability in both groups (p<0.05). No significant differences in any of secondary outcome variables between the groups was found.

Conclusions: The mechanism of our hypothesis was that in opposite of cold therapy which has local effects, IPC may affect circulatory control. In conclusion, IPC may be an effective modality in improving range of motion, muscle strength, pain intensity and disability in patients with knee OA.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5696
SATURDAY, 17 JUNE 2017

HPR patients’ perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0717-HPR

PREGNANCY AND DELIVERY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS

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Background: Inflammatory rheumatic disease do have an influence on pregnancy course and outcome. There is little knowledge about the comparison between two rheumatic diseases.

Objectives: To analyze pregnancy complications, pregnancy outcome and delivery mode in patients with rheumatoid arthritis (RA) and spondyloarthritides (SpA).

Methods: Patients with RA and SpA were compared with those of matched healthy controls (HC) with respect to pregnancy complications, pregnancy outcome and delivery mode. Patients and controls were prospectively followed at the University of Bern.

Results: We analysed 244 pregnancies, of which 96 pregnancies occurred in 86 RA patients. 78 in 70 SpA patients and 70 in healthy women. Pregnancy complications (gestational diabetes, preeclampsia, infection, preterm rupture of membranes) were more frequent in RA patients (11.5%) and in SpA patients (17.9%) than in HC (1.4%).

Pregnancy outcome of 174 pregnancies in RA and SpA patients resulted in 178 live born infants, 6 sets of twins, one stillbirth and one induced fetal demise. The induced fetal demise was performed in a twin pregnancy on a fetus with a congenital anomaly. Congenital anomalies occurred in 6 infants (3 in RA and 3 in SpA patients). All HC had live births. Median birth weight was lower in RA and SpA patients compared to HC (RA: 3100g, SpA: 3245g, HC: 3455g). RA and SpA patients had more often small for gestational age infants (birth weight <10th percentile; RA: 16.2%, SpA: 11.4%, HC: 1.4%) and preterm deliveries (RA: 18.8%, SpA: 11.5%, HC: 1.4%).

With regard to delivery mode, most women had vaginal deliveries (RA: 51.0%, SpA: 57.7%, HC: 72.9%). Birth by caesarean section (elective and emergency) was more frequent in RA and SpA patients than in the healthy controls (RA: 44.8%, SpA: 39.7%, HC: 27.2%). Emergency caesarean sections were indicated in 22.9% of pregnancies among RA patients, in 21.8% of SpA patients and in 14.3% of healthy women.

Conclusions: Pregnancy complications, caesarean section, and adverse child outcomes were more frequent in patients with RA and SpA compared to healthy women. However, no significant differences in pregnancy outcomes were observed between RA and SpA patients indicating comparable risks induced by the autoimmune inflammatory process.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6086

SATURDAY, 17 JUNE 2017

HPR measuring health (development and measurement properties of PROs, tests, devices) –

SAT0718-HPR

INFLUENCE OF PATIENT GLOBAL ASSESSMENT ON THE DISEASE ACTIVITY ASSESSMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A METEOR CROSS-SECTIONAL STUDY

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Background: Disease activity indices (DAI) are used to guide immunosuppressive therapy in rheumatoid arthritis (RA). The inclusion of patient global assessment (PGA) in these indices has been questioned as it conveys mainly disease impact rather than disease activity.

Objectives: To determine the influence of PGA on patient disease states and to determine PGA correlations with inflammatory parameters, disease impact, demographic, clinical and contextual factors.

Methods: The METEOR international database was used, namely data from patients’ first available visit with no missing values on PGA, tender and swollen joint counts (TJC28, SJC28) and C-reactive protein (CRP). Remission rates were compared according to the DAS28CRP4v vs 4v and ACR/EULAR Boolean remission vs near-remission (failing 1 of the 4 criteria) definition. We assessed the correlation of PGA with (predominantly) inflammatory (TJC28, SJC28, CRP) and disease impact (pain and HAQ) factors. We used hierarchical modelling to explain PGA by 4 blocks (B) of independent variables (B1: gender, age, disease duration; B2: biologic DMARD, Gross National Income; B3: pain, HAQ; and B4: TJC28, SJC28, CRP).

Results: Among the 18280 patients analysed, 1930 (10.6%) were in DAS28CRP4v remission, and 2197 (12.0%) in DAS28CRP3v remission. According to the Boolean definition, 1207 (6.6%) patients were in remission. PGA was the main obstacle to Boolean remission: 2090 (79.0%) of the 2645 near-remission patients (Table 1). A considerable proportion of patients with low inflammation perceived high PGA (Figure 1).

PGA correlated better with Pain (r p=.79) and HAQ (r p=.55) than with TJC28 (r p=.45), SJC28 (r p=.36) or CRP (r p=.25).

In the entire dataset, 60.2% of PGA variance was explained by Pain and HAQ, 1.8% by B1 and B2 of covariates and only 1.3% by B4 (TJC28, SJC28, CRP) (Table 2).

In near-remission patients, B4 did not contribute significantly to changes in the model.

Conclusions: Two thirds of patients that achieve TJC28, SJC28, and CRP ≤1 still perceive high PGA despite disease “inflammatory” control. The weight of PGA in DAI could lead to immunosuppressive overtreatment. In these patients, disease impact management, including non-pharmacological treatments delivered by Health Care Professionals, are more likely to be effective.

Disclosure of Interest: R. Ferreira Grant/research support from: MERIT foundation, M. Ndosi: None declared, C. Duarte: None declared, P. Carvalho: None declared, A. Chopra: None declared, K. Salomon-Escoto: None declared, D. Vega: None declared, D. van der Heijde: None declared, P. Machado: None declared, J. da Silva: None declared

DOI: 10.1136/annrheumdis-2017-eular.4895
HPR patients’ perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0719-HPR

"AND SUDDENLY YOU ARE A PERSON AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS!" DIFFERENT PERSPECTIVES OF INDIVIDUALS ON PREDICTIVE TESTING – RESULTS OF AN INTERNATIONAL QUALITATIVE INTERVIEW STUDY


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Background: People at risk of developing rheumatoid arthritis (RA) may be candidates for interventions aimed at preventing RA development [1]. The identification of such ‘at risk’ populations includes testing for genetic and other (e.g. autoantibody) biomarkers. However, little is known about the people’s perspectives on these tests, how they react and cope when identified as being a person ‘at risk’ and what their unmet needs are.

Objectives: To explore the perceptions about RA and predictive testing and to understand the various reactions and coping strategies used when identified as being at risk of developing RA from the perspective of those directly concerned.

Methods: As part of the EuroTEAM project, a qualitative interview study with people who were informed of being at risk of developing RA was conducted. An interview schedule was developed and pilot-tested. Interviews were audio-recorded, transcribed verbatim and analyzed using thematic analysis.

Results: A total of 34 individuals (with rheumatoid factor and/or ACPA positive) already informed of being at risk of developing RA participated in the study, from Austria (n=15), Germany (n=15), and the UK (n=4). In Vienna, people who had been tested within an expanded health exam participated in this study. In Birmingham and Erlangen, people with arthralgia were recruited from the outpatient clinics. Analysis of the interview data revealed five overarching themes related to perceptions in the context of predictive testing. There were differences between the perceptions of arthralgia patients and asymptomatic individuals. People suffering from pain were much more frightened and worried when informed of being at risk of developing RA. As a consequence, they modified their lives in a larger extent and had greater knowledge about RA than those without any symptoms who were rather surprised, kept calm and hardly changed their lifestyle after being tested positive. Almost all participants in this study would appreciate precise predictive tests in the context of RA. However, more than half of them would refuse synovial biopsy (even if this could help quantify risk more accurately) or preventive medication. Recommendations for an improved procedure of predictive testing in the field of RA were given, which could promote uptake of preventive strategies.

Conclusions: Participants showed large differences in views about predictive testing in the context of RA risk and offered specific suggestions that should be incorporated into service design and delivery in the context of future predictive testing programmes. These findings may also be relevant to prediction and prevention in the context of other diseases where multiple genetic risk factors interact with environmental risk factors to drive disease development.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4705

HPR service developments, innovation and economics in healthcare

SAT0720-HPR

LONGITUDINAL ANALYSIS OF RESPONSE, COSTS AND RESOURCE USE OF PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (BDMARDS) IN TAIWAN USING THE NATIONAL HEALTH INSURANCE RESEARCH DATABASE


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Background: Rheumatoid arthritis (RA) is an inflammatory disorder associated with a significant physical and psychological burden. Patients with RA experience a lower quality of life than patients without RA. This study utilizes Taiwan’s National Health Insurance Database (NHIRD) which is a claims-based database recording all interactions with the National Health Insurance (NHI) system.

Objectives: The objective of this study was to use the NHIRD to estimate the percentage of newly treated patients with inadequate response (IR) to biologic disease-modifying antirheumatic drugs (bDMARDS) as well as the costs and resources.

Methods: Data were from the catastrophic illness file within the NHIRD from 1/1/2009 to 12/31/2013. The index period spanned 2010 with a pre-index period consisting of the index date – 365 days, and patient follow-up was index date to 365 days post-index. Patients with a catastrophic illness card for RA were included in the study. Biologically-naive patients were included through the first time showed an IR to their treatment within a year. Patients with any symptoms who were rather surprised, kept calm and worried when informed of being at risk of developing RA. As a consequence, they modified their lives in a larger extent and had greater knowledge about RA than those without any symptoms who were rather surprised, kept calm and hardly changed their lifestyle after being tested positive. Almost all participants in this study would appreciate precise predictive tests in the context of RA. However, more than half of them would refuse synovial biopsy (even if this could help quantify risk more accurately) or preventive medication. Recommendations for an improved procedure of predictive testing in the field of RA were given, which could promote uptake of preventive strategies.

Conclusions: A significant proportion of patients with RA initiating a bDMARD for the first time showed an IR to their treatment within a year. Patients with an IR had increased resource utilization and higher non-medications costs than those with stable disease. This level of IR suggests an unmet need in the RA treatment paradigm.


DOI: 10.1136/annrheumdis-2017-eular.5315

HPR epidemiology and public health (including prevention)

SAT0721-HPR

EXPOSURE TO PASSIVE SMOKING AND RA RISK; RESULTS FROM THE SWEDISH EIRA STUDY

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Background: Smoking has consistently been associated with increased risk of developing rheumatoid arthritis (RA). However, no studies have been performed investigating the effect of exposure to environmental tobacco smoke (i.e. passive smoking) on RA risk.

Objectives: The aim of this study was to estimate the influence of passive smoking on the risk of developing the two major subsets of RA, defined by anti-citrullinated protein antibodies (ACPA) status.
FAMILIAL RISKS OF RHEUMATOID ARTHRITIS: EVIDENCE FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS CASE-CONTROL STUDY

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Objectives: We investigated the association between family history of RA and the risk of anti-citrullinated peptide antibody (ACPA)-positive and ACPA-negative RA in the Malaysian population.

Methods: Data from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) population-based case-control study involving 1,055 early RA cases and 1,055 age, sex and residential area-matched controls were analyzed. Information from interview-reported family history of RA or rheumatic stiff back among first degree relatives was used to estimate the risk of developing ACPA-positive and ACPA-negative RA. The odds ratio (OR) with 95% confidence interval (CI) was calculated.

Results: In this study, 64% of the RA patients were ACPA-positive and 40% of the overall RA carried HLA-DRB1 shared epitope (SE) alleles. Family history of RA was significantly associated with an increased risk of developing RA in the Malaysian population (RA versus controls, 17.0% vs. 7.7%, OR 2.4, 95% CI 1.8–3.2, p < 0.0001). The association between positive family history and risk of RA was unadjusted for the presence of ACPA-positive RA (OR 2.5, 95% CI 1.8–3.3, p < 0.0001) and ACPA-negative RA (OR 2.3, 95% CI 1.6–3.2, p < 0.0001) subsets, respectively. A dramatically increased risk for ACPA-positive RA was seen in individuals who both were having positive family history of RA and carried HLA-DRB1 SE alleles (OR 14.7, 95% CI 7.7–27.8). We also observed a lesser risk magnitude in the ACPA-negative RA patients (OR 5.7, 95% CI 2.7–11.9).

Conclusions: Our data demonstrate that family history of RA remains an important clinical risk factor for RA. In addition, positive family history of RA was associated with an increased risk of developing both the ACPA-positive and ACPA-negative RA in the Malaysian population, suggesting that the two RA subsets are similar in genetic risk factor content and overlap with these diseases.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3389

SAT0724-HPR

1512 Saturday, 17 June 2017

PATIENTS WITH RHEUMATOID ARTHRITIS – A NATIONWIDE CROSS-SECTIONAL STUDY

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Background: There is an increasing focus on how patients with inflammatory arthritis (IA) manage living with arthritis. There are a preponderance of women with RA (70%), thus previous research has overall focused on female patients and their management. Research in other long term conditions suggests men need their own health strategy. It is important to investigate whether there are gender differences in coping strategies and illness acceptance within chronic IA.

Objectives: To explore gender differences in IA as reflected by coping strategies and illness acceptance. Furthermore, to identify factors associated with high degree of illness acceptance.

Methods: The study was conducted as a nationwide cross-sectional study using online survey during 2016. Patients ≥18 with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) were invited to contribute through: The Danish Rheumatism Organization, local arthritis networks, diagnosis networks, and rheumatology departments across the country. The self-report online questionnaire comprised Socio-demographics, Diagnosis, Symptoms (pain, fatigue, global), Medications, Disease Activity, Functional Status, Coping (i.e. confrontation, avoidance and acceptance-resignation) and Illness Acceptance. As recommended by EULAR 2 patients with RA (KJ & LA; male and female, respectively), were included as equal research partners in all phases of the study. Descriptive statistics were applied to explore gender differences, and logistic regression analyses were performed to test for factors associated with illness acceptance.

Results: In total, 664 (85% women) were included in the study; RA 53%, PsA 27% and axSpA 20%. More men (40%) than women (30%) were treated with biological DMARDs (p=0.048). No significant gender differences were found in disease activity, symptoms and functional status. Overall, the total sample had high degree of illness acceptance and no significant difference was found between males and females. Regarding illness coping, women with IA tend to use avoidance as a coping strategy significantly more than men (p=0.015). In the final multivariable regression model, higher education (OR=1.46; 1.02–2.11), longer time diagnosed (OR=1.21 per 1 yr. increase: 1.01–1.05), lower physical function (OR=0.86, 0.76–0.95), better coping with fatigue (OR=1.13; 1.05–1.22), less avoidance (OR=0.93; 0.87–0.99) and acceptance-resignation (OR=0.62; 0.62–0.75) as coping strategies were significantly associated with high degree of illness acceptance.

Conclusions: No significant differences were found in illness acceptance among women and men with IA. However, women tended to use avoidance as a coping strategy more than men. High levels of illness acceptance may be explained by high education, longer disease duration, and better physical function, better coping of fatigue and less use of passive coping strategies.

References:
[1] White A, McKee M, Richardson N, et al. Europe’s men need their own health strategy 1, thus it is important to investigate whether there are gender differences in coping strategies and illness acceptance within chronic IA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5027

SAT0722-HPR

FAMILIAL RISKS OF RHEUMATOID ARTHRITIS: EVIDENCE FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS CASE-CONTROL STUDY

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Objectives: We investigated the association between family history of RA and the risk of anti-citrullinated peptide antibody (ACPA)-positive and ACPA-negative RA in the Malaysian population.

Methods: Data from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) population-based case-control study involving 1,055 early RA cases and 1,055 age, sex and residential area-matched controls were analyzed. Information from interview-reported family history of RA or rheumatic stiff back among first degree relatives was used to estimate the risk of developing ACPA-positive and ACPA-negative RA. The odds ratio (OR) with 95% confidence interval (CI) was calculated.

Results: In this study, 64% of the RA patients were ACPA-positive and 40% of the overall RA carried HLA-DRB1 shared epitope (SE) alleles. Family history of RA was significantly associated with an increased risk of developing RA in the Malaysian population (RA versus controls, 17.0% vs. 7.7%, OR 2.4, 95% CI 1.8–3.2, p < 0.0001). The association between positive family history and risk of RA was unadjusted for the presence of ACPA-positive RA (OR 2.5, 95% CI 1.8–3.3, p < 0.0001) and ACPA-negative RA (OR 2.3, 95% CI 1.6–3.2, p < 0.0001) subsets, respectively. A dramatically increased risk for ACPA-positive RA was seen in individuals who both were having positive family history of RA and carried HLA-DRB1 SE alleles (OR 14.7, 95% CI 7.7–27.8). We also observed a lesser risk magnitude in the ACPA-negative RA patients (OR 5.7, 95% CI 2.7–11.9).

Conclusions: Our data demonstrate that family history of RA remains an important clinical risk factor for RA. In addition, positive family history of RA was associated with an increased risk of developing both the ACPA-positive and ACPA-negative RA in the Malaysian population, suggesting that the two RA subsets are similar in genetic risk factor content and overlap with these diseases.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4714
HPR interventions (educational, physical, social and psychological)  

SAT0725-HPR  
GOTHENBURG NURSE LED TIGHT CONTROL STUDY - GOTTNET: A STUDY COMPARING "CARE AS USUAL" WITH NURSE LED CLINIC, TIGHT CONTROL AND PERSON CENTRED CARE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND WITH MODERATE/HIGH DISEASE ACTIVITY  

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Background: The treatment guidelines of EULAR recommend treatment according to “tight control” (TC), clear treatment goals (Treat-to-Target, T2T) and patient centered care. The treatment guidelines of EULAR recommend treatment according to “tight control” (TC), clear treatment goals (Treat-to-Target, T2T) and patient centered care would result in better outcome compared to care as usual. The treatment guidelines of EULAR recommend treatment according to “tight control” (TC), clear treatment goals (Treat-to-Target, T2T) and patient centered care would result in better outcome compared to care as usual. One way to overcome this could be nurse led clinics of RA patients, which for patients in remission have shown positive effects on patient’s pain, knowledge and self-efficacy. We hypothesized that a nurse-led clinic based on the above principles of TC, T2T and Person-centered care would result in better outcome compared to care as usual.  

Objectives: The aim of the study was to compare the effect of such nurse-led clinic with frequent visits and person-centered care with regular care of patients with established RA and a moderate to high disease activity.  

Methods: This was a randomized, controlled, blinded assessor study that aimed to compare the effect of nurse-led clinic with regular care of patients with the established RA. Inclusion criteria were: duration of RA >2 years, DAS28>3.8, age >85 years, and not having experience with all available csDMARDs and bDMARDs. Patient with any severe current comorbidity were excluded. Intervention Group (IG): intervention included two elements; 1) disease activity control every 6th week, with clear treatment goals (DAS28 >2.6) and escalation of pharmacological therapy according to existing Swedish guidelines, 2) a written person-centered care health plan with shared goal setting and decision making between patient and healthcare provider. Control Group (CG): Patients in the control group followed a protocol of care at baseline, 3 and 6 months and at 1, 2, 5 and 8 years. SOFI consists of 3 parts measuring hand, arm (upper), and leg (lower) function. One hand function is tested by 4 movements: cylinder grip (H1), pen grip (H2), pincer grip (H3) and opposition of the thumb (H4). Arm function is assessed by 3 movements: hand behind the head and the ability to touch the cervical spine processes with fingers (A1), elbow supination (A2) and elbow extension (A3). Leg function is tested by 4 movements: the ability to touch the opposite knee with the heel while sitting (A1), knee extension in supine position (L2), dorsiflexion of the foot standing on a balance board (L3), and the ability to stand on tip toes without shoes (L4). An assessor scores the patient’s ability to perform the different tests on an ordinal scale (0=normal, 1= partly impaired and 2= unable to perform). The range of SOFI scores is 0–44 (best to worst).  

Results: At baseline the mean (SD) SOFI was 7.2 (5.8), and at 1 year follow up the improvement was 2.75 (5.65), p<0.001. From 1 year to 8 year follow up the deterioriation was 1.5 (4.6), p<0.001. When studying hand, upper and lower function separately, the pen grip and the ability to stand on tip toes improves most during the first year. From 1 to 8 year the pincer grip and the ability to stand on tip toes improved with 0.5 (2.4) and 1.1 (2.7) respectively. The ability to touch the opposite knee with the heel while sitting and the ability to stand on tip toes without shoes improved with 1.8 (3.6) and 2.1 (4.3) respectively. The difference in the improvement was not statistically significant. Pre-study power calculation estimated group sizes to 60 patients in each group. Due to difficulties in the recruiting process the study was stopped preterm.  

Conclusions: This controlled trial suggest that a nurse-led clinic for RA patients with moderate/high disease activity may be effective. Although not shown, it likely to be cost-effective and possible to implement in clinical care.  

Disclosure of Interest: None declared  
DOI: 10.1136/annrheumdis-2017-eular.2659
SAT0727-HPR

THE EFFECT OF INSPIRATORY MUSCLE TRAINING ON AEROBIC CAPACITY, PULMONARY FUNCTION AND FUNCTIONAL STATUS IN PATIENTS WITH ANKYLOSING Spondylitis: A RANDOMIZED CONTROLLED STUDY


Background: In ankylosing spondylitis (AS) the chronic inflammatory process mainly affects the axial skeleton with ensuing pain and limitation of thoracic and spinal mobility. Most of the AS patients have the complaint of reduced exercise capacity due to cartilage and meniscus impairment, chest wall restriction, weak respiratory muscle performance, peripheral muscle weakness and deconditioning which have been reported as the hypotheses for reduced exercise capacity.

Objectives: The aim of this study was to evaluate the effects of inspiratory muscle training on exercise capacity, pulmonary function and functional status in patients with AS.

Methods: A total of 32 patients (18 female, 16 male; mean age: 37.3±10.4 years) were included in this study. The patients were randomized as two groups; Group I consisted of 16 patients, received inspiratory muscle training (IMT) in addition to conventional exercise (CE), Group II consisted of 16 patients, received only CE. All assessments were done before and after the training (8 weeks) for every patient. Standard pulmonary function tests were applied for pulmonary volumes. Maximum inspiratory pressure (Pilmax), maximum expiratory pressure (PEmax) were also measured as respiratory muscle strength. Six-minute walk test (6MWT) was used for the assessment of aerobic capacity. For the evaluation of functional status, the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI) were used. CE training program consisted of 20 exercises: motion and flexibility exercises of the cervical, thoracic, and lumbar spine, myofascial stretching of the hamstrings, quadriceps, erector spine muscle, and shoulder muscles. IMT training load was based on 50% of the patient’s sustained maximum inspiratory pressure. The patients started performing ten loaded inspiration with a 60 second rest period between each inspiration for three sets every day. The exercises were performed as home program for five days per week, 40 minutes per session.

Results: After eight weeks follow-up, patients in Group I had a significant increase in Pilmax (p=0.001), PEmax (p=0.05), and 6MWT (p=0.041) compared with Group II (p=0.134, p=0.281, p=0.281 respectively). There were no significant differences of spirometric measurements. Comparison of the groups showed significantly superior results for group I in BASDAI (p=0.049).

Conclusions: Ankylosing spondylitis patients who performed eight weeks of inspiratory muscle training in addition to conventional exercise training, had an increased respiratory muscle strength, a better aerobic capacity, and disease activity than those who performed conventional exercise only. Inspiratory muscle training should be disseminated with these patients due to advantages.

References:

Acknowledgements: Inspiratory muscle training should be disseminated with these patients due to advantages.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6076
are related to poor perception of health but not to pain sensitivity or cerebral processing of pain. Arthritis & Rheumatology Journal 62(11).


Acknowledgements: NIL.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1445

SAT0730-HPR DIFFERENCES IN PERCEPTION OF THE DISEASE CONSTRAINTS BETWEEN THE CHILD AND PARENTS IN JIA

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Background: Studies suggest that the perception of the child and family differ in juvenile idiopathic arthritis. This may pose a problem for the clinician’s assessment (1,2).

Objectives: The aim of this study was to evaluate the differences in perception of the disease constraints between child and parent in JIA.

Methods: 129 children with JIA were included in the study. The main complaint about the illness was requested to be expressed in writing by both the child and the family. Individuals’ expressions and demographic data were recorded. The main complaints were considered nominal. The correlation between the parent’s and child’s expressions were examined. The types of complaints were classified as none, functional, symptomatic, and both functional and symptomatic.

Results: The age range of children ranged from 6 to 21 (mean±SD; 12.86±3.68). When the complaints of the 129 children and the parents were compared, 45.7% were different, 20.2% were partially similar and 34.1% were perfectly similar complaints. When the answers of the 59 children and parents who differ in their complaints were examined, 67.8% of the children expressed a milder disease than their parents (Table 1). While the family mostly concentrated on the symptoms, the children were worried on functional complaints (Table 1).

Table 1. Results of the evaluations

<table>
<thead>
<tr>
<th>Group of complaint - Child</th>
<th>Group of complaint - Parent</th>
</tr>
</thead>
<tbody>
<tr>
<td>None n (%)</td>
<td>None n (%)</td>
</tr>
<tr>
<td>Function n (%)</td>
<td>Function n (%)</td>
</tr>
<tr>
<td>Symptom n (%)</td>
<td>Symptom n (%)</td>
</tr>
<tr>
<td>Function + Symptom n (%)</td>
<td>Function + Symptom n (%)</td>
</tr>
</tbody>
</table>

Conclusions: As a result of this study, there was a difference between parent’s and child’s perception of the disease. While children report functional complaints, parents focus on symptomatic complaints. Exercise approaches should focus on the child’s functional complaints and identify common goals with the family.

Families should be educated about the importance of the complaints that the child expresses.

Acknowledgements: The author declare that they have no conflict of interest.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5749

SAT0732-HPR RESILIENCE AND POSITIVE AFFECT ARE RELATED TO THE EXPERIENCE OF FATIGUE IN PATIENTS WITH A RHEUMATIC DISEASE

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Background: Fatigue is a common symptom in patients with a rheumatic disease. Resilience, the ability to bounce back or recover from stress, has been found to be related to lower fatigue in patients with cancer, traumatic brain injury, cardiac disease and fibromyalgia (see e.g. [1]).

Objectives: To study the relationships of resilience and the resilience related factors positive affect, acceptance and engaged living with fatigue in patients with rheumatic diseases.

Methods: 57 patients with a rheumatic disease (rheumatoid arthritis, 70%; osteoarthritis, 11%; others, 9%) completed an online questionnaire. Fatigue was measured with SF-36 vitality scale, pain with a VAS; Resilience with BRS and resilience related factors with PANAS (positive affect), AAQ-II (Acceptance) and ELS (engaged living). Data were analysed with hierarchical multiple regression analyses.

Results: Resilience, positive affect, acceptance and engaged living were multi-variate significantly related to fatigue ($R^2=0.54$; $P<0.001$). Resilience ($|b|=0.29$; $P<0.05$) and positive affect ($|b|=0.39$; $P<0.01$) were significant individual predictors of lower fatigue in multiple regression analysis. Acceptance and engaged living were not significantly related with fatigue in the multivariate model. The relationship between resilience and fatigue was partially mediated by positive affect. When pain was included in the model the relations of resilience ($|b|=0.27$; $P<0.05$) and positive affect ($|b|=0.34$; $P<0.05$) with fatigue remained significant.

Conclusions: Resilience and positive affect may be predictors of decreased fatigue in rheumatic patients. Further longitudinal studies are needed to examine the causality of these relationships.

Acknowledgements: The author declare that they have no conflict of interest.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4624

SAT0731-HPR SYMPTOMS OF PAIN, FATIGUE AND SELF-EFFICACY IN YOUNG PATIENTS WITH SPONDYLOARTHITIS – A COMPARISON BETWEEN WOMEN AND MEN

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Background: Spondyloarthritis (SpA) often has an early disease onset with inflammatory back pain debuting already in young adulthood. Studies have shown gender differences in disease specific areas but few studies have focused only on the younger subjects. Extended knowledge based on self-reported information can help to better understand the characteristics of these younger women and men with SpA.

Objectives: To study the differences between young women and men with SpA with regard to self-reported pain measures, disease activity, fatigue, self-efficacy and health status.

Methods: A cross-sectional population based cohort of 201 patients age 18–36 years with SpA identified through a health care register by searching for ICD-10 codes for SpA between the years 2003–2007. They all responded to a questionnaire survey in 2009, 29% were diagnosed with ankylosing spondylitis, 39% with psoriatic arthritis, and 32% with undifferentiated spondyloarthritids. The survey included questions concerning pain (NRS 0–10 and a pain mannequin), fatigue (NRS 0–10), self-efficacy (ASES 10–100, low-high), The pain mannequin was used to categorize patients into groups; no chronic pain (NCP), chronic regional pain (CRP) or chronic widespread pain (CWP). Self-reported disease activity (BASDAI), health status (EQ5D, 0–1) were used to describe the group. Characteristic symptoms are reported as mean, standard deviation (SD) and frequencies. T-Test and Chi2 test were used to study gender differences.

Results: The mean age (SD) was 30 (5) years, 60% were women. The group reported disease activity scores (BASDAI) of 3.8 (2.3), health status 0.75 (0.16), and a disease duration of 7.5 (5) years. One third were smokers or former smokers, and 69% reached WHO’s recommended level of health enhancing physical activity. 21% reported CRP, 41% CWP and the remaining 38% reported NCP. More women reported CWP pain than men, (48% vs. 30%, p=0.026). Women also reported worse pain compared to men, (3.9 (2.4) vs. 2.9 (2.1), p=0.001), worse fatigue (5.0 (2.6) vs. 3.9 (2.7), p<0.003), less self-efficacy for pain (53 (20) vs. 59 (21), p=0.040) and also for symptoms (59 (19) vs. 65 (20), p=0.038).

Conclusions: A significant proportion of both women and men reported symptoms consistent with chronic widespread pain already at young age. Women reported in general worse health compared to men, including pain distribution, pain intensity and pain management. This information could be valuable for clinicians in the care of young patients with SpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5749

SAT0733-HPR A QUALITATIVE STUDY ON OBSTACLES AND MOTIVATIONS TO VACCINATIONS IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is characterized by an increased risk of infection, which is further enhanced by the associated treatments like corticosteroid therapy or biologics. To diminish this risk, influenza and...
pneumococcal vaccinations have been recommended prior to initiating treatment with biological agents. The COMEDRA trial, conducted in France, revealed the usefulness of a nurse-led consultation in the management of RA-associated comorbidities. Despite this, however, only 40% of patients were shown to be appropriately vaccinated (1).

Methods: This qualitative study was conducted at the rheumatology department by means of semi-directed nurse-led interviews lasting about 45 minutes, between July and November 2015. Four topics were analyzed: obstacles and motivations to influenza vaccination, obstacles and motivations to pneumococcal vaccination, post-vaccination follow-up, and information sources. The interviews were registered and transcribed within 45 hours post-interview, and were pursued using content analysis. The final data analysis was carried out by the nurse in charge of the interview, then by a second nurse, with the two analyses assembled according to the traditional concept of double reading. Differences between both analyses were thoroughly discussed, with a consensus sought by a third researcher, namely a rheumatologist, as necessary.

Results: Overall, 15 interviews were conducted involving 11 women and 4 men, with a mean age of 63 years (29–83). All patients were suffering from RA and undergoing at least one immunosuppressant therapy. Most (80%) were vaccinated against pneumococcus, but only 33% against influenza, with eight patients declaring having been affected by influenza and one by pneumococcus-related pneumonia.

The obstacles to vaccinations, revealed during the interviews, primarily concerned fears of unwanted effects in relation with the vaccinations, particularly concerning the influenza vaccination. The patients also reported anxieties in relation with the vaccines’ excipients, with overdoses, or with disease reactivation. Moreover, media impact, contradictory information, the fact that vaccinations were not always proposed, and the lack of traceability may also be considered obstacles against vaccinations. Influenza is often considered a benign disease, and the vaccine poorly efficacious. Patients with prior influenza were more motivated towards vaccination. The primary motivation reported by the patients, and especially as to the pneumococcal vaccination, was the protection provided by the vaccine. The perception of frailty and increased infection risk associated with the disease and its treatments were other sources of motivation, and particularly when vaccination was highly recommended by the physicians, and when there had been no public controversy.

Conclusions: The fears and motivations associated with these two vaccinations are not identical. Influenza vaccination appears to be poorer perceived, patients reporting more fears related to it. With respect to pneumococcal vaccination, we only collected a few comments, given that the vaccine is less well known, and thus better accepted.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4994

THE EFFECT OF RHEUMATIC DISEASES ON WORK ABILITY: A STUDY OF SELF-ASSESSMENT OF SF-36 IN PATIENTS WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)


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Background: A variety of rheumatic diseases can significantly affect the patient’s quality of life and work ability. SF-36 is a commonly used tool to assess the quality of life and work ability in patients with chronic disease. In the past, most patients were guided by doctors/nurses to assess SF-36 in a paper form. At present, there is a lack of research on the quality of life in patients with rheumatic disease by using new mobile tools in the real world.

Objectives: To explore the effect to the life ability of rheumatic disease and the potential association between the disease activity and SF-36 in patients with rheumatic diseases (RA) using SSDM.

Methods: SSDM is a new smart disease management mobile tool, which includes physicians’ and patients’ application system. After entering the results of SF-36 assessment by patients, all data can be synchronized automatically to the mobile terminal of authorized rheumatologist. According to the scores of SF-36 (<12.5, 12.5–50 and >.50), the quality of life was divided into three levels: poor, moderate and good.

Results: From June 2016 January 2017, data were extracted online from the mobile terminals of 839 adult patients (284 male and 555 female) in 62 hospitals across China. All patients performed self-assessment of SF-36 for a total of 1,065 times. The mean age was 38.12±13.87 (18 to 81) years and the median disease duration was 20.60 (0 to 573) months. There are 25 kinds of rheumatic diseases involved, including RA (23%), ankylosing spondylitis (AS, 19%), systemic lupus erythematosus (SLE, 13%), osteoarthritis (OA, 11%), Sjogren syndrome (SS, 10%), polyarthralgia/dermatomyositis (PM/DM, 6%), mixed connective tissue disease (MCTD, 6%) and others (12%).

The 8 items of SF-36 index were averaged between 49.07 (General Health perceptions, GH) to 74.12 (Physical Functioning, PF). The overall mean score of patients with different rheumatic diseases was higher than 50. However, there were significant differences in the scores of 5 kinds of rheumatic diseases with average score of 5 items less than 50, including: MCTD, SS, PM/DM, AS and SLE in patients with GH score: 44.24, 44.60, 47.87, 47.93 and 49.16, PM/DM in patients with the Emotional Role functioning (RE): 47.52, Physical Role functioning (RP): 44.68 and AS patients with Reported Health Transition (HT): 49.64, respectively. In RA patients, 39% and 37% of patients reported that their ability to work were affected by disease and mood changes respectively. Bivariate correlation analysis showed that DAS28 was negatively correlated with the two items scores (RP and RE) of SF-36 index in RA patients, p<0.01.

Conclusions: SSDM can be used to assess SF-36 in patients with rheumatic diseases. The Quality of life scores in patients with MCTD, SS, PM/DM, AS, and SLE were more likely to be affected by rheumatic disease. The disease activity (DAS28) of RA patients was negatively correlated with the work ability (RP and RE of SF-36 score).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4990
Background: Fatigue, sleep disturbances and pain, are symptoms of primary Sjögren’s syndrome (PSS). However, current clinical interventions predominantly focus on treating patients’ dryness symptoms. 

Objectives: To explore the experience of fatigue, sleep disturbances and discomfort in people with PSS, to investigate the impact of these symptoms on patients’ daily lives and to develop an intervention strategy to address them.

Methods: Qualitative focus groups with open-ended questions allowed participants to explore ideas together and focus on issues they perceived as being important. PSS patients (n=10) and spouses (n=3) took part in three focus groups divided into six sessions which were facilitated by two clinician researchers using a topic guide. Discussion topics included; the symptoms, strategies used by participants to explore ideas together and focus on issues they perceived as being important.

Results: Patient participants all experienced these symptoms. Symptom severity varied within individuals and flares occurred unpredictably. Fatigue, sleep disturbances and discomfort, all affected patients’ lives and those around them and sometimes felt overwhelming. Discomfort symptoms included oral and ocular dryness, tingling, nausea and difficulties tolerating light and noise. The invisible nature of these features meant patients often struggled to meet others’ expectations, which affected their mood and resulted in social withdrawal. Fatigue was a major barrier to engaging in work, productivity and leisure activities. Sleep disturbances further compounded the fatigue. Patients employed a range of strategies to self-manage their symptoms to varying degrees of success.

Participants expressed a need for tailored support from health care professionals which included information provision, access to peer support and professional support to apply symptom management information. A three stepped model of care was proposed. The model includes different modes of delivering intervention content, including written information, education groups, peer support, digital self-management and one-to-one therapy. Intervention intensity increased with each step in the model.

Conclusions: Symptoms of fatigue, sleep disturbances and discomfort all impact on PSS patients’ daily lives and individualised interventions are needed to support self-management. Care needs to be tailored as different patients require variable levels of support. A stepped model of future symptom management delivery is proposed.


Acknowledgements: This project was funded by Arthritis Research UK (grant 20169) and the United Kingdom Occupational Therapy Research Foundation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1246
with 15 patients with RA who had taken part of the tele-health follow-up. The selection of participants was purposive and participants with different sex, age, disease duration and severity were included. Age ranged from 28 – 77 years and disease duration from 4 – 41 years. The analysis of the interview transcripts was inductive with a constant comparative approach. First, we identified the main themes that could describe the participants’ experiences. Subsequently, we constructed patient types that could explain different perspectives on the tele-health follow-up.

Results: Five themes covered the participants’ experiences with PRO based tele-health follow-up: (A) flexible solution”, “Responsibility”, “Knowledge of RA”, “Communication and involvement” and “Continuity”. Two different types of perspectives were identified: “the keen patient” and “the reluctant patient”, representing opposite perspectives and preferences regarding the core value of and approach to the tele-health follow-up compared to usual out-patient care.

Conclusions: In general, the participants had positive perceptions towards the PRO based tele-health follow-up and saw this as a flexible, time and resource saving solution. Disadvantages were mainly related to the missing face-to-face contact with health professionals. The two types of perspectives, ‘the keen patient’ and ‘the reluctant patient’, contribute to the understanding of patients’ different needs, wishes and abilities to take part in tele-health follow-up. Thus, our findings call for more insight into how tele-health follow-up could be integrated in routine clinical practice with a special attention on how to support ‘the reluctant’ patient’.

References:


Acknowledgements: We are grateful to the participants who shared their experiences. We also thank an international research foundation at Aarhus University Hospital for supporting this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2903

PATINGTS’ PREFERENCES TOWARDS CHARACTERISTICS OF TREATMENT WITH BIOLOGICAL AGENTS DIFFER ACROSS EXPERIENCE WITH THEIR RHEUMATIC DISEASE AND TREATMENT RECEIVED OR PRESCRIBED: RESULTS FROM THE CARA STUDY

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Background: The development of biologic therapies has created a more complex decision-making process to select the treatment option for patients. In order to optimize the decision of the decisions, it is necessary to be informed and aware of the preferences of the interested parties and the influence of their experiences on their preferences for the different treatments.

Objectives: To estimate preferences of relevant treatment characteristics valued by different patient subgroups involved in the management of patients with rheumatic diseases. This abstract focuses on patients’ preferences.

Methods: We involved patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) or psoriatic arthritis (PsA), who according to clinical practice, at the time of data collection had for the first time a prescription of (PsA), we constructed patient types that could explain different perspectives on the rheumatic disease and treatment received or prescribed: RESULTS FROM THE CARA STUDY.

Results: Four categories were revealed: (1) Feelings and thoughts related to significant others, where participants would feel like being someone’s burden, taking away opportunity, and express anxiety about how relationships and activities would function in the future. (2) The importance of physical contact, referring to the problematic and manageable impact RA could have on intimate live, as well as body contact in the form of hugging. (3) Getting the support you want, where participants distinguished getting help they had not asked for, from helping each other out. The first being experienced as a degradation, and the latter as feeling more involved in the activity. (4) Adaption of daily activities, referring to how the person and significant others consciously modified their activities and activity choices when needed.

Conclusions: Significant others can either be a barrier or facilitator for participation in daily activities, for persons with early RA. From a clinical point of view it is important to further involve significant others in the rehabilitation process, in order to enhance participation in daily activities for persons with RA.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2780

PHYSICAL PERFORMANCE AND GAIT SPEED OF FALLER AND NON-FALLER ELDERLY PEOPLE WITH KNEE OSTEOARTHRITIS LIVING IN THE COMMUNITY

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Background: Osteoarthritis (OA) is the most prevalent chronic degenerative joint disease in the elderly population. The main signs and clinical symptoms of this disease are pain, edema, stiffness, and articular instability. OA is considered to be an intrinsic risk factor for the occurrence of falls. Falls constitute one of the major public health concerns. They frequently have a negative impact on the daily activities of elderly people and could lead to an increase of dependence, fear of falls, fractures, immobility and death.

Objectives: The purpose of this study was to compare physical performance and gait speed among older people with knee osteoarthritis with and without a history of falls.
THE EFFECT OF A NEOPRENE KNEE SLEEVES ON KNEE JOINT PROPRIOCEPTION IN PATIENTS WITH TOTAL KNEE PROSTHESIS

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Background: Proprioception has been defined as the perceived sense of knee joint position (joint position sense) and movement (kineesthesia) (1). The sensory input from the joint capsule, muscles, ligaments, skin improve proprioceptive acuity. With total knee arthroplasty (TKA) surgery articular cartilage, meniscuses, articular ligaments are removed. Also articular effusion and hematoma formation increase following surgery. Therefore, proprioceptive acuity decrease after TKA surgery (2). The proprioceptive improvement might prevent patients with TKA from falling down and increase their sense of security during physical activities. The clinical effect of neoprene knee sleeves on knee proprioception has been evaluated by studies in both injured and uninjured populations (3). But there is not any study research on the effect of neoprene knee sleeves on knee proprioception in patients with TKA.

Objectives: The aim of this study was to determine the effect of the neoprene knee sleeves on joint proprioception in patients with TKA.

Methods: Sixty patients (50 female/10 male) with a median age 64.9±8.84 years were included in the study. Knee joint proprioception of all the patients was evaluated with and without a neoprene knee sleeves preoperatively and at discharge. Patients attempted to replicate target angles (in knee joint angle 15°, 30°, 60°) using active knee extension movements in sitting position. The average of the 3 repetitions of active joint repositioning test was recorded as position sense score. The angular displacements from the target angles (in knee joint angle 15°, 30°, 60°) at the end of the active reproduction tests were recorded as position sense deficit scores.

Results: Preoperatively (p<0.001) and after surgery (p<0.001) patients’ proprioceptive acuity measured with neoprene knee sleeves in knee joint angle 15°, 30°, 60°, had a significant improvement. When the proprioceptive acuity measured without neoprene knee sleeves before and after surgery were compared, had a significant decrease in proprioceptive acuity (p<0.001) in early stage after TKA. Multiple logistic regression analysis showed that age (odds ratio=12.5, p=0.011), body mass index (odds ratio=14.5, p=0.030), pain intensity (odds ratio=3.5, p=0.045), range of motion (odds ratio=9.8, p=0.012), and knee swelling (odds ratio=8.4, p<0.001) were independent risk factors for fear of falling among patients with knee OA.

Conclusions: We conclude that age, body mass index, pain intensity, range of motion and knee swelling influence the fear of falling. They are viewed as an important predictor of fear of falling in knee OA. Our results could be used to help select knee OA patients who should be enrolled in fall prevention programmes.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5714

THE USE OF HEALTH ASSESSMENT QUESTIONNAIRE (HAQ) TO GIVE A PICTURE OF PATIENT EVERYDAY LIFE WITH RHEUMATOID ARTHRITIS

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Background: HAQ is used to monitor physical disability in patients with Rheumatoid arthritis (RA). At our department patients are planned to answer HAQ at every visit. The suitability for use in connection with ordinary clinical controls are questioned (1, 2) and furthermore we have the impression that the patients fill in the HAQ questionnaire because the staff wants it, and not because it make sense to the patients themselves.

Objectives: Evaluation of the HAQ from the patient perspective

Methods: A survey where all patients with RA who visited the outpatient clinic over a period of 3 weeks were invited to participate. Patients were asked to fill in a questionnaire to evaluate (20) in the HAQ on a scale from 1 – 10, 1 = no meaning and 10 = most meaningful. Values less or equal to five were evaluated as “no meaning”. Furthermore a literature review was done, afterwards a Critical Appraisal Skills programme (CASP) was performed on publications found

Results: 100 patients were asked to participate, in total 67 questionnaires were returned, twelve patients were excluded because of incomplete answers, twenty-one did not return the questionnaires or did not want to participate. Depending on which of the 20 questions, different fractions of the patients did not find any meaning in the questions: 18.6% (are you able to shampoo and wash your hair?) up to 40.4% (are you able to use the bathtub?)

In the literature (3, 4) we found several themes of importance for everyday life with RA seen from the patients’ perspective. Pain and impaired physical performance is of great significance for patients living with rheumatoid arthritis. It affects patients both physically, mentally and socially, as it may be necessary to cut back on social activities, to ask for help for ordinary everyday chores, changing or dropping work etc. This has implications for the role of the patient in the family. Powerlessness, frustration and uncertainty about the future affect the mood in form of anger and depressive thoughts.
Overall, it affects the patients' self-image and the patients' independence may be lost.

Conclusions: HAQ questionnaire is relevant in the term of defining the areas in everyday life, where the patients have problems. But the questionnaire does not contribute to elucidate the implications for the patient, which probably is the reason why many patients do not find the meaning of the questions. To evaluate the everyday living with and of treatment arthritis embedding the patient values, patient involvement in designing questionnaires is vital.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2153

SA0745-HPR

IMPACT OF AN INTERDISCIPLINARY INTERVENTION ON RA PATIENTS

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Background: Rheumatoid arthritis (RA) impairs patient function and quality of life (QoL) which, in turn, may lead to invalidity and chronicity of pain.1 Even though a variety of effective treatments are available, there is still a significant portion of patients not attaining remission, of whom many continue to report moderate to high pain and fatigue despite low levels of inflammation.1 Interdisciplinary interventions are promising approaches that may complement the medication effect on patient well-being and disease control, however previous studies on the effectiveness of interdisciplinary interventions seem conflicting.

Objectives: The primary objective is to compare the DAS28 response between patients receiving an interdisciplinary intervention (Intervention group) and patients followed under standard rheumatologic practice (Control group). Secondary objectives are to compare patient-reported outcomes such as pain, fatigue, general health, and patient empowerment between the two groups.

Methods: Prospective quasi-experimental, matched cohort (age, gender) study. Adult patients with a diagnosis of RA and DAS28 (CRP)≥2.6 are eligible for the study. The Intervention group (n=28) benefits from interdisciplinary team intervention with the following professionals: rheumatologist, nurse, physiotherapist, social worker, kinesiologist, occupational therapist, and nutritionist. The Control group (n=32) receives a conventional rheumatologist-nurse intervention. Both groups see the rheumatologist approximately three times over 12 months. Interdisciplinary meetings take place in the hospital setting with the patients at Month 0 and Month 12 and without them at Month 6. The following outcome measures are used at each visit to the rheumatologist: patient pain, fatigue (Multidimensional Assessment of Fatigue; MAF), disability (HAQ), quality of life (SF-36), patient empowerment (Patient Activation Measure; PAM13), and patient satisfaction (OSC-F; only in Intervention group at Month 12).

Results: A total of 28 patients were enrolled in the Intervention group and 32 in the Control group without any significant differences in demographics or disease parameters with the exception of disease duration which was significantly higher in the Intervention group (10.9 vs. 5.8 years; p=0.021). Within 6 months of treatment, clinically important and statistically significant (p<0.01) improvements in DAS28 were observed in both groups which were maintained until 12 months. Overall, at 12 months, DAS28 response was comparable between groups (68% vs. 63%; p=0.140). However, when looking at patients with established RA (≥2.6) on AS in ERA patients.120 patients with

Disclosure of Interest: I. Fortin Grant/research support from: grant UCB, H. Sylvain Grant/research support from: Grant UCB, F. Banville Grant/research support from: UCB

SA0747-HPR

TOWARDS MEASUREMENT OF PERSON-CENTERED CARE OUTCOMES IN OUTPATIENT NURSE-LED CLINICS

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Background: Person-centered care (PCC) is increasingly emphasized as a key component of effective illness management and of developing high quality of care. Despite considerable progress of PCC in many areas of care there is currently a need and a need for means to assess PCC practice in outpatient care. In rheumatology, PCC is considered an unmet need and further development and evaluation of this approach to care is thus of high priority.

Objectives: To develop an instrument for measuring person-centered care from the perspective of the person with rheumatoid arthritis (RA) in nurse-led outpatient clinics.

Methods: A conceptual framework of PCC in the outpatient context and focusing on the meeting between the person with RA and the nurse and on the patient as an active care partner was undertaken. Based on this framework, qualitative interviews (1,2) and a literature review, a 35-item questionnaire was proposed and qualitatively tested regarding content validity and construct validity with patients attending RA with a nurse-led outpatient clinic. Two versions of the questionnaire were tested: one using four response categories (0 = Totally disagree; 3 = Completely agree) and one using two response categories (0 = Disagree; 1 = Agree). Content validity was estimated by calculating Content Validity Index of the individual items (I-CVI) and of the overall instrument (S-CVI).

Results: Respondents found the items easy to understand (77%) and relevant (93%). Seventy-three percent of the respondents preferred the questionnaire version with four response categories. This version took a mean (SD) of 5.3 (2.5) minutes to complete. I-CVI values ranged from 0.87 to 1.00 and S-CVI was 0.94. About 80% of the respondents considered some items to be redundant. This resulted in a reduced 24-item draft questionnaire that yield a total score between 0–72.

Conclusions: A preliminary 24-item patient-reported PCC questionnaire was developed. Psychometric testing is needed for validation of this tool before implementation.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6530

SA0748-HPR

CAN ACHIEVING SUSTAINED DAS REMISSION PREVENT PROGRESSION OF SUB-CLINICAL ATHROSCLEROSIS? A PROSPECTIVE COHORT STUDY IN EARLY RHEUMATOID ARTHRITIS (ERA)

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Background: Patients with rheumatoid arthritis (RA) have higher incidence of cardiovascular disease (CVD) and prevalence of arterial stiffness (AS) due to TNFα. Whether inhibition of proinflammatory pathway or suppression of inflammation remains uncertain. While achieving Disease Activity Score in 28joints (DAS) remission was associated with significant benefits in articular disease, its effect on co-morbidities such as CVD risk is uncertain.

Objectives: To investigate the effect of achieving sustained DAS remission on AS.

Methods: This randomized control trial investigates the effect of 2 tight-control interventions: intensified, intensified disease activity suppression anti-TNF. We examined the difference in 2.minimal disease activity [DAS<2.6] vs 2.3 years on AS in ERA patients.120 patients with active disease (DAS>3.2), symptoms onset <2years and bDMARDs naive were recruited and received 1-year treatment.Treatment are adjusted based on the standardized protocol every 3months aiming at either 1 of the 2 targets. AS is measured by branch-ankle plethysmography wave velocity (bPWV) using a dedicated tonometry system (Omron VP-2000).

Results: In the interim analysis, results of 100 patients [male (23.0%); 52.8±13 years] completed 1year follow-up were analyzed. No significant differences between groups in clinical features, DMARD use and bPWV at month12
(M12) was observed yet significant improvement in disease activity was found in both groups. Hence, results from the 2 groups were combined to ascertain if achieving sustained DAS remission can prevent AS progression. The disease activity improved significantly [DAS: 4.8 (4.2-5.6) at baseline (BL) vs 2.38 (1.6-3.0) at M12, p < 0.001]. 57% patients achieved DAS remission at M12 and 36% patients achieved CR at M12 from interventions that focused on coping with pain and fatigue management, as well as those that raise awareness amongst employers.

No significant differences were found in disease activity, cardiovascular risk factors (CRF) and baPWV at BL between groups who can (CA) or cannot achieve (NA) sustained remission. At M12, no significant differences in CRF and baPWV were found between groups. However, the change in baPWV was significantly different between CA and NA group [-65.5 (-147.2, 44.0) cm/s vs 39 (-65.25, 124.75) cm/s, p = 0.005]. The differences remained significant in the change of baPWV [4.4 (-9.67-2.84) vs 2.51 (-4.34-10.28)%, p = 0.006]. In univariate analysis, association of change in baPWV and potential predictors included BL baPWV, blood pressure (systolic & diastolic) and sustained DAS remission was found. By multivariate analysis, achieving sustained DAS remission was an independent predictor for baPWV reduction.

**Table 1 – Changes in baPWV over a period of 12 months in patients who can or cannot achieve sustained DAS remission in 3 consecutive visits**

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>No (n=40)</th>
<th>Yes (n=36)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (n, %)</td>
<td>47 (73.4%)</td>
<td>30 (83.3%)</td>
<td>0.259</td>
</tr>
<tr>
<td>Age (year)</td>
<td>51.6 ± 12.8</td>
<td>54.9 ± 13.2</td>
<td>0.232</td>
</tr>
<tr>
<td>DAS 28</td>
<td>5.01 ± 1.04</td>
<td>4.81 ± 0.92</td>
<td>0.327</td>
</tr>
<tr>
<td>SDI</td>
<td>27.4 (20.02, 41.08)</td>
<td>26.35 (18.95, 33.3)</td>
<td>0.243</td>
</tr>
<tr>
<td>Diabetes (n, %)</td>
<td>5 (7.8%)</td>
<td>3 (8.3%)</td>
<td>0.927</td>
</tr>
</tbody>
</table>

**Mean baPWV (cm/s)**

- Baseline: 1422.5 (1207.5-1518) vs 1478.5 (1286.3-1624), p = 0.166.
- Month 12: 1436 (1264, 1636) vs 1394.3 (1244.5, 1567.3), p = 0.698.
- Changes in PWV (cm/s): 39.65 (42.75, 24.75) vs 65.5 (147.25, 44), p = 0.005.
- Percentage change in PWV: 2.51 (-4.34, 10.28) vs -4.4 (-9.67, 2.84), p = 0.006.

* Adjusted for blood pressure and baPWV

**Conclusions:** Effective suppression of inflammation by achieving sustained DAS remission may prevent progression of AS in ERA patients.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.3367

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**SAT0748-HPR**

**WORKING WITH A MUSCULOSKELETAL DISORDER – A QUANTITATIVE STUDY OF WORKERS’ EXPERIENCES**


**Methods:** Semi-structured interviews conducted with 19 individuals who had attended musculoskeletal assessment clinics in three Irish hospitals within the preceding year with a confirmed diagnosis of non-inflammatory musculoskeletal disorder. Participants were only included if they had been in paid employment continuously for at least six of the previous 12 months. The interviews were audio-recorded and transcribed. Data were analysed using thematic analysis.

**Results:** Participants ranged in age from 21 to 50 years, most were female (n=16). Fifteen participants were continuing to work, while experiencing pain and some functional limitations. Job control emerged as a key factor in continued work participation. Specifically, being able to organise workload and make modifications to work practices enabled participants to maintain an acceptable level of work performance. The value of work, both personal and financial, motivated people to continue to work. While some co-workers and supervisors were considered to be helpful, interviewees were concerned that they could lose their job if they asked for assistance or took time off work. Fatigue had a considerable impact on participation in social activities.

**Conclusions:** While continuing to work was beneficial, negative spillover effects on performance and well-being were commonly reported. Workers with MSD may benefit from interventions that focus on coping with pain and fatigue management, as well as those that raise awareness amongst employers.

**Acknowledgements:** This research is funded by the Health Research Board [RCGPS-2014-2].

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2909

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**SAT0749-HPR**

**THE RELATIONSHIP BETWEEN SPINAL MOBILITY AND STATIC AND DYNAMIC BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

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**Background:** Ankylosing spondylitis (AS) is a major chronic rheumatic disease that predominantly affects axial joints, determining a rigid spine from the occiput to the sacrum. The disease can lead to permanent spinal deformity and postural disorder during the later stages. Changes in axial mobility may lead to impaired postural control, with altered postural control being associated with increased fall risk and low-quality of life. Although correlation with AS has been rarely studied regarding postural control, both dynamic and static.

**Objectives:** The aim was to investigate the relationship between spinal mobility and static and dynamic balance of patients with mild to moderate AS.

**Methods:** The study included 137 (74 male and 63 female) patients with a mean age of 51.9 ± 10.72 (20–78) years who were diagnosed with AS according to the modified New York criteria. Patients were divided into two groups as tragus to the wall distance (TWD) > < 15 cm (Group I = mild AS, n=51) and TWD > > 15 (Group II = moderate AS, n=84). The mean duration of disease in Group I was 17.83±11.3 (1- 50) years and the mean duration of disease in Group II was 20.78±9.67 (2 - 48) years. Spinal mobility measurements (TWD, cervical rotation (CR), modified Schober test (MST), lumbar lateral flexion (LLF), intermeomeral distance (IMM), thoracic expansion (TE) tests) were compared with static and dynamic balance tests in the groups. Static balance was assessed with one-foot standing with eyes open and closed. Dynamic balance was assessed with timed up and go test and Berg balance scale.

**Results:** A statistically significant difference was found between spinal mobility measurements and Berg balance scale scores between the groups. Spinal mobility values of Group II were worse than Group I (p < 0.05). Berg balance scale scores were better in Group I vs Group II (p = 0.026). No statistically significant difference was found between the two groups in terms of static balance and timed up and go (p > 0.05). There was a weak and significant correlation between spinal mobility measurements (CR, MST, LLF, IMM, and TE) and static and dynamic balance in the positive direction (r=0.177-0.284, p < 0.05). There was no significant correlation between TWD and static and dynamic balance (p > 0.05).

**Conclusions:** In patients with AS, as the severity of the disease progresses, spinal mobility and dynamic balance worsen; however, the static balance does not change. These changes in the posture and balance can negatively affect patients’ participation in daily life and increase their risk of falling. For this reason, we think that detailed evaluation of balance, balance training and fall preventing approaches should be included in the rehabilitation programs for the patients with AS.

**References:**


**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.2278

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**SAT0750-HPR**

**“IS THIS REALLY THE WAY WE SHOULD GO?” – PATIENT PERSPECTIVES ON RHEUMATOID ARTHRITIS MANAGEMENT**

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**Background:** Current rheumatoid arthritis (RA) treatment guidelines suggest aggressive management in order to minimize disease activity. To achieve this goal, clinicians will need to engage patients in shared decision making. Currently little is known regarding patient’s preferences and goals for treatment.

**Objectives:** To understand patient perspectives on their goals with regard to RA disease and flare management and the barriers to, and facilitators of achieving those goals.

**Methods:** Participants were interviewed utilizing open-ended questions focused on understanding their goals of managing their disease (both disease flares and remission) and the disease (as well as the barriers and facilitators of achieving those goals. We explored the following: disease impact; disease beliefs and behaviors; medication use; provider relationship and communication; availability of insurance coverage; and community resources. Interviews were recorded and transcribed. Data were categorized using content analysis techniques. Convenience sample of persons living with rheumatologist-diagnosed RA was recruited from rheumatology practices in 4 states to participate in telephone interviews.

**Results:** Twenty-seven participants completed an interview from March-August 2015. Mean age was 63 years; 82% were female and 82% Non-Hispanic White. Participants reported living with RA for an average of 12 years and 44% reported...
that their RA was not well controlled. The most common participant goal was to improve or maintain physical function. Barriers to RA and flare management included: 1) Patient Level- lack of knowledge of how to manage flares and a reluctance to change or use medications, related to concerns about potential side effects, and limited understanding of the potential benefits; 2) Provider Level- inadequate communication between patient and provider, specifically in relation to flare management and; 3) Health System Level- difficulty navigating insurance, handling coverage gaps, affording high medication costs. Facilitators of RA and flare management included: 1) Patient Level- successful use of non-medication approaches to disease management and the willingness to initiate conversation with their provider about changing medications; and; 2) Provider Level- a positive relationship with their provider, including having trust in the provider, easy access to the provider, and positive communication.

Conclusions: We identified patient-, provider and health system-barriers and facilitators experienced by RA patients achieving their treatment goals. A common theme that emerged was inadequate shared decision making between patients and their providers related to patient knowledge, inadequate communication, and mistrust.

Disclosure of Interest: C. Lemay Grant/research support from: Pfizer Inc. K. Mazor Grant/research support from: Pfizer Inc. J. Kremer Shareholder of: Corrona, Grant/research support from: Abbvie, Genentech, Lilly, Novartis, Pfizer, Employee of: Corrona, Speakers bureau: Genentech (non-promotional only), W. B. Nowell: None declared, C. Bingham III Consultant for: Bristol-Myers Squibb, J. Curtis Grant/research support from: Roche, Genentech, UCB, Janssen, Corrona, AbbVie, Pfizer, BMS, Crescendo, AbbVie, Consultant for: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie, E. Ruderman Grant/research support from: Pfizer Inc, Amgen, Consultant for: AbbVie, Amgen, Lilly, Novartis Pharmaceutical Corporation, Pfizer Inc., Janssen Pharmaceutica Product, L.P., L. Harrold Shareholder of: Corrona, Grant/research support from: Pfizer Inc, Consultant for: Roche Pharmaceuticals, Employee of: Corrona
DOI: 10.1136/annrheumdis-2017-eular.3930

SAT0751-HPR
THE RELATIONSHIP BETWEEN ANAEROBIC EXERCISE CAPACITY AND ISOMETRIC LOWER EXTREMITY MUSCLE STRENGTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is a chronic disease that occurs before the age of 16 years. It was shown that anaerobic exercise capacity, which is important for most daily activities in children such as jumping, hopping and climbing was diminished in JIA. Previous studies showed that anaerobic exercise capacity was related to well-being level, functional status, and aerobic exercise capacity in JIA. However, no data is available about the relationship between lower extremity muscle power and anaerobic exercise capacity parameters in children with JIA.

Objectives: To determine the possible relationships between lower extremity muscle strength and anaerobic capacity.

Methods: Forty-six children with JIA (14 F, 32 M), with a mean age of 13.74±2.29 years (min-max: 9–17 years) were included in the study. Isometric lower extremity muscle strength was assessed with a hand-held dynamometer at the end points of knee flexion, knee extension, hip flexion and hip extension movements, which are generated from gross lower extremity muscles and important for anaerobic power. All the muscle testing was performed on the right leg. Anaerobic exercise capacity was measured performing a 30-second Wingate test. Both absolute and per kilogram values for peak power and average power were noted. The relationships between the parameters were determined with Pearson’s correlation coefficient.

Results: All children completed the assessments without any adverse effects. Demographics, average isometric lower extremity muscle strengths and parameters related to the anaerobic exercise capacity testing were shown in Table 1. Moderate to good correlations were determined between isometric muscle strength and anaerobic exercise capacity parameters r <0.001 (Table 2).

Conclusions: The results of the study suggested that lower extremity muscle strength might influence the anaerobic exercise capacity. Exercise regimes including lower extremity strengthening might help improving anaerobic exercise capacity in children with JIA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5697

Table 1. Demographics, isometric lower extremity muscle strength and anaerobic exercise capacity parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13.74±2.29</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.7±11.08</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>36.7±6.14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>20.7±6.32</td>
</tr>
<tr>
<td>Hip Flexion (kg)</td>
<td>16.8±5.47</td>
</tr>
<tr>
<td>Hip Extension (kg)</td>
<td>13.5±4.50</td>
</tr>
<tr>
<td>Knee Flexion (kg)</td>
<td>17.2±5.83</td>
</tr>
<tr>
<td>Knee Extension (kg)</td>
<td>22.0±6.94</td>
</tr>
<tr>
<td>Peak Power (W)</td>
<td>386±6.14</td>
</tr>
<tr>
<td>Peak Power (W/kg)</td>
<td>6.99±2.33</td>
</tr>
<tr>
<td>Average Power (W)</td>
<td>287.69±129.53</td>
</tr>
<tr>
<td>Average Power (W/kg)</td>
<td>5.22±1.60</td>
</tr>
</tbody>
</table>

Table 2. The relationships between isometric muscle strength and anaerobic exercise capacity parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Peak Power</th>
<th>Average Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip Flexion (kg)</td>
<td>0.688*</td>
<td>0.629*</td>
</tr>
<tr>
<td>Hip Extension (kg)</td>
<td>0.618*</td>
<td>0.532*</td>
</tr>
<tr>
<td>Knee Flexion (kg)</td>
<td>0.642*</td>
<td>0.530*</td>
</tr>
<tr>
<td>Knee Extension (kg)</td>
<td>0.647*</td>
<td>0.465*</td>
</tr>
</tbody>
</table>

Pearson Correlation Test: kg; kilogram; W; watt; W/kg; watt/kilogram. *Significance at level p <0.001.

SAT0752-HPR
THE MEASUREMENT OF PATIENTS’ EXPECTATIONS OF A MULTIDISCIPLINARY AND DEDICATED FIBROMYALGIA PROGRAM

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Background: Fibromyalgia (FM) is a chronic and multidimensional condition impacting the physical health and psychosocial state of the individuals. In addition to performing clinical and psychological assessments, evaluating patients’ expectations may help address their specific needs and improve outcomes.

Objectives: The aim of this study was to assess the expectations of a cohort of FM patients participating in a multidisciplinary, dedicated fibromyalgia program.

Methods: This was a survey of 86 consecutive FM patients who were initiating a multidisciplinary program delivered by a rheumatologist, nurse, physiotherapist, occupational therapist, psychotherapist and GP with a special interest in FM. Patients were diagnosed using the 2010 ACR diagnostic criteria. Demographic data, Widespread Pain Index (WPI), Symptom Severity Score (SSS) were recorded. Patients filled in the self-administered questionnaires including the Revised fibromyalgia impact questionnaire (FIQR), Hospital Anxiety and Depression Scale (HADS) and a patients’ expectations questionnaire. The latter consisted of both open ended and closed questions using a five-point Likert scale (1=strongly agree to 5=strongly disagree) about the following domains: physical, psychological, coping and social aspects.

Results: Eighty-six patients (92% females) participated in the survey. The average age was 51.2 years (SD 10.60) and mean duration of symptoms 13.3 years (SD 11.17). The mean HADS-A was 11.6 (SD 4.37), HADS-D 8.67 (SD 3.47) and FIQR 55.9 (SD 21.64). In response to an open question about what was their main expectation from this program, just over half of the patients (52.3%) reported improvement of pain and fatigue as their most important outcome. This was followed by improved quality of life (19.3%), being able to cope better with ADLs, family and work (17.4%), obtain more knowledge about the condition (5.8%), while 15.1% did not have any expectations. When asked to rate their expectations for each specific domain: 64% expected significant improvement of physical symptoms, 74% to be able to cope better with family, hobbies and work and 66% expected an improvement of their psychological state, namely depression and anxiety. By the end of the program, 66% of the patients expected to have minimal or no symptoms. When asked to identify any lifestyle changes which could help, 30.2% mentioned a better work-life balance, 12.8% starting an exercise routine, 10.5% weight loss, 11.6% a mixture of house adaptations while 34.9% could not come up with any suggestions.

Conclusions: Expectations of fibromyalgia patients were high in all domains. This study highlights the need for multidimensional assessment and a personalised multidisciplinary approach in managing fibromyalgia. Moreover, it is very important to assess patients’ expectations in order to guide interventions and set realistic achievable goals which are acceptable to both patients and clinicians. Patients’ expectations are an important patient reported outcome measure, which need to be assessed.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1599

References:
**SAT0753-HPR** AWARENESS OF POSSIBLE SIDE EFFECTS OF NSAIDS AMONG THE ALBANIAN PATIENT POPULATION

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**Background:** No official published figures are available regarding the annual use of NSAIDs in Albania. Nonsteroidal anti-inflammatory drugs are used primarily to manage different pain conditions, less commonly they are used for their antiplatelet effect. Although generally well tolerated, conventional NSAIDs have been associated with a wide range of adverse effects. The most common of which are gastrointestinal tract (GIT) side effects like: dyspepsia, abdominal pain, heartburn, and the most serious life-threatening gastrointestinal (GI) ulceration.

**Objectives:** To investigate patient awareness of the proper use and frequency of side effects in nonsteroidal anti-inflammatory drugs (NSAIDs) patients in Albania. Methods: This was a cross-sectional study, a prospective 15 question interview of patients purchasing medications, during randomized 1 hour/day pharmacy visits over a one month study period (May 2015).

The study was conducted in 4 community pharmacies located in the city of Tirana (capital of Albania). Two hundred and ten patients were included in this study.

**Results:** Overall NSAIDs use during last year was 63%: ibuprofen and diclofenac was the most used NSAIDs. The majority of patients (58%) reported having side effects upon NSAIDs use; gastrointestinal upset was the most frequently reported side effect. Patients awareness regarding proper NSAIDs use was poor, and pharmacist role in counselling was inadequate.

However, user ability to discover the most common side effect to the drug seemed not to be affected.

**Conclusions:** Nonsteroidal anti-inflammatory drugs use awareness and knowledge of probable side effects and how to handle them was not adequate. This probably reflected on high incidence of side effects. Nonsteroidal anti-inflammatory drugs are available on prescription as well as over the counter drugs. Pharmacist involvement in education of patients using them is highly recommended and much needed to help decrease frequency of side effects. However this is a small scale study and further studies need to be done.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1089

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**SAT0755-HPR** VARIATION IN SLE-RELATED PAIN: A SEVEN YEAR FOLLOW-UP STUDY

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**Background:** In a previous study we have shown that 24% of the SLE patients in our cohort reported high level of SLE-related pain, ≥40 mm on VAS (0–100 mm). These patients with high pain level also reported significantly more fatigue, anxiety and depression and reduced health-related quality of life compared to the SLE patients with low pain level, <39 mm on VAS.2

**Objectives:** To investigate the variation in self-reported SLE-related pain and its association with presence of chronic widespread pain (CWP) and patient-related outcomes after seven years of follow-up.

**Methods:** 64 of 84 patients agreed to participate in the 7-year follow-up and answered questionnaires on pain (VAS/mm), fatigue (MAF), HROQL (SF-36), anxiety and depression (HADS) and, in case of remaining pain – three months, marked painful body regions on a pain-drawing. Disease activity and damage (SLAM, SLEDAI, SLICC) were also captured. Nonparametric statistics were used to compare the different groups. Difference in measures (diff) between inclusion and follow-up was calculated.

**Results:** For patients with low degree of SLE-related pain the previous week (<39 mm on VAS) at inclusion, n=50, there were no significant differences at 7 years follow-up in pain, fatigue, anxiety, depression and all dimensions of SF-36, except for deterioration in physical function median diff (IQR) 0 (-10 to 5), p=0.024. Of these patients with low level of pain, 26% indicated chronic widespread pain on the pain drawing.

Among patients with high degree of pain (≥40 mm on VAS) at inclusion, n=14, half of the patients reported significantly decreased pain, diff (IQR) 45 (35 to 65), p=0.021, fatigue, 8 (8 to 17), p=0.018, anxiety, 4 (1 to 6), p=0.035 and depression, 4 (2 to 5), p=0.018 and improvements in all dimensions of SF-36 except for role emotional and social function at follow-up, p<0.05.

However, half of the patients with high degree of pain at inclusion reported no significant changes at follow up regarding pain, median diff (IQR) -13 (-20 to 28), fatigue, 5 (-0.3 to 6), anxiety, 2 (-1 to 3) and depression, 0 (3 to 2). These patients reported significantly deterioration in vitality in SF-36, diff (IQR) 20 (15 to 35), p=0.0018 but no significant changes in the other dimensions of SF-36. All patients with high levels of remaining pain indicated chronic widespread pain on the pain drawing. These patients with remaining pain had significantly higher SLAM at follow-up compared to the patients with decreased pain at follow-up, p=0.017 and the patients with low levels of pain at inclusion, p=0.006. No significant differences were found regarding SLEDAI and disease damage.

**Conclusions:** Self-reported level of disease-related pain remain low in most patients and in some patients also significantly reduced. However, half of the patients with high level of pain at inclusion still experienced high level of pain and pain-related problems including widespread pain after 7 years of follow-up. These results suggest a transition from SLE-related pain to chronic widespread pain, which requires different pain management.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1446

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**SAT0754-HPR** A NECESSARY INVESTMENT IN FUTURE HEALTH. PERCEPTIONS OF PHYSICAL ACTIVITY MAINTENANCE AMONG PEOPLE WITH RA PARTICIPATING IN AN OUTSOURCED HEALTH-ENHANCING PHYSICAL ACTIVITY PROGRAM

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**Background:** Health-enhancing physical activity (HEPA) is an active treatment in rheumatoid arthritis (RA) that may be difficult for patients to maintain over time. A two-year HEPA program including twice-weekly circuit training at public gyms and 150 weekly minutes of moderately intense aerobic exercise was conducted in Sweden between 2011 and 2013. Regular peer support sessions were held to promote the maintenance of HEPA. Patient perceptions on maintained physical activity in RA have been minimally explored.

**Objectives:** To describe perceptions of physical activity maintenance during the second year of an outsourced 2-year HEPA-program among people with RA

**Methods:** A descriptive design with a qualitative inductive approach was used. Interviews were conducted with 18 participants with RA, including men and women differing in age, disease duration, activity limitation, perceived pain, levels of physical activity, training centers and peer support groups. Qualitative content analysis was used, and a pattern of theme, subthemes, categories, and subcategories was constructed based on the participants’ perceptions of the phenomenon.

**Results:** A main overarching theme and three subthemes were established, called ‘A necessary investment in future health through dedication, affinity and awareness’; which described participants’ experiences of maintenance during the second year of an outsourced 2-year HEPA-program. This was further described in eight categories with 16 subcategories. The categories described the participants’ ‘mindsets, habits, commitments, social support, PA contexts, monitoring, insights in PA, and health gains’. 

**Conclusions:** The findings are partly in line with the theoretically derived explanations for maintenance of behavior change formulated to date, such as maintenance motives (self-determination and identity), self-regulation (skills and processes, lapse, relapse and coping) habits, resources (psychological and physical) as well as environmental and social influences. The results of this study could also be transferable to similar groups of people with RA in similar settings and can be useful in designing future HEPA interventions to facilitate maintenance of behavior change.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6219

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**SAT0756-HPR** EFFECT OF NSAID INTAKE ON KINESIOPHOBIA IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Spinal stiffness and loss of spinal mobility, explained byspinal inflammation and structural damage due to extensive osteoporosis, are characteristics of Ankylosing Spondylitis (AS). AS usually disables a person with severe back pain and, in later stages, remarkable spinal kyphotic deformity. The deformity may initially only be present as reduced spinal movement, thereby controlling the symptoms and progression of AS in early stages by effective medication is the main step in the management of AS.

**Objectives:** The aim of this study was to investigate the effectiveness of DMARD therapies on NSAID intake and kinesiophobia in patients with AS.

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**Health Professionals in Rheumatology Abstracts**

Saturday, 17 June 2017 1523
SIGNIFICANT IMPROVEMENT OF RHEUMATOID ARTHRITIS (RA) OUTCOME WITH REPEATED SELF-ASSESSMENT APPLYING SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILES TOOLS: A COHORT STUDY OF RA PATIENTS IN CHINA

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Background: There are more than 5 million RA patients in China, but only 5,000 rheumatologists. Treat-to-Target (T2T) strategy are critical for the treatment of RA, but the Chinese rheumatologists can hardly provide patients with a complete assessment in the clinic due to limited time. The SSDM includes interfaces of both physicians’ and patients’ application. After entering the data of lab test records, treatment regiments, and executing DAS28 assessment by patients themselves, all data can be synchronized automatically to the authorized physicians’ mobile tool. The rheumatologists can rationally adjust treatment for RA patients can achieve better T2T result. SSDM can assist rheumatologist to improve disease activity.

Methods: A total of 74 patients, diagnosed according to the modified New York criteria for AS, were enrolled. Patients were assessed to measure disease activity using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Fear of movement was assessed with the Tampa Scale for Kinesiophobia [TSK]. To calculate NSAID intake and the type of NSAID, percentage of days with intake were recorded, along with DMARD therapy, age, body mass index (BMI), and disease duration. The BASDAI equivalent scoring was calculated according to recommendations from longitudinal clinical studies. The drug therapy groups were compared using the Kruskal-Wallis test and the Chi-square test. Correlation analysis was evaluated by Spearman's correlation coefficient.

Results: Seventy-four patients (36 women, 38 men; mean age: 43.8±10.18 years; mean disease duration: 9.89±8.50 years; BMI: 28.20±5.07) treated with 4 types of DMARDS (adalimumab-golimumab=17; infliximab=19; etanercept=13; sulfasalazine=25) were included. There were no drug group differences in terms of age (p=0.586), sex (p=0.886), or BMI (p=0.821). BASDAI scores (mean: 3.9±2.4) and NSAID intake (mean: 68.1±76.1; p=0.003) were significantly higher in the sulfasalazine therapy (ST) group compared to other drug groups. BASDAI scores were not correlated with age (p=0.103), disease duration (p=0.131), BMI (p=0.641) or the TSK scores (p=0.376). Different NSAID intake groups (p=0.089) had similar TSK scores.

Conclusions: Patients with AS had fear of movement independent of age, BMI or disease duration, even when they experienced positive results from drug therapies and concomitant therapy with a single oral dose of NSAID or oral corticosteroids in stable dosages.

References:

Acknowledgements: We would like to thank Rheumatology Nurse Ayten Yuksek in our department for monitoring and documenting of the data, and our patients for assistance with their valuable participation to our study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1389
References:
Acknowledgements: Arthritis Research UK (grant 20169) and the United Kingdom Occupational Therapy Research Foundation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4996

SAT0760-HPR

PSYCHOLOGICAL VARIABLES PREDICTIVE OF DISORDERS OF SLEEP IN PATIENTS WITH SPONDYLARTHRITIS AND PSORIATIC ARTHRITIS. PRELIMINARY MULTICENTER STUDY

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Objectives: To study the psychological variables associated with the severity of insomnia and hypersomnia according to the Oviedo sleep questionnaire (COS) in patients with spondylarthritids (SPA) and psoriatic arthritis (PA), including the disease activity BASDAI and DAS28.

Methods: Design. Cross-sectional descriptive study. Patients: Patients with consecutive SPA or PA were selected by consecutive sampling in follow-up in rheumatology units of 4 Spanish hospitals. Inclusion criteria: Adults (age >16 years) with SPA (ASAS criteria) or PA (CASPAR criteria) capable of understanding and willing to perform questionnaires. Exclusion criteria: other rheumatic diseases, age <16 years. Protocol: Upon arriving at the consultation, he was offered to participate in the study, he was explained and the patient was given the battery of questionnaires; His physician performed the evaluation of disease activity and recorded the comorbidities and current medication. Main outcomes: the 3 dimensions of COS: (1) Subjective satisfaction with sleep, (2) Insomnia and (3) Hyperinsomnia. The COS is a semi-structured interview to aid the diagnosis of insomnia and hypersomnia according to the diagnostic criteria ICD-10 and DSM-IV. Other variables: current medication for SPA or PA, comorbidities, use of sleeping pills and/or CPAP according to COS questionnaire (insomnia was divided into mild <15 and moderate-severe >15), disease activity: ADAS and PsA (DAS28); Health-related quality of life (HRQL) using SF-36; Pain perception (Brief Pain Inventory BPI questionnaire), SPA (BASDAI) and PA (DAS28, BASDAI) and FACIT fatigue, TMMS emotional intelligence. Resilience with resilience questionnaire, anxiety and depression screening using HADs. Statistical analysis: descriptive, bivariate analysis using T-Student, Mann-Whitney and χ2; Followed by binary logistic regression (BLR) (Vd. moderate/severe insomnia).

Results: A total of 126 patients participated: 65 patients with SPA (33.8% women, 42% <40.92 years) and 61 patients with PA (60.7% women, 49.4±5.5 years) with an average of 8.4±6.8 years of disease. They used biological therapy SPA 29 (23%) and PA 28 (45.9%). The most common comorbidity were in SPA and PA: disc disease 33 (50.8%) and 18 (29.5%), 16 (24.6%), Both patients with SPA and PA were dissatisfied with their sleep (3.4±1.39). We did not find correlation of the COS variables with the HRQoL, the fatigue or the pain. There were no differences in COS scale according to biological treatment and/or FAME. Logistic regression analysis demonstrated an association between insomnia and TMMS repair, resilience and anxiety in PA. Insomnia in SPA showed an association with depression and BASDAI.

Conclusions: Insomnia is a common health problem in these diseases. Moderate-intense insomnia in patients with SPA was associated with an increase in BASDAI and depression. Also in patients with PA, the insomnia was associated with TMMS repair, resilience and anxiety. The patient assumes the sleep disorder as part of this chronic illness, this justifies the good evaluations of resilience and emotional intelligence of the evaluated patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2544

SAT0761-HPR

IDENTIFICATION OF FACTORS THAT CONTRIBUTE TO SUCCESSFUL ONLINE MONITORING OF DISEASE ACTIVITY: EXPERIENCES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: In order to encourage patients to take an active role in their disease management and to enhance the dialogue between patients and healthcare providers, iMonitor was developed. iMonitor is a Software Medical Device developed and funded by Pfizer. Patients can complete patient-reported outcome measures (PROMs) in this online system. This allows for monitoring of disease activity in between visits, identification of patients who need medical attention in between visits, and it may lead to reduction of consultations for patients with stable disease activity. Moreover, completion of a PROM might help a patient to prepare for his or her consultation and might improve the communication between physician and patient.

Objectives: This study aims to identify factors that contribute to adequate online monitoring of disease activity, by collecting experiences from patients with RA with iMonitor.

Methods: Patients were recruited at Bernhoven (Uden, the Netherlands) by an announcement of the study on the hospital website, leaflets and by specific meetings. Four instruction classes were organised in which two researchers gave live instructions about the programme. Patients received log-in codes and chose their PROM-preference(s) and PROM-frequency. After nine months a focus group interview was performed and three telephone interviews were held. Questions were semi-structured using a topic list based on Flottorp. Data will be transcribed, coded and grouped.

Results: Currently 33 patients with RA are using iMonitor. Of these patients 17 (52%) attended the instruction classes and six patients (18%) attended the focus group discussion. Preliminary results reveal six themes (Technological aspects, Patient factors, Need for feedback, Incentives and resources, Reduction of consultations and Security aspects). The Flottorp domain “Patient factors” provided most rich information. Most patients said they developed more knowledge about their disease activity and that they felt more aware about their disease activity. Additionally, iMonitor supported them in taking actions such as adjustments in lifestyle and becoming more prudent when noticing a flare. Some patients felt more prepared for a consultation and less dependent from their rheumatologist. With regard to the domain “Capacity for organisational change”, patients were confident that iMonitor could contribute to reduction of consultations, but contacting the outpatient clinic when feeling worried should be required.

Conclusions: Patients’ experiences with an online remote monitoring system were mainly positive. Instruction classes helped patients to get familiar with the programme. Patients experienced to have more control over their disease and to have developed more knowledge. This may result in enhanced self-management, which is important with regard to retain control over disease.

References:

Disclosure of Interest: L. Renskers Grant/research support from: Pfizer, S. Rongen: None declared, A. Huis: None declared, M. Hulscher: None declared, P. van Riel Grant/research support from: Pfizer DOI: 10.1136/annrheumdis-2017-eular.2294

SAT0762-HPR

THE ACCESSIBILITY AND USABILITY OF AN AUSTRALIAN WEB-BASED SELF-MANAGEMENT PROGRAM (MYJOINTPAIN) FOR PEOPLE WITH LOWER HEALTH LITERACY AND JOINT PAIN IN THE UK

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Background: Osteoarthritis (OA) is disproportionately prevalent in people from lower socio economic groups (1). People from lower socio economic groups are also more likely to have lower health literacy. Health literacy influences people’s capacity to understand, acquire, appraise and use health information. Currently, health professionals over estimate patients’ health literacy (2), potentially reducing the impact of OA self-management interventions that rely on educational approaches (3). As internet usage increases, online OA self-management resources are an option for delivering patient education. Currently, there is no evidence as to whether online education resources are suitable and accessible for people with joint pain and lower health literacy.

Objectives: To identify facilitators and barriers experienced by people with joint pain and low health literacy to access and utilise information available on the MyJointPain website. (https://www.myjointpain.org.au).

Results: Currently 33 patients with RA are using iMonitor. Of these patients 17 (52%) attended the instruction classes and six patients (18%) attended the focus group discussion. Preliminary results reveal six themes (Technological aspects, Patient factors, Need for feedback, Incentives and resources, Reduction of consultations and Security aspects). The Flottorp domain “Patient factors” provided most rich information. Most patients said they developed more knowledge about their disease activity and that they felt more aware about their disease activity. Additionally, iMonitor supported them in taking actions such as adjustments in lifestyle and becoming more prudent when noticing a flare. Some patients felt more prepared for a consultation and less dependent from their rheumatologist. With regard to the domain “Capacity for organisational change”, patients were confident that iMonitor could contribute to reduction of consultations, but contacting the outpatient clinic when feeling worried should be required.

Conclusions: Patients’ experiences with an online remote monitoring system were mainly positive. Instruction classes helped patients to get familiar with the programme. Patients experienced to have more control over their disease and to have developed more knowledge. This may result in enhanced self-management, which is important with regard to retain control over disease.

References:

Disclosure of Interest: L. Renskers Grant/research support from: Pfizer, S. Rongen: None declared, A. Huis: None declared, M. Hulscher: None declared, P. van Riel Grant/research support from: Pfizer DOI: 10.1136/annrheumdis-2017-eular.2294
Methods: A qualitative interview study was conducted. Participants were invited to use the website for two weeks and then participated in semi-structured interviews. The interview topic guide had been developed in line with current literature. The interviews were audio recorded and transcribed verbatim. Thematic analysis was used by the main researcher (with independent verification) to interrogate the data and identify themes.

Results: Six people with low health literacy (S-TOFHLA 17±3) were recruited from community groups from an inner-city area with a high index for social deprivation. Four key themes were identified. 1) Dealing with technical issues, where participants demonstrated that they could persevere with technical problems in using online resources. 2) Information over provision, here participants found there was too much complex health information provided, that hindered usability; 3) Motivation for information seeking, where participants discussed that it was pain that encouraged resource use but motivation to self-manage was influenced by personal beliefs; 4) Specialist professional insights: some participants whilst willing to use and engage with the website recalled that they also want to have access to a health professional and felt the website could supplement but not replace this contact.

“I think you have it from the health care where the healthcare are telling you and explaining to you”. 

Conclusions: Digital online OA self-management presented by MyJointPain showed potential for use by people with joint pain and lower health literacy levels. This is important as outcomes for this group are poor (1). Text volume, detail and image use should be carefully considered when designing new online resources and involvement of people with lower health literacy when designing websites will help to ensure inclusion and useful content is accessible to all OA patients. Clinicians should consider their patients’ health literacy levels, computer literacy and readiness to change behaviour before prescribing web based self-management tools.

References:

Acknowledgements: Prof D. Hunter, A. Cahill and C. Dickson from Arthritis Australia.

Disclosure of Interest: None declared


SAT0763-HPR FUNCTIONAL OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS ON THE BACKGROUND CORRECTION OF PROGESTERONE INSUFFICIENCY M. Salokhiddinov 1, T.G. Woodworth1, F. Guillemin2, D.E. Furst1, J. Brook1, S. Kafaja1, 3Rheumatology, Saudi German hospital, Jeddah, 2Rheumatology, Saudi German hospital, Medinah; 3Rheumatology, Saudi German hospital, Riyadh, Saudi Arabia; 4Rheumatology, Thumbay Hospital, Dubai, United Arab Emirates

Background: Chronic pain is a common condition that affects one-third of the population, accounting for a large number of medical consultations and a significant proportion of health care costs. Evidence suggests that anxiety and depression are associated with increased pain sensitivity and pain-related disability, co-morbid conditions that are more disabling than either condition alone (1). Pain management in OA patients is complicated in the setting of chronic pain and depression, and the effect of OA management on these co-morbid conditions is not well understood.

Objectives: The objective of this study was to determine the prevalence of anxiety, depression, and sleep disorders, painful musculoskeletal conditions in a sample of adults with disabilities.

Methods: This cross-sectional study analyzed data of 1692 adults aged 18 or older who have disabilities over 10 years (2005 to 2014). We examined the following chronic conditions, in which pain is a key symptom and forms part of the diagnostic process, and organized them into 3 groups. Group 1 consisted of (rheumatic diseases), arthritis, osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis; group 2 consisted of muscular dystrophy; and group 3 consisted of neck or back pain. The prevalence (95% confidence interval) of painful musculoskeletal conditions was determined according to the diagnosis. Factors associated with these painful conditions were analyzed separately for men and women by using a logistic regression model.

Results: The prevalence of painful musculoskeletal conditions was 66.9% (95% CI, 66.0%–67.7%). Factors associated with these conditions in both men and women included older age, a sleep disorder, and comorbid chronic anxiety and/or depression was 23.5% (95% CI, 22.5%–24%), all of which were higher in women than in men. Of the 1692 adults with disability included in the study, 65% were women. The average age was 50.5 (standard deviation, 12.5 y), and 65% of participants were 50.5 or older. In addition, 48% of participants were married. Of the participants, 16% had been diagnosed with chronic anxiety and 22% with chronic depression; and 32% with sleep disorder (sleeping 6 hours or less per day. Prevalence of Painful Conditions in Adults with Disabilities, by Group of Conditions was developed to facilitate and standardize detection and measurement of RA flares in an American English version of the FLARE questionnaire to detect and measure RA flares in rheumatoid arthritis.

CITERI ON AND CONCORDANCE VALIDITY OF THE AMERICAN-ENGLISH VERSION OF THE FLARE QUESTIONNAIRE TO DETECT AND MEASURE FLARES IN RHEUMATOID ARTHRITIS N. Barros1, T.G. Woodworth1, F. Guillemin2, D.E. Furst1, J. Brook1, S. Kafaja1, N. Borazan1, D.A. Elashoff1, B.J. Fautrel3, V.K. Ranganath1, 1Rheumatology, Saudi German hospital, Jeddah, 2Medicine, UCLA, Los Angeles, United States; 3Université de Lorraine, Paris Descartes University, APEMAC, EA 4360; 4Pitié Salpêtrière Hospital, Paris, France

Background: Despite advances in rheumatoid arthritis (RA) therapeutic agents, difficulty in managing RA flares persists, and remission or the persistent absence of inflammation remains challenging to achieve. The French FLARE (F-FLARE) was developed to facilitate and standardize detection and measurement of RA flares between clinic visits. Here we report validation of the American English version of FLARE (Am-E FLARE-RA).

Objectives: To assess whether the Am-E FLARE questionnaire performs comparably to the French version of FLARE in detecting RA flare in an American English-speaking clinic population.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1067
Methods: We enrolled patients attending UCLA rheumatology clinics. After informed consent, patients completed a questionnaire to collect demographics, Am-E FLARE, RAPID3, patient global visual analog scale (VAS), and self-reported flare at time of visit or between visits (yes/no). Questions were provided to patients without specific instruction. From the electronic medical records, we extracted MD global, VAS, MD-reported flare, seropositivity, disease duration, swollen/tender joint counts (SJC/TJC), and calculated the clinical disease activity index (CDAI). Analyses included Wilcoxon rank sum tests and Spearman correlations to assess criterion and concurrent construct validity.

Results: Eighty-five RA patients diagnosed by the 1987 American College of Rheumatology (ACR) criteria enrolled in our study. For the study population as a whole, mean age was about 50 years and most were female. Mean disease duration was about 10 years and about 65% were seropositive. (see Table). Am-E FLARE scores were significantly higher in patients' self-reporting flare compared to those without (p = 0.008), and to patients who did not report flare compared to those without flare (p = 0.008) (see Table). Interestingly, there were no significant differences in SJC (p = 0.82) and physician global (p = 0.19) between patients who self-reported flare versus those who reported no flare. In addition, the Am-E FLARE scores correlated moderately with both CDAI (corr=0.46) and RAPID3 (corr=0.57).

Conclusions: The Am-E FLARE is feasible for use in clinic, and shows good criterion validity, with scores significantly higher in patients who self-report flare. In addition, Am-E FLARE shows good discriminant validity, distinguishing patients who are flaring according to MD or patient self-report from those who are not. Finally, Am-E FLARE demonstrates construct validity comparable to that of the original French version of FLARE.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3329
Objective measures of cognitive impairment and the importance of considering cognitive dysfunction. Findings emphasize the gap between subjective and objective measures of cognitive impairment in persons with chronic disease. 

Background: There is an increased appreciation of the burden of cognitive impairment in persons with rheumatoid arthritis (RA). Research shows a gap between subjective and objective measures of cognitive impairment in persons with chronic disease.

Objectives: This study explored the relationship between subjective cognitive dysfunction and computerized neuropsychological performance in Korean older adults with RA.

Methods: Individuals with RA were recruited by their rheumatologists during follow-up visits at a university hospital in Korea. After getting signed consents, a trained research nurse assessed participants with a range of physical, psychosocial, and biological metrics. Subjective cognitive dysfunction was assessed using the Perceived Deficits Questionnaire (PDQ; range 0–20, higher score=greater impairment). Objective cognitive impairment was assessed using a set of 6 computerized neuropsychological tests yielding 18 indices covering a range of cognitive domains. Subjects were classified as “impaired” if they performed 1 SD below age-based population norms on each test [1]. A total cognitive impairment score was calculated by summing the transformed scores (range: 0–18, higher score=greater impairment). Multiple regression analysis controlling for education, disease severity, and depression was conducted to identify the relationship between objective and subjective cognitive measures.

Results: Fifty four subjects with a mean (±SD) age of 63.6 (±10.5) years were included in the final analyses. 85% were female and 87% were married. Mean education level was 10.2 (±4.9) years and mean depression (SE) was 8.9 (±8.5) years. 25.9% had depression and 55.6% had sleep difficulty. Mean PDQ score was 11.8 (±4.5, range 5–25) and mean total cognitive impairment score was 11.0 (±4.1, range 2–18). 92% were classified as cognitively impaired on five or more test indices. There was no significant correlation between PDQ score and total cognitive function score (r=0.26, p=0.086). However, psychological factors including depression (r=0.18, p=0.001) and sleep problem (r=0.577, p=0.001) were significantly correlated with PDQ score. In the multivariate analysis, there was no significant relationship between PDQ score and total cognitive impairment score. However, functional limitations and depression (r=0.317, p=0.048; r=0.334, p=0.019) were significantly associated with the PDQ score.

Conclusions: There was no significant relationship between subjective cognitive dysfunction and computerized neuropsychological performance in this cohort. Functional limitations and depression were significantly associated with perceived cognitive dysfunction. Findings emphasize the gap between subjective and objective measures of cognitive impairment and the importance of considering psychological factors in the context of cognitive complaints in clinical settings.

References:

Acknowledgements: This research was supported by the 2015 Inje University research grant (No.20151092).


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6809
HPR measuring health (development and measurement properties of PROs, tests, devices) __

**AB1195-HPR**  
**PSORIATIC ARTHRITIS PATIENTS INITIATED ON APREMILAST: A RETROSPECTIVE ANALYSIS OF PATIENT OUTCOMES FROM A WEST LONDON TEACHING HOSPITAL**

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**Background:** Apremilast is an oral phosphodiesterase 4 (PDE-4) inhibitor that reduces disease activity in psoriatic arthritis (PsA) by modulating the expression of inflammatory cytokines. In December 2015, apremilast received a negative National Institute of Clinical Excellence (NICE) appraisal for its use in PsA, owing to a lack of robust evidence on its long-term impact on patient outcomes and efficacy in improving radiographic progression (TA372).

The role of the drug in the PsA treatment pathway remains uncertain. We present a retrospective analysis of the use of apremilast in 14 patients with PsA within our hospital trust.

**Methods:** Pharmacy funding applications and medication dispensing records were used to identify patients. All patients commenced on apremilast at Imperial College NHS Healthcare Trust (ICH) for PsA were included in the analysis.

**Results:** A total of 14 patients were initiated on apremilast between June 2015 and September 2016 (Table 1). Of these patients, 9 (64%) achieved an adequate response to treatment, defined by NICE as an improvement in at least 2 of the 4 PsA response criteria (PsARC) scores, with no worsening in any of the four criteria. Of the 5 patients not achieving response, 3 patients discontinued treatment prior to assessment due to intolerable side effects, whilst 2 further patients did not achieve the appropriate therapeutic response (primary failure).

From the 9 patients that achieved an adequate response only 5 are currently taking therapy, with intolerable side effects causing discontinuation in a further 4. This gives an overall discontinuation rate of 65% (9 out of 14). In the 5 patients remaining on therapy, one patient needed to reduce the drug dose due to side effects, whilst one continued treatment despite tolerable side effects. Of our 14 remaining patients only 3 remained on treatment in the absence of any side effects. The most common side effects causing discontinuation were nausea and vomiting (Spaltins, 21%) and mood changes (2 patients, 14%).

Conclusions: Apremilast was poorly tolerated in our population with only 3 patients continuing the drug with response and without ongoing side effects. Discontinuation rates within ICHT were found to be much higher than those in the original trial data (65% versus 15%). Patients who have continued the medication and tolerated side effects, however have shown a good response to treatment.

**References:**

Acknowledgements: Dr Benjamin Ellis, consultant Rheumatologist, Imperial college NHS Healthcare trust. Dr Matthew Pickering, consultant Rheumatologist, Imperial college NHS healthcare trust

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3220

**AB1196-HPR**  
**A COMPARISON OF PATIENT PREFERENCE AND USABILITY BETWEEN TWO ELECTRONIC GONIOMETRIC GLOVES IN THE MEASUREMENT OF JOINT MOVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Patients with Rheumatoid arthritis suffer from pain, stiffness and reduced mobility of their finger joints. Instrumented electronic goniometric gloves have been developed which can enable dynamic measurements to be made with accuracy and efficiency [1]. This technology could be employed in assessing patients with rheumatoid arthritis and could also be used as an aid to rehabilitation. However, pain and swelling in the joints might limit the applicability of these measurement devices as to date they have not been tested in this patient group.

**Objectives:** The purpose of this pilot study was to establish the usability of two different electronic gloves in patients with mild to moderate Rheumatoid arthritis. We wished to establish if patients experienced difficulty donning or doffing either glove or if carrying out a series of measurements with the gloves on caused a change in pain and stiffness. We also investigated differences in the usability and preference between the two Datagloves.

**Methods:** We compared a commercially available electronic glove (the 5DT dataglove 14 Ultra) with a bespoke IMU based electronic glove produced to our specifications by Tyndall National Institute, University College Cork (Figure). We developed a programming interface for both devices to facilitate calibration and detailed evaluation of joint movement. Nine patients with mild to moderate rheumatoid arthritis who were experiencing significant but not severe pain and early morning stiffness in their hands were recruited. After calibration, the patients worked through a protocol of finger flexion and extension movements, which were repeated for each glove and again to test repeatability. The patients completed questionnaires before and after using the gloves on their pain and stiffness levels and at the end of the session on glove donning and doffing usability and preference between the two gloves.

**Results:** All nine patients were able to don and doff the IMU glove without any difficulty compared to 4/9 for the 5DT glove. Seven of 9 patients expressed a preference for the IMU glove or if carrying out a series of measurements with the gloves on caused a change in pain and stiffness. We also investigated differences in the usability and preference between the two Datagloves.

**Conclusions:** Electrogoniometric gloves are usable in patients with rheumatoid arthritis.
arthritis, but patients cannot tolerate longer protocols without an increase in discomfort.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5202

**AB1197-HPR**

**VALIDITY AND RELIABILITY OF A SMARTPHONE GONIOMETER APPLICATION FOR MEASURING HIP RANGE OF MOTION IN PATIENTS WITH HIP OSTEOARTHRITIS: A PILOT STUDY**

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**Background:** Osteoarthritis (OA) of the hip affects the entire joint structure and function and leads joint capsule changes which result limitation in range of motion (ROM). Therefore, measuring ROM is an essential part of the hip assessment. Various measurement tools are available for determining the ROM such as universal goniometers (UG), digital inclinometers, motion analysis systems. Recently, smartphones equipped with suitable applications are able to measure ROM.

**Objectives:** The aim of this study was to determine the inter-rater and intra-rater reliability of a smartphone application “PT Goniometer®” 2015 Mark Busman (PTG) and investigate the agreement within PTG versus UG for active hip ROMs in patients with OA.

**Methods:** This study included eight people who were diagnosed with hip OA. Two physiotherapists performed the ROM measurements on affected hips by using PTG and UG. UG was employed as the reference standard. Hip ROM tests were performed in the following order: flexion, abduction, internal and external rotation. Inter-rater correlation coefficient were used to determine the inter-rater and intra-rater reliability. The Spearman correlation coefficients were used to establish validity of PTG.

**Results:** The PTG smartphone application demonstrated good to excellent inter-rater and intra-rater reliability (ICCs > 0.75) for all measured hip movements in patients with hip OA. ICC scores, minimum detectable change (MDC95) and standard error of measurement (SEM) values were indicated in Table 1 and Table 2. Additionally, UG and PTG application methods demonstrated positive correlations for all hip movements (p < 0.05).

**Conclusions:** Results showed the application potential of PTG in clinical practice. PTG might be a valid and a reliable method for measuring hip ROM in patients with hip OA and smartphone applications can be used in clinical settings. Studies with larger population are required for further investigation of smartphones psychometric properties on measuring hip ROM.

**Disclosure of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.6283

**AB1199-HPR**

**IMPROVING TRIAGE TO APPROPRIATE TREATMENT LEVEL BY USING A COMBINATION OF SCREENING TOOLS IN PATIENTS AT RISK OF DEVELOPING CHRONIC BACK PAIN**

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**Background:** The screening instrument STaR (Subgroups for Targeted Treatment) Back Screening Tool (SBST) identify patients at risk of developing chronic back pain in order to facilitate triage to appropriate treatment level. The SBST takes into account known risk factors such as activity limitations, kinesiophobia and psychological health. However, SBST does not consider pain distribution which is a known predictor of chronic widespread pain (CWP). According to evidenced clinical practice patients with CWP should be referred to multidimensional rehabilitation (1).

**Objectives:** The purpose of the study was to compare screening by SBST with screening of multisite chronic widespread pain (MS-CWP) in a group of patients with back pain and to analyze to what extent the two screening methods identify the same patients at higher risk.

**Methods:** 73 individuals with a report of chronic back pain (>3 months during last year) age 40–70 years responded to both screening tools. The SBST stratifies patients into low, medium or high risk groups. A pain mannequin was used to categorize patients into no chronic pain (NCP), chronic regional pain (CRP) or chronic widespread pain (CWP) and number of painful areas (0–18). A presence of ≥ 7 painful areas was stratified as MS-CWP. The outcome of the different screening tools was analyzed by cross tabulations. The Roland-Morris Disability Questionnaire (RMDQ, 0–24), health related quality of life (EQ5D, 0–1), Fear-Avoidance Beliefs Questionnaire about physical activity (FABQ-PA, 0–24) and work (FABQ-Work, 0–42), Hospital Anxiety (HAD-A, 0–21) and Depression scale (HAD-D, 0–21) were used to describe physical function, health related quality of life, kinesiophobia and mental health.

**References:**

**Acknowledgements:** The authors declare that they have no conflict of interest.

**Disclosure of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.5710

**AB1198-HPR**

**PRESENTATION OF A NEW SCALE ASSESSING THE BIOPSYCHOSOCIAL ASPECTS OF HEALING PROPERTIES IN RHEUMATIC PATIENTS**

E. Ünal1, P. Kisacik1, G. Arin1, E. Karabulut2, D. Gökşülük2, N. Vardar Yalğı1, A. Aydın Özcan1, U. Berberoğlu1, N.B. Karaca1, A. Akdoğan3, Ö. Karadağ3, 1 Department of Internal Medicine, Rheumatology Subdivision, Hacettepe University, Ankara, Turkey

**Background:** Exercise programs have been providing in Hacettepe University for 12 years. The group exercises were transformed into a book named as "Bilisel Egzersiz Terapi Yaklaşımı (BETY)" (1) in 2014 and were registered as a trademark by the Turkish Patent Institute in 2015. This approach includes cognitive processes in pain management, clinical pilates exercises and awareness of mood state during patients therapy (2).When rheumatic patients participating in BETY sessions, they are evaluated with appropriate scales for their diseases and it is stated that these scales do not express enough the healing properties they feel with BETY.

**Objectives:** The aim was to develop a new scale assessing the biopsychosocial aspects of healing properties in rheumatic patients.

**Methods:** After 12 years of treatment, cognitive beliefs about health perceptions were gathered from the patients who participates in the BETY group for at least 5 years, with the open-ended question “What kind of changes did you make in this group? What kind of methodology did you apply?”. After that, 51 rheumatologists, 2 and physiatrists for expert opinion. 15 rheumatologists and 1 physiatrist were returned. When the survey items were examined on a question-based basis, the acceptance rate of all questions was 78.83%. According to this result, the scale was finalized. Structural validity of the created draft will be investigated in the subheadings of functional activity, pain, sexual life, fear of movement, and psychological health.

**Conclusions:** As a result, an original scale which will assess the biopsychosocial aspects of healing properties in rheumatic patients is developed. Our future purpose is to investigate the validation of this scale in different rheumatic diseases.

**References:**

**Acknowledgements:** The authors declare that they have no conflict of interest.

**Disclosure of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.6283
Results: The mean (SD) age was 59 (8) years, 63% were women. Self-reports of physical function (RMDQ) were 4.5 (4.8), health related quality of life (EQ5D) 0.71 (0.21), kinesiophobia (FABO-PA and FABO-Work) 8.3 (5.9) and 14.7 (11.1), and mental health (HAD-A and HAD-B) 8.8 (2.0) and 4.5 (1.7). Comparing the different screening methods, 5 patients (7%) were at high risk as captured by SBST while using the pain mannequin 38 (52%) patients had CWP and 22 (30%) had MS-CWP. No patients in the SBST high risk group had NCP, but 31 (50%) in the SBST low risk group reported CWP, and 16 (26%) reported MS-CWP. In the medium risk group 3 reported CWP, and 3 were also categorized as MS-CWP.

Conclusions: SBST and the pain mannequin as screening tools partly capture different patients at high risk of developing chronic back pain. Using a combination of the two instruments may improve the ability to triage to appropriate treatment level.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8065

**AB1200-HPR**
THE RELIABILITY OF ROMANIAN MORRIS DISABILITY QUESTIONNAIRE IN PEOPLE WITH LOW BACK PAIN: A PRELIMINARY STUDY

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Background: Patient reported assessments are widely recommended by the clinical guidelines and an important part of a comprehensive assessment. Patient-reported questionnaires should be translated into local language accordingly and validated in the translated language (1). The clinicians in Romania suffer from lack of validated questionnaires in Romanian language. The Roland Morris Disability Questionnaire is one of the most recommended questionnaires evaluating low back pain. Although, the Romanian translation was performed before, there is no effort regarding to its validation in Romanian language until now.

Objectives: To investigate the test-retest reliability Romanian version of the Roland Morris Disability Questionnaire (RMDQ-Ro) in people low back pain.

Methods: The permission to conduct such a study was asked to the original author Prof. Martin Roland, before starting to the study. The Romanian translated form of Roland Morris Disability Questionnaire which is provided on the web site “http://www.rmdq.org/” was used in the study. A total of 100 people with low back pain filled the RMDQ-Ro as well as Numeric Rating Scales for rest (NRS-R) and activity (NRS-A). Due to the lack of other validated measures such the Oswestry Disability Index in Romanian, these additional assessments (VAS-R and VAS-A) were performed for investigating convergent validity. For test-retest reliability 30 people filled the RMDQ-Ro after 3–14 days later as recommended. Test-retest reliability was assessed with intra-class coefficient correlation (ICC). Non-parametric tests were employed due to the heterogeneity of the data. Therefore, the Spearman correlation test was used for determining the relationship between RMDQ-Ro and VAS-R and VAS-A.

Results: The characteristics of the participants were shown at Table 1. The test-retest reliability of RMDQ-Ro was found at an excellent level (ICC: 0.95). Moderate positive correlations were determined between RMDQ-Ro and NRS-R (rho: 0.518, p<0.001), and NRS-A (rho: 0.484, p<0.001).

Table 1. Characteristics of the Participants

<table>
<thead>
<tr>
<th>Characteristics of the Participants</th>
<th>Male (n: 52)</th>
<th>Female (n: 48)</th>
<th>Total (n: 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median (IQR 25/75)</td>
<td>Median (IQR 25/75)</td>
<td>Median (IQR 25/75)</td>
</tr>
<tr>
<td></td>
<td>32 (28.5-46.5)</td>
<td>35 (28.5-54.5)</td>
<td>34.5 (28.5-46)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>179.5 (175/183)</td>
<td>168 (163/170.5)</td>
<td>174 (168/180)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81 (72/90)</td>
<td>61 (55.5/61)</td>
<td>71 (61/81.5)</td>
</tr>
<tr>
<td>RMDQ-Ro (0–24)</td>
<td>6 (3/8)</td>
<td>4 (3/7)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>NRS-R-a (0–10)</td>
<td>3.5 (2.5)</td>
<td>3.5 (2.5)</td>
<td>3.5 (2.5)</td>
</tr>
<tr>
<td>NRS-R-b (0–10)</td>
<td>2 (1.5)</td>
<td>3 (1.6)</td>
<td>2 (1.5)</td>
</tr>
</tbody>
</table>


Conclusions: RMDQ-Ro was found reliable regarding test-retest reliability. This questionnaire can be performed in the repeated measures for evaluating low-back pain patients. However, more psychometric characteristics of RMDQ-Ro such as internal consistency and construct validity should be investigated in further studies.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8649

**AB1201-HPR**
THE VALIDITY AND TEST-RETEST RELIABILITY OF THE TURKISH PATIENT SPECIFIC FUNCTIONAL SCALE IN CHRONIC NECK PAIN PATIENTS. A PRELIMINARY REPORT

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Background: Current clinical guidelines recommend to use both clinical and self-reported measurements for evaluation of chronic neck pain. Among the self-reported outcomes, Neck Disability Index (NDI) and Patient Specific Functional Scale (PSFS) are the most widely used and recommended instruments. Although, NDI was validated in Turkish language before, no validation study related to the PSFS was detected in the literature.

Objectives: The aims of this study were to translate PSFS in Turkish language and to establish the test-retest reliability and validity of the PSFS-T in chronic neck pain patients.

Methods: The PSFS was translated into Turkish by using the “translation-backward translation” method as recommended in the guidelines. The demographic information, PSFS-T and NDI were recorded at the first visit of the patients. Thirty patients were called by phone for the retest evaluation of PSFS-T. The construct validity of PSFS-T was determined by investigating the correlation between NDI and PSFS-T scores. The Cronbach’s alpha was used for the internal consistency. Intra-class coefficient (ICC) was employed to determine the test-retest reliability.

Results: The final form was completed by 42 chronic neck pain patients (18 F) until now. The mean age was 42±14. The internal consistency was found as good (Cronbach’s alpha:0.9). A positive moderate correlation was determined between NDI and PSFS-T scores (p<0.05; r=0.5). The ICC for test-retest reliability was determined in high level (ICC: 0.88).

Conclusions: The PSFS-T is a reliable and valid instrument for chronic neck pain patients. However, the preliminary results should be confirmed by completing the study.

References:


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5686

**AB1202-HPR**
RELATIONSHIP OF WORK DISABILITY BETWEEN THE DISEASE ACTIVITY, DEPRESSION AND QUALITY OF LIFE IN HOUSEWIFE AND WORKING PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The aim of this study was to determine the work status in patients with rheumatoid arthritis (RA) while also defining the factors related to work disability.

Objectives: In this study, our objective was to determine the work productivity, work disability and quality of life in time-off daily activities of the housewife and working patients with rheumatoid arthritis (RA) and to investigate the relation of the parameters with disease activity, anxiety, depression and quality of life.

Methods: 82 patients with the diagnosis of RA (26 males, 56 females) and 29 healthy control subjects (5 males, 24 females) were included in the study. In patients with RA, DAS28 was used to evaluate the disease activity. Duruöz hand index was used to determine the functional status. In addition, HAQ (Health Assessment Quality) and The Short Form (SF-36) Health Survey was used to evaluate the health status, Hospital Anxiety and Depression Scale (HADS) was used for the evaluation of depression and anxiety and Work Productivity and Activity Impairment Questionnaire: Specific Health Problem v2.0 (WPAI-SHP) was used to evaluate the work productivity.

Results: Demographic characteristics such as age and gender, were comparable in both patient and control groups (p>0.05). The difficulty in the time off daily activities were worse in the patient group compared with the control group (p<0.05). Anxiety, were significantly higher in housewife RA group (p<0.05). Difficulty in time-off daily activities was correlated with VAS-fatigue and DAS28,HAQ,Duruöz hand index was correlated. (p<0.05).

Conclusions: Even if they are not working in housewives, we have found that...
as much as the least active RA patients, it is difficult for activities in daily life, that the quality of life associated with the illness is low, and that depression and anxiety are similar to employees. As a result, disease activity, quality of life and functional status control in RA patients are as important as those who are working as housewives. Particularly in increasing productivity and participation in everyday activities, the mood is influential and it is must examine the patients in this regard. There is a need for more extensive cohort studies on this topic.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4614

AB1023-HPR COMPARISON OF QUALITY OF LIFE OF PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIARTHSITIS AND ANKILOSING SPONDYLITIS WITH TREATMENT OR PULSATION WITH BIOLOGIC DRUGS: RESULTS FROM THE CARA STUDY

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Background: Chronic rheumatic conditions such as rheumatoid arthritis (RA), ankyllosing spondylitis (AS), and psoriatic arthritis (PsA) are associated with severe morbidity and significant impairment of patients’ health related quality of life (HRQoL). Several treatments are available but not all the patients respond positively to them. Biologic therapies such as anti-TNFs agents are shown to benefit who fail or have partial responses to standard DMARD therapy.

Objectives: Within a multicenter stated preferances study (CARA Study), we assessed HRQoL in patients with RA, AS and PsA, and estimated relationship of HRQoL with the different diagnoses, clinical characteristics and biological treatment experience.

Methods: Patients with RA, AS, or PsA, who at the time of enrollment were following a treatment (experienced) or received a first prescription (naïve) of biological drugs were enrolled. Together with preferences data, clinical and HRQoL information was reported. HRQoL was assessed with the recently developed and successfully validated version of the EQ-5D-5L, which allows to obtain a description of health (in 5 domains and 5 levels of severity each), a measure (EQ-VAS) and a valuation (utility) of health. Multiple linear regression analyses were conducted to assess the association between EQ-5D VAS score, EQ-5D utility with age, sex, diagnosis, treatment experience, years from symptoms onset and years from diagnosis.

Results: 513 patients were enrolled (mean±SD = 50±13.6, 42.5% female). As regards the diagnosis, 33.9% had RA, 34.9% PsA and 31.2% AS. The mean±SD time from the symptoms onset was 10.8±5.4 and from the diagnosis was 6.0±6.2 years. Almost half of the patients (47.4%) were naïve to biological treatment. Patients reporting severe or extreme problems were: 7.1% in mobility, 3.6% in self-care, 10.3% in usual activities, 18.6% in pain/discomfort, 5.5% in anxiety/depression. The mean±SD of the VAS was 60±22.5 and of the utility was 0.77±0.11. From the regression model the VAS and utility are significantly (p<0.05) associated with age, sex and disease activity, treatment experience, years from symptoms onset and years from diagnosis.

Conclusions: Patients naïve to biological treatment have significant lower levels of HRQoL, suggesting that their current situation is not satisfactory and need to start with a more effective treatment.

DOI: 10.1136/annrheumdis-2017-eular.4904

AB1204-HPR EVALUATION OF CARBOHYDRATE METABOLISM IN RHEUMATOLOGIC PATIENTS AFTER PULSE THERAPY WITH GLUCOCORTICOIDS

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Background: Chronic inflammation – the crucial pathogenic mechanism of rheumatoid arthritis is the main cause of accelerated atherosclerosis, insulin resistance and well-known consequences related to it. The conservative treatment of rheumatoid arthritis may provide a significant influence on glucose metabolism. When the duration of rheumatic diseases of administration and dosage of glucocorticoids (GC) are significant predictors of the development of impaired glucose tolerance and diabetes mellitus.

Objectives: To study the effect of pulse-therapy (PT) of the GC on the violation of carbohydrate metabolism in rheumatologic patients.

Methods: The study included 35 patients (7 men, 18 women) with a variety of rheumatic diseases (systemic lupus erythematosus - 23, systemic vasculitis - 12) between the ages of 18 to 68 years (mean age 42.3±14.3 years) and duration of disease from 6 months to 12 years (mean 3.55±3.36 years). Pulse-therapy of GC included intravenous prednisolone 600–1000 mg per day for 3 consecutive days (course dose of 1800–3000 mg). Oral glucose tolerance test (OGTT) was performed after the course. The first group included patients with a normal result of OGTT (glucose concentration of <7.8 mmol/L at 2 hours after taking 75 g of glucose). There were 23 patients in this first group at the age of 30–54 years and 8±0.2±1.6 days (p<0.05) at the age of 52±6±4 years. The second group had OGTT was >7.8 mmol/L. This group included 12 people aged from 44 to 61 years (mean age 52±6±4 years).

All patients underwent the measurement of blood glucose levels prior to PT, 2, 4, 6, 10, 24, 48 and 72 hours and after the PT.

Results: All patients included in the study, after the PT session there was an increase in blood glucose levels with a peak at 4 hours after the start of administration - 12±0.82 in the first group, in the second to 21.95±0.25 mmol/L (p<0.05). Normalization of glucose levels in the first group of patients occurred within 1.75±0.18 days (1 to 3), whereas in the second - for 5.0±1.0 (3 to 5; p<0.05). During the OGTT the mean fasting blood glucose levels in patients with the first group was 4.49±0.12 mmol/L, and the second - 5.85±0.35 (p<0.05), after 2 hours - 6.0±0.21 and 10.0±1.5 mmol/L, respectively (p<0.05).

Conclusions: Application PT of GC in rheumatologic patients causes blood glucose levels to change values, indicating the development of impaired glucose tolerance. Predictors of disorders of carbohydrate metabolism in these patients are high levels of glycemia during the PT more continuous glucose normalization indices after the course PT GC.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1169

AB1205-HPR THE EFFECTS OF KINESIOTAPING ON JOINT POSITION SENSE AND POSTURAL STABILITY FOLLOWING FATIGUE PROTOCOL

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Background: Muscle fatigue is common in sports activities and has been shown to adversely alter proprioception, impair neuromuscular control, and increase the risk of injury. Kinesiotaping has recently gained popularity among sports professionals for its assumed injury prevention and performance enhancement (1). Two studies have reported conflicting findings with respect to the effects of KT on proprioception. Halseth et al reported that KT produced no significant change in the absolute error in ankle joint position sense (2). However, Chang et al reported that KT decreased the force sense error in grip strength measurements among 21 healthy college athletes (3). Thus, the current literature does not provide clear information about the effects of KT on proprioception. Although there are published articles about investigating KT on joint position sense and postural stability, the effects of KT is still unknown after muscle fatigue, to our knowledge.

Objectives: There is a lack of literature examining the KT on joint position sense and postural stability following fatigue protocol. Therefore, the aim of this study was to investigate the effects of KT on knee joint position sense and postural stability after muscle fatigue. It was hypothesized that KT applied on quadriceps femoris muscle would partially compensate for the proprioceptive and postural stability losses caused by muscle fatigue.

Methods: Thirty – six healthy subjects were evaluated in the study. Knee joint position sense was assessed by Biodex System Pro 4 during active repositioning tests at the target angles of 30°, 50° and 70° of knee flexion in sagittal plane. Postural stability was assessed by Pedalo Sensamove® System in antero –
posterior and medio – lateral plane. Joint position sense and postural stability were assessed three times: during rest, following the fatigue protocol, and following the taping. The subjects were received a clinically-used fatigue protocol on a cycle ergometer. The Modified Borg’s Rate of Perceived Exertion Scale has been used for fatigue determination. 

Regarding position sense and postural stability were significantly decreased following fatigue compared to the condition during rest (p < 0.05). However, no significant difference was found in terms of joint position sense and postural stability after taping compared to the condition following fatigue (p > 0.05).

Conclusions: The hypothesis of this study, that KT could partially compensate for the proprioceptive and balance-related deficits induced by muscle fatigue, was not supported. According to the results of our study, we concluded that the subjects do not benefit from the use of KT for compensating joint position sense and postural stability in condition following fatigue.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5888

AB1206-HPR

ADAPTATION INTO SPANISH OF THE SCLERODERMA HEALTH ASSESSMENT QUESTIONNAIRE (S-HAQ)

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Statistics, British Hospital, Buenos Aires; 6Luis Lagomaggiore Hospital, MENDOZA, Argentina; 7Georgetown University, Washington, United States

Background: The Health Assessment Questionnaire (HAQ) is an instrument administered to patients to self-report functional status originally in rheumatoid arthritis (RA). In Argentina, it has been translated and validated for RA in 2004.

For diffuse SSC, HAQ has been associated to morbidity and mortality.

Objectives: To adapt S-HAQ into Spanish and to assess its validity in SSC patients in Argentina.

Methods: S-HAQ was translated following a forward-backward translation procedure of the original English version, and transcultural adaptation was performed by a comprehension test reaching the final Spanish version. SSC patients that fulfilled ACR 80 criteria and early Systemic Sclerosis according to Le Roy and Medsger criteria were included. Patients with overlap were excluded. Cronbach’s alpha and item-total correlation were used to assess internal consistency.

Construction validity was analyzed through factor analysis with Varimax rotation. Construct validity was compared by t-test, Mann-Whitney or Kruskal-Wallis test, and categorical variables by chi-square or Fisher’s test. A value of p < 0.05 was considered significant.

Results: 19 an adapted Argentine-Spanish version of S-HAQ was developed. One hundred patients were surveyed; 84% were female, mean age 54±12.8 years and disease duration 8.8±1.9 years. Limited SSC was more frequent (63%), followed by diffuse SSC (36%). Serologically, 89% were ANA positive, 27% had anti Scl 70 and 41% had anti centromere antibodies. Median Rodnan score (mRSS) was 9.8 (±4.05) and median activity measured by EUSTAR was 1.25 (0–6). Median S-HAQ was 0.62 (0–2.5), Cronbach’s alpha 0.89, and when removing questions one by one the coefficient decreased. Median VAS (visual analogue scale) was 0.57 (0–2.8). Factor analysis identified two factors for the S-HAQ: factor 1: dressing (0.61), arising (0.68), reaching (0.63), and personal hygiene (0.70); factor 2: reaching (0.49), usual activities (0.68). For questions, these factors were identified through VAS: factor 1: overall disease severity (0.63) and gastro-intestinal symptoms (0.57); factor 2: Raynaud’s (0.66), digital ulcers (0.56); factor 3: respiratory symptoms (0.43). There was a statistically significant association between higher values of S-HAQ and higher values of mRSS (1.1±0.74 vs. 0.64±0.5 p=0.002) and also with seropositivity for anti-Scl 70 (p=0.003). Higher values of total VAS were associated to female gender (0.75±0.5 vs. 0.49±0.71, p=0.01). There was a significant association between S-HAQ and MEDSGER (p=0.04) and EUSTAR (p=0.03) scores; likewise, between VAS and MEDSGER (p=0.09) and EUSTAR (p=0.03) scores.

Conclusions: A Spanish version of S-HAQ was developed, showing an acceptable reliability and validity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4025

AB1207-HPR

PATIENT SATISFACTION IN A RHEUMATOID ARTHRITIS SPECIALIZED CENTER

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Background: According to the Beryl Institute’s, patient experience (PX) is “the sum of all interactions, shaped by an organization’s culture, that influence patient perceptions across the continuum of care”. Nowadays patient satisfaction is considered as one of the quality for performance in health systems [1]. In order to provide a multidisciplinary quality care to patients with RA in centers of excellence (CoEs) under the coordination of a rheumatologist, provide comprehensive management of patients with this pathology, ensuring a probability to medical appointments and treatment, in order to get better clinical outcomes and improve patient safety and satisfaction of the health services provided.

Objectives: To measure levels of satisfaction of RA patients treated at a specialized center and to evaluate patient service.

Methods: In a RA specialized center during a 24 month period we performed a satisfaction survey in order to evaluate the health services provided. We evaluated the timing on appointment, appointment assignment, information provided, the treatment received by the healthcare team, facilities among others. Patients evaluated the services provided in a scale from 1 to 4, were 1 was very bad, 2 regular, 3 good and 4 excellent. Descriptive epidemiology was performed for each variable presented.

Results: We collected 1125 surveys during 2015 and 2016, 45% considered to have a timely care, the mean of waiting time for an appointment was 9 min ± 8; regarding the appointment assignment 96% of the patients evaluated it as good or excellent (mean 3.5±0.7), 80% considered that the information provided was clear and useful, 90% reported to receive a kind and friendly treatment and to considered the facilities as good or excellent. When we evaluated the satisfaction regarding the health care team 50% of patients evaluated the rheumatologist, nurse, nutritionist, physical therapist, psychologist and physiatrist as good and 40% as excellent.

Conclusions: Although we found that our patients are highly satisfied, there is a large opportunity to improve our services. Also, this evidence can support further research projects in order to increase the patient’s satisfaction.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5380

AB1208-HPR

PSORIASIS INDUCED BY TNF ANTAGONIST THERAPY. ANALYSIS OF 13 CASES

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Background: Tumor necrosis factor (TNF) antagonist drugs have been shown to be effective in different inflammatory arthropathies and autoimmune pathologies, including psoriasis. However, an unexpected side effect has been observed: the new occurrence or worsening of psoriasis in patients treated with TNF antagonist therapy in our center.

Objectives: The aim of this study is to describe the cases of induction or worsening of psoriasis in patients treated with TNF antagonist therapy in our center.

Methods: Retrospective observational study, review of cases of new or worsening psoriasis in patients with TNF antagonist at the University Hospital Dr. Peset from October 2008 to November 2016. A total of 13 cases were obtained.

Results: Thirteen patients, 8 females and 5 males with mean age 46 years (±16), 38% of patients received treatment for Crohn’s disease, 31% for rheumatoid arthritis (RA), 31% for psoriatic arthritis (PsA), 8% for ankylosing spondylitis (AS) and another 8% for psoriasis. Two patients were diagnosed of more than one pathology: Crohn’s disease associated with PsA and Crohn’s disease associated with RA. Sixty one percent had no known personal history of psoriasis, in one of these patients the family history of psoriasis was recorded. Infliximab was used in 38% of cases, followed by adalimumab and golimumab in 23% each and etanercept in 15.4%. The mean latency time since drug introduction was 9.3 months (2–26). There were 12 cases of psoriasis and 1 case of pityriasis lichenoides (histologically confirmed). Lesion morphology included pustular psoriasis in 91%, scalp psoriasis in 8%, and guttate lesions in 25%, plaques psoriasis in 8%, and inverse psoriasis in 8%; 58% experienced lesions of more than one type. There were no cases of nail, mucosal or erythrodemic psoriasis. The psoriasisform lesions resolved without interruption of TNF antagonist therapy in 53.85%. Of the 6 patients who required discontinuation, 3 patients were switched to another anti-TNF drug (adalimumab,
golimumab and certolizumab) and all 3 had recurrence of the lesions, in 2 patients the anti-TNF was replaced by a non-anti-TNF biological. Topical treatment was used in all cases, one patient also required systemic treatment with methotrexate.

Conclusions: TNF antagonist induced psoriasis is a well-described adverse event. Pustular psoriasis is the most frequent presentation. In most cases there is no personal or family history of psoriasis. Topical therapy may be effective but some patients require discontinuation of the drug. Skin lesions can reappear when switching to another anti-TNF drug.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2877

AB1210-HPR  THE PREVALENCE OF DENTAL AND SINUS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE BIologic THERAPY INITIATION: USEFULNESS OF A SYSTEMATIC SCREENING?

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Background: Introduction of the biologic therapies has dramatically improved the outcome of severe rheumatoid arthritis (RA). Biologic therapies play a central role in the control of synovial inflammation. However they also decrease host defenses leading to an increased rate of infection. Because of their adverse effects, a careful assessment is needed before their initiation. A systematic assessment of dental and sinus infections before a biologic therapy is not required.

Objectives: The aim of our study was to assess the prevalence and the usefulness of a systematic screening of oral (dental and/or sinus) infection of RA patients before biologic therapy initiation.

Methods: This was a monocentric retrospective study. We included RA (ACR/EULAR 2010 criteria) patients with active disease despite disease-modifying anti-rheumatic drugs (DMARDs) and requiring biologic therapy initiation between 2010 and 2016. The following parameters were collected: demographic and disease characteristics, disease activity (CRP, disease activity score (DAS) 28), current therapies (DMARDs, corticosteroids). Dental infections were assessed by stomatologist after clinical and panoramic dental X-ray evaluation. Sinusitis was defined on sinus computed tomography as partial or complete opacification of one or more sinuses cavities. Factors associated with oral infections were analyzed in uni- and multivariate models.

Results: We included 223 RA patients (79.4% of female, mean ± SD disease duration of 8.9±8.6 years). The mean age was 54±10.9 years, 70.3% rheumatoid factor (RF) positive, 64.4% anti–citrullinated protein antibody (ACPA) positive and 68.1% had radiographic damages. The mean DAS 28 was 5.5±2.6; 71% of patients received corticosteroids (mean 7mg per day of equivalent prednisone) and 63% methotrexate (mean 17.8mg per week). No patient had pain or other sinus or dental symptoms. Before biologic agent initiation, systematic dental and sinus screening revealed an oral infection in 31.5% of patients (dental: 20.2% and sinus: 14.8%). In univariate analysis, active smoking was associated with a higher risk of oral infection (OR=2.16 [1.02–4.57], p=0.038) and methotrexate with a lower rate (OR=0.43 [0.23–0.81], p=0.006). Corticosteroid, disease duration, DAS 28, RF, ACPA and structural damages were not associated with oral infection. No significant association was confirmed with oral infection using multivariate analysis.

Conclusions: In our study, one third of RA patients requiring biologic agents had asymptomatic oral infection. The high prevalence of oral infection in RA patients suggests the usefulness of systematic dental and sinus screening before biologic therapy initiation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5601

AB1211-HPR  THE USE OF SUBCUTANEOUS METHOTREXATE IN POLISH PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (Mtx) should be the drug of the first choice in rheumatoid arthritis (RA) if there are no contraindications to use it. The efficacy of Mtx is measured by remission or low disease activity and depends on the dose taken. Higher doses (25–30 mg/week) are more effective, but intolerance is the main cause of discontinuation of oral treatment. Subcutaneous Mtx is efficient alternative in those cases.

Objectives: The aim of this study was to evaluate subcutaneous Mtx use frequency in Polish patients and change oral form for subcutaneous as well.

Methods: The disease activity was assessed by Disease Activity Score 28 (DAS 28) during the first visit (V1) and after 3 months therapy (V2) and compliance with therapy as well.

Results: There were 194 RA patients diagnosed by the ACR and 1997 and/or ACR/EULAR 2010 criteria. 144 patients were treated by oral Mtx (group A) and 50 patients (group B) by subcutaneous Mtx at the time of study enrolment (V1). 37 patients of group A (28%) required changes in therapy during V2. 24 (17%) were switched to subcutaneous Mtx (group A1). 6 patients of group B (12%) required change of treatment during V2, including 2 patients (4%) with subcutaneous Mtx, who were switched to oral Mtx. The main cause of changing therapy from oral to subcutaneous was gastrointestinal intolerance of high dose of Mtx. 69 patients (12%) of group A required additional steroid therapy compared to 18 (36%) of group B. Average DAS 28 decreased by 0.58 in group A1 in oral treatment and during the subcutaneous treatment time decreased by next 0.23, in group A1 during oral treatment 14 (58%) patients used 25 mg/week and 20 patients (83%) used 25 mg/week during subcutaneous treatment time.

Conclusions: Patients treatment by oral Mtx often require modification of therapy in comparison to patients treated by subcutaneous Mtx, including more frequent use of steroids.

The main cause of oral intolerance are ailments of the digestive system. Change of oral to subcutaneous therapy allows administration of higher doses of Mtx and results in decrease of DAS28 in comparison to the patients continuing their oral treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6963

AB1212-HPR  DYNAMICS OF ARTICULAR SYNDROME IN RHEUMATOID ARTHRITIS AGAINST CORRECTION OF PROGESTERONE INSUFFICIENCY

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Background: According to the literature, sex hormones manifest themselves as immune modulators that inhibit the ones and stimulate other immune functions. Studies have shown that patients with RA, decrease of estradiol and particularly
progesterone in the blood serum is found in the women of reproductive age. According to the literature, progesterone has a close relationship with T-cell immunity. A value of T-cell deficiency plays an important role in the cause of the autoimmune process.

**Objectives:** To study of progesterone correction in RA patients. The aim of this study was to evaluate the effectiveness of progesterone deficiency correction in patients with rheumatoid arthritis based on the analysis of articular syndrome

**Methods:** The study involved 40 patients with a documented diagnosis of RA, women of reproductive age. The study group consisted of 30 patients who had correction of progesterone deficiency background in the pathogenic therapy. The control group consisted of 10 female patients who are on the pathogenic therapy. We used the following criteria: disease activity and severity of the articular syndrome with determining of the number of tender and swollen joints, indices of DAS and HAQ. Statistical analysis of the results of research used the method of parametrics of Student criterion

**Results:** Among the patients studied disease duration ranged from 3 months to 19 years (mean age 10±7.2 years), 20 patients (50%), from 5 to 10 years – 15 (37.5%), and more than 10 years – 5 patients (12.5%). X-ray picture of joint damage in the majority of patients corresponded to stage 2–3 – 87.5% (35 patients). Less common muscular disorders (7.5%), mainly in patients taking long-term GC, myalgia and muscle malnutrition were detected in 7.5% and 25% of patients, respectively. In addition to the articular syndrome, the most frequent complaints of general weakness (75%), irritability, sleep disorders and attention (50%), anxiety and anxiety (75%), low-grade temperature (10%).

**Conclusions:** Progesterone deficiency correction in RA patients against pathogenic therapy has improved performance of articular syndrome and improves quality of life, such as vitality, general health and social function as well as it contributes to the positive dynamics of mental health.

**References:**

2. Wells G et al. Validation of the 28-joint Disease Activity Score (DAS28) and it contributes to the positive dynamics of mental health.

**AB1213-HPR**

A NATIONAL RHEUMATOID ARTHRITIS REGISTRY SUPPORTED BY A PUBLIC POLICY AS A STRATEGY FOR DISEASE CONTROL AND RISK MANAGEMENT IN COLOMBIA

**Background:** Rheumatoid arthritis (RA) is a chronic disease that implies high direct and indirect costs for the health system (1.2). According to the needs of the health care system, the clinical interests and the national regulatory framework, it was developed a national registry information of RA patients (3).

**Objectives:** To show how a registry of information that would meet the RA situation was developed and to present the results obtained from the analysis of the Registry on this first year.

**Methods:** A national RA Registry was created after a comprehensive literature review to identify the relevant variables to determine monitoring indicators used by health insurers and health services providers in the attention of patients with RA. Variables were selected and defined by an agreement with clinical experts, rheumatic and methodological experts and were evaluated by the Ministry of Health in order to review and approve the structure to gather the information.

**Results:** A structure of 89 variables contained was defined. All entities must report annually to the Registry all the patients with a diagnosis of RA, their clinical and demographic characteristics, and the process of care and costs (3). On its first year the Registry provided a baseline of the disease situation of 68.357 patients with RA. Prevalence, incidence, state of disease and drugs including synthetic and biologic DMARDs were analyzed (Table 1). Most important results were: mean age 57 years; relation women: men 5.2:1; age at onset of disease: 36 years; mean evolution time of disease-7 years; population with DAS 28 measured 45.6%; mean DAS-28 2.8; percentage of the patient with DMARD therapy 78.9% and bDMARD 16.5%.

**Conclusions:** A national Registry supported by an official policy, with data from the real world provided for healthcare insurers gives an opportunity to obtain a global vision and to identify failures and strengths in the attention process of RA, and to develop indicators to obtain better outcomes. In the future, through continuous efforts towards improving the quality of care provided, these will allow to monitoring and decreasing the burden of RA in the country and may serve as a model to other countries.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1306

**AB1214-HPR**

**AB1215-HPR**

**SPINAL BRUCELLOSIS: A RETROSPECTIVE STUDY OF 30 CASES**


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**Background:** Brucellosis is a major health problem in Mediterranean countries including Tunisia. The clinical presentation of this zoonosis varies considerably but osteoarticular involvement and spinal brucellosis particularly is the commonest complication.

**Methods:** This study was carried out between 2000 and 2015. One hundred and six patients with infectious spondylodiscitis hospitalized in the department of rheumatology were analyzed. All patients were thoroughly interrogated subjected to a rigorous clinical examination aned, battery of investigations including: complete blood count, urine analysis, blood culture, erythrocyte sedimentation rate, C - reactive protein (CRP) and serology for brucellosis. The imaging of spine ordered including: X-ray, bone scan and magnetic resonance imaging (MRI) with contrast enhancement.

**Results:** Thirty of the 106 patients (28%) proved to have spinal brucellosis. The mean age of these patients was 53 years (range 15–68 years) and female/men ratio at 1.5. The mean delay of diagnosis was 8 months. The following symptoms were observed: fever in 14 patients and back pain in all of patients. Other symptoms were less frequent observed, such as splenomegaly (2 patients), peripheral adenopathy (5 patients) and diarrhea (2 patients). Laboratory exams showed elevated erythrocyte sedimentation rate in 13 patients, high levels of CRP in all patients and leukocytosis in 11 cases. Wright serology was positive in 21 of the patients. Brucella melitensis was isolated in blood cultures in 2 cases. Standard X-rays were performed in all patients. They showed signs of spondylodiscitis in the lumbar spine in 20 cases, cervical in 2 cases and dorsal in 8 cases. Ct-scan and MRI confirms the diagnosis and showed associated epiduritis in 2 cases or abscess in 6 cases. Bone biopsy with histopathological examination was performed in 7 cases. A combination of rifampicin and doxycycline was given to all patients. The duration of therapy was between 6 and 8 weeks.

**Conclusions:** Brucellosis is present with various clinical signs in endemic areas and may simulate many diseases. The need for prompt diagnosis and treatment of spinal brucellosis is of utmost importance to prevent serious bone destruction and severe neurological Sequelae.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.6301

**HPR interventions (educational, physical, social and psychological) —**

**AB1215-HPR**

**EFFECTS OF BEETROOT JUICE SUPPLEMENTATION N ENDOXILATION FUNCTION AND MARKERS OF INFLAMMATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Nitric oxide (NO) is central in the process of vasodilatation (1). Limited bioavailability of NO often associates with endothelial dysfunction, a precursor to atherosclerosis (1). Such dysfunction is often observed in patients with chronic conditions such as Rheumatoid Arthritis (RA) (2) and Chronic Obstructive Pulmonary Disease (COPD) (3). Common therapies for this include the administration of nitrate-rich medication. However, in the general population beetroot juice supplementation has been shown to increase NO bioavailability (4). It could therefore have beneficial effects on endothelial function of these patients as well.
AB1216-HPR
THE EFFECTS OF APPLICATION OF IONTOPHORESIS AND PHONOPHORESIS IN PATIENTS WITH SUBACROMIAL IMPINGEMENT SYNDROME
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¹Physiotherapy and Rehabilitation, Marmara University Health Sciences Faculty; ²Physiotherapy and Rehabilitation, Kosyolu Medipol Hospital, Istanbul, Turkey

Background: Subacromial impingement syndrome (SIS) is defined as the mechanical compression of subacromial structures between the coraco-acromial arch and the humerus during active elevation of the arm above shoulder height. Objectives: The aim of this study was to investigate the effects of applications of iontophoresis and phonophoresis, which has been used in addition to physiotherapy program on pain and disability level in patients with SIS.

Methods: The study was conducted with subjects (n=43) diagnosed with SIS. The subjects were divided into two groups randomly as iontophoresis group (IG) and phonophoresis group (PG). Diclofenac sodium iontophoresis was applied to the first group (n=22), diclofenac sodium phonophoresis was applied to the second group (n=21). In addition all of groups therapy program includes superficial heat, transcutaneous electrical nerve stimulation and exercise. The groups were evaluated before and after treatment in terms of pain and scores of shoulder disability. Visual analog scale was used to assess of pain (night pain, rest pain, pain with motion and pain in functional use), Shoulder Disability Questionnaire (SDQ) and Disabilities of the Arm Shoulder and Hand (DASH) were used to assess of shoulder disability.

Results: 43 patients with age range of 18 to 65 years were recruited in this study. After treatments pain severity (night pain and pain in functional use) was decreased in both groups (p<0.05) and in the scores of disability of shoulder (p<0.05) in both groups. Pain relief was similar in groups. SDQ and DASH scores remained relatively unaffected by blackcurrant consumption (Overall: 3.9% [0 – 5.1] vs 4.2% [2.3 – 6.1]; p=0.26).

Conclusions: A two week consumption of beetroot juice seems to be able to significantly improve endothelial function both in RA and COPD. A two week consumption of beetroot juice is a safe supplement for both patients’ groups (RA: 2.6% [0.9 – 6.2] vs 10.7% [6.2 – 11.7], p=0.013; COPD: 3.4% [1.2 – 4.8] vs 7.8% [3.6 – 10.2], p=0.034).

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4519

Table 1. The level of pain, functionality and disability scores in groups

<table>
<thead>
<tr>
<th></th>
<th>IG Before</th>
<th>SD mean ± sd</th>
<th>p</th>
<th>PG Before</th>
<th>SD mean ± sd</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night pain severity</td>
<td>5.59±3.01</td>
<td>1.77±1.99</td>
<td>*</td>
<td>4.47±2.42</td>
<td>1.42±1.8</td>
<td>*</td>
</tr>
<tr>
<td>Severity of general pain</td>
<td>5.09±1.23</td>
<td>2.63±1.59</td>
<td>*</td>
<td>5.42±2.17</td>
<td>2.28±1.45</td>
<td>*</td>
</tr>
<tr>
<td>SDQ</td>
<td>48.00±10.26</td>
<td>28.38±20.41</td>
<td>*</td>
<td>3.39±0.12</td>
<td>2.18±0.55</td>
<td>*</td>
</tr>
<tr>
<td>DASH</td>
<td>38.90±14.74</td>
<td>19.36±9.37</td>
<td>*</td>
<td>4.17±5.93</td>
<td>2.64±10.37</td>
<td>*</td>
</tr>
</tbody>
</table>

IG: Iontophoresis group, PG: Phonophoresis group. *p<0.001.

DASH scores were improved in two groups after treatments. But there was no difference between the groups in terms of functionality and disability scores. Conclusions: This study shows that diclofenac sodium iontophoresis and phonophoresis that are used in patients with subacromial impingement syndrome have similar positive therapeutic effects on shoulder functions.
EFFECTIVENESS OF PLATELET-RICH PLASMA ON FUNCTION AND PERFORMANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS: PRELIMINARY RESULTS

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Background: Osteoarthritis is one of the most painful conditions and the most frequent cause of functional limitation and disability. There are variety of methods used in osteoarthritis (OA) treatment, including, physical therapy, exercise, intraarticular injections, surgery, etc. Platelet-rich plasma (PRP) is a relatively new autologous biologic treatment that is used for stimulating cartilage healing process and improving the symptoms. Although the effects of PRP injection on pain and function investigated before, as to our knowledge there are no studies related to performance.

Objectives: Aim of this study was to investigate effectiveness of PRP on improving function and performance in patients with knee osteoarthritis.

Methods: This study included 28 patients (16 F, 12 M) who were affected by grade 1–3 bilateral knee OA according to Kellgren-Lawrence Scale. Patients received three injections of PRP that were performed at monthly intervals by the same doctor. All patients were evaluated before and six months after the first injection. Primary outcome measures were: Stair Climbing Test (SCT), 50-Foot Walk Test (50 FWT), 30-sec Chair Stand Test (30 CST) and Timed Up and Go Test (TUG). IOWA Score. Additionally, Hospital for Special Surgery Score (HSS) was also recorded as a secondary outcome measure. Wilcoxon signed-rank test is used for interpreting the differences between before and after the injections.

Results: All patients completed the study with no adverse effects. The mean age of the patients was 67.6 years (range 29–83). Improvements were determined for all outcome measures after 6 months regard to baseline results (p<0.01) (Table 1).

Table 1. Comparison of Primary and Secondary Outcomes at Baseline and After 6 months.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Baseline Median (IQR)</th>
<th>After 6 months Median (IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stair Climbing Test</td>
<td>16(10.55/19.75)</td>
<td>13.1 (8.26/16.75)</td>
<td>0.001</td>
</tr>
<tr>
<td>50-Foot Walk Test</td>
<td>29.5 (27.03/32.45)</td>
<td>27.26 (25.13/30.32)</td>
<td>0.001</td>
</tr>
<tr>
<td>30-sec Chair Stand Test</td>
<td>10.5 (9.3/14.0)</td>
<td>12.5 (10.15/15.75)</td>
<td>0.001</td>
</tr>
<tr>
<td>Timed Up and Go Test</td>
<td>9.25 (7.25/14.5)</td>
<td>8.1 (6.58/10.15)</td>
<td>0.001</td>
</tr>
<tr>
<td>IOWA Score</td>
<td>10.2 (8.9/12.87)</td>
<td>9.8 (8.12/10.75)</td>
<td>0.008</td>
</tr>
<tr>
<td>HSS Post</td>
<td>63.5 (55.0/75.0)</td>
<td>75.66 (66.6/78.75)</td>
<td>0.001</td>
</tr>
<tr>
<td>HSS Left</td>
<td>68.65 (55.29/79.25)</td>
<td>78.5 (70.80/85.0)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: Our preliminary findings show that PRP is safe and effective autologous biologic agent that might improve function and performance in patients with mild to moderate knee OA and; could be considered as a treatment option in patients with knee OA.

Disclosure of Interest: None declared


EXPERIENCES OF SWEDISH “PAIN SCHOOL - COMPETENCE FOR LIFE” OF PATIENTS WITH CHRONIC WIDESPREAD PAIN - A QUALITATIVE INTERVIEW STUDY

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Background: Chronic pain is generally associated with low activity level, low work capability, and negative health consequences (1). Education and exercise have shown effective results for patients with chronic pain (2), and is according to EULAR 2016 recommendations first line interventions for patients with fibromyalgia (3). This educational program “Pain school - Competence for life” for patients with chronic pain was developed by the Swedish Rheumatoid Association together with health care professionals for use in primary health care, but is not used in clinical practice. The aim of the study was to describe the participants’ experiences of the educational program, was held 10 weeks after completion of four educational group sessions. Interviews were conducted by two authors and transcribed verbatim.

Methods: One theme and four categories were identified. An overarching theme, increased understanding and support to patients.

Results: We found optimal adherence in 52% of patients: the average (SD) adherence rate was 71.1±9.42. We didn’t find any significant differences between adherent and nonadherent patients regarding patient age, gender, the diagnosis of rheumatic disease and disease duration time, however, patients with higher education level (at least graduate level) were more compliant than those without any formal education (p<0.006). In addition there was no association between adherence and the type of medication (csDMARD, bDMARD) (p=0.39). Patient data are presented in the table 1.

Table 1. The adherence according to the patient diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
<th>Adherence</th>
<th>Total score</th>
<th>Mean (SD)</th>
<th>Leahest adherent (%)</th>
<th>Most adherent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA 65 (56%)</td>
<td>10.8</td>
<td>69.90 (9.56)</td>
<td>12 (28%)</td>
<td>29 (28%)</td>
<td>58% (28%)</td>
<td>0</td>
</tr>
<tr>
<td>PSA 14 (12%)</td>
<td>14.7</td>
<td>74.18 (10.62)</td>
<td>3 (22%)</td>
<td>7 (71%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>AS 14 (12%)</td>
<td>9.7</td>
<td>73.43 (10.73)</td>
<td>2 (14%)</td>
<td>22 (78%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other 22 (20%)</td>
<td>12</td>
<td>70.81 (11.59)</td>
<td>6 (27%)</td>
<td>12 (55%)</td>
<td>15% (55%)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Our study showed lower adherence rate than expected. To improve patient adherence we should work more in the future on providing additional knowledge and support to patients.

Acknowledgements: Special thanks to our colleagues Tadeja Šušteršič and Aliba Stanovnik

Disclosure of Interest: None declared


COMPARISON OF DMARD THERAPIES ON NSAID INTAKE, DISEASE ACTIVITY, FEAR OF MOVEMENT, AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) may result in loss of mobility and function; therefore, patients can experience pain and stiffness with a loss of physical function in addition to severe impairment in their quality of life. Standard treatment of AS consists of nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy.

They expressed new strategies relating to managing pain, physical activity, and everyday life. Both individual and social value of participation was described, such as increased well-being, decreased anxiety and improved relationships. Group dynamics, structure of education and former knowledge was described to predispose change in perception of pain and lifestyle.

Conclusions: The results provide deeper knowledge about patients’ experiences of the educational program Pain School Competence for life. The educational program appears to provide a meaningful and well-functioning structure for education for patients with chronic widespread pain in primary health care. Further, this can contribute to improve education and rehabilitation for patients with CWP provided by physiotherapists and occupational therapists in primary health care.

References:

Disclosure of Interest: None declared

Objectives: The aim of this study was to compare the effectiveness of DMARD therapies on requirements for NSAIDs, disease activity, fear of movement, and quality of life in AS patients.

Methods: A total of 74 patients diagnosed according to the modified New York criteria for AS were enrolled. To calculate NSAID intake, the type of NSAID, dose, and percentage of days with intake were recorded in conjunction with DMARD therapy, age, body mass index (BMI), and disease duration. Patients were assessed to measure several parameters: 1) disease activity using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); 2) fear of movement as assessed by the Tampa Scale for Kinesiophobia (TSK); and 3) quality of life using the Ankylosing Spondylitis Quality of Life Scale (ASQoL) from the patient’s perspective.

Results: Seventy-four patients (36 women, 38 men; mean age: 43.8±10.18 years; mean disease duration: 9.8±5.50 years; BMI: 28.20±5.07) treated with different DMARDs (ADA+GO=17; Infliximab [INF/X]=19; Etanercept [ETA]=13; Sulphasalazine [ST]=25) were included. NSAID intake was significantly lower in the INF/X group compared to the ADA+GO (mean: 28.1±81.5) compared to the ADA+GO (mean: 33.3±76.0), ETA (mean: 33.5±58.2), and ST therapy groups (mean: 68.1±76.1) (p=0.003). BASDAI scores (mean: 3.9±2.4), NSAID intake (mean: 68.1±76.1; p=0.003), and ASQoL scores (mean:10.2±7.4) were significantly higher in the ST group compared to the other drug groups. TSK scores were also similar between different NSAID intake groups (p=0.089).

Conclusions: According to our results, ST was not effective enough even with concomitant therapy consisting of a single oral dose of NSAID or standard doses of concomitant drugs in terms of disease activity, fear of movement, and quality of life in AS patients.

References:

Acknowledgements: We would like to thank Rheumatology Nurse Ayten Yuxsek in our department for monitoring and documenting of the data, and our patients for assistance with their valuable participation to our study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1391

AB1222-HPR

EXERGAMES VERSUS SELF-REGULATED EXERCISES WITH INSTRUCTION LEAFLETS TO IMPROVE ADHERENCE IN GERIATRIC REHABILITATION: A RANDOMIZED CONTROLLED TRIAL

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Background: Improving mobility in elderly persons is a primary goal in geriatric rehabilitation (Bachmann 2010). Self-regulated exercises with instruction leaflets are used to increase training volume but adherence is often low. Exergames may improve adherence. This study therefore compared exergames with self-regulated exercise using instruction leaflets.

Objectives: To evaluate short-term effects of exergames versus self-regulated exercise using instruction leaflets. Primary outcome was adherence. Secondary outcomes were enjoyment, motivation and balance.

Methods: Design: single center parallel group non-blinded randomized controlled trial with central stratified randomization (Hasselmann 2015). Setting: center for geriatric inpatient rehabilitation. Included were patients over 65 with mobility restrictions who were able to perform self-regulated exercise. Patients were assigned to self-regulated exercise using a) exergames on Windows Kinect® (exergame group EG) or b) instruction leaflets (conventional group CG). Physical therapists instructed self-regulated exercise to be conducted twice daily during thirty minutes during ten working days. Patients reported adherence (primary outcome), enjoyment and motivation daily. Balance during walking was measured blind with an accelerometer. Analysis was by intention to treat. Repeated measures mixed models and Cohen’s d effect sizes (ES, moderate if >0.5, large if >0.8) were used for between-group effects and effect sizes over time.

Results: We evaluated 217 patients and included and 54, 26 in the EG and 28 in the CG. Adverse effects were observed in two patients in the EG who stopped because of pain during exercising. Adherence was comparable at day one (38 min. in the EG and 42 min. in the CG) and significantly higher in the CG at day 10 (54 min. in the CG while decreasing to 28 min. in the EG, p=0.007, ES (0.94, 0.39–0.151). Benefits favoring the CG were also observed for enjoyment (p=0.001, ES 0.88, 0.32 – 1.44) and motivation (p=0.046, ES 0.59, 0.05–1.14). There was no between-group effect in balance during walking.

Conclusions: Self-regulated exercise using instruction leaflets is superior to exergames regarding adherence, enjoyment and motivation in a geriatric inpatient rehabilitation setting. Effects were moderate to large. There was no between group difference in balance during walking.

References:

Acknowledgements: The present study is part of the GameUp Project, focusing on game-based mobility training and motivation of elderly persons, and is co-funded by the European research and development joint program “Ambient Assisted Living” (AAL-2011–4-090). We thank Viviane Hasselman and Stine Staubach for data collection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1176

AB1223-HPR

BELIEFS AND ATTITUDES OF ITALIAN NURSES TOWARDS PLACEBO AND NOCEBO RESPONSES INDUCED BY CONTEXTUAL FACTORS IN CLINICAL PRACTICE

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Background: Placebo and nocebo represent psycho-neuro-immuno-endocrinological responses commonly encountered in nursing care (1,2). A new paradigm proposed the contextual factors (CF) as mediators and moderators of these responses (3). To date, the knowledge about the awareness of CF and their use in nursing is scant.

Objectives: The goal of this study was to examine frequency of use, beliefs and attitudes of Italian specialised nurses regarding the contextual factors.

Methods: In December 2016, through SurveyMonkey Software®, an online survey was conducted by sending a questionnaire to the members of four Italian Nursing Association, grouping nurses specialized in Neuroscience, Medical, Geriatric and Diabetic care. Behaviours, beliefs and attitudes of nurses about the implementation of CF in clinical practice were assessed by a 17 items questionnaire and resulting data were analysed by descriptive statistic.

Results: Of the 1441 members of the involved Nursing Associations invited to participate to the survey 425 responded (30.1%). An high number of respondent nurses adopts CF often in their practice (42%). They believe that CF can positively influence acute pain (47.5%), chronic pain (61%) and rheumatologic disorders (42%), 34% of responders consider the use of CF, if it can determine beneficial psychological effects, as ethically acceptable. 15.5% responders oppose to the adoption of CF when based on deception or if they undermines trust between nurses and patients. A relevant number of nurses (24%) do not communicate the use of CF to their patients and 19% implement CF as addition to other nursing interventions to optimize clinical responses. Nurses explain the power of CF through patient’s expectation and psychological mechanism (11%).
Conclusions: The Italian specialised nurses use CF quite frequently and believe that their use has the capacity of positively influencing the clinical outcome. Larger surveys are needed to understand the proportion of use of CF by nurses in common clinical practice in Italy.

References:

Disclosure of Interest: None declared

AB1224-HPR

COULD WE USE THE LAY REFERRAL SYSTEM TO IMPROVE THE EARLY ARTHRITIS CLINIC EFFICIENCY?
M. Dobroiu1, M. Trandafir1, C. Ioan1, D. Vasile1, D. Predeteanu2, R. Ionescu 2

Background: The professional’s monopoly on knowledge about disease and its treatment is something gone now, in the era of internet and patient consumerism. In addition, the interest of rheumatologists (and the interest of the society, too) shifted toward early recognition of the disease and early arthritis clinics. Education is definitely one of the solutions to increase the awareness of potential patients regarding rheumatic disease. However, most of rheumatic diseases are not very frequent in the population that raise the problem of cost efficiency of the education process. Per Eliot Freidson’s view, the members of every community of whatever kind share some cultural understandings about disease, treatment, and cure. The lay community network could be considered an instrument for dissemination of proper knowledge regarding health and could help to earlier recognition of a sign of disease related to early arthritis.

Objectives: To identify the opportunity of using lay network for early arthritis referral. In addition, we intended to identify the most suitable vectors from this network to be used for education and dissemination of medical knowledge.

Methods: 48 rheumatic patients (mean age (SD): 50.8 (14.7)) consecutively declared between first sign of disease and professional examination, 71.7% use the professional’s referral. In addition, we intended to identify the most suitable vectors from this network to be used for education and dissemination of medical knowledge.

Results: In 28.3% cases the first sign of disease was noticed not by the patient but by somebody else, for 36.7% a delay of several months to one year was declared between first sign of disease and professional examination, 71.7% use to discuss bout health problems with their lay network (often and very often), 76.1% consider them able to give pertinent advices regarding the disease they suffer from, 45.7% are ready to act as an education vector and 41.3% are ready to participate in additional education programs. They interest in such activity is not related to gender, education level or work status.

Conclusions: Lay network referral could be a powerful instrument to reduce the duration between onset of rheumatic symptoms and medical visit, to increase the awareness regarding rheumatic disease, to reduce the cost of health education. Health professionals should understand how to use these networks.

References:

Disclosure of Interest: None declared

AB1225-HPR

A PROGRAM BASED ON PSYCHOEDUCATION FOR RHEUMATOID ARTHRITIS PATIENTS
P. Orquía1, L. Villarreal2, P. Santos-Moreno3, D. Buitrago-García4, G. Cajado5, A.M. Orozco6, Psychology and processes: 1Rheumatology; 2Epidemiology, Biobam, Center for Rheumatoid Arthritis, Bogota; 3Psychology, El Bosque University, Bogota, Colombia

Background: The National Institute of Arthritis and Musculoskeletal and Skin Diseases defines rheumatoid arthritis (RA) as a chronic disease that affects the joints, causing pain, swelling, stiffness, reduced mobility and affection of internal organs. In order to learn to accept and integrate the disease as a part of their daily life, it is important that they have enough information and knowledge about their health condition. The strategy of psychoeducation is important because it involves the patient actively and seeks to have specialist who provide relevant, clear, and comprehensive information. In this way, a change is generated at level of beliefs and myths on the disease, and suggests suggestions for coping with situations for the management of the disease's impact on the patient’s life.

Objectives: To determine the effect of a psychoeducation program on the quality of life and commitment to the treatment of patients diagnosed with RA from a specialized center in Bogotá.

Methods: We conducted a quasi-experimental study with two independent groups, one experimental and one for control. The Inclusion Criteria was: patients with RA over 30 years old that knew how to write and read with mobility resources. We excluded patients with emotional stress, stroke, and diagnosed cognitive deficit or with patients with consumption of psychotropic substance. We applied the Arthritis Visual Scale (EVA), a Quality of Life Questionnaire - Specific for patients with Rheumatoid Arthritis (QOL-RA). Data Analysis: when performing the normality test, the QOL-RA results were parametric and the analysis was performed with Student’s t test for independent measurements. On the other hand, the results of the EVA and QOR were non-parametric, for that reason we worked with the Mann Whitney U test.

Results: We included 36 patients, men (4) and women (32), aged between 35 and 75 years, with diagnosis of RA, which belong to the integral model of RA specialized center. The subjects that patients preferred were: Disease recognition, changes in lifestyle, training educational resources for self-care among others. Statistical analysis showed that, when we evaluated quality of life T-student test did not show any statistical differences between pre and post test results in both groups. The Man Whitney test showed statistical differences between groups (u=70,500, z=241,500, p<.004) regarding the compromise with the RA treatment, but it did not showed differences in regards of pain intensity between groups.

Conclusions: We recommend a strategy to facilitate the process of data collection in pre-test and post-test. For the next application of the program, it is suggested that the sample of patients must be increased, to increase the duration of each session and the number of sessions of the program. In order to achieve the patients’ attendance at the program, maintain permanent telephone contact (may be by telephone). To have printed or recorded material (Brochures, guides, CDs, etc.) is recommended with more relevant to each session of the program.

Disclosure of Interest: None declared

AB1226-HPR

VACCINATION COMPLIANCE IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIRDs): ROLE OF SPECIALIST NURSE

Background: The patients with autoimmune inflammatory rheumatic diseases (AIRDs) have double the risk of infections as compared to the general population. This may be due to highly inflammatory nature of the disease, the drug used, and the co-morbidities. In recent years, the efficacy of vaccinations has been proven in decreasing morbidity and mortality among these patients, hence, it reduces the cost of the treatment and improves the quality of life of the patients. However, low vaccination compliance is a global problem. Therefore, in this study, we tried to assess the effect of nursing counselling on vaccinations compliance.

Objectives: To assess the efficacy of counseling by the specialist rheumatology nurses in vaccination compliance among AIRDs patients.

Methods: All the adult patients (>18yrs), suffering from AIRDs, were advised vaccinations between January to December 2016 were enrolled in this study. The basic demographic and disease-related data captured with details of vaccinations such as date of advice of vaccination and reasons for non-compliance were recorded. The patients were counselled by specialist nurses about the importance and needs of vaccination, clarifying their doubts. Reinforcement of the same was carried out in the follow-up visits.

Results: A total of 506 patients (374 female, 73.9.2% and 132 male, 26%), with mean age 48 years, of which 87.5% had rheumatoid arthritis, 76% (74.75%), Spondyloarthropathy: 80 (15.81%) other autoimmune rheumatic disease 48 (9.48%), Co-morbidities status: 309 (61%) having multiple co-morbidities and 197 (38.9%) have no co-morbidities. The vaccination compliance outcome is shown in table.

Table 1

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Patients who received</th>
<th>Patients who did not receive</th>
<th>Same day</th>
<th>Within 3 months</th>
<th>Within 6–9 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumovac</td>
<td>23</td>
<td>506</td>
<td>456 (90.1%)</td>
<td>50 (9.9%)</td>
<td>306 (67.1%)</td>
</tr>
<tr>
<td>Prevnar 13</td>
<td>3</td>
<td>244</td>
<td>211 (86.4%)</td>
<td>33 (13.6%)</td>
<td>143 (58.8%)</td>
</tr>
<tr>
<td>Influenza</td>
<td>6</td>
<td>506</td>
<td>443 (87.5%)</td>
<td>63 (12.5%)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: The compliance rate of all vaccinations was highest on the same day when it was prescribed. This was despite the fact that the patients that they had their own vaccinations without any third party payment. However, the compliance decreases with increase in the period when it was prescribed with the passage of time. This suggests that intensive counselling, availability of vaccines at premises (pharmacy) and administration of vaccination free of cost are a few of the important factors which can boost the compliance of the vaccination among patients with AIRDs.

References:

Background: Osteomalacia is caused by a deficiency of vitamin D and can be corrected by changes in diet, lifestyle and supplementation. Consequently, it is a condition where education has a primary role in prevention.

Objectives: If educational interventions are to be developed and evaluated, then an instrument for measuring knowledge is required. This has led us to develop a novel Osteomalacia Knowledge Questionnaire (OKQ).

Methods: Based on nominal group technique, a steering group of people who are knowledgeable about osteomalacia, educational theory and questionnaire development was convened. The group decided to use true and false questions. Important areas of knowledge of osteomalacia were first determined by the group and then relevant statements which were true or false were written and grouped into 8 sections of 5 questions, each covering the different areas of knowledge. This resulted in a knowledge instrument with 40 questions in all. The questions were tested for utility and ambiguity in the group and modified and replaced accordingly.

The questionnaire was then trialled in 37 people of South Asian origin (an osteomalacia susceptible population), in three groups. Participants were initially administered the OKQ and then received an educational intervention comprising a practitioner led education session on osteomalacia, including a presentation and written or electronic material. Participants were re-tested with the OKQ after 6 weeks.

Although there is no “gold standard” for measuring knowledge about osteomalacia, if effective, increased knowledge should lead to an increase in vitamin D (Vit D) levels and a decrease in parathormone (Pth) levels. Vitamin D and Parathormone levels were measured alongside the OKQ in 2 of the groups before and after the educational intervention.

Results: Baseline knowledge about osteomalacia was low pre education averaging only 12.7 out of 40 (range 0–29) (n=27).

A total of 30 participants (81%) attended for the follow up test. They averaged a score of 13.9 at baseline and 23.4 at follow up. This was statistically significant (p=0.002 Mann Whitney) and demonstrated sensitivity to change of the OKQ.

Knowledge at baseline was correlated with vit D and Pth blood levels for two of the groups (n=27). This showed correlation coefficients of 0.128 and -0.407 respectively. For change of knowledge and change of parathormone (n=21) the r value was -0.324 suggesting a relationship between knowledge and Pth that is worthy of confirmation through further studies.

Conclusions: A novel questionnaire has been developed that has face validity and can be corrected by changes in diet, lifestyle and supplementation. Consequently, it is a condition where education has a primary role in prevention. Reduced in diet K in RA group was more pronounced for women. All patients tested normokalemic (mean serum K: 4.37 mEq/l). No meaningful correlation between diet components and disease measures (data not shown). Food avoidance patterns identified a-priori did not seem to impact disease measures (data not shown). 44% RA and 77% controls consumed vegetarian diet (excluding eggs). Patient dependence for diet recall and measure was the important limitation.

Table 1. Women RA subjects and healthy control

<table>
<thead>
<tr>
<th>Component</th>
<th>Patient (n=115)</th>
<th>Control (n=122)</th>
<th>RDA</th>
<th>P (1)</th>
<th>P (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>2825</td>
<td>3436</td>
<td>2230</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>Carbohydrate (g/d)</td>
<td>457</td>
<td>532</td>
<td>NA</td>
<td>0.21</td>
<td>0.50</td>
</tr>
<tr>
<td>Protein (g/d)</td>
<td>94</td>
<td>127</td>
<td>55</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Fat (g/d)</td>
<td>69</td>
<td>84</td>
<td>25</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Sodium (mg/d)</td>
<td>3112</td>
<td>3221</td>
<td>1902</td>
<td>0.56</td>
<td>0.03</td>
</tr>
<tr>
<td>Potassium (mg/d)</td>
<td>1223</td>
<td>3393</td>
<td>3225</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 2. Men RA subjects and healthy controls

<table>
<thead>
<tr>
<th>Component</th>
<th>Patient (n=22)</th>
<th>Control (n=43)</th>
<th>RDA</th>
<th>P1</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>2737</td>
<td>2829</td>
<td>2730</td>
<td>0.74</td>
<td>0.87</td>
</tr>
<tr>
<td>Carbohydrate (g/d)</td>
<td>439</td>
<td>422</td>
<td>NA</td>
<td>0.67</td>
<td>0.67</td>
</tr>
<tr>
<td>Protein (g/d)</td>
<td>92</td>
<td>109</td>
<td>50</td>
<td>0.33</td>
<td>0.07</td>
</tr>
<tr>
<td>Fat (g/d)</td>
<td>68</td>
<td>77</td>
<td>50</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>Sodium (mg/d)</td>
<td>3156</td>
<td>3180</td>
<td>2012</td>
<td>0.5</td>
<td>0.03</td>
</tr>
<tr>
<td>Potassium (mg/d)</td>
<td>1755</td>
<td>3562</td>
<td>3750</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Conclusions: The diet of RA patients seemed adequate except for an intriguingly low K. We speculate that patients eat less vegetables and fruits that source K. K sub serves several physiological functions that may be deranged in RA and contribute to disease progression. This would need further investigation.

Acknowledgements: In contrary to our expectations and reassuringly, the diet of RA patients seemed adequate except for an intriguingly low potassium which should be investigated. We speculate that patients eat less vegetables and fruits that source K potassium.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4335

EVALUATION OF RHEUMATOLOGY NURSE-LED CLINIC IN MANAGING PATIENTS WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY

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Background: Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease characterized by inflammation of the synovial joints. Management of RA patients is usually provided by rheumatologists only. Enhanced care provided by rheumatology nurses between rheumatologist consultations may have beneficial effects in terms of symptom control. In Hong Kong, whether rheumatology nurse care model can favor to patient outcomes remained uncertain.

Objectives: The aim of the study was to examine the clinical effectiveness of rheumatology nurse clinic in controlling disease activity as expressed in change of Disease Activity Score in 28 joints in RA patients compared with usual care led by rheumatologists only.

Methods: This was a retrospective study. Two historical groups of RA patients (30 patients at each group) were identified from attendance records between 1/1/2015 and 20/7/2015 at the rheumatology outpatient clinics. Group 1 comprised of patients who attended rheumatology nurse clinic in between the doctor clinic and nurse clinic.

Results: The mean follow up duration for the study cohort was 20 weeks (median: 22.5 weeks). Patient global assessment and DAS 28 were similar for both groups at baseline. At follow-up, patient global assessment and in the nurse group (Group 1) decreased from mean ± SD: 42±24.7 at baseline to 28.7±24.8 at follow-up, and DAS28 decreased from mean ± SD: 3.7±15. With regards to DAS28, there was a 8.2% decrease (absolute change: -0.38±1.14) in DAS28 in group 1 suggesting a trend of improvement (p=0.081).

Conclusions: This study demonstrates the short-term benefit of a nurse-led program on RA disease management. Future multi-center studies with a randomized controlled design and a larger sample will be required to confirm our findings.
Background: Inflammatory arthritis strongly correlates with work disability. Treatment guidelines recommend work support but data are lacking on rheumatology clinicians’ perspectives on work referral and extent of work support within current rheumatology services for this population.

Objectives: To scope the need for and patterns of work referral, and examine the extent and type of work support currently available in Irish rheumatology services for people with inflammatory arthritis. To identify factors that help or hinder employment-related service provision. To explore the role of occupational therapy in addressing work with this population from the perspectives of the other members of the rheumatology team and current practices and challenges.

Methods: A questionnaire concerning work support provision was distributed via online survey to doctors, nurses and physiotherapists working in clinical rheumatology in Ireland.

Results: Response rate of 22% was achieved and total sample of 73 analysed. Respondents indicated that 71% of service users were of working age and the majority of respondents (85%) agreed that addressing employment-related service provision was within the remit of rheumatology services. Over half of respondent (55%) of respondents estimated that 25–49% of their caseload had work needs. Work was usually addressed if clients raised work concerns (94%), client reports work absenteeism (83%), client’s work involved manual component (75%). Barriers to addressing work included limited time in clinical setting (92%); unfamiliarity with best practice for work support (91%); lack of perceived competency to address work included limited time in clinical setting (92%); unfamiliarity with best practice for work support (91%); lack of perceived competency to address work; client’s work involved manual component (75%).

Conclusions: Work support provision was distributed via online survey to doctors, nurses and physiotherapists working in clinical rheumatology in Ireland.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6236
hematoma formation increase following surgery. Therefore, propioprocitave acuity decrease after TKR surgery (1). Drainage is a common procedure in TKR, but its effectiveness is controversial. Some studies have claimed that drainage decreases the risk of articular effusion and hematoma formation. However, some studies have demonstrated that drainage increases postoperative blood loss and does not improve the surgical result (2). Several studies have examined the effects of using drainage, but they have not involved improvement in proprioception for patients who had drains compared with those who did not after TKR.

Objectives: The aim of this study was to compare the effect of the drainage on proprioception acuity impairments with total knee prosthesis.

Methods: The study group consisted of 34 patients (35 knees), 15
two TKR because of arthrosis were consecutively allocated to a drainage group (n=26 (41 knees), with median age; 66.23±8.63 years), and were allocated to a non-drainage group (n=14 (54 knees), with median age; 63.97±9.99 years).

Patients were evaluated regarding knee proprioception (in knee joint angle 15°, 30° and 60°), knee function score (Hospital for Special Surgery (HSS) score), pain (Numeric Pain Rating Scale (NPRS)), knee circumference, knee range of motion. Functional activities were evaluated using the Iowa Level of Assistance Scale and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Patients were evaluated preoperatively and at discharge. All patients underwent the same rehabilitation program.

Results: At baseline, demographic and anthropometric characteristics were similar in groups and there was no statistically difference between groups (p>0.05). When knee proprioceptive acuity measurements (in knee joint angle 15°, 30° and 60°) were compared before and after surgery there was no statistical differences in proprioceptive acuity between groups (p>0.05). It was determined that; the drainage group had better results in terms of reduction of pain severity after surgery (p<0.001). When the HSS knee scores were compared there was statistically difference between groups (p<0.001) and the knee joint angles were lower in non-drainage group after surgery. There were no statistical differences in knee circumference, knee range of motion, the IOWA help level score and IOWA walking speed score between groups after TKR (p>0.05).

Conclusions: According to our results, the use of drainage did not improve the knee proprioceptive acuity impairments with TKR. But, it is suggested that using drainage decreases pain severity and improves the HSS knee score. Also the use of drains has no effect on patients’ outcomes after TKR, in terms of improvements knee range of motion, knee circumference, functional activities and walking speed.

References:


Disclosure of Interest: None declared


AB1223-HPR COGNITIVE COMPLAINTS IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS AND PAST NEUROPSYCHIATRIC SYMPTOMS

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Objectives: Cognitive complaints are common in patients with systemic lupus erythematosus (SLE). Their association with disease and non-disease related factors have been inconsistently reported. We studied their relation to disease related factors including disease activity, neuropsychiatric history and non-disease related factors such as anxiety or depression.

Methods: We used cognitive symptoms inventory (CSI) for measuring cognitive impairment at 3 time-points 12 months apart/2015–2016/ and Hospital Anxiety and Depression Scale (HADS)-HADS-A and D.Disease activity was measured by SLAM.

Results: 93 SLE patients were recruited at baseline (T0). Among them 59 had first re-evaluation (T1) and 34 had second re-evaluation (T2) at 12-month interval. Majority (72%, 24/34) of patients had stable CSI whereas 5.5% (2/34) of patients worsened CSI over 12 months. At T0, multivariate analysis revealed that higher CSI was associated with history of NPSLE (p=0.001), depression (p=0.04), higher HADS-A (p<0.001) and HADS-D (p=0.001) scores. CSI of active patients (SLEDAI–6) was not different from inactive patients. It did not change despite regression of disease activity in 12 months. There was no difference in CSI between T0 and T1 regardless of history of NPSLE, change in anxiety and depression at T1 (HADS-D≥11 as cutoff).Multivariate linear regression analysis revealed change in HADS-A as the only significant predictive factor of change in CSI over time (p=0.774, 95% CI 0.43 –1.12, p<0.001).

Conclusions: 11.5% of SLE patients reported persistent cognitive symptoms.CSI had worsened in patients with NPSLE and psychiatric illness, anxiety or depression.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5186

AB1234-HPR PHYSOTHERAPY EFFECTS ON GAIT SPEED AND PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS THREE DAYS AFTER APPLYING KINESIOTAPE

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Background: Knee osteoarthritis is a chronic degenerative disease, known as the most common cause of difficulty walking in older adults and subsequently is associated with slow walking, also one of the most main symptoms is a degenerative and mechanical type of pain. Pain is very noticeable while walking in rugged terrain, during ascent and descent of stairs, when changing from sitting to standing position as well as staying in one position for a long time. Many studies have shown that the strength of the quadriceps femoris muscle can affect gait, by improving or weakening it. Kinesiotape is a physiotherapeutic technique, which reduces pain and increases muscular strength by irritating the skin receptors.

Objectives: The aims of this study was firstly to verify if the application of Kinesiotape on quadriceps femoris muscle increases gait speed in patients with knee osteoarthritis and secondly if applying Kinesiotape on quadriceps femoris muscle reduces pain while walking.

Methods: 73 patients with primary knee osteoarthritis, aged 50–73 years, participated in this study. Firstly we observed the change of gait speed, while walking for 10 meters at normal speed for each patient, before and three days after the application of Kinesiotape on quadriceps femoris muscle, with the help of the 10-meter walk test. Secondly we observed the change of the pain, while walking for 10 meters at normal speed for each patient, before and three days after the application, with the help of Numerical Pain Rating Scale-NRS.

Results: Our results indicated that there was a significant increase of gait speed while walking for 10 meters one day and also three days after application of Kinesiotape, also there was a significant change of pain. Before applying Kinesiotape on quadriceps muscle was shown that 41.1% chose score 6, 30.1% chose score 7 and 28.8% chose score 8 of the numerical pain rating scale. Three days after the application 15.1% chose score 2, 37% chose score 3 and 47.9% chose score 4 of numerical pain rating scale.

Conclusions: Our results indicated that there was a significant decrease of pain and increase of gait speed while walking for 10 meters. Kinesio-Tape can be used in patients with knee osteoarthritis, especially when changing walking stereotypes is a long term goal of the treatment.

References:


Disclosure of Interest: None declared


AB1235-HPR SEXUAL DISTURBANCES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND IT'S RELATION WITH DISEASE ACTIVITY

L. Villarreal 1, S. Henao 2, D. Buitrago-Garcia 3, P. Santos-Moreno 4, 1Psychology and processes; 2Patient service; 3Epidemiology; 4Rheumatology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia

Background: Sexuality is an important dimension of personality and human body, therefore any involvement in this area should be considered as important. Sexual disturbances in rheumatoid arthritis (RA) patients are poorly described in literature. In other chronic conditions studies had shown that sexual disturbances can be common problem in but, sexual dysfunction has a high risk of under treatment because providers frequently do not initiate the conversation with the patient.

Objectives: The purpose of this study was to describe sexual disturbances in
a meaningful relationship between functional ability and disease activity in a specialized rheumatology center.

**Methods:** A descriptive cross-sectional study was performed in a specialized clinic dedicated to care patients with rheumatoid arthritis (RA). Data was collected during a two year period at a psychology consultation, through semi-structured interviews. Descriptive epidemiology was applied for continuous variables, using measures of central tendency and dispersion for categorical and qualitative variables by averages and percentages. We analyzed bivariate association with Pearson’s X².

**Results:** We included 1398 patients attending to our psychology consultation. Mean age was 55 years ± 8; 80% were female and 20% male. Mean DAS28 was 2.6±1.3, mean HAQ was 1.6±1.6; patients had the disease for an average of 12 years ± 8; 41% of patients had comorbidities associated with non-autoimmune disease, 14% comorbidities related to autoimmune disease; 35% of our patients did not report any specific comorbidities. Most of patients were married 50%, followed by divorced 19%, single 14% and widowed 7%. Regarding occupation 33% were employees, 25% were housekeepers or retired due to age, 12% were retired due to disabilities, and 3% unemployed. Of the total population 45% had elementary school, 32% high school, 8% college education, 7% graduate education and 7% were illiterate. Concerning sexual disorders, 38% reported no to have any sexual activity, 32% reported to have a satisfactory sexual life, 11% dyspareunia, 9% had an unsatisfactory sexual life, 5% loss of desire, 3% premature ejaculation and 2% orgasmic decrease. Regarding predisposing factors of sexual disorders 63% of our population did not present any, 11% had insecurity related to the sexual role, 10% inadequate information related to sexuality; 10% infidelity and 6% physical and biological predisposing factors. Regarding precipitant factors of sexual disorders 63% report no to have any, 19% had biological or physical factors, 12% infidelity, 3% inadequate information and 3% insecurity related to the sexual role. There was no statistical association between disease activity and predisposing or precipitant factors.

**Conclusions:** We found that a third of patients with RA have sexual disorders and a high percentage reported not having any sexual activity. Also, it is important to have a multidisciplinary care team for the patient with RA, including a psychologist and a sexologist for managing this kind of illness in order to improve the life quality of patients.

**Disclose of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5635

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**Table 1. Socio-demographic status of respondents**

<table>
<thead>
<tr>
<th>Married status</th>
<th>Education level</th>
<th>Working status</th>
<th>Monthly revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Married 70</td>
<td>Primary school 40</td>
<td>Employed 27</td>
<td>up to 500 € 32</td>
</tr>
<tr>
<td>Divorced 27</td>
<td>High school 27</td>
<td>Housekeeper 2</td>
<td>500 € – 1000 € 27</td>
</tr>
<tr>
<td>Single 6</td>
<td>University 27</td>
<td>Student 1</td>
<td>900 € – 1300 € 19</td>
</tr>
<tr>
<td>Widowed 19</td>
<td>Master’s degree 3</td>
<td>Unemployed 5</td>
<td>1300 € – 1700 € 4</td>
</tr>
<tr>
<td>Separate life 2</td>
<td>Doctor’s degree 3</td>
<td>Retired 65</td>
<td>1700 € and up 3</td>
</tr>
</tbody>
</table>

Respondents of our study described their functional ability good by the average of the entire sample 2.06. This value shows us a relatively good functional ability of patients most days or very often. Patients had some problems with function of hand and wrist in particular by opening jars (43%) and on area walking and bending with intensive activity (42%). Correlation between functional ability and socio-demographic data show us some statistical deviation in age group 41 to 50 year (p=0.94), in patients with higher education level (p=0.09) and in group of patients who monthly earns more than 900 € (p=0.96). But we didn’t find any statistically significant difference in the entire sample including patients treated with biological drugs (functional ability patients and control: results of a cross-sectional pilot study. J Am Podiatr Med Assoc. 2013 Nov-Dec;103(6):489–97.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4669

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**Table 2.**

**AB1237-HPR**

**CONNEXION BETWEEN FUNCTIONAL ABILITY AND SOCIO-DEMOGRAPHIC DATA IN PATIENTS WITH RA IN SLOVENIA**

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**Background:** Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis, characterized by progressive, destructive course when left untreated, resulting in severe patient disability and significantly reduced quality of life. RA has an important impact on work ability and economic status of patients.

**Objectives:** In our study we focused on specific consequences of arthritis in terms of functional ability and we were looking for correlation with socio-demographic data.

**Methods:** The study was conducted between January 2016 and May 2016 at the Department of Rheumatology, UMC Ljubljana and included patients with RA. Data were collected using Arthritis Impact Measurement Scales 2 (AIMS2) questionnaire.

**Results:** One hundred RA patients (76% women, mean age (SD) of 61.1±15.29 years) participated in the study. Disease duration was ± 5.6 year. Most of our patients were married, retired with elementary education and lower incomes (Table1).

**Conclusions:** We found fairly good functional ability of patients; which might be explained by relatively short duration of RA. The most important functional-related issues from patient perspective were identified. Despite that we not find a statistically significant relationship between socio-demographic data and functional ability of patients, it is very important that we pay attention on socially unprivileged patients and we offer our support in managing disease.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2523

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**AB1237-HPR**

**POSTURAL STABILITY AND ANKLE PROPRIOPCEPTION IN DIFFERENT SUBGROUPS OF SUBJECTS WITH HALLUX VALGUS**

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**Background:** Hallux valgus (HV) is lateral deviation of the great toe towards the second with subluxation of the first metatarsophalangeal joint and medial deviation of the second metatarsophalangeal joint. Increasing HV severity has been shown to negatively impact on health-related quality of life and self-reported function, and HV has been linked to increased falls risk in older adults (2). HV, in particular, is associated with poorer performance during postural stability and functional testing in older adults (3).

**Objectives:** Despite the findings of impaired postural stability in older adults with hallux valgus, the links between functional status and postural stability, ankle proprioception are not well established in HV. One of clinical significance of this study was to determine whether impaired postural stability was caused by deficits in ankle proprioception and impaired functional status in HV subjects. Our purpose of this study was to assess postural stability and ankle proprioception in different subgroups of HV. In this study, we hypothesized that subjects with severe deformity would exhibit poorer postural stability and ankle proprioception performance compared to subjects with mild and moderate deformity in HV.

**Methods:** Thirty-five adults diagnosed with unilateral HV according to the Manchester Oxford Foot Questionnaire deformation grade 2 and on were participated in the study. They were distributed among three groups: Mild (grade 2), moderate (grade 3), and severe deformity (grade 4). Functional status was measured with a disease specific score (the hallux valgus scale of the American Orthopaedic Foot and Ankle Society). While postural stability was measured with Pedalo Sensamove® System, ankle proprioception was measured with Biodex Balance System Pro 4.

**Results:** Subjects in HV with severe deformity group showed poorer postural stability performance than groups in HV mild (p=0.024) and moderate (p=0.039) deformity groups. However, there was no significant difference between the groups in ankle proprioception. There was a significant correlation between postural stability and functional status (p<0.05, r=0.771) in all subjects with HV. In addition, it was found that ankle proprioception was not correlated to functional status and postural stability (p>0.05).

**Conclusions:** It has been concluded that HV with severe deformity affects postural stability according to the results of our study. On the other hand, ankle proprioception is not as an important predictor as postural stability for rehabilitation in different subgroups of HV. Therefore subjects in HV with severe deformity should be focused on stability exercises, in particular, in addition to home – based exercise programs, foot orthoses, footwear recommendations, and patient education in their rehabilitation.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.5803

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**AB1238-HPR**

**PEOPLE’S PERCEPTIONS OF THEIR PHONE CALL WITH RHEUMA DIRECTLY, A RHEUMATIC DISEASES HELPLINE**

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**Background:** Information on rheumatic diseases is often complex to understand or scary, and additional support is often necessary. Rheuma Directly (RD) is a helpline with working nurses on rheumatic diseases, funded by the Swedish Rheumatism Association and Spenshult Research and Development Centre. Little is known of how people calling a helpline perceive the contact.

**Objectives:** To describe the variation in how people perceive the contact with the helpline RD.

**Methods:** The study had a descriptive, qualitative design with a phenomenographic approach and was carried out by means of 27 semi-structured telephone interviews. The informants were 22 female and 5 men, and their ages ranged from 22 to 69 years (mean 54 years).

**Results:** The informants called RD when they had problems getting answers

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.2524
to their questions through the Internet or from healthcare professionals. Three different description categories emerged: Specific competence, Constructive dialogue, and Applicability. The informants’ perceived specific competence when the nurses were knowledgeable, the call was complementary to previously received information and when the informants had greater knowledge after the consultation. It was considered that it was worth to continue to have Constructive dialogue when they got someone to discuss with, a “sounding board”, and perceived emotional support, felt reassured and were satisfied with the answer. The informants perceived Applicability because RD was available and they could make different choices according to their own desire, before (how and when they would contact RD), during (what to tell and when the question they would ask) and after (how and what they would do after the contact with RD).

Conclusions: People calling RD perceived that the telephone call with the nurses meant meeting specific competence, gaining constructive dialogue and that the helpline was applicable. This knowledge ad to a fuller understanding of factors that from a callers perspective, are important when calling a helpline with specially trained nurses on rheumatic diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2466

AB1239-HPR

FATIGUE AT DIAGNOSIS OF INFLAMMATORY JOINT DISEASES - A PREDICTOR OF FATIGUE DURING THE COURSE OF DISEASE DESPITE OF LOW DISEASE ACTIVITY

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Background: Fatigue is a common symptom in patients suffering from inflammatory rheumatic diseases. Several patients still present with fatigue, although they are well treated with anti-TNF-therapy (1).

Objectives: To investigate disease-related aspects of fatigue in patients with inflammatory rheumatic diseases using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-F) with the aim later to develop methods to improve the patients quality of life in a more specific way.

Methods: All patients with inflammatory diseases including Rheumatoid Arthritis (38) and Spondyloarthropathy (15) and Psoriatic arthritis (2) treated with Intravenous biologic from 15.10 until 31.12.16 were invited to fill out the FACT-F questionnaire during intravenous (IV) infusion of the drugs in the rheumatology outpatient clinic. Furthermore hemoglobin and disease activity score were extracted from patients electronic records.

Results: Of 72 patients, 53 patients completed the questionnaire. 5 patients did not want to participate. In 11 patients treatment was discontinued during the study and 3 patients were not able to answer the questions.

Patients with a fatigue score of >30 had few problems with any of the subgroups within the FACT-F questionnaire (A-E), whereas more than 30% of patients with a fatigue score of >30 had challenges in one of the FACT-F subgroups (somewhat, quite a bit and very much) A. Physical well-being: lack of energy and troubles with meeting the needs of their family because of their physical condition. B. Social/family well-being: patients were not feeling close to their friends, not getting enough emotional support from their family and not satisfied with the emotional support they received. C. Emotional well-being: patients worry if their conditions might get worse. D. Functional well-being: patients feel they are partly unable to work, not satisfied with their performance at work and they have sleeping and quality of life problems. E. Additional concerns: patients had problems with fatigue, weakness, tiredness, starting and finishing things because of tiredness, not having energy, not being able to do usual activities, frustration by being too tired to do the things they want to do as well as they want to limit social activities because of tiredness and they need to sleep during the day. Furthermore, there was a moderate correlation between fatigue at diagnosis and fatigue at time of data extraction (r =0.53). The fatigue was not correlated with anaemia or high disease activity.

Conclusions: Our results demonstrated that patients with a fatigue score of >30 had different challenges mentioned in the fatigue questionnaire. In addition, patients who experience fatigue at time of diagnosis, they often remain fatigue, proving fatigue is not correlated with inflammatory joint disease. Maybe more explorative questions about fatigue at the consultation could be a part of improving the patients’ quality of life.


Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2485

AB1240-HPR

PATIENTS’ DOGMA, NUMBER OF SWOLLEN JOINTS AND PHYSICIANS’ AND PATIENTS’ AGE PREDICT NON-ADHERENCE TO MEDICATIONS AND NON-PHARMACOLOGICAL INTERVENTIONS IN RHEUMATOID ARTHRITIS – A MIXED METHODS STUDY

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Background: In rheumatoid arthritis (RA), up to 80% of patients were found to be non-adherent to prescribed medication and non-pharmacological recommendations. These patients do not achieve an optimal clinical outcome.

Objectives: In the present study, we therefore explored predictors that may lead to non-adherence to both medicines and/or non-pharmacological recommendations. Methods: In a mixed methods study, retrospective observational data from patients meeting the ACR/EULAR criteria for RA who were non-attenders/missed the routine check up visits for at least 9 months to the rheumatology clinic and had had an initial DMARD therapy were queried of the databases of two rheumatology centers in Austria (Graz, Vienna). Subsequently, we invited all patients to take part in a qualitative semi-structured interview study with a meaning condensation data analysis. In the interviews, patients were assigned to the subgroups “adherent” (e.g. having regular rheumatology visits in another clinic) or “non-adherent” (e.g. having stopped taking the prescribed medication). Possible predictors derived from the qualitative analysis and the retrospective observational data were then tested in a logistic regression model.

Results: In total, data of 459 patients (346 [75.4%] females; mean age 63.0 [SD ± 14.8]) were extracted out of the databases. 131 patients (109 [83.2%] females; mean age 64.8 [SD ± 14.1]) participated in the qualitative interviews. In addition to already known themes, new topics arose from the analysis: (i) patient’s disease inhibited adherent behavior, in that patients felt that pain was an important part of life and attributed to having had a high manual workload during life of which patients were proud; (ii) patients had less trust in physicians when they were seeking support from other physicians, because they appeared to be “young or inexperienced”; (iii) Some patients did not feel properly understood if physicians only prescribed medication without giving advice on non-pharmacological aspects of treatment.

Two clinical variables were found to be predictors for non-adherent behavior (table 1): swollen joint count (patients with higher numbers of swollen joints were less adherent) and age (younger patients were less adherent).

Table 1. Logistic regression models. Odds ratios of relevant factors for non-adherent behavior in RA: results of the logistic regression analysis

<table>
<thead>
<tr>
<th>Regression Model</th>
<th>Odds Ratio</th>
<th>CI 95%</th>
<th>Significance at 0.05 (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the last visit</td>
<td>1.033</td>
<td>1.005 to 1.063</td>
<td>0.022</td>
</tr>
<tr>
<td>Swollen Joint Count using a 32 joint count form</td>
<td>0.876</td>
<td>0.767 to 1.000</td>
<td>0.050</td>
</tr>
</tbody>
</table>

Conclusions: In order to achieve a good clinical outcome, it is important to provide evidence based treatment recommendations, but also to ensure adherence to these. The predictors found in our study could be used to enhance patient adherence and therefore improve clinical outcome.

Acknowledgements: This project was partially funded by AbbVie Inc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5227

AB1241-HPR

EVALUATION OF PATIENT COMPLIANCE WITH LONG TERM PRESCRIBED RHEUMATIC MEDICATION AT LOCAL LONDON HOSPITAL RHEUMATOLOGY UNIT

V. Sodhi, C.B. Coelho, M. Hoffman, J. Kirk on behalf of Central Middlesex Hospital Rheumatology (Patient) Support Group. LNWHT, London, United Kingdom

Background: Non-Compliance with Long term medication is reported as high 60% [1]. Health belief model suggests four elements contribute to this problem. The Beliefs About Medicines Questionnaire (BMQ) is a tool for evaluating people’s beliefs about medicines (1).

Objectives: A Service Evaluation of compliance with prescribed medication for Long Term Rheumatologic Conditions at Central Middlesex Hospital. This was conducted to assess any relationship between compliance with medicines and beliefs or concerns of patient’s ethnicity.

Methods: The design was a voluntary self-reported, cross-sectional paper based questionnaire survey of people with Rheumatic Conditions. Twelve questions were grouped within three categories (healthcare utilisation, necessity beliefs and concern beliefs) to capture compliance behaviour for later analysis and comparison.

The Beliefs about Medicines Questionnaire was adapted from ref (1) to distinguish patients beliefs of ‘necessity’ or ‘concerns’. In line with principles of PPH, the questionnaire was discussed prior to the audit with a sample focus group of 5
patients who contributed to the wording and the simplification of the questions re: ethnicity.

Questionnaires were offered to all patients attending the CMH Rheumatology Unit. The evaluation was discontinued when a target of 100 was reached (n=102). No questionnaires were excluded. And up to 5% of questions were unanswered. Data was collected on a voluntary basis.

Results: The Number of questionnaires returned for this service evaluation was 102.

- Most respondents (94%) showed compliance with rheumatic medication as prescribed.
- More than half the respondents (66%) agreed or strongly agreed that their arthritis medications are necessary for their health.
- 54% were concerned about potential adverse consequences.
- The overall necessity score (19.32 S.D. 3.17) was higher than the concerns score (13.48 S.D. 3.35).1, 61.57, P =0.001.
- Concerns about the long-term effect of rheumatic conditions correlate positively with perceptions of health in the future P < 0.01 level (2-tailed Pearson).
- No significant correlation was found between compliance and patient's ethnicity/individual demographics.

Conclusions: Most people with Rheumatic conditions have positive beliefs about the necessity of their medication. However, levels of concern are high, especially towards the long-term effects of the medication. This concurs with a similar study in Rheumatoid Arthritis.(2). The service evaluation using the Beliefs about Medicines Questionnaire has helped to identify people at risk of poor compliance locally. This illustrates a need to discuss patients' beliefs and concerns in targeted drug counseling sessions with specialist nurses. A post study patient focus group recognised the high level of compliance yet recommended a fixed weekly walk in session with a nurse and pharmacist to sustain this high quality outcome. Further methods of continued patient re-education will be explored.

References:

Disclose of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4738

HPR service developments, innovation and economics in healthcare

Ab1242-HPR NUMERICAL PREDICTION OF THE OPTIMUM SHEET METAL THICKNESS Implanted as the JOINT CARTILAGE

M. Moayedfar, A.M. Rani, H. Hanaei. Mechanical Engineering, Universiti Teknologi Petronas, Bandar Seri Iskandar, Malaysia.

Background: The combination of computer-aided-design (CAD), digital image processing techniques and finite element method (FEM) has been successfully employed to create the customized distal condyle implants in human joints during arthroplasty surgery when the manufacturing method is incremental sheet forming (ISF) technique. However, due to the high time of process in the FEM analysing of human joints, finding the optimum material thickness with respect to the joint cartilage has been neglected.

Objectives: To apply a numerical investigation based on the FEM to predict and propose the sheet metal thickness for joint cartilage in the ISF process in a timely method for the human knee as a case study.

Methods: To reduce the expense of experiments and save the time of production, a numerical investigation method based on FEM is designed for the ISF. The user subroutine is employed to navigate the tool motion and material behaviour for reducing the time of simulation in the analysing tool. Hence, the sequence of FEM process was as follows: 1) Create the geometric model of the clamping system and sheet metal. 2) Choosing associated nodes together with Shell elements to increase the accuracy of the simulation and simplify the process. 3) Applying the specifications of every element. 4) Assign and render the material properties for sheet metal. 5) Apply the initial boundary conditions. 6) Assigning the asymmetric boundary conditions using the subroutine for time reduction purpose. 7) Apply the loads related to the complete FEM. Consequently, the proper thickness from MRI based on the previous study is sent to the CAD system for the mechanical and anatomical modification.

Sheet metal thickness and also material selection were based on the joint mechanical properties, shape and size. Therefore, by using the optimum pressure profile, the FEM can be performed to predict the sheet stretch and also shear failure to illuminate the optimum sheet thickness used in customized medical implants.

Results: The result of this study is based on the validation of predicted sheet thickness with the real patient cartilage thickness. This result showed a good agreement with the hospital data (for cartilage thickness of −2.20mm) and simulation result (~2.23mm for sheet thickness). It was not possible to divide the model into some sections and only analyse one particular part as a sample.

Therefore, the time of calculation was 23 hours for FEM when a high-performance computer was used. Regarding the same issue, the mesh was not uniform distributed so the time of analysing for each particular location was not the similar and predictable. The shear failure happens on the edge of design and also some locations that a turning point existed.

Conclusions: A numerical simulation is required to predict the material thickness replaced with the joint cartilage. Thus, the mathematical solution is investigated to predict the sheet thickness in the customized production process. Therefore, the result showed 98.5% similarity thickness of sheet metal with cartilage.

References:
[2] B. Huzjan, Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia

Background: The use of information and communication technology (ICT) in occupational therapy should allow management of chronic diseases by providing support programs in education including the use of multimedia services.

Objectives: In order to determine the presence of information and communication technologies use in the options of telerehabilitation, a survey was conducted 224 newly diagnosed patients with rheumatoid arthritis (RA).

Methods: The quantitative research approach was used with the newly created patients with RA treated on Department of Rheumatology at the University Medical Centre Ljubljana. The questionnaire included basic demographic information and questions about the use extent and possibilities for using ICT. The population also accounted for patients with RA diagnosed between 1 January 2014 and 31 December 2015. The data obtained was statistically analysed with the SPSS program IMB 20. The total of 64 survey questionnaires were completed, which represents 28% of the selected population.

Results: 23.4% RA patients don’t use internet. 48.4% RA patients use personal computers (PC), and 51.6% patients use smart phones. 35.3% of patients that use PC use it for e-mailing, searching health information (35.4%), video calls (13.3%) and sending messages (15%). Patients who use smart phones use them for calls (31.9%), texting and calls (26.7%), e-mailing (25%), searching health information (12.9%), and video calls (3.4%). There is a positive correlation between the use of modern ICT and the opinion that the interviewed patients would use telerehabilitation services during their rehabilitation. Pearson correlation coefficients are statistically significant with all the ICT. With using a PC (r =0.602) and smartphones (r =0.542) there is a medium strong positive correlation Positive coefficients indicate that the surveyed patients who are increasingly using ICT think they could help themselves with telerehabilitation. Increased frequency of ICT usage is associated with potentially greater possibility of using telerehabilitation.

Conclusions: The need for rapid access and exchange of information is the main reason for the use of information and communication technologies in healthcare, and is conditional for the development of e-health. Research provided answers questions about the possibilities of using information and communication technology and rehabilitation services at a distance – telerehabilitation in occupational therapy.

Disclose of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2046

Ab1243-HPR USING INFORMATION-COMMUNICATION TECHNOLOGIES AND OPPORTUNITIES FOR TELEREHABILITATION IN OCCUPATIONAL THERAPY

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Background: Fatigue is reported to be a common symptom in people with inflammatory rheumatic diseases. It is a complex symptom, characterized by an individual interplay of biopsychosocial factors that has been associated with different factors such as: pain, sleep problems, depression, fatigue. Pain and psychosocial factors like depression.

Objectives: The main objective was to contribute to improved coping and quality of life in people with inflammatory rheumatic disease and fatigue. Cognitive therapy is one of the common psychological interventions used in the rehabilitation...
of people with rheumatic diseases and fatigue. The current intervention was developed as a supplement to medical treatment to strengthen coping and quality of life, and reducing fatigue, depression and pain.

Methods: People with inflammatory rheumatic diseases and fatigue were recruited for 6–9 sessions of cognitive therapy sessions, in addition to treatment as usual at a rheumatology outpatient clinic in Norway. The intervention aimed at reducing fatigue, depression and pain, consisted of four main elements: understanding fatigue, assessment and activity planning, mental and cognitive self-help skills.

Results: This pilot project recruited 40 people with inflammatory rheumatic disease from a rheumatologic outpatient clinic in Norway. Participants had a disease duration of mean 14 years, they were mainly women (n=36) with a mean age of 45 (Standard Deviation =10) years (Table 1). Repeated ANOVA analyses and Paired t-tests showed promising statistically significant changes on a group level for fatigue and depression, not for pain (Table 2).

Conclusions: This pilot project supports the idea of conducting a trial on the effectiveness of a brief cognitive therapy intervention for people with inflammatory rheumatic diseases and fatigue. ANOVA analyses and Paired t-tests showed promising statistically significant changes on a group level for fatigue and depression, but not for pain, whether these changes are clinically meaningful, and if there is a difference, compared to treatment as usual remains to be explored.

Acknowledgements: This project would not have been possible without the support from the national patient organization, through a grant from the Norwegian ExtraFoundation for Health and Rehabilitation. We acknowledge patients who contributed to this project and the staff at the rheumatological outpatient clinic at Diakonhjemmet Hospital.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6906

AB1245-HPR NEW HEALTH TECHNOLOGIES AND LIFESTYLE MANAGEMENT FOR PATIENTS WITH OSTEARTHRITIS

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Background: Osteoarthritis (OA) is one of the most common chronic diseases of the elderly worldwide. It represents significant impairments in terms of quality of life [1]. It notably affects self-care-tasks, body-image, self-esteem, well-being, social-activities and relationships. A wide-ranged field of therapy concepts exist. Medication is often one part, but it cannot solve other existing problems due to OA [2]. The demographic trends combined with the growth of mobile devices among the older population suggest that using digital devices, as a platform for health care services, is a promising option. OA patients and (B) to evaluate existing health applications. The demographic trends combined with the growth of mobile devices among the older population suggest that using digital devices, as a platform for health care services, is a promising option.

Methods: The areas most commonly found were disease- and treatment information (n=23), social support regarding the level of patient empowerment [4], self-management, social-activities and relationships. A wide-ranged field of therapy concepts exist.

Results: This study included 40 people with inflammatory rheumatic disease from a rheumatologic outpatient clinic in Norway. The intervention aimed at reducing fatigue, depression and pain, consisted of four main elements: understanding fatigue, assessment and activity planning, mental and cognitive self-help skills. The project was developed, and data collected at the rheumatology outpatient clinic at Diakonhjemmet Hospital in 2014–2016.

Conclusions: The areas most commonly found were disease- and treatment information (n=23), social support regarding the level of patient empowerment [4], self-management, social-activities and relationships. A wide-ranged field of therapy concepts exist.

Abstract AB1244-HPR – Table 2. Self-reported fatigue and depression at baseline, after treatment and at 6 months follow-up

<table>
<thead>
<tr>
<th>Measure</th>
<th>VAS</th>
<th>WOMAC Pain</th>
<th>WOMAC Stiffness</th>
<th>WOMAC Total</th>
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<tbody>
<tr>
<td>Before</td>
<td>7.6±2.0</td>
<td>9.3±4.4</td>
<td>2.3±2.4</td>
<td>40.8±9.0</td>
</tr>
<tr>
<td>After</td>
<td>6.0±2.5</td>
<td>8.1±4.7</td>
<td>1.7±2.4</td>
<td>20.4±5.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Measure</th>
<th>HA Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>7.1±3.2</td>
</tr>
<tr>
<td>After</td>
<td>3.0±1.4</td>
</tr>
</tbody>
</table>

References:


Disclosure of Interest: S. A. Raisseadat Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None

DOI: 10.1136/annrheumdis-2017-eular.5484

HPR professional education, training and competencies

AB1247-HPR AN INTEGRATED APPROACH TO CUSTOMIZED MEDICAL FEMORAL COMPONENT PRODUCTION TO MINIMIZE THE CONDYLERT CUT OFF DURING THE TKA

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Background: To prepare the femoral component during the Total knee arthroplasty (TKA), it is needed to cut off the damaged condyle to a dimension matched with one of the available implant sizes in the market. Since there is a variety of humans’ knee size and shape, therefore, some parts of the distal femoral are over cut. This problem is to customisation of the implants via a cohesive procedure specifically designed for medical orthopaedic implant production. Objectives: This research aims to provide a fully integrated system of digital image processing of Magnetic Resonance Imaging (MRI) data and Finite Element Method (FEM) for testing and analysing prior to manufacturing of customized medical femoral component. Methods: An automatic algorithm to segment MR images from end-of-femur condyle is developed and employed for 3D reconstruction followed by computer-aided design (CAD) system, FEM and incremental sheet forming (ISF) process. In femur segmentation, multi-resolution edge detection is applied that extracts all the edges at bone surfaces. The edge detection process followed by the selection and extraction of strong edges with enhanced active contour technique that results in separation between femur and tibia components. Morphological processing is applied for creating a solid part and solid body. The Proper femoral component is designed using region growing technique then exported to FEM system to calculate the best metal thickness and angles, regarding the normal cartilage, to bear the maximum load with the lighter material. The process of ISF that involves machining and sheet forming parameters is using to manufacture customized medical metal femoral component but in low surface quality which increases the risk of ion release at in vivo condition. Therefore, during this technique, optimum parameters using Design of Experiment method are applied to modify and enhance the sheet stretching of final parts. Results: The integrated system demonstrates a cohesive user-friendly system for creation of patients specific implants while it showed a substantial reduction in implant production time compares to the current manufacturing method. In ISF process optimum parameters are used to increase the rate of stretching together with the best sheet thickness ~2.5 mm based on validated sheet stretching simulation. The results of this study also show that the high surface quality for femoral component up to ~Ra 2.527 is achievable using this newly developed method. Conclusions: An integrated system that combines computational method, CAD, FEM and ISF procedure is developed that shows its potential for manufacturing of customized medical femoral component. Flexibility in size and shape make this system prominent. The best sheet thickness with respect to the cartilage thickness is calculated and obtained with the optimum process parameters for manufacturing section.

Acknowledgments: The authors are thankful to the Ministry of Higher Education, Malaysia for supporting this research via FRGS/1/2014/TK01/UTP/02/8 research grant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1351

AB1249-HPR THE EFFECT OF TASK ORIENTED TRAINING ON FUNCTIONALITY, DEXTERITY AND ADL PERFORMANCE IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis is the most common and most serious of the inflammatory arthropitides, and it dominates clinical rheumatological practice (1). This inflammation leads gradually to a destruction of bone and cartilage, responsible for loss of function (2). The main goals of treatment for RA are to prevent or control joint damage, prevent loss of function, and decrease pain (3).

Objectives: The purpose of the study is to investigate the effect of task oriented training on functionality, dexterity and ADL performance in rheumatic hands. Also the other goal of this study is to bring a new perspective to RA rehabilitation.

Methods: Thirty seven women (16 patients in control group and 17 patients in study group) performed therapy programme. Control group received hand exercise therapy (MCP, DIP,PIP mobilization, range of motion exercise, isometric exercise), and study group received both hand exercise therapy and task oriented training (fork use, drinking water with a glass, face washing, sit up-stand up and t-shirt wearing) twice a week for 5 weeks. Every therapy sessions took 40–45 minutes for study group and 20–25 minutes for control group. According to the patient’s condition, the rest interval was given and it was said that the exercises should be done too three times a day. The results were evaluated with therapy programme with Jamar Hand Dynamometer, Nine Hole Peg Test, Health Assessment Questionnaire and Duruöz Hand Index.

Results: Age distribution of participants was 49, 57 (p<0.005) and were found to be homogeneously dispersed (p<0.15). Hand grip strength was not statistically
significant, although it increased in both groups except left hand grip strength which was decreased after the program (control group: $r=0.552$ (right hand), $p=0.066$ (left hand)/study group: $p=0.136$ (right hand), $p=0.723$ (left hand)). The NHP showed a decrease in the duration of the test within both groups, but this decrease was not statistically significant (control group: $p=0.113$ (right hand), $p=0.265$ (left hand)/study group: $p=0.215$ (right hand), $p=0.291$ (left hand). The HAQ showed a statistically significant decrease in both groups (control group: $p=0.001$/study group: $p=0.01$). Although DHI decreased in both groups, the decrease in the study group was not statistically significant (control group: $p=0.003$/study group: $p=0.440$). Treatment efficacy between groups after treatment was evaluated by Independent-t test and change in parameters other than HAQ and DHI was not statistically significant.

**Conclusions:** Hand exercise program and task oriented training are safe methods that can be used to increase the grip strengths of patients with rheumatoid arthritis, daily life activities and hand skills. The statistical significance of the results may be due to the low number of patients. We assume that this study can be done in a larger sample, the effect of task-oriented training on patients with rheumatoid arthritis will be better.

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.1065
People with Arthritis and Rheumatism in Europe
Abstracts
**GROWING STRONGER TOGETHER: IMPLEMENTING EULAR YOUNG PARE’S STRATEGY**

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**Background:** In a recent European youth survey, 53% reported that rheumatic and musculoskeletal diseases (RMDs) affected their ability to work, while 75% reported that RMDs interrupted their education. Therefore, in 2017 and 2018, while continuing to achieve the objectives reached in 2015 and 2016, EULAR Young PARE will focus on two key points from EULAR Young PARE’s strategic objectives: work and education.

**Objectives:** In 2017, in line with EULAR’s efforts to raise awareness of the needs of people with RMDs among employers and other stakeholders, the specific and still unmet needs of young people with RMDs will be highlighted, so that employers and other stakeholders will be more aware of the needs of young people with RMDs and young people will receive better support to find a suitable job. In 2018, education for young people with RMDs will be in focus, so that educational institutions across Europe will be more flexible and assistive in supporting high quality education for young people with RMDs.

**Methods:** In 2017, we will support EULAR’s lobbying activities by raising awareness among employers and other stakeholders about the needs of young people with RMDs, and young people will receive better support to find a suitable job.

**Results:** In 2017, we will support EULAR’s lobbying activities by raising awareness among employers and other stakeholders about the needs of young people with RMDs. In 2018, education for young people with RMDs will be in focus, so that educational institutions across Europe will be more flexible and assistive in providing high quality education for young people with RMDs by offering training and support to national youth leaders.

**Conclusions:** The objectives reached by EULAR Young PARE in 2015 and 2016 are closely related to its future aims and achievements, allowing EULAR Young PARE to grow stronger and continue its work by the side of young people with RMDs, in order to improve their quality of life.

**References:**


**Acknowledgements:** Special thanks to EULAR and EULAR PARE for supporting the vision of EULAR Young PARE. EULAR Young PARE would also like to acknowledge all of the patient organisations that they continue to work with.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4891

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**CELEBRATING TEN YEARS OF SUCCESSFUL PATIENT INVOLVEMENT IN RESEARCH OF INFLAMMATORY CONDITIONS**

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**Background:** In 2016, the Research Institute (RI), Primary Care and Health Sciences, Keele University, UK, celebrated 10 years of Patient and Public Involvement and Engagement (PPIE) in research of musculoskeletal and other long term conditions. Our Research User Group (RUG) with over 90 members with a range of long-term conditions, actively work with research teams on studies. Many of whom have been involved in ten studies of different inflammatory conditions. We provide two case studies: 1) CONTACT: a trial comparing the effectiveness and side-effects of two commonly-used drugs (Naproxen and low-dose Colchicine) to treat acute gout in primary care; 2) A qualitative interview study with people with rheumatoid arthritis (RA) who had attended a nurse-led review clinic, which included identifying people at risk of anxiety and depression.

**Objectives:** To describe how PPIE helped shape the design and delivery of the CONTACT and qualitative interview studies.

**Methods:** 1) For the CONTACT trial, two RUG members with experience of gout joined the Trial Steering Committee. Another seven RUG members formed an advisory group to provide the patient perspective on trial procedures.

2) For the qualitative interview study, a group of eight people with RA from a local rheumatology centre (Haywood User Group) commented on the documents for the ethics application and met to discuss data analysis and dissemination.

**Results:** 1) In the CONTACT trial, RUG members made a difference by:

- Helping to produce clear and user-friendly information sheets for participants in the trial.
- Providing practical advice regarding how participants were recruited.
- Future RUG involvement will include helping to interpret the trial findings planning further dissemination and discussing future research studies.

2) In the qualitative interview study, the PPIE group:

- Contributed to the development of readable patient questionnaires for use in the clinic.
- Offered their perspectives on the interpretation of the qualitative data.
- Helped develop a leaflet to inform patients about mood problems related to rheumatoid arthritis and where help could be sought.
- Contributed to the establishment of an RA annual review clinic at the local hospital.

**Conclusions:** Both studies demonstrated the wide-ranging benefits of PPIE input throughout the research cycle of identification, designing, managing and disseminating research. The RI will continue to involve patients with long-term conditions in studies for the benefit of the wider patient community.

**Acknowledgements:** We thank all of our Research User Group members for their valuable time and contribution to the RI’s research. CONTACT was funded by the NIHR School for Primary Care Research. The RA qualitative study was funded by the NIHR School for Primary Care Research. The RA qualitative study was funded by the Scientific Foundation Board of the Royal College of General Practitioners and the Haywood Foundation. KD is part-funded by a NIHR Knowledge Mobilisation Research Fellowship (KMF-2014–03–002). CCG is part funded by the NIHR Collaborations for Leadership in Applied Research and Care West Midlands.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.3144

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**THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017 Work and rehabilitation**

**ASSESSMENT OF PAIN AND IMPORTANCE OF EXERCISE IN HIP OSTEOARTHRITIS**

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**Background:** Osteoarthritis (OA) of the hip is a common condition which affects men and women of all ages. The cartilage becomes damaged. Stiffness and reduced range of movement are common. The pain experienced from OA of the hip may be felt in your lower back, buttocks and groin. You may also feel pain from your hip in your leg and down into your knee. This is called referred pain. The goals of OA treatment include alleviation of pain and improvement of functional status. Optimally, patients should receive a combination of nonpharmacologic and pharmacologic treatment. A physiatrist may help in formulating a nonpharmacologic management plan for the patient with OA.
Guidelines from Osteoarthritis Research Society International (OARSI) advise that nonpharmacologic treatment of hip and knee OA include the following: patient education; heat and cold; weight loss; exercise; physical therapy; occupational therapy; unloading in certain joints (eg, knee, hip).

Objectives: The aim of this study was to investigate the importance of exercise and TENS (transcutaneous electrical nerve stimulation) therapy in patients with OA of the hip on the pain and functional status.

Methods: This was a prospective clinical study involving 20 patients with primary hip OA treated at stationary at the Center for Physical Medicine and Rehabilitation during 2016. On receipt of all the respondents filled out the social survey, questionnaire; Direct telephone questionnaire. Patients were asked the same questions: 1. Describe the best you feel at present following the exercise programme; 2. Did you feel the programme was too long, just right or too short? 3. Do you feel the programme was worthwhile? 4. Did you feel the programme was worthwhile.

Results: There was 100% of women, mean age 64.15±0.06 years. The most represented were retired, 60%, followed by workers and unemployed 10% and 30%. BMI was 27.3±2.22 kg/m². After a month there was a statistically significant reduction in pain measured by VAS (at the beginning it was 6.7; at the end 3.2; p<0.001). At the end of the study there was a statistically significant increasing range of motion for active flexion (p<0.05) and active abduction (p<0.05), while there was no statistically significant increasing for active extension, adduction, internal and external rotation in the hip joint (p>0.05).

Conclusions: The ER strongly recommends the following nonpharmacologic measures for patients with knee or hip OA: cardiovascular or resistance land-based exercise, aquatic exercise, weight loss, for overweight patients. TENS may have a role in reducing pain measured by VAS (at the beginning it was 6,7; and it is a huge burden on primary care (Peat, McCarnyn, & Croft, 2001). The knee joint is one of the most affected in elderly, influencing directly physical function and affecting psychological and social parameters. Therefore, it is imperative to develop strategies that help individuals to change the way they affect their lives. International recommendations reinforce educational and exercise programs as the core of non-pharmacological approaches to enhance physical functional and relieve pain and others osteoarthritis symptoms.

Objectives: The purpose was to assess the effectiveness of a three months educational program for older adults with knee osteoarthritis (KOA).

Methods: Participants recruitment was done in the community using various marketing strategies. Forty individuals with 60 years or more, bilateral or unilateral KOA diagnosed according to clinical and radiological criteria of the ACR [1] and independently mobile and literate participated in the program. Educational sessions regarding exercise and joint protection strategies were offered. Telephone calls were done 15 days after each educational session. Patients received a book (2), with a core exercise section. Patients in the first attendance session were taught to do registration in an exercise training diary. Self-reported measures were used for other symptoms, activities of daily living (ADL), and quality of life assessed by Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire (3). Patient Global Impression of Change Scale (PGICS).

Results: Final sample included 32 adults (age: 67.8±5.3 years; bilateral KOA: 93.8%; female, 59.4%; BMI: 30.1±5.3 kg/m²). Eight participants did not complete the program (3 due to health problems and 5 for personal reasons). KOOS pain improved 10% (p<0.042), and other symptoms 8%. Improvement in KOOS ADL (6.7±13.6) and quality of life (8.2±11.8) were also observed. 47% of the participants reported significant changes (scores 5–7) after intervention and a decrease in medication use of 31%.

Conclusions: The educational program can be an effective and suitable way for osteoarthritis management and to improve pain and health-related quality of life, leading individuals with KOA to better control their pathology and consequently better living.
Objectives:  
- Mapping beliefs of researchers and PRs about the potential value of patient involvement in basic research.  
- To document experiences of both patient representatives and researchers of a pilot project of PRs participating in basic research.

Method:  
A mixed-method study with a participatory action research has been used. This is a research approach that emphasizes both participation and action [2]. In this case two working groups were involved. The coordinator participated in meetings of the working groups, made notes during these meetings about the nature and degree of participation, evaluated the meetings with the participants and kept a diary. At the start and at the end of the pilot 6 researchers of the working groups were interviewed by the coordinator. The findings of the interviews were categorized and summarized. During 6 months, 5 PRs were invited to attend once a month, in one of the working group meetings. In the first meeting expectations of both researchers and PRs were exchanged. In the following meetings one researcher presented a lay version summary of his/her work. There was room for PRs to ask questions.

Results:  
Prior to the pilot, some researchers had doubts about the added value of PRs, others were more positive and even curious. All PRs were open minded about the pilot, although none of them had experience with involvement in basic research.

At the end of the pilot, researchers expressed positive statements, such as: “(very) nice, good initiative and interesting discussions.” Positive experiences included: exercise in explaining their work to lay persons; stimulation in developing a more holistic (helicopter) view of their research, and getting a better insight in problems in daily life that patients encounter.

The PRs experienced the atmosphere during meetings as open and pleasant; they felt that the degree of participation was limited, but worthwhile. The coordinator observed that interaction between the researchers and PRs mainly consisted of asking questions for clarification. Besides, the coordinator observed after presentations exchanges between PRs and about research-related issues such as the availability of human tissues for research and conversations about personal experiences.

Critical comments were made about the difficulty in understanding the complex matter for PRs and the chosen method (researchers present, PRs listen) that does not encourage interaction.

Conclusions:  
There is a potential value of patient involvement in basic research. A first result is that junior researchers develop a more holistic view of their research subject.

An open atmosphere and low expectations may contribute to success. Continuation of this pilot with modifications, including more research groups and PRs, are needed to find ways to increase patient involvement in basic research.

References:  

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4898

PARE0007  
HOPES AND FEARS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN SPAIN. THE VALUE OF PATIENT OPINION: RESULTS FROM THE SPANISH ATLAS

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Background:  
Not much attention has been paid to listening to the opinions of patients in most scientific studies on Spondyloarthritis, despite their opinions playing an increasingly important role in decision-making alongside clinical and public health criteria.

Objectives:  
To assess the opinions of patients with Axial Spondyloarthritis (axSpA) using qualitative information.

Methods:  
A sample of 680 patients diagnosed with axSpA was interviewed during a pilot as part of the Spanish Atlas, which aims to promote early referral and improve healthcare and the use of effective treatments in patients with axSpA. The Atlas is a CEADE initiative (Spanish Coordinator of Patients with axSpA in Spain) developed by the University of Seville and Max Weber Institute in collaboration with GRESSER (Spanish Rheumatology Society spondyloarthropathy study group). Responses to qualitative items about patients’ hopes and fears for their disease and their personal aims regarding their treatment were analysed.

Results:  
53% were females, mean age 46 years and 77.1% were HLA-B27+.

The five main hopes of patients are: stopping the disease, dream of a cure, elimination of pain, improve their quality of life and live without limitations. Additionally, patients has expectations on the medical research outcomes. Thus, 81% of patients hope that the research will make possible to find the cause and a cure for axSpA, developing more efficient biologic therapies (11%), and finding new techniques or medication (8%).

The following stand out among drug treatment-related concerns: having more effective treatments (32%), sustaining the results of biologic therapies (29%), being able to start on biologics (8%), the public health system funding non-drug treatments for AS (8%), eliminating secondary effects (15%), reducing prices (4%), and correct use (4%).

With respect to their fears, patients stated that their main concern was mobility loss (31%), followed by loss of independence (23%), disability (22%), stiffness (12%), structural damage (3%), organ damage (3%), other illnesses and diseases related (3%), physical decline (3%), and sight loss (1%).

Patients who expressed fear regarding their disease listed their greatest concern related to the disease (12%), structural damage (3%), organ damage (3%), other illnesses and diseases (3%), physical decline (3%), and sight loss (1%).

Patients who expressed fear regarding their disease listed their greatest concern related to the disease (12%), structural damage (3%), organ damage (3%), other illnesses and diseases (3%), physical decline (3%), and sight loss (1%).

With respect to patients’ personal objectives in terms of their treatments, they highlighted the wish that their treatment would, first, help them to reduce and eliminate pain, increasing in mobility, improved quality of life, the avoidance of structural damage and the disease eventually being cured.

Conclusions:  
Analysis of patient opinion using qualitative information has enabled the identification of important concerns for patients such as discovering the cause of the disease, reducing pain and structural damage, loss of self-sufficiency and disability.

Acknowledgements:  
This project has been supported by Novartis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.8711
A TAXONOMY OF DISEASE EXPERIENCES OF WOMEN WITH SJÖGREN’S SYNDROME FROM THE PERSPECTIVE OF THE PATIENT

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Background: In earlier studies of experiences of patients with Sjögren’s Syndrome (SS), professionals interpreted the data and drew conclusions and implications. In the current study, patients had a major share in the interpretation and structuring of experiences, and a patient research partner was part of the research group in all phases of the study: planning, collecting data, organizing, analyzing, and reporting.

Objectives: The aim of this study was to examine the full spectrum of life experiences of women with SS in an integrated, hierarchical model, and to examine the degree to which the research participants experienced the sorted experiences themselves.

Methods: Patients structured and interpreted the data using a concept mapping technique. In a card-sorting task, 52 patients with SS from the Netherlands grouped 75 experiences in piles. These experiences came from previous in-depth interviews with Chilean patients [1]. Hierarchical cluster analysis yielded an integrated, hierarchical model of these sortings. The 52 patients indicated on a Likert scale whether they had had these experiences themselves: agree, agree a little, disagree a little, disagree.

Results: Hierarchical cluster analyses showed a main 6-category clustering of experiences with primary symptoms, emotional processing, social interaction, self-management, ignorance, and physicians. Four of these categories showed underlying clusters of experiences (see Figure). Patients generally agreed to have common experiences of “primary symptoms”, “role functioning barriers”, and “diagnosis” and they commonly disagreed with the “psychologizing” symptoms, while they differed in the degree to which they had individually experienced the other experiences.

Conclusions: Life experiences of women with SS were summarized in an integrated, hierarchical model consisting of 14 clusters in 6 overarching categories. The results may be colored by the cultural background of the participants. This year this concept mapping study will be extended to patients from Chile, which will increase the generalizability of the findings and allow cross-cultural comparison. The final hierarchical overview with life experiences from the patient’s view can be used to improve screening in clinical consults, develop a questionnaire, give direction to future research, and enhance education and self-management support [cf. 2]. The method gives ample room to really incorporate the patient perspective in research.

References:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2923

SIGNIFICANCE OF FOOT PROBLEMS FOR PATIENTS WITH RHEUMATOID ARTHRITIS: A PATIENT-LED QUALITATIVE STUDY

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Background: Patients with rheumatoid arthritis (RA) commonly report problems with their feet. It is known that foot joint involvement begins early in the course of RA and even patients on biologic therapy and/or with low disease activity can still experience high levels of foot pain. Current UK guidance states that “All people with RA and foot problems should have access to a podiatrist for assessment and periodic review of their foot health needs.”

Objectives: To understand how foot health problems affect patients with RA.

Methods: Adult patients, with a diagnosis of rheumatoid arthritis and ability to converse in English, were recruited by clinicians based at a London hospital rheumatology outpatient clinic to participate in two focus groups on foot health. These were conducted by the lead patient researcher and comprised 8 females and 1 male of diverse ethnicities, aged 27-68 years old with 4-46 years disease duration. The focus groups were audio-recorded and transcribed verbatim. Transcripts were verified for authenticity by a random sample of 4 participants, and were systematically coded with the assistance of qualitative data analysis computer software. Themes were generated and cross-checked by the co-researcher to negate any potential bias by the lead patient researcher.

Results: Four interlinked themes were identified: 1) dependence on feet, e.g. for standing and walking; 2) physical impact e.g. pain, swelling and deformities; 3) social impact e.g. hard to keep appointments and participate in leisure activities; 4) psychological impact e.g. low self-esteem, worry and using humour to cope. The sole male participant was unaffected by theme 4. One patient in the group had not experienced foot problems since diagnosis. No differences were identified across age, ethnicity or disease duration.

Conclusions: Foot problems can significantly lower quality of life for patients with RA. It is therefore essential that foot health is adequately addressed during rheumatology outpatient consultations with onward referral to podiatry services as necessary.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1400
EDUCATING YOUNG CHILDREN, PARENTS AND DOCTORS THROUGH THE MEDIUM OF AN ILLUSTRATED CHILDREN’S BOOK

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Background: Chronic illness in a child is a complex reality for all involved. The child often feels confused and afraid. He doesn’t understand why he is sick and in pain, he worries about the doctor and hospital visits, as well as the medications and shots to which he is subjected. Parents are unsure how the illness will affect their child, and how to best prepare him for future challenges. Both parent and child are not always sure how to communicate to the Doctor their needs and concerns. Communication, however, between parent, doctor, child and health professionals is critical for effective treatment of the disease.

Objectives: This book attempts to open lines of communication between parent and child, to educate, give coping tools, and a voice to the young patient in a fun and optimistic manner. The book targets many of the children’s challenges through identifying with Kipo, the young monkey who also has JIA. The objectives are: 1. To give the child strength and tools to deal with his illness. 2. Improve compliance through a better understanding of treatment.

Methods: A list of challenges young children with JIA face was compiled through meetings with parents, doctors and children. Next, a list of coping strategies was produced based on discussions with parents and health professionals. The book addresses the challenges and methods of dealing with them in a fun and optimistic manner through young Kipo’s routine. Included are also messages addressed to the parent and doctor. To keep the child an active part of the story, thus allowing him to voice his concerns and discover coping skills, the story line requires active participation through “reading the pictures” which accompany the text. (The book includes a “how to read” guide). The back page includes a brief description of the illness, as well as other useful web addresses: parents associations, PRINTO, etc.

Results: Working jointly with the illustrator an illustrated children’s book in 3 different languages (Hebrew, English and Arabic) was published. The book addresses the challenges and difficulties of a young child with JIA through the story of Kipo the monkey who is also ill. Included are a visit to the doctor, getting an injection, going to the physiotherapist, etc. The book is distributed free of charge through the paediatric rheumatologists to the families, and is received very enthusiastically by parents, children and doctors. The children read and reread the book sharing it with family, friends and kindergarten classrooms. They use the terminology introduced in the book to describe their own physical and emotional feelings, and adopt coping strategies used by Kipo.

Conclusions: The success of the book motivated us to allow for a more international distribution. The illustrations and the text are available allowing it to be used by any national group.

Acknowledgements: Inbar, Mitrakim Zeerim, ENCA, Dror Adam (Illustrator), anonymous junior doctors, parents and translators.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1887

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Patient information and education

PARE0012

EXPLORING THE ADDED VALUE OF A BOOSTER SESSION AFTER COMPLETING THE DUTCH SELF-MANAGEMENT TRAINING “CHALLENGING ARTHRITIS”

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Background: In the Netherlands, the peer-guided self-management training “Challenging Arthritis” exists for over 15 years and is being organized by the Dutch Arthritis Foundation and the University Medical Center Utrecht. The training is based on the “Arthritis Self-Management Program”1 but has recently gone through several updates, improvements and extensions2. The goal of the training is to improve self-management skills of patients and thereby improving their physical and emotional health and quality of life. Evaluations show that participants highly appreciate the training, but some of them have suggested that they would like to have an extra moment of training, (i.e., a booster session) after the ending of the regular program. Research shows that self-management programs are effective but mostly in the short term3. The effects of “Challenging Arthritis” may be enhanced and prolonged by organizing booster sessions.

Objectives: Aim of this research is to make recommendations about organizing booster sessions based on 1) a literature search and 2) a needs assessment among former participants and peer trainers.

Methods: A literature search was performed in databases like Google Scholar, PubMed and Science Direct, focusing on articles about the use of boosters in self-management interventions. Up to the year 2016. Next to that, a needs assessment was conducted among participants and trainers on needs and preferences, using two separate online surveys. The survey for the participants, who followed a live training between 2012 and 2015, included items on the need for a booster, reasons and on preferences regarding its form, content and frequency. The survey for peer trainers addressed the perceived usefulness and the trainers’ willingness to provide booster sessions. The resulting data were analyzed using SPSS and thematic analysis.

Results: The literature search yielded 27 articles describing health interventions with aspects of self-management, including one or more booster sessions. From a theoretical perspective, boosters are a way to maintain new behavior over an extended period of time. As of yet, there is little evidence that the use of boosters lead to better outcomes in terms of health or health behavior, but it has been suggested that tailoring may lead to better results4.5. Regarding the needs assessment, 124 participants and 34 trainers completed the survey. Results showed that almost half of the participants (47.5%) expressed a need for a booster, while the other half (52.5%) expressed little or no need. Participants who prefer a booster want to share experiences, learn how to stay active with self-management and hold on to skills they have already achieved without the experiences of the users. We presented the support of Donna Saunders, NRAS Member & Volunteer, on hand to comment and ensure authenticity of how the actress moved and dealt with every day activities. The final scene shows the character of Jane attending her clinic appointment with her rheumatologist and even then putting on a brave face and hiding behind the smile of the typical response “I’m fine”. In addition, Donna who lives with RA, was filmed giving her personal comments on the awareness film and insights into her personal struggles. Finally, Prof. Iain McInnes, was filmed giving the clinicians perspective and offering advice as to how health care professionals need to keep at the forefront of their minds that patients are people and to be truly effective as physicians they should always make the time to open the dialogue on how the individual is truly “feeling”.

Results: The films were released on World Arthritis Day 2016 via Lilly and NRAS social media channels in the UK. To date the “Jane” clip has been viewed in access of 200,000 times. The feedback from patients has been overwhelmingly that it has truly captured their “story”. Physicians and industry staff have been left speechless and moved by the emotive film. NRAS and Lilly continue to utilise the films at health care professional training, staff and patient events.

Conclusions: Plans for 2017 is to develop more similar awareness raising videos as it is evident that using social media with video has impact and reach.

Acknowledgements: Acknowledge the support of Lilly Pharmaceuticals for the funding to develop these resources. The invaluable support of Prof. Iain McInnes and patient Donna Saunders

Disclosure of Interest: C. Jacklin Grant/research support from: Lilly Pharmaceutical, D. Saunders: None declared


PARE0014

BEHIND THE SMILE - RA AWARENESS VIDEOS - RAISING AWARENESS OF THE HIDDEN IMPACT OF RHEUMATOID ARTHRITIS

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Background: NRAS was approached by Lilly Pharmaceuticals to contribute to the design and production of a series of videos to raise awareness of the hidden impact of rheumatoid arthritis. As this clearly met the charity’s own objectives of raising awareness to a variety of audiences NRAS gladly collaborated on this project.

Objectives: The key aim of developing these resources to be utilised in European countries was to raise awareness of the impact of RA on daily life to 1) the general public, 2) clinicians, 3) payers, 4) industry and 5) people living with RA and their families. The challenge was to capture, in a two minute video, key messages that would resonate with all these stakeholders.

Methods: NRAS worked with a PR agency to develop an appropriate script for the main Behind the Smile resource. The main character, Jane, who lives with RA, was to be in her mid 30s – to represent that RA is not associated with ageing; a school teacher – to represent that RA hits people of all ages. She is a valued contributor to society; and a daughter, wife and mother – to represent how many other people depend on her and that she has commitments to. We filmed with the support of Donna Saunders, NRAS Member & Volunteer, on hand to comment and ensure authenticity of how the actress moved and dealt with every day activities. The final scene shows the character of Jane attending her clinic appointment with her rheumatologist and even then putting on a brave face and hiding behind the smile of the typical response “I’m fine”. In addition, Donna who lives with RA, was filmed giving her personal comments on the awareness film and insights into her personal struggles. Finally, Prof. Iain McInnes, was filmed giving the clinicians perspective and offering advice as to how health care professionals need to keep at the forefront of their minds that patients are people and to be truly effective as physicians they should always make the time to open the dialogue on how the individual is truly “feeling”.

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Conclusions: Plans for 2017 is to develop more similar awareness raising videos as it is evident that using social media with video has impact and reach.
part of the participants expresses the need for a booster and trainers are highly motivated to provide it. Therefore, we think it’s worthwhile to start experimenting with organizing booster sessions on a small scale and, depending on the outcomes, consider further implementation.

References:
[1] References can be obtained from the first author.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6171

THE IMPORTANCE OF FACE-TO-FACE NETWORKS: FINDINGS FROM THE 2ND EULAR YOUNG PARE CONFERENCE, “CHANGE THE FUTURE”

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1. Sele/Lupus Ung Dk, Gigvetorenjen, Gentofte, Denmark, Gentofte, Denmark;
2. Lupus Europe, Essex, United Kingdom, Essex, United Kingdom;
3. Slovak League Against Rheumatism, Piestany, Slovakia, Piestany, Slovakia;
4. EULAR Standing Committee of PARE, Zurich, Switzerland, Zurich, Switzerland;
5. Youth-H-Well.com, Lisse, The Netherlands, Lisse, Netherlands;
6. ANMAR Young, Rome, Italy, Rome, Italy; 7. ELEANA Hellenic League Against Presentation; each liaison had the opportunity to share recent work in their
8. School of Healthcare, University of Leeds, Leeds, United Kingdom, Leeds;
9. Fibromyalgia Action UK, Paisley, Renfrewshire, United Kingdom, Paisley, United Kingdom;
10. Österreichische Rheumaliga, Salzburg, Austria, Salzburg, Austria;
11. Arthritis Ireland, Dublin, Ireland, Dublin, Ireland.

Background: EULAR YOUNG PARE’s strategy for 2020 is to establish and strengthen liaisons for young people with rheumatic and musculoskeletal diseases (RMDs) across Europe, by developing a collaborative network. We aim to empower young leaders to ensure the voice of young people with RMDs is heard. To facilitate this, the 2nd EULAR YOUNG PARE Conference was held in Retie, Belgium in October.

Objectives: To empower and educate EULAR YOUNG PARE youth liaisons, focusing on developing academic and interpersonal skills to best support young people across Europe living with RMDs. This was achieved through a series of practical, skills-based workshops and plenary sessions.

Methods: The EULAR YOUNG PARE working group reflected on the conference during a debrief meeting. A post-conference evaluation was completed by liaisons. A five-point Likert scale (1= very bad, 5= very good) was used alongside open questions. In addition, there was an informal meeting to generate discussions and receive input from participants regarding the future direction and focus of EULAR YOUNG PARE in 2017 and 2018.

Results: The conference was attended by 22 youth liaisons from 20 organisations. The programme was well received with the face-to-face interactions favoured over digital. A five-point Likert scale (1= very bad, 5= very good) was used alongside open questions. In addition, there was an informal meeting to generate discussions and receive input from participants regarding the future direction and focus of EULAR YOUNG PARE in 2017 and 2018.

Conclusions: The ‘Change the Future’ conference was a successful meeting of youth liaisons from across Europe, who were highly satisfied with the programme and mechanism of delivery. Meeting in person facilitated the growth and continued involvement within the EULAR YOUNG PARE network. The activities of EULAR, and specifically the Standing Committee of PARE, were shared with liaisons, encouraging liaisons to become involved in a wider number of EULAR activities. The method is based on the capacity of a motivated patient to positively influence others also worried by their health situation by sharing their experiences. The campaign spread online, allowing ANMAR YOUNG to gather different experiences, expand its network, contribute in the process of empowerment and engagement of Italian young rheumatic patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6175

EMPOWERING PATIENTS WITH OSTEARTHROSIS WITH NON-PHARMACOLOGICAL MEASURES

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Background: Osteoarthritis (OA) and other joint pains are generally seen as ailments that affect people with age. With the increase in life expectancy over recent decades, the prevalence of people with OA is drastically growing. Estimates suggest that there are 242M people with OA in the world 1; 30M live in Europe 2. The most commonly affected joint at the present time is the knee, followed by hips and shoulders.

Objectives: To run an educational program that will provide elderly people with tools to tackle their problems of joints so that they can improve their quality of life by adopting non-pharmacological measures. A well-informed patient knows how to address their disease. Thus, they can improve their quality of life.

Methods: The method is based on the capacity of a motivated patient to positively influence others also worried by their health situation by sharing their experiences and awareness of the disease.

Stage I. Preparatory actions:
1. Elaboration of contents: An expert team (psychologist, nurse, rheumatologist, family doctor, physiotherapist and rehabilitator) elaborates the content: Knowledge, Weight control, Doing the right exercise, Dealing with the disease.
2. Engagement of the target group: “La Caixa” Banking Foundation is supporting this study by giving access to its 63 senior centers in Catalonia (Spain)
3. Selection of senior centers: The educational program is planned to be run in 6 centers. Currently, 20 centers are conducting initial presentations to evaluate interest and ensure the selection of 6 final centers
4. Enrollment of smart seniors: 12 people will be selected (2 per center), called hereafter as “smart patients” through a survey so we can assess interest of enrolling and quality of the presentation.

Stage II. Training and implementation:
5. Training of smart patients: Train selected smart patients during 9 sessions, 90 minutes each
6. Test of groups of patients: Every smart patient will train 2 groups of 10 people also interested in joint health. A nurse will be in every session, giving support only if necessary
7. Evaluation and follow-up: Improvement of participants in the course will be assessed (anticipated sample size 240 people) by surveying level of satisfaction
Conclusions: Based on results to date, after the 20 sessions the team expects to collect 763 surveys and identify 190 potential smart patients and 483 people willing to participate in the program. There is a clear interest or concern for OA disease in elderly people and they want to take more responsibility for their disease and age with quality of life.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2463

WE DO THE IMPOSSIBLE, BECAUSE THE POSSIBLE EVERYONE CAN DO WAD AWARENESS CAMPAIGN

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Background: One of the main priorities that Bulgarian organization for people with rheumatic diseases follows is dissemination of knowledge and information about RMD’S and their impact on people’s life and to the society. The WAD awareness campaign is the culmination of the organization’s activities during the whole year.

Objectives: The main goal of the 2016 WAD awareness campaign was to:
- To inform the society and BOPRD’s members about the social importance of RMD’s.
- To inform BOPRD’s members what are their rights as people with long term chronic condition.
- To inform the society about RMD’s and the challenges that people with RMD’s face.
- To challenge the people with RMD's to look into their inner world and to define what are their strengths and weaknesses.
- To make the informing process more attractive, by visualizing the key features of life with an RMD.

Methods: In 2016 BOPRD organized an awareness campaign - "We do the impossible, because the possible everyone can do”.

The start of our campaign was on 1st of October and lasted for more than two weeks till the World arthritis day and ended on 16th of October. Informative and motivating pictures, with information about different RMD’s, were published every day on the official BOPRD’s Facebook page and were shared in the closed group for people with rheumatic diseases as well.

A social experiment among the members of the organization was made. They were asked to explain what the disease means to them, like they are telling the story to a person who do not know anything about it. The aim of this experiment was to identify the meaning and significance which people with rheumatic diseases give to their condition, as well as the basic problems result from the illness.

Based on the social experiment and analysis of 33 small biographical narratives 17 basic characteristics of the rheumatic diseases are identified. These characteristics form the problematic areas for people with RMD’s and bases for their study.

The main characteristics are life with chronic pain, the process of disabling, life in continuous compliance with the environment and the high degree of uncertainty and ambiguity, imposed by chronic illness.

An e-booklet, containing the results of the social experiment was published on BOPRD’s Facebook page and website on 12th October. On the same day we published the WAD video, of the PARE WAD campaign: "The future is in your hands". At the end of the awareness campaign we published an online booklet, which contained translated articles about RMD’s and the different aspects of life with a chronic condition.

Results:
- The total number of all publications is 22.
- The publications were seen from over 3 000 people.
- The WAD video was seen by 1000 people.
- The results of the social experiment were seen by 1500 people.
- The most popular were those pictures that managed to touch people’s feelings.

Conclusions: Main common characteristics of rheumatic diseases were identified and can help patients in getting the right diagnosis. The most popular were the posts that were related to emotions and experience of life with a chronic condition.

By publishing the results of the social experiment we managed to help those who read the narratives get the feeling that they are not alone.

The results of the social experiment will be used as a basis in developing a manual for the main symptoms of RMD’s (the patient perspective).

Acknowledgements: Miglena Ivanova

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2595

PARE0018 ADHERENCE TO THERAPY: A COMPARISON BETWEEN THREE PATIENT POPULATIONS WITH AUTOIMMUNE INFLAMMATORY DISEASES

U.G. Viora1, R. Giannelli2, M.G. Pisu3, G. Voltan4 on behalf of ANMAR Italia.
1Anmar Italia, Torino; 2Anmar Italia, Firenze; 3Anmar Italia, Milano; 4Anmar Italia, Roma, Italy

Background: Non-adherence to therapy is one of the main obstacles achieving the goals of care in chronic autoimmune inflammatory diseases, including Rheumatic diseases (RMDs). In the “ MOSAICO” study, ANMAR along with two other associations of Italian patients (AMICI chronic inflammatory bowel diseases (IBD) and ANAP - psoriasis (PSO) and chronic dermatological diseases) wanted to compare the adherence to therapies for IBD, RMDs and PSO and identify key problems that can affect it positively or negatively. This paper presents the results related to adherence to treatment, the obstacles that are disadvantageous and to the factors that, conversely, favor adherence and persistence.

Objectives: to fix the degree of adherence to therapy - with DMARDs and biological indifferently - in the three different pathologies; to identify obstacles and factors predisposing good adherence and persistence by patients; to compare the different populations, highlighting similarities and significant differences.

Methods: A 72 questions questionnaire - about 50% of which were dedicated to adherence and persistence to therapy and the predisposing factors and impediments - prepared in collaboration with Doxapharma was administered to patients with RMDs, IBD, PSO via web and by volunteers of the three associations.

The evaluation of adherence to therapy (“degree in which a person’s behavior in taking medication, following a diet and/or change the lifestyle, corresponds to the specific recommendations made in agreement with the Medical”) was assessed by Morisky Medication Adherence Scale - 8 items (MMAS-8).

Results: 1.017 patients - 233 with RMDs (AR e SA), 449 with IBD (Crohn and ulcerative colitis), 273 with PSO and 62 APs – answered to the questionnaire useful for the purpose of the study.

Non-adherence varies in a range from 50% of dermatological patients, to 44% of them with IBDs, to 40% of patients with APs, to 36% of them with RMDs. Only 74.8% of adherent people is persistent (83% in biologic therapy; 76% in DMARDS) and non-persistent patients does not ask and/or inform their doctors.

Patients with Psoriasis take therapies more discontinuously and inaccurately then patients with RMDs, IBDs and APs. The most popular were the posts that were related to emotions and experience of life with a chronic condition.

Conclusions: Our study shows that patients who enjoy a better health state, both physically and psychologically, are more likely to follow the treatment prescribed by their doctor, according to the mode and the specified time, especially if properly informed and well supported in choices, shared by medical and health professional staff.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3102

PARE0019 ADHERENCE TO THERAPY: A COMPARISON BETWEEN THREE PATIENTpopulations WITH AUTOIMMUNE INFLAMMATORY DISEASES

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1Anmar Italia, Torino; 2Anmar Italia, Firenze; 3Anmar Italia, Milano; 4Anmar Italia, Roma, Italy

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Conclusions: Our study shows that patients who enjoy a better health state, both physically and psychologically, are more likely to follow the treatment prescribed by their doctor, according to the mode and the specified time, especially if properly informed and well supported in choices, shared by medical and health professional staff.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3095
25 YEARS OF PATIENTS’ ASSOCIATIONS OF ANKYLOSING SPONDYLITIS IN SPAIN: ACEADE

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Background: Patients’ associations can provide to the ankylosing spondylitis (AS) patient all the information and support that his/her rheumatologist cannot give and that is necessary to fight against the disease having a greater quality of life. The knowledge about AS is fundamental and Patients’ associations play an important role in education on disease (2). In 1991, the first association dedicated to AS in Spain, was born: ACEADE (Asociacion Cordobesa de Enfermos Afectados de Espondilitis). The Rheumatologist, Dr Eduardo Collantes, after having spent some years in several countries, brings together several patients affected by this disease, in the city of Cordoba, to create the first Patients Association dedicated to this disease in Spain. There were some associations of this kind in the UK and France, and they decided to create their own association to promote the knowledge about AS and to help the AS patient. More than 25 years later, there are many AS patient associations in Spain that were created following the example of ACEADE, and with the help of this pioneering association.

Objectives: The aims of ACEADE during these 25 years has been:
1) Disseminate the knowledge of the disease.
2) Collaborate with medical researchers.
3) Improve the quality of life of the AS patient.
4) Organize and participate in scientific meetings, congresses and specialized courses.
5) Nativise the patients in socio-labor aspects.
6) Inform associates of the advances related to the disease.

Methods: Several activities are being carried out in the Association, some of them were exposed previously (3): educational seminars, rehabilitation courses, patient guides, social events, legal advice, employment bureau, newsletter, web page, ... In order to develop these activities, we have several sources for fundraising, donations, local and regional governments, pharmaceuticals, foundations, ...

Results: ACEADE is formed by 415 members distributed in the province of Cordoba (Spain), although some of them are from outside this city (11%), 67% of them are men and the average age of the members is 53 years. Of these, 32% have a recognized legal disability. After ACEADE, up to 18 patient associations have been created in Spain. There is also a national organization of AS patient associations: CEADE.

Conclusions: ACEADE was the pioneering AS Association in Spain and has been the mother of others that have been appearing. Today there are associations of AS in virtually all territories of Spain, helping patients to have a better quality of life. The next 25 years appear, for our association, full of illusions, ideas and a lot of work ahead, to help in the fight against AS.

References:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4754

PUBLIC AND PATIENT INVOLVEMENT AT ARTHRITIS RESEARCH UK: ENSURING BENEFIT FOR ALL

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Background: Since 2008, Arthritis Research UK have utilised the valuable experience and perspective of people with arthritis to review and evaluate the research applications we receive, through the USER stakeholder committee. The world of public and patient involvement (PPI) has developed and progressed hugely in that time. So too has Arthritis Research UK, becoming an insight-led charity that can now genuinely say that people with arthritis are at the centre of everything we do, helping those people to be in control, independent and recognised. As such, our approach to PPI must not only meet the high new standards of meaningful PPI set by the research community but also serve to anchor our research activities and the work that we fund in genuine relevance and patient benefit.

Objectives: To present our new approach to involving people with arthritis in the decision-making processes of research and the wider charity.

Methods: We carried out a UK-wide scope exercise, consisting of questionnaires and one-to-one interviews, of key stakeholder groups and PPI leaders. This included: our funded researchers and centres of excellence; medical research charities; and people with arthritis including ex- and current USER members. The findings were written up in to a report.

Results: The findings of the report highlighted to us that we need to 1) scale up our PPI activities in order to ensure that insight of people with arthritis can be integrated at all stages of the research cycle 2) improve the quality of our PPI ensuring that all the things we do are carried out with clear purpose, that they are meaningful and add mutual value to all involved 3) increase the numbers of people with arthritis in our PPI processes. To help realise this vision, whilst improving our support, training and guidance processes for those people 4) recognise and support the already excellent PPI activities going on in the musculoskeletal community, and providing resources and training for those also wishing to start or develop similar activities.

Conclusions: After implementing this new approach for over a 18 months, we are now confident that our research activities and the research we fund have the utmost relevance and potential benefit to people with arthritis.

Disclosure of Interest: None declared
LOVE YOUR HEART – AN INTERACTIVE ON-LINE EDUCATION PROGRAMME TO ENABLE PEOPLE WITH RHEUMATOID ARTHRITIS TO ASSESS THEIR CARDIOVASCULAR RISK AND SET PERSONAL GOALS TO IMPROVE THEIR CARDIOVASCULAR HEALTH

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Background: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular disease, akin to type 2 diabetes. However, screening for, management of, and education about co-morbidities is not always adequate and as a result, the co-morbid risks may be overlooked by the general public, some health professionals and policymakers alike. Dr. John originally developed and piloted a programme in group format in Dudley to educate RA patients about their cardiovascular risk and help them change their lifestyle to improve their health; it achieved promising results. The format however limited the number of people who could access it and NRAS wanted to make it as widely available as possible. The sad reality is that it is not unusual to meet someone with RA who does not realise that they are at an increased risk of heart disease, so they are far less likely to address factors such as smoking, weight and diet which are firmly within their control.

Objectives: Our aim was to create an engaging and interactive online programme to educate people with RA about heart disease and atherosclerosis. This programme should; explain in simple terms why they are at increased risk; include the opportunity to determine individual risk factors thereby allowing a QRisk2 score to be performed; provide a cognitive-behavioural framework to empower people to change their behaviours and achieve a healthier lifestyle, thereby reducing risk of premature death from heart disease.

Methods: The participant manual created for the group programme and working closely with Dr. John and other health professionals in Dudley (exercise physiologist, smoking cessation nurse, dietician, health psychologist) and patients who had attended the programme, we explored with our creative film production team the best way to adapt this to create a really engaging on-line experience which would allow participants to undertake the programme over time whilst working through the behaviour change goal-setting process. Two days of filming were done in Dudley and Maidenhead followed by a period of editing, additional recording and review. Beta testing of the programme will be conducted in February, piloting in March and launch anticipated for April 2017.

Results: Evaluation of both the programme and the potential to change health behaviours will be measured on completion of the programme and actual behaviour change will be measured at 6 months.

Quote from a patient who participated in the face to face programme: “Before I did this programme I thought that I was doing pretty well in terms of diet and exercise but it showed me that there was a lot I wasn’t aware of, that my knowledge of lifestyle factors wasn’t adequate and I needed to do more to help myself. I found it a valuable and life-changing experience to do this programme.”

Conclusions: We are very excited about the launch of this programme as it is an important new resource addressing the major co-morbidity which shortens the lives of those with RA. It is unique in that not only does it provide patient education, but it also provides a structure through which patient can change their behaviour. Furthermore, it also illustrates what can be achieved when patient-led charity organisations work alongside healthcare professionals; we are hugely excited about its potential.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6299

THE NEEDS AND PRIORITIES OF YOUNG PEOPLE LIVING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES IN ITALY: A SUB-ANALYSIS OF THE PARE YOUTH RESEARCH PROJECT

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Background: In 2014 EULAR Young PARE conducted a research (PARE Youth Research) to gather information about how young people (aged 18–35) living with rheumatic and musculoskeletal diseases (RMDs) are organized in different European countries and to explore their specific needs, obstacles, preferences and priorities. The research was developed through a survey launched in countries with EULAR members organizations and a total of 2,339 validated responses from the target population were obtained. In 2015 ANMAR Young, Italian National Association for people with RMDs (ANMAR) youth group, was born aimed to create a network of young people with RMDs living in this country.

Objectives: Taken the socio-economical and cultural differences across countries, as well as the need to tailor interventions, activities and projects of national youth groups accordingly, the purpose of this study was to map out specific insights about Italian young people living with RMDs.

Methods: Data from Italian responders to the survey of the PARE Youth Research Project survey were extrapolated and answers were encoded to be analyzed using SPSS 21.0 software. Descriptive statistics were calculated in the whole group as well in subgroups of subjects as needed.

Results: 81 young Italian people living with RMDs responded to the survey: 75 females and 6 males. The conditions reported most often are rheumatoid arthritis (38%), juvenile idiopathic arthritis (23%), ankylosing spondylitis (15%). The work on PARE Youth Research’s Italian data shows some important insights, among which the most significant are the following: 84% report a delay in their studies due to the rheumatic condition, 92% report that the condition has affected their ability to work; 90% report the impact of RMD on social life, 70% report an impact on sexual life and 83% on mental health. Focusing on mental health issues, we highlight that 69% express the need for psychological support while only 43% have the possibility to access psychological support. Although all patients reported that after being diagnosed with an RMD they have access to a rheumatologist for regular follow-up visits, an average 3-year diagnostic delay is reported.

Conclusions: The results from the analysis of Italian responders to the survey represent a crucial starting point to put in light the unmet needs of Italian young people living with RMDs. These findings will be of great help to develop a fruitful national network of young people with RMDs on one hand and a focused collaboration with patient representatives, physicians, and health professionals (HPs) on the other. We believe that the awareness of physicians and HPs working in the field of rheumatology about the needs and priorities of young people with RMDs will ensure a better management of the disease and therefore lead to the reduction of the RMD burden in this subgroup of patients.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6190

TO RAISE AWARENESS OF RHEUMATIC AND MUSCULOSKELETAL DISEASES AND TO PROVIDE THE OPPORTUNITY TO THE FINANCIALLY LESS ABLE TO RECEIVE TIMELY DIAGNOSIS AND INTERVENTION IN RMDs


Background: The timely and accurate diagnosis in most rheumatic diseases is still a big issue for patients as the choice of the appropriate doctor’s specialty is still at the discretion of the patient, mainly due to the poor organized health care services. Furthermore, the success of our campaign two years ago, when we gave the opportunity to people who might suffer from an RMD but who could not afford a rheumatologist to be examined for free, prompted our organization to offer not only free consultations but free lab tests as well.

Objectives: To raise awareness of RMDs and at the same time to enable people of lower income who may have the early warning signs of rheumatic diseases to be examined by a rheumatologist and have lab tests done at no cost.

Methods: Firstly, we found a sponsor who embraced our initiative and was willing to cover the cost of the whole campaign. Secondly, we contacted various medical laboratories to give us low estimates on the RMD tests and then we chose to collaborate with the ones offering us the lowest prices. Then we came into contact with all the rheumatologists in all the prefectures of the island and asked them to offer consultations free of charge according to their availability. On WAD, 12 October, we erected four stands in four central locations of our island with our logo, a banner, informative leaflets and a large number of well-informed volunteers to answer questions. From WAD we had to work in the mass and social media. A lot of people visited our stands, told us their problem and their signs and we wrote down the names and phone numbers of those we deemed needed a rheumatologist. As last time, there were people who had already been seeing a rheumatologist who wanted to take advantage
of this opportunity; we had to reject them as this was only available to people who had not been diagnosed previously. The following two days our office made an appointment for these people with a rheumatologist in their area. The doctors prescribed the necessary laboratory tests and gave a free voucher for the tests to those that needed them. The cost of the lab tests was covered by our association. Our office received a large number of calls from people who wanted to be tested and unfortunately, we could not accommodate all of them as our budget was limited.

Results: More than 267 people visited our stands and 209 people phoned our office asking to be tested. We made appointments for 123 people of whom 111 showed up for their appointments. The rheumatologists gave vouchers and prescribed lab tests for 89 of them. 12 rheumatologists volunteered their services gratis and more than 40 volunteers took part in the campaign.

Conclusions: People's awareness of RMDs is growing but there are still undiagnosed people due to financial constraints, inadequate health insurance coverage and lack of information. Since the demand for free testing is very high we will make every effort to be able to provide this opportunity to undiagnosed people again in the future!

Acknowledgements: BMS

Disclosure of Interest: A. Stara Grant/research support from: BMS

DOI: 10.1136/annrheumdis-2017-eular.2625

AB1253-PARE

KID'S GET ARTHRITIS TOO - EXPANSION OF TARGET GROUPS

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Background: The Finnish Rheumatism Association is generally perceived as a very strong alliance of older people. However in Finland there are more than 2000 children and youth suffering JIA and around 250 new ones get diagnosis yearly. Children will have their whole lives ahead with rheumatic disease, so they and their families also need information, support and friends.

Objectives: Support children and families living with JIA in different ways

Get in touch with families, understand what their needs are, provide them with the correct information and promote their interests

Bring new energy into the families' challenging lives affected by illness

Build a supporting network for the families and increase mental well-being

Rejuvenate the brand of our association

Methods: Ordered international top photographer to photograph the JIA children and families. Created an entirely new high-quality imagery and expression to all Rheumatism Association children communications.

Created the “Puppana” bunny soft toy and the mascot costume.

Have the rheumatism-week campaign: Kids Get Arthritis Too: one week nation wide big radio campaign with a child’s voice, a poster campaign in hospitals, our local associations and public spaces.

First aid packet with information of JIA, some toys, and the Puppana mascot. Packets were delivered to all Finnish hospitals, juvenile rheumatoid arthritis units. The rheumatologist gives a packet for a child who receives a diagnosis.

Introduced the action program of two annual nationwide large children’s events Joy of Life.

New juvenile rheumatoid arthritis sites for children and families on our new website.

Support the activities of local associations directed for children and families.

Create a new web portal support activities “Reumanakanssa.fi”. International Trials Organisation) in co-operation. Translated into Finnish and added to the new website where we built ABC for JIA.

Results: The brand of the Finnish Rheumatism Association has become more modern and wider.

People have experienced an eye opening campaign, the children suffer from rheumatism–arthritis can be a disease at all ages

Families with children have been reached more, they have joined our social media groups, the event attracted more than 250 children and their families, new families with children have joined the association, some of the local association has begun to organize groups of juvenile rheumatoid arthritis

Fund-raising, it was very easy to find sponsors for children activities and it also helped in common fundraising.

Children suffering from rheumatoid have experienced a positive campaign, it feels better when people’s attitudes change, and no longer think that they’re suffering from “a disease of the elderly”.

Cooperation with arthritis professionals has intensified and improved. Their want to do more co-operation and they guide patients to more actively explore the Finnish Rheumatism Association activities.

Conclusions: Operation for JIA children and their families are needed.

Children’s powerful vision of the activities have a positive impact on the brand and fundraising organization.

The positivity of this type of cooperation with arthritis professionals to approximate intervals and supported by more co-operation

It’s relatively easy to receive sponsor funds for the development of children’s activities

Children and families inclusion will bring new energy and confidence in the future among local associations

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2724
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